THE ESSENTIAL, HOLISTIC GUIDE TO PALLIATIVE CARE

OXFORD HANDBOOK OF PALLIATIVE CARE

Max Watson | Rachel Campbell
Nandini Vallath | Stephen Ward | Jo Wells

Fully updated to include the latest management options for supporting patients at the end of life

Includes new sections on international access to palliative care, Advance Care Planning, and palliative care for non-malignant diseases

Provides detailed guidance on the physical, emotional, and spiritual aspects of palliative care



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Oxford Handbook of Palliative Care

Third Edition

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Foreword

Palliative care has a unique balance of professional, emotional, and existential issues. All are necessary to guide our patients through the last stages of their lives, and poetry can be an excellent reflection of this.

We introduce this new edition with the challenge of the poem *Don't Tell Me*, written by a UK palliative care consultant under her pseudonym, Jo Hansen.

Don't tell me

Don't tell me, 'He was a good old age … '—I know that.

Don't tell me, 'it was great that you were all there … '—I know that too.

Don't tell me, 'with time this will pass … '—I didn't ask if it would.

Words belittle the enormity,
The aching deepness of existence
And loss.

Don't say anything at all
Please, just be there.

Jo Hansen 2017

Preface to the second edition

I am always willing to learn, however I do not always like to be taught.
Winston Churchill

The first edition of the Oxford Handbook of Palliative Care has been warmly received. We have been encouraged by colleagues to make the material presented here more relevant to non-medical readers. We therefore welcome to our team, Jo Wells, who is a nurse consultant in palliative care. We have added new sections on antibiotics, increased emphasis on non-malignant disease, learning disabilities, palliative care in developing countries and communication. All the chapters of the first edition have been reviewed and many have been completely rewritten.

We hope that the result will be a Handbook which that is useful to the whole of the multiprofessional team and will achieve a better balance than its predecessor. Although the Handbook is somewhat larger than the first edition, we feel that this is a reflection of the rapid changes and progress of this field of clinical practice in a relatively short period.

The aim of the Handbook remains as originally stated. We would like to provide a readily accessible source of help to all those who care for people who cannot be cured. This will include generalists and those whose specialty is not palliative care. We hope that the Handbook may also be a useful ready reference for those engaged in full-time palliative, hospice or end-of-life care. We remain proud to be associated with the Oxford University Press Handbook series, and are well aware of the heavy responsibility which this confers.

MW
CL
AH
JW

Preface to the first edition

Most clinical professionals have been affected by caring for patients with palliative care needs. Such patients may challenge us at both a professional and at a personal level in areas where we feel our confidence or competence is challenged.

I wanted to help her, but I just didn't know what to do or say

As in every other branch of medicine, knowledge and training can help us extend our comfort zone, so that we can better respond to such patients in a caring and professional manner. However, in picking up this Handbook and reading thus far you have already demonstrated a motivation that is just as important as a thirst for knowledge, the central desire to improve the care of your patients.

It was out of just such a motivation that the modern hospice movement began 40 years ago, and it is that same motivation that has fuelled the spread of the principles of palliative care—in fact the principles of ALL good care—across the globe: respect for the person, attention to detail, scrupulous honesty and integrity, holistic care, team caring and con- summate communications (often more about listening than telling and talking).

I knew we couldn't cure him, but didn't know when or how to start palliative care

Increasingly it is being recognized that every person has the right to receive high-quality palliative care whatever the illness, whatever its stage, regardless of whether potentially curable or not. The artificial distinction between curative and palliative treatments has rightly been recognized as an unnecessary divide, with a consequent loss of the border crossings that previously signified a complete change in clinical emphasis and tempo.

Medical knowledge is developing rapidly, with ever more opportunities for and emphasis on curative treatment, to the point when any talk of palliative care can sometimes be interpreted as 'defeatist'.

Today the principles of palliative care interventions may be employed from the first when a patient's illness is diagnosed. Conversely, a patient with predominantly palliative care needs, late in their disease journey, may benefit from energetic treatments more usually regarded as 'curative'.

I just felt so helpless watching him die. Surely it could have been better?

Governments and professional bodies now recognize that every nurse and doctor has a duty to provide palliative care and, increasingly, the public and the media have come to expect—as of right—high-quality palliative care from their healthcare professionals irrespective of the clinical setting.

Many of these palliative care demands can best be met, as in the past, by the healthcare professionals who already know their patients and families well. This Handbook is aimed at such hospital- or community-based professionals, and recognizes that the great majority of patients with palliative needs are looked after by doctors and nurses who have not been trained in specialist palliative care but who are often specialist in the knowledge of their patients.

Even though I knew she had had every treatment possible, still, when she died I really felt that we had failed her and let her family down.

Junior healthcare staff members throughout the world have used the Oxford Handbook series as their own specialist pocket companion through the lonely hours of on-call life. The format, concise (topic-a-page), complete and sensible, teaches not just clinical facts but a way of thinking. Yet for all the preoccupation with cure, no healthcare professional will ever experience greater satisfaction or confirmation of their choice of profession, than by bringing comfort and dignity to someone at the end-of-life.

I had never seen anyone with that type of pain before and just wished I could get advice from someone who knew what to do.

The demands on inexperienced and hard-pressed doctors or nurses in looking after patients with palliative care needs can be particularly stressful. It is our hope that this text, ideally complemented by the support and teaching of specialist palliative care teams, will reduce the often expressed sense of helplessness, a sense of helplessness made all the more poignant by the disproportionate gratitude expressed by patients and families for any attempts at trying to listen, understand and care.

It was strange, but I felt he was helping me much more than I was helping him.

While it is our hope that the Handbook will help the reader access important information quickly and succinctly, we hope it will not replace the main source of palliative care knowledge: the bedside contact with the patient.

It is easier to learn from books than patients, yet what our patients teach us is often of more abiding significance: empathy, listening, caring, existential questions of our own belief systems and the limitations of medicine. It is at the bedside that we learn to be of practical help to people who are struggling to come to terms with their own mortality and face our own mortality in the process.

Readers may notice some repetition of topics in the Handbook. This is not due to weariness or oversight on the part of the editors, but is an attempt to keep relevant material grouped together—to make it easier for those needing to look up information quickly.

It is inevitable that in a text of this size some will be disappointed at the way we have left out, or skimped on, a favourite area of palliative care interest. To these readers we offer our apologies and an invitation to make any comments to https://global.oup.com/academic/contactus/editorial/

Acknowledgement

We are indebted to Caroline Lucas, for checking and amending the proofs of this edition. She has added her expertise and experience to this book, and it would not have been possible without her.

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List of abbreviations

5HTP	5- hydroxytryptophan
AAC	alternative augmentative communication
ACE	angiotensin-converting-enzyme (inhibitors)
ACh	acetylcholine
AChEI	acetylcholinesterase inhibitor
ACTH	adrenocorticotropic hormone
ADL	activity of daily living
ADT	androgen deprivation therapy
AED	anti-epileptic drug
AF	atrial fibrillation
AHP	allied health professional
AIDS	acquired immune deficiency syndrome
AIE	acute inflammatory episode
ALK	anaplastic lymphoma kinase rearrangement
Amp.	ampoule
APTT	activated partial thromboplastin time
ARV	antiretroviral
AVP	arginine vasopressin
b.d./BD	twice daily
BBB	blood– brain barrier
BCG	bacillus Calmette-Guérin
BEDS	Brief Edinburgh Depression Scale
BiPAP	bilevel positive air pressure
BIPP	bismuth iodoform paraffin paste
BNF	British National Formulary
BP	blood pressure
BPH	benign prostatic hypertrophy
BPSD	behavioural and psychological symptoms of dementia
BZ	benzodiazepine
C/T	chemotherapy
CABG	coronary artery bypass graft
CAG	cytosine- adenine- guanine
CAM	complementary and alternative medicines
Caps	capsules
CBCT	cone beam CT
CBD	cannabidiol
CBT	cognitive behavioural therapy

CD	controlled drug
CDR	clinical dementia rating
CEA	carcinoembryonic antigen
CHF	congestive heart failure
CKD	chronic kidney disease
CMV	cytomegalovirus
CNS	central nervous system
CO2	carbon dioxide
COMT	catechol-O-methyl transferase
COPD	chronic obstructive pulmonary disease
COX	cyclo-oxygenase
CPAP	continuous positive airway pressure
CSCI	continuous subcutaneous infusion
CSPCT	community specialist palliative care team
CSU	catheter specimen of urine
CT	computed tomography
CTLA-4	cytotoxic T-lymphocyte-associated protein 4
CTPA	CT pulmonary angiogram
CTZ	chemoreceptor trigger zone
CVA	cerebrovascular accident
CXR	chest X-ray
DCIS	ductal carcinoma in situ
DDI	drug-drug interaction
ddI	didanosine
DIC	disseminated intravascular coagulation
DisDAT	Disability Distress Assessment Tool
DLT	decongestive lymphatic therapy
DN	district nurse
DOAC	direct oral anticoagulant
DVT	deep vein thrombosis
EBV	Epstein–Barr virus
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
EDDM	equivalent daily dose of morphine
EFT	enteral feeding tube
EGF	epidermal growth factor
EGRF	epidermal growth factor receptor
EORTC	European Organization for the Research and Treatment of Cancer
EOL	end of life
ERCP	endoscopic retrograde cholangio-pancreatography

ESA	erythropoiesis- stimulating agent
ESRF	end- stage renal failure
FASP	Focused Abdominal Sonography in Palliative Care
FBC	full blood count
FEV1	forced expiratory volume in one second
FFP	fresh frozen plasma
FNA	fine needle aspiration
g	gram
GDS	Global Deterioration Scale
GERD	gastro-oesophageal reflux disease
GFR	glomerular filtration rate
GI	gastrointestinal
GIST	gastrointestinal stromal tumour
GIT	gastrointestinal tract
GMC	General Medical Council
GNRH	gonadotrophin-releasing hormone
GORD	gastro-oesophageal reflux/oesophagitis
GP	general practitioner
GSF	Gold Standard Framework
Gy	Gray(s): a measure of radiation
h	hour or hourly
HAART	highly active antiretroviral therapy
HCP	healthcare professional
HHM	humoral hypercalcaemia of malignancy
HHV-8	human herpesvirus 8
HIV	human immunodeficiency virus
HNSCC	head and neck squamous-cell carcinoma
HPV	human papillomavirus
HRQoL	health-related quality of life
HSPCT	hospital specialist palliative care team
HSV	herpes simplex virus
HTLV-1	human T-lymphotropic virus 1
i/r	immediate release
i/t	intrathecal
IAPC	Indian Association of Palliative Care
ICD	implantable cardioverter defibrillator
ICP	intracranial pressure
IGFs	insulin-like growth factors
IDDM	insulin-dependent diabetes mellitus
IGRT	image-guided radiotherapy
IM	intramuscular

IMCA	independent mental capacity advocate
IMT	intensity-modulated radiotherapy
IMRT	intensity-modulated radiotherapy
INCB	International Narcotics Control Board
INI	integrase inhibitor
Inj.	injection
IV	intravenous
IVC	inferior vena cava
IVDU	intravenous drug use
IVI	intravenous infusion
IVU	intravenous urogram
JVP	jugular venous pressure
KS	Kaposi's sarcoma
kV	kilovolt
L	litre
L/A	local anaesthetic
LCIS	lobular carcinoma in situ
LEMS	Lambert–Eaton myasthenic syndrome
LFT	liver function test
LHRH	luteinizing hormone-releasing hormone
LMWH	low molecular weight heparin
LPA	lasting power of attorney
LVAD	left ventricular assist device
LVF	left ventricular failure
m/r	modified release
m/w	mouthwash
MA	marketing authorization
MAC	Mycobacterium avium complex
MAHA	microangiopathic haemolytic anaemia
MAI	mycobacterium avium intracellulare
MAOI	monoamine oxidase inhibitor(s)
max	maximum
MCA	Mental Capacity Act 2005
MCCD	Medical Certificate of Cause of Death
mcg	microgram
MeV	mega electronvolt
MI	myocardial infarction
MHRA	Medicines and Healthcare Products Regulatory Agency
MLD	manual lymphatic drainage
MND	motor neurone disease
MRI	magnetic resonance imaging

MRN	magnetic resonance neurography
MS	multiple sclerosis
MSA	multisystem atrophy
MSCC	metastatic spinal cord compression
MSM	men who have sex with men
MSU	midstream specimen of urine
MUPS	multiple unit pellet system
MV	megavolt
NaSSA	noradrenergic and specific serotoninergic antidepressant
NCDs	non-communicable diseases
NCPC	National Council for Palliative Care
NCSE	Non- convulsive status epilepticus
neb	nebulizer
NG	nasogastric
NHL	non-Hodgkin's lymphoma
NICE	National Institute of Clinical Excellence
NIPPV	non-invasive positive pressure ventilation
NMDA	N-methyl-D-aspartate
NMP	non-medical prescribing
NNRTI	non- nucleoside reverse transcriptase inhibitor
NNT	number needed to treat
NOAC	novel oral anticoagulant
nocte/o.n.	at night
NP II	neurophysin II
NPI	neuropsychiatric inventory
NPPC	National Program for Palliative Care
NRTI	nucleoside reverse transcriptase inhibitor
NSAID	non-steroidal anti-inflammatory drug
NSCLC	non small-cell lung carcinoma
NYHA	New York Heart Association
o.d./OD	once daily
o.m.	in the morning
OMS	opsoclonus-myoclonus syndrome
ONJ	osteonecrosis of the jaw
OT	occupational therapy
OTFC	oral transmucosal fentanyl citrate
p.o./PO	by mouth
p.r./PR	per rectum/progesterone receptor
p.r.n.	when required
p.v.	per vagina

PACA	Palliative Care ASsessment Tool
PaP	The Palliative Prognostic score
PCA	patient-controlled analgesia
PCF	palliative care formulary
PCI	percutaneous coronary intervention
PCP	*Pneumocystis carinii* pneumonia,
PCT	palliative care team
PD	peritoneal dialysis
PD-1	programmed cell death 1
PDGF	platelet-derived growth factor
PD-L1	programmed cell death ligand 1
PE	pulmonary embolism
PEG	percutaneous endoscopic gastrostomy
PEP	post- exposure prophylaxis
PET	positron emission tomography
PHCT	primary healthcare team
PI	protease inhibitor
PIG	Prognostic Indicator Guidance
PIL	patient information leaflet
PLWH	people living with HIV
POS	Palliative Care Outcomes Score
PPCS	Pain and Palliative Care Society
PPI	proton pump inhibitor
PPM	permanent pacemaker
PPV	positive pressure ventilation
PrEP	pre- exposure prophylaxis
PROs	patient-reported outcomes
PSA	prostate-specific antigen
PSP	progressive supranuclear palsy
PT	prothrombin time
PTH	parathyroid hormone
PTHrP	parathyroid hormone- related peptide
PTSD	post-traumatic stress disorder
q.d.s.	four times daily
QoL	quality of life
RBL	renal bone liver (investigations)
RCT	randomized controlled trial
RIG	radiologically inserted gastrostomy
RLS	restless legs syndrome
RT	radiotherapy
RVF	right ventricular heart failure

S/D or SD or SP	syringe driver (CSCI)
SA-AG	serum ascites-ascitic albumin gradient
SAA	serum anticholinergic activity
SALT	speech and language therapy
SC	subcutaneous
SCLC	small-cell lung carcinoma
SD	syringe driver
SE	side effects
SECPAL	Spanish Society of Palliative Care
SERM	selective oestrogen-receptor modulator
SF36	36-Item Short Form Health Survey
SIAD	syndrome of inappropriate antidiuresis
SIV	simian immunodeficiency virus
SL	sublingual
SLD	simple lymphatic drainage
SLT	speach and language therapy
SNRI	serotonin-noradrenaline reuptake inhibitor
soln	solution
SN	sensory neuropathy
SPC	specialist palliative care/summary of product characteristics
SPECT	single photon emission computed tomography
SPICT	Supportive & Palliative Care Indicators Tool
SR	slow or modified release
SRS	stereotactic radiosurgery
SSRI	selective serotonin reuptake inhibitor
stat	immediately
STN	subthalamic nucleus
supps	suppositories
susp.	suspension
SVC	superior vena cava
SVCO	superior vena cava obstruction
t.d.s./TDS	three times daily
tabs	tablets
TAF	tenofovir alafenamide
TB	tuberculosis
TBM	tubercular meningitis
TCA	tricyclic antidepressant
TCC	transitional-cell carcinomas
TCM	traditional Chinese medicine
TDF	tenofovir disoproxil fumarate

TENS	transcutaneous electrical nerve stimulation
TFT	thyroid function test
THC	tetrahydrocannabinol
TIA	transient ischaemic attack
TKI	tyrosine kinase inhibitor
TNM	tumour/node/metastasis
TPN	total parenteral nutrition
TSD	therapeutic standard dose
TURP	transurethral resection of the prostate
U&E	urea and electrolytes
URTI	upper respiratory tract infection
USS	ultrasound scan
UTI	urinary tract infection
UVB	ultraviolet B
V/Q	ventilation/ perfusion
VEGF	vascular endothelial growth factor
VTE	venous thromboembolism
VZV	varicella-zoster virus
WHO	World Health Organization
WHOCC	WHO Collaborating Centre
WTHD	wish to hasten death

Introduction

Palliative care definitions

Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychological and spiritual.[1, 2]

Palliative care

- provides relief from pain and other distressing symptoms
- affirms life and regards dying as a normal process
- intends neither to hasten nor postpone death
- integrates the psychological and spiritual aspects of patient care
- offers a support system to help patients live as actively as possible until death
- offers a support system to help the family cope during the patient's illness and in their own bereavement
- uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated
- will enhance quality of life, and may also positively influence the course of illness
- is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy and radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications

Principles of palliative care

No single sphere of concern is adequate without considering the relationship with the other two. This usually requires genuine interdisciplinary collaboration.[3] (See Fig I.1)

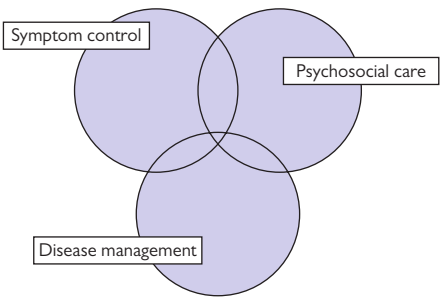


Fig I.1 Spheres of concern in palliative care.

General palliative care is provided by the usual professional carers of the patient and family with low-to-moderate complexity of palliative care need. Palliative care is a vital and integral part of their routine clinical practice, underpinned by the following principles:

- focus on quality of life, which includes good symptom control
- whole-person approach, taking into account the person's past life experience and current situation
- care, which encompasses both the person with life-threatening illness and those who matter to the person
- respect for patient autonomy and choice (e.g. over place of care, treatment options)
- emphasis on open and sensitive communication, which extends to patients, informal carers, and professional colleagues

Specialist palliative care

These services are provided for patients and their families with moderate-to-high complexity of palliative care need. The core service components are provided by a range of NHS, voluntary, and independent providers staffed by a multidisciplinary team whose core work is palliative care.[2]

Supportive care for cancer is that which helps the patient and their family to cope with the disease and its treatment—from pre-diagnosis, through the process of diagnosis and treatment, to cure, continuing illness or death, and into bereavement. It helps the patient to maximize the benefits of treatment and to live as well as possible with the effects of the disease. It is given equal priority alongside diagnosis and treatment. This definition can be applied equally to non-cancer diagnoses.

The principles that underpin supportive and palliative care are broadly the same.

Hospice and **hospice care** refer to a philosophy of care rather than a specific building or service, and may encompass a programme of care and array of skills deliverable in a wide range of settings.

Terminal care or end-of-life care

This is an important part of palliative care and usually refers to the management of patients during their last few days, weeks, or months of life from a point at which it becomes clear that the patient is in a progressive state of decline. However, end-of-life care may require consideration much nearer the beginning of the illness trajectory of many chronic, incurable non-cancer diseases.

Fig 1.2 shows aspects of palliative care through the patient's illness trajectory.

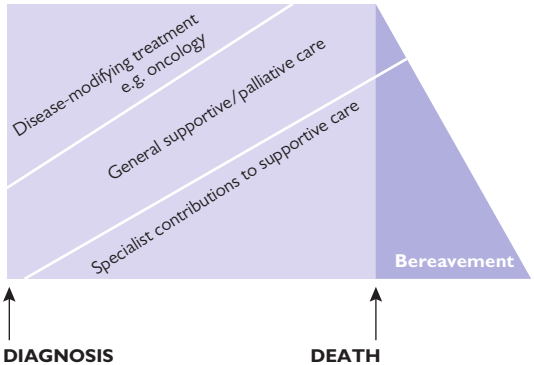


Fig 1.2 Palliative care through the illness trajectory.

History of palliative medicine as a specialty

The specialty of palliative medicine as a specific entity dates from the mid-1980s. However, medical activity related to terminal care, care of the dying, hospice care, and end-stage cancer is, of course, as old as medical practice itself.[4] Palliative medicine is the medical component of what has become known as palliative care.

The history of the hospice movement during the nineteenth and twentieth centuries demonstrates the innovations of several charismatic leaders. These practitioners were enthusiasts for their own particular contribution to care of the dying, and they were also the teachers of the next generation of palliative physicians. Although they were products of their original background and training, they all shared the vision of regarding patients who happened to be dying as 'whole people'. They naturally brought their own approaches from specific disciplines of pharmacology, oncology, surgery, anaesthetics, or general practice. This whole-person attitude has been labelled as 'holistic care'. Comfort and freedom from pain and distress were of equal importance to diagnostic acumen and cure. However, rather than being a completely new philosophy of care, palliative medicine can be regarded more as a codification of existing practices from past generations.

Histories of the development of palliative medicine illustrate the thread of ideas from figures such as Snow, who developed the Brompton Cocktail in the 1890s, to Barrett, who developed the regular giving of oral morphine to the dying at St Luke's, West London, to Saunders, who expanded these ideas at St Joseph's and St Christopher's hospices. Worcester, in Boston, was promoting the multidisciplinary care of whole patients in lectures to medical students at a time when intense disease specialization was very much the fashion, as it was yielding great therapeutic advances.[5] Winner and Amulree, in the UK in the 1960s, were promoting whole-person care particularly for the elderly, first challenging and then re-establishing the ethical basis for palliative medicine.

The early hospice movement was primarily concerned with the care of patients with cancer who had missed out on the surge of post-war medical innovation.

This movement was responding to a need perceived across the world, as evidenced by the exponential growth in palliative care services throughout the UK and across the globe since the opening of St Christopher's Hospice in south-east London in 1967.

The expansion is set to increase further, as the point has now been reached where patients, doctors, and governments alike are calling for the same level of care to be made available to patients suffering from non-malignant conditions as for those with cancer.

If this new challenge is to be met, healthcare professionals from early in their training will need to be exposed to palliative care learning, which can be applied across the range of medical specialties.

The essence of such palliative medicine learning—both for generalists and specialists—remains that of clinical apprenticeship. Alfred Worcester, in the preface to his lectures, notes:

> The younger members of the profession, although having enormously greater knowledge of the science of medicine, have less acquaintance than many of their elders with the art of medical practice. This like every other art can of course be learned only by imitation, that is, by practice under masters of the art. Primarily, it depends upon devotion to the patient rather than to his disease.[5]

Hope

> Hope is the physician of each misery.
>
> Irish proverb

The ways in which hope is spoken about suggests that it is understood to be a fragile but dynamic state. For example, hope:

- is intended–we hope in … or for … or of … or to … someone or something
- is associated with longing, as in 'hopes and dreams'
- is usually passive: hope is brought, given, revived, restored, inspired, provided, maintained, offered, injected, developed, pinned, or lost; it can be kept alive or it can be crushed
- can be hoped against
- can be false, mistaken for wishfulness, optimism, desire, or expectation
- can be new, fresh, big, strong

Hope is closely linked with wants and desires. The phrase 'Freud had hoped to revisit Paris' says something about a future-oriented desire Freud nurtured when he left Vienna en route to London. The phrase implies an expectation that the desired thing might be achieved. This expectation may itself be realistic or unrealistic, but assessment of what might or might not be realistic depends on one's perception of reality.

Because hope is future orientated, the question posed by terminal illness may become: 'What hope can there be if death is this patient's only and impending future?'.

Hope has long been associated with belief.

> Now faith is being sure of what we hope for and certain of what we do not see.
>
> The New Testament, Hebrews 11:1

Hope nurtures within it the belief that that which is hoped for has the potential to be realized: a trip to Paris. The dilemma for healthcare professionals is: How can I work with a terminally ill patient in a way that avoids

collusion and yet sustains hope? Addressing this question locates healthcare professionals firmly on the terrain of psychospiritual care.

> Hope is a dynamic inner power that enables transcendence of the present situation and fosters a positive new awareness of being.[6]
>
> Reproduced from Herth K. (1993) Hope in the family caregiver of terminally ill people. *Journal of Advanced Nursing*, **18**: 538–48, with permission from Wiley.

But part of the difficulty in answering this question is in understanding

- *what* hope is
- *how* it differs from wishfulness, and
- *why* it can remain hope even when it sounds like despair

The development of hope: Rumbold's three orders

Building on a psychiatric description of the defences deployed by patients to shield themselves from the knowledge of imminent death, Rumbold (1986) describes hope developing through 'three orders' (see Fig I.3).[7]

First order: denial of symptoms—hope for recovery

Diagnosis of a terminal illness is often met with denial. Symptoms are ignored or interpreted as something other than what they are said to be. Denial serves to protect the person from the reality of their condition, but it also prevents them from accepting treatment. However, as symptoms progress, the fantasy sustaining denial breaks down, and acceptance generates hope that either recovery may be possible, or that at least death may be long delayed. Rumbold suggests hope may emerge

- from a straightforward transition from admitting the reality of their illness to affirming a hope for recovery; or
- from a period of despair following the breakdown of denial

(The transition is delicate, and admitting illness may actually plunge patients into a despair and resignation from which they do not emerge.)

Second order: denial of non-recovery—hope beyond recovery

Hope for recovery, paradoxically, supports a higher level of denial, which is actively supported by medical staff and by family and friends. Whereas denial of symptoms keeps the person from becoming a patient, the denial of possibilities other than recovery allows clinicians the freedom to focus on symptom management without having to engage with the bigger issues and uncertainties of disease progression or the worries connected with mortality.

Yet, for hope to continue developing and become hope beyond mere insistence on recovery, patients need to face and explore the possibilities for dying. The social support that once buoyed hope of recovery now works against patients contemplating dying as part of their hope. Lack of support at this point can mean that the acceptance emerging in the patient as this denial breaks down results in resignation and despair, for the withdrawal from community can be, for many people, particularly destructive of hope.

The breakdown of this denial of non-recovery is a critical transition: 'If all our hope has been invested in recovery, then that hope may virtually be destroyed by the new perception of second-order acceptance'.

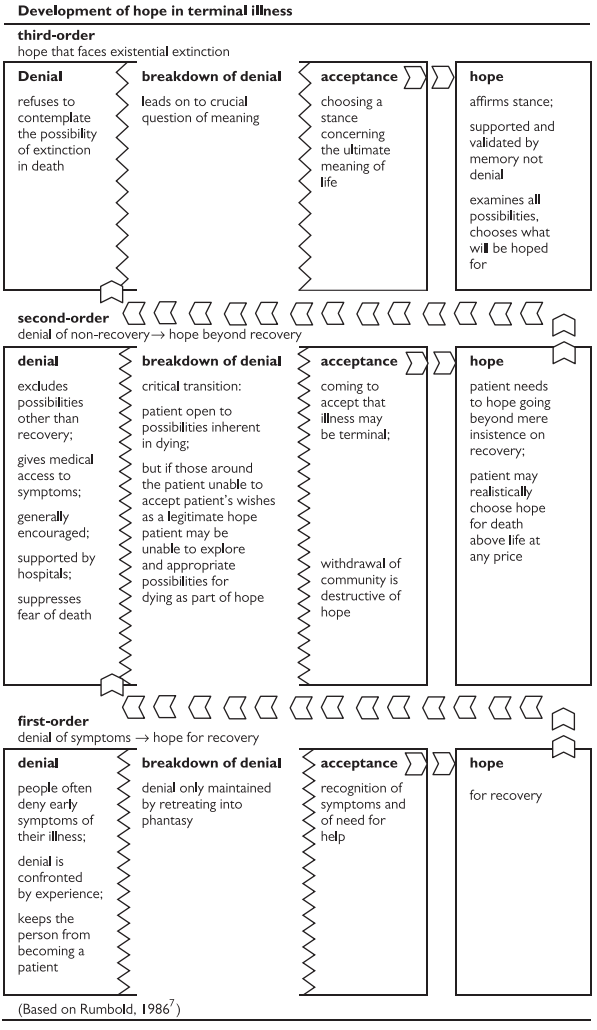


Fig 1.3 Development of hope in terminal illness. Based on Rumbold B. D. (1986) Helplessness & Hope: Pastoral Care in Terminal Illness, pp. 59–75. London: SCM Press.

Hope beyond recovery is a more varied hope than the single-minded hope for recovery. The patient may simply hope

- to die with dignity
- for the continuing success of children
- that a partner will find the support they need
- that their life's contribution will continue and be found useful

> Most terminally-ill people do seem to reach this second stage where such a hope becomes possible; but those who can find a meaningful hope which they are allowed to affirm are distressingly few.
>
> Bruce Rumbold, 1986

Third order: hope that faces existential extinction

Hope beyond recovery has the capacity for yet further development:

- hope for recovery (which supported denial of the terminal reality of their illness) develops into the higher-level hope beyond recovery
- hope beyond recovery (which realistically accepts death 'rather than crave life at any price') may develop into a higher level yet: hope that accepts the existential possibility of extinction at death, but nevertheless finds a sense of ultimate meaning in the life that has been lived

Such hope may hold to a belief in a life after death, but recognizes this belief as a contingency of faith.

Prior to her first hospice admission, Elaine had been very angry about her illness (second-order denial). Her realization that she didn't want to die angry broke down her denial, opening new possibilities to her.

> **Elaine:** I was angry … very angry—angry at the world; and that's not me. I'm not like that. I'm usually very calm. That's not the way I want to be. I think that's a quite natural reaction, but I don't want to be angry; I don't want to die angry … actually, I feel as if I'm moving on from that now. I feel as if I'm moving into trying to make sense of what is ahead.

By allowing her to say and think what she needed to, those around Elaine supported her to explore the possibilities for her dying. When she returned for terminal care, she was in a different place spiritually.

> **Elaine:** It's that the anger has gone. I've worked through a lot of stuff while I was at home. We talked about a lot of things. This is the way it is going to be and there's no use fighting it. We'd rather things were going to be different, but they're not. There's no point in being angry; it takes up so much energy. I know I'm going to be on a gradual, slow decline now, so I have to get on with it. My body is getting weaker, but I feel emotionally stronger. I hope I will.

Hope and the psychospiritual value of denial

When healthcare professionals deny the legitimacy of patients' hopes, they are likely to be expressing their own fears about death and dying.

- Healthcare professionals need to validate patients' exploration to allow patients the possibilities of acknowledging their dying.
- Patients should not be pressured to confront their denying—denial should be respected as a legitimate psychological defence strategy.
- Healthcarers should not think that challenging denial will help patients to explore their dying—only the patient can determine the right time to be open to their dying.

To attempt to steal 'denial' from another is an act of righteousness and separatism.[8]

Dignity

'Dignity' as defined by the *Oxford English Dictionary* is 'the state of being worthy of honour or respect' or 'high regard or estimation'. The 1984 Universal Declaration of Human Rights and Article 1 of the Charter of Fundamental Rights of the European Union recognize dignity as a human right. The Department of Health in England launched a policy in 2007 to 'create a zero tolerance of lack of dignity in the care of older people in any setting'. Upholding the dignity of patients within a palliative care setting is essential not only for the patients themselves but also for the family, particularly in their bereavement.

Patients approaching the end of life fluctuate in their will to live, a situation closely associated with dignity. The meaning and experience of human dignity relate to the following:

- presence of symptoms
- loss of independence
- fear of becoming a burden
- not being involved in decision-making
- lack of access to care
- lack of adequate communication between patients, families, and professionals
- some attitudes of staff
- spiritual matters, especially when people feel vulnerable

Patients with a terminal illness become vulnerable to a loss of dignity if they begin to feel that they are no longer respected as the person that they once were. As they become increasingly dependent, patients often feel that professionals no longer see them as an individual, which can compound a sense of loss of self. Patients may suffer the ultimate indignity of feeling that their life has no worth, meaning, or purpose.

A core framework of dignity-conserving care has been developed by Chochinov[9] with the aim of reminding practitioners about the importance of caring for, as well as caring about, their patients. The mnemonic ABCD stands for attitude, behaviour, compassion, and dialogue.

Attitude

Professionals need to be respectful in their attitudes towards patients, acknowledging the patient as an individual with cognisance of many issues including culture and ethics. Professionals unwittingly make incorrect assumptions; e.g. seeing a patient who has difficulty in communicating does not mean that they are not competent to have an opinion about their care. The attitude of the professionals to a patient plays a large part in determining the patient's ongoing sense of worth, a factor which is often underestimated.

Behaviour

An awareness of one's attitude may lead to a more positive behaviour towards patients. Small acts of kindness and respect boost a patient's sense of worth. Taking a little time to explain to patients what is happening dispels fear. Practising open and honest communication and giving patients full attention allows them to develop trust, thereby enabling more personal and appropriate care.

Compassion

Compassion refers to a deep awareness of the suffering of another coupled with the wish to relieve it. Compassion is felt beyond simply intellectual appreciation. Compassion may be inherent in the healthcare provider and hopefully develops over time with both professional and life experience. Demonstrating compassion does not need to take time and can be both verbal and non-verbal.

Dialogue

Healthcare professionals speak to patients about their illness but may fail to touch on the issues that are most important to the patient, such as the emotional impact of the illness and the importance of being recognized as an individual and not another sick person. Healthcare decisions need to be taken considering not only the medical facts but also the life context of the patient. Psychotherapeutic approaches, such as life review or reminiscence, can be used to support patients to regain or retain a sense of meaning, purpose, and dignity.

These four facets compromise a framework for upholding, protecting, and restoring dignity, which embraces the very essence of medicine.

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Resilience

> Hercules himself must yield.
>
> Henry VI Part III, Scene I

Strengths exist in everyone. Any strength is a pathway to resilience. Even people facing the end of their lives or bereavement can be resilient. The concept of resilience is an approach, philosophy, or mindset which is consistent with the holistic model in palliative care.

Resilience is the ability to thrive in the face of adversity and stress: 'the capacity to withstand exceptional stress and demands without developing stress-related problems'.[10] People demonstrate resilience when they cope with, adjust to, or overcome adversities in ways that promote their functioning. It is a process that allows for some kind of psychological, social, cultural, and spiritual development despite demanding circumstances. It is, therefore, important that those involved in delivering palliative care appreciate the nature of resilience and how to enhance it. We should promote methods of enhancing and supporting coping mechanisms with the same vigour applied to assessing risk and defining problems.

Resilience has been described as a 'universal capacity which allows a person, group or community to prevent, minimize or overcome damaging effects of adversity'.[11] It is not just about re-forming but about the possibility of growth. The concept of resilience is important to the future delivery of end-of-life care and the significant challenges it faces. It offers a unifying concept to both retain and sustain some of the most significant understandings of the last four decades of palliative care and to incorporate more effective investment in a community approach and a public health focus, in addition to the direct care of patients and families. This integration is vital if we are to resolve the ever-increasing tension between the rhetoric of choice and equity coupled with the demands of rising healthcare expectations in ageing populations, and the inevitably limited availability of informal and professional carers and financial resources.[12]

Resilience has been defined as 'the capacity of an individual person or a social system to grow or to develop in the face of very difficult circumstances'.[13] Resilience can be promoted at different levels in

- individuals
- families and carers
- groups
- communities
- staff, teams, and organizations

Each of these components has strengths and resources that can be encouraged and reinforced. It is important to remember that resilience is a dynamic process, not a static state or a quality that people do or do not possess—it can change over time. Resilience is a combination of internal and external characteristics in the individual and their social, cultural, and physical environment.

Everyone needs opportunities to develop coping skills, and it is important that individuals are not excessively sheltered from the situations

that provide such challenges. Some of the characteristics of resilience that health professionals can recognize and use to encourage it are the following:

- secure attachments
- self-esteem
- belief in one's own self-efficacy
- realistic hope, whether or not mediated by faith[14]
- use of 'healthy' defence mechanisms, including humour and denial
- capacity to recognize achievements in the present
- ability to find positive meaning in stressors
- good memories
- community support
- one supportive person

Even the existence of just one of these features can promote resilience and growth.

Various interventions and tools can promote the process of resilience in clinical practice (see Table I.1).

Table I.1 Interventions to promote resilience

Intervention	Resilience and growth
Accurate and timely information	knowledge is power and can promote control
Use of stories and narratives, e.g. life review	assists the integration and surmounting of difficult events
Brief, short-term, focused interventions	maximize opportunities for change and boost confidence
Cognitive restructuring, e.g. cognitive behavioural therapy	develops coping and self-confidence
Creative activities	provide opportunities for expression of thoughts and emotions, affirmation, and opportunities to learn new skills
Family systems' approach	harnesses the potential of those involved to find their own solutions
User involvement	invites users and carers to give back and to leave a legacy of better services
Self-help groups	promote mutual exchange and peer support, reducing isolation
Public education and social marketing	share some of the lessons with users, carers, and the public, including children, remembering that the values and attitudes of society affect the ways in which people cope with loss
Empowered communities	engage with communities to minimize harm and maximize care, potentiating social capital so that communities themselves respond sensitively and supportively to the dying and bereaved
Robust management/organizations	provide structure for empowered staff to achieve objectives

Prognostication in end-of-life care

The natural history of disease has been documented over many years. This has become increasingly less relevant as successful therapies have developed. In present-day palliative care, prognosis frequently relates to chronic progressive disease in patients with multiple co-morbidities, and not to the recovery prediction of a young adult with an acute illness, as was more common in the nineteenth century.

The reasons for making an attempt at predicting how long a patient with incurable disease might live include the following:

- providing information about the future to patients and families so that they can set goals, priorities, and expectations of care
- helping patients develop insight into their dying
- assisting clinicians in decision-making
- comparing like patients with regard to outcomes
- establishing the patient's eligibility for care programmes (e.g. hospice) and for recruitment to research trials
- policy-making regarding appropriate use and allocation of resources and support services
- providing a common language for healthcare professionals involved in end-of-life care

Prognostic factors in cancer

There is a good literature on the probability of cure for the different cancers. Although individual cancers behave differently, as a generalization, predictions relate to tumour size, grade, and stage. Other factors include

- hormonal status (for hormone-dependent tumours such as cancer of the breast and prostate)
- age
- biochemical or other tumour markers
- length of time taken for the disease to recur

In palliative care, such prognostic indices may not be so relevant.

Factors such as physical dependency (due to, for example, weakness or low blood pressure), cognitive dysfunction, paraneoplastic phenomena (e.g. anorexia–cachexia, cytokine production), certain symptoms (weight loss, anorexia, dysphagia, breathlessness), lymphopenia, poor quality of life, and existential factors (either 'giving up' or 'hanging on' for symbolically important times) may be more important.

Some patients may survive for a long time (months and years) with a seemingly high tumour load, while others succumb within a short time (days) for no obviously identifiable reasons.

Several scores have been developed to aid prediction of survival. The Palliative Prognostic (PaP) score is predictive of short-term survival and summarizes scores for dyspnoea, anorexia, Karnovsky performance status, the clinician's estimate of survival (in weeks), total white count, and percentage of lymphocytes.

Oncologists rely on prognostic assessments in order to predict which patients are likely to benefit from oncological interventions. Many of their decisions are based on the patient's functional status.

Patients with an ECOG score greater than two are usually deemed unsuitable for most chemotherapy interventions (Table I.2).

Table I.2 Eastern Co-operative Oncology Group (ECOG) scores

ECOG	Grade
Fully active; able to carry on all activities without restriction	0
Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature	1
Ambulatory and capable of all self-care but unable to carry out any work activities. Up and about more than 50% of walking hours	2
Capable of only limited self-care; confined to bed or chair 50% or more of waking hours	3
Completely disabled; cannot carry out any self-care; totally confined to bed or chair	4
Dead	5

Reproduced from Oken MM et al (1982) Toxicity and response criteria of the Eastern Co-operative Oncology Group. Am J Clin Oncol 5: 649–655 Copyright © 1982, © Lippincott-Raven Publishers, with permission from Wolters Kluwer

Prognostic factors in non-malignant disease

Predicting prognosis in patients with a non-cancer diagnosis is very difficult. These patients often remain relatively stable, albeit at a low level, only to deteriorate acutely and unpredictably. They are usually then treated acutely in hospital, and the disease course may consist of acute exacerbations from which recovery may take place.

One study showed that even during the last 2–3 days of life, patients with congestive heart failure (CHF) or COPD were given an 80% and 50% chance, respectively, of living 6 months.

There are, however, general and specific indicators of the terminal stage approaching.

General predictors

Those predicting poorer prognosis include reduced performance status, impaired nutritional status (greater than 10% weight loss over 6 months), and a low albumin.

Specific predictors

Congestive heart failure (CHF)

- more than 64 years old
- left ventricular ejection fraction less than 20%
- dilated cardiomyopathy
- uncontrolled arrhythmias
- systolic hypotension
- CXR signs of left heart failure
- a prognosis of less than 6 months is associated with NYHA Class IV (chest pain and/or breathless at rest/minimal exertion) and already optimally treated with diuretics and vasodilators

Chronic obstructive pulmonary disease (COPD)

- advanced age
- FEV_1 less than 30% of predicted
- pulmonary hypertension with cor pulmonale/right heart failure

- short of breath at rest
- on 24-hour home O_2 with pO_2 less than 50mmHg (6.7kPa) and/or pCO_2 more than 55mmHg (7.3kPa) and documented evidence of cor pulmonale

Cortical dementias (Alzheimer's disease)

- functional status—the onset of being unable to walk unaided
- unable to swallow
- unable to hold a meaningful conversation
- increasing frequency of medical complications, e.g. aspiration pneumonia, urinary tract infections, decubitus ulcers

Stroke

- impaired consciousness
- lack of improvement within 3 months of onset
- age
- incontinence
- cognitive impairment
- dense paralysis

Communicating prognosis

Prognostication is a notoriously difficult task to perform accurately. The world abounds with stories of patients who have been told by their physicians that they have only a matter of months to live who, 20 years later, can recount in vivid detail the day they were given the news.

One of the reasons that prognostication is so difficult is that it is fraught with uncertainty and also with opportunities for misunderstandings between doctors and patients, who often have very different agendas as to what they want to get out of the interview.

Mr Jones listened carefully as the consultant went into great detail about the nature and the extensive spread of his metastatic prostate tumour. The explanations were detailed and scientific and long. Eventually the consultant stopped. 'Now Mr Jones, do you have any more questions?'

'Well, I didn't like to interrupt you but I was only asking how long I had before I needed to go down to get my X-ray'.

Over the past 20 years there has been a huge shift in attitudes regarding disclosure of information to patients, and a culture of complete disclosure has now become the norm. Yet prognostication does not just involve passing on clinical details and predictions of disease progression; it also involves assessing the following:

- What does the patient actually want to know? (Giving too much information to a patient who does not want to have the exact details spelt out is as unprofessional as the patronizing attitude of 'best not to trouble the patient'.)
- How is the patient dealing with the information that is being given?
- How can the patient be helped to deal with the implications of the news?

To pass on facts without regard for the implications of those facts is to increase the risk of dysfunctional communication taking place (➔ see Chapter 2).

Risk and chance

While doctors are used to describing risk in terms of percentages, when such percentages are measuring out your own longevity it is hard to translate the mathematical chances into personal experience.

Doctors may feel that they have provided the patient with the clear facts when they state that in 100 patients with the particular malignancy, 36 will be alive after 5 years following treatment. Such sentences can be easily misunderstood, and the patient may hear something very different from what the doctor is saying.

Professional discomfort

Doctors are also particularly vulnerable to miscommunication at the time of passing on prognostic information:

- Western society is now death-denying, and if the prognosis is poor it can be uncomfortable for the doctor to pass on the information and confront the patient with their imminent death.
- There is increasing fear of litigation, particularly if disease is not responsive to treatment, and any admission of failure may come across as an admission of guilt.
- Doctors may feel uncomfortable in dealing with the emotional impact that their news may have on the patient, and develop techniques to protect themselves from this discomfort.

Prognostic information can be extremely important to patients as it allows them to focus on tasks and goals which they want to achieve before their disease takes over. Communicating such information effectively is a skill which all healthcare professionals should covet.

Further reading

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Chapter 1

Ethical issues and the person in the patient

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Clinical decision-making

Clinical decision-making in the palliative care setting can present numerous challenges on a daily basis for all involved. Healthcare professionals will regularly be faced with a variety of complex ethical issues including the following: withholding or withdrawing treatments (e.g. cardiopulmonary resuscitation); capacity; autonomy; confidentiality; consent; truth-telling and hope; rationing of services; and sedation, nutrition, and hydration at the end of life. The decision-making around such ethical dilemmas and paralleling communication with patients and their families can be daunting, requiring a degree of skill, time, and, where possible, the collaboration of a wider multiprofessional team (MPT).

The management of the more explicit ethical issues faced by 'actively dying' patients is integral to the work of palliative care professionals. Though the underpinning good practice is common across all healthcare, it may only be when facing the reality of impending death that patients, their families, and their clinicians begin to fully consider the most difficult questions around the meaning and quality of their life, provoking a reassessment of the goals of treatment. Differences of opinion and conflicts of interest can emerge, creating increasingly difficult scenarios. Though not easily answered, many ethical issues can be adequately addressed with sensitive, well-informed, honest communication, without even becoming a dilemma. Misunderstandings can be unraveled; fears and uncertainties dispelled. Thereby, skilled discussions can promote a trusting patient-professional relationship, leading to consensus; many patients will feel some sense of relief, even when facing great adversity.

A life-threatening illness will often be inherently daunting, particularly if someone has never experienced the death of a loved one. Simple explanations of what to expect, can, for some, significantly calm their fears of the unknown. For example, if a patient suggests that they cannot face living any more, there may be misplaced fears of untreatable symptoms, areas of 'unfinished business', guilt, or other issues that need to be explored and hopefully addressed, at least in part.

The 'clinical world' has become increasingly complex. As society evolves and medicine continues to advance, there are more healthcare technologies, inputting MPTs, patients living longer with multiple co-morbidities, and spiralling health and social costs. Decision-making has shifted: historical paternalism has tended to be replaced in Western healthcare models by a more patient-led—or at least patient-involved—approach. The parallel information revolution means that the insight as well as the expectations of our patients and the wider public have grown, with some patients being more 'expert' in their own disease than their professionals, feeding more defensive and more consumer-led medical practices. Similarly, public and political interest in medical ethics continues to grow, with increased media attention on important topics such as end-of-life care, resuscitation, and euthanasia.

Consequently, the ethical issues around ceilings of care at the end of life are increasingly discussed. Although well meaning, the care of dying patients may inadvertently become over-medicalized, in a blinkered attempt to prolong life without any realistic chance of meaningful benefit. This can happen easily, with ever more life-prolonging treatment options and multiple clinicians split across different settings and organizations—where no one is willing or able to make the 'right' or the more 'difficult' decisions. Conversely, the 'right' or the more 'difficult' decision may be to offer active

medical management, despite a known poor prognosis, in order to best manage potentially reversible pathology, to optimize quality of life and quantity of life benefits.

Consequently, we have entered a new era for medical ethics, facing relatively uncharted clinical dilemmas in an emerging group of patients. Complex ethical decisions are best taken with the support of MPT colleagues, keeping patients' and families' wishes at the centre. This may not be straightforward: there may be clinical complexities (with unfamiliar or conflicting information); continuity of senior medical care may be limited; patients are likely to be unwell and vulnerable; and similarly their family, who may have limited contact with the patient or each other up to this point, will also be under great strain. Thus, while predictably well meaning, the most vocal contributors to a decision may not be the best informed or well placed.

Though decisions on current treatments and expected levels of intervention must always be individualized to the patient's disease and wishes, equally they remain clinical decisions that must be based on up-to-date medical evidence and robust ethical reasoning. Engaged clinical ethics is a best-practice framework that provides a reminder of the common pitfalls to avoid in everyday practice, thereby enhancing decision-making and reducing the stresses experienced by stakeholders.

Engaged clinical ethics

- **timeliness**: well-timed discussions and decisions, with the right people, to prevent breakdowns in communication
- **holistic care**: valuing compassion and empathy, towards patients, families, colleagues, and ourselves
- **values diversity**: non-judgemental acceptance and appreciation of the different approaches from other stakeholders
- **contextual openness**: allowing for shifts in plans as situations change, to be comfortable with inconsistencies in views/choices
- **consensual understanding**: developing mutual negotiation, until agreement is found or, if not, constructively agreeing not to agree

Different ethical approaches

There are several different ethical approaches that can be recruited to consider whether our clinical care is appropriate; however, these will potentially lead to different 'answers' and/or questions:

- **duty-based ethics**: the focus is on following the rules, whatever the outcome
- **consequentialism**: the priority is to get the desired result, whatever it takes
- **virtue ethics**: the key requirement is to match the approach of someone of good character, being 'worthy'

In Western healthcare, arguably the most influential ethical framework is the 'duty-based' ethics approach of principlism, which describes four key principles (or 'rules') that must be considered and adhered to as far as is possible:

- **autonomy**: deliberated, self-determination (i.e. self-governing); patients have the right to be fully informed and make decisions regarding their care according to their own values
- **beneficence**: to do good
- **non-maleficence**: to not do harm
- **justice**: fairness in allocation of resources; treating patients justly and balancing the needs of individuals with those of society

When faced with making complex clinical decisions, the priority is to apply each of the four principles to help evaluate each potential course of action. However, subjective balancing of the principles is then needed to find the 'best' solution, whereby no one principle should outweigh the others. The most ethically commendable action will be the one that causes the least infringement of all four of these principles, while remembering that professional and legal constraints may well have a disproportional impact!

At the bedside, the four principles can be condensed into three questions and considered in the following order, halting the process if 'No' is ever the answer. This approach can provide greater clarity and consistency to treatment decisions, reducing potential discord:

- **Will this treatment potentially help?** The presence of net gain (the product of beneficence and non-maleficence): in your judgement of the medical evidence base, as applied to this individual, will the treatment be of overall benefit?
- **Do we have this treatment?** The availability of an intervention (justice): are we able to give it, from the resources that we currently have?
- **Does the patient want this treatment?** That is, a considered choice from what is on offer (autonomy): exercising free will, informed and uncoerced.

Three 'Yeses' are needed to pursue a treatment. Despite its prime importance, consent must be asked last; it's a mistake to ask whether a treatment is wanted only to later find out that it would be harmful or is unavailable—so never actually on offer.

Four quadrants approach

In particularly difficult ethical scenarios, the 'four quadrants' approach can further assist clinical decision-making in applying the four principles, balancing conflicting opinions, or helping to reveal what 'good moral character' may look like. The quadrants approach consists of four broad topics:

- **medical indications**: What is the impact of the treatment/decision? What are the best-case/worst-case/likely-case outcomes?
- **patient preferences**: explore the range and strength of wishes; complete a 'best interests checklist' if lacking capacity
- **quality of life**: What is the patient's current quality of life? What impact will the proposed treatment/decision have?
- **contextual features**: additional factors (e.g. legal, family, resources, religion)

Completing each quadrant provides confidence that all the key elements have been examined, enhances communication, and builds consensus. In doing so, the 'best' way forward often becomes clear.

Scenario 1: 'My father is not drinking adequately. Why are you not giving him extra fluids?'

Ethical issues

- **beneficence**: what will be the benefits of clinically assisted hydration (CAH) in this patient?
- **non-maleficence**: what will be the harms of CAH in this patient?
- **justice**: are the necessary resources already in place (e.g. trained staff, time, drugs, equipment, space), to deliver CAH as an explicit part of the service we provide?
- **autonomy**: what is the patient's informed, deliberated, competent opinion on the current appropriateness of CAH?

The provision of food and fluids to loved ones is a natural human instinct. As patients approach the end of their life, typically they have a naturally reduced oral intake as their activity and then level of consciousness decreases. It is common for families to become anxious regarding a perceived lack of adequate fluids. There are many clinical situations in palliative care when CAH might be needed (e.g. hypercalcaemia, oropharyngeal obstruction, or profuse diarrhoea or vomiting). The accompanying dehydration may be reversible, allowing patients to return to their recent best level of functioning, albeit on a background of predictably deteriorating overall health. However, when someone is considered to be dying in hours or short days at most, without an obvious indication for CAH, routinely administering CAH is unlikely to be in the patient's best interests.

Clinically assisted hydration (CAH)

- A blanket policy to always or never give CAH is ethically indefensible.
- If dehydration is potentially the cause of a clinical deterioration or symptoms, the need for a trial of CAH should be considered and always offered if of overall benefit.
- The ongoing appropriateness of CAH should be weighed in terms of benefits and harms on a day-to-day basis for each patient.
- CAH decisions need to be made along with other ceiling-of-care decisions, e.g. the plans for clinically assisted nutrition.

Background: CAH at the very end of life

There is limited research addressing the issue of CAH at the very end of life. At present there is no definitive evidence that either giving or withholding of fluids interferes with the length of remaining life when patients are dying. However, though some fluid may help, maintaining a strict fluid balance is rarely appropriate in patients' final hours or days.

- There is some evidence that sedation and myoclonus can be helped by CAH, but with an apparent risk of worsening ascites, pleural effusions,

and peripheral oedema. This highlights the need for individualized decision-making; considering trials of CAH with regular reviews.[1]
- There is no conclusive evidence that thirst or dry mouth (in particular) will improve with CAH.
- Starting CAH can become a diversion from quality time with a patient, if families spend time worrying about infusions running out or plastic cannulae being displaced and causing discomfort.
- The simple measure of keeping patients' lips moist with wet sponges offers families the opportunity to care for their relatives and focuses care on maintaining patient comfort.

The need to withhold or withdraw CAH is inevitably an emotive issue, signifying finally and clearly for all involved, perhaps for the first time, that the patient is now dying. In practice, many patients are able to take small amounts of fluids until shortly before death. This may suffice; it can be explained that as the body is gradually shutting down, it is unable to handle extra fluid. Patients and families should be reassured that everything will be done to prevent pain or other distressing symptoms, with explanations given of the measures that will be taken. These will include medication including CAH where necessary and, most importantly, meticulous mouth care to address the common symptom of dry mouth.

Palliative care is about living remaining life to the fullest; it includes all active as well as conservative management options: 'to cure sometimes, to relieve often, to comfort always'.

Conservative management does not automatically lead to shortening of life—patients can live longer when spared toxic interventions.

Active management is not automatically inappropriate in end-stage disease; it can be the best means to provide meaningful improvements to quality of life, without the fear of 'prolonging dying'.

Occasionally, families cannot bring themselves to accept the inevitability of death, and insist on CAH at the very end of life. Although healthcare professionals must act only in the best interests of the patient, it would be unwise to ignore the views of the family, who know the patient better and have to go on surviving with vivid memories of the dying phase. On occasion, as the evidence is unclear, a careful trial of CAH can legitimately be tried. It can be particularly helpful to make a contract with the family, to try a relatively small volume of fluid subcutaneously or intravenously for a defined, short period to look for benefit, on the understanding that it would have to be discontinued if at any time it was thought to be causing distress.

Key considerations for end-of-life discussions on clinically assisted hydration

- Fully assess the individual clinical need and potential indications for CAH. Use the 'three-question sequence': Will CAH help? Is CAH available? Is CAH wanted?

1 Good P, et al. (2014) Medically assisted hydration for adult palliative care patients, Cochrane Database of Systematic Reviews.

- Explore, acknowledge, and validate any concerns of the patient, family, or colleagues about CAH.
- Discuss the potential benefits and risks of CAH that have to be carefully considered when making the final clinical decision.
- Reassure the patient and family that CAH will be provided if of overall benefit and that this individualized decision will regularly be reviewed.
- Reassure the family that the patient will be looked after optimally, with all appropriate measures, whether receiving CAH or not.
- Remember to emphasize that good mouth care is always essential and is arguably the priority ahead of CAH.

Scenario 2: 'How long have I got left?'

Ethical issues

- **beneficence**: what will be the benefits of telling this patient their prognosis?
- **non-maleficence**: what will be the harms of telling this patient their prognosis?
- **justice**: are the necessary resources already in place (e.g. trained staff, time, space, administrative support), to tell this patient their prognosis, as an explicit part of the service we provide?
- **autonomy**: what is the patient's informed, deliberated, competent opinion on the current appropriateness of being told their prognosis?

Prognosis is a very common question asked by palliative care patients and their families. In responding, healthcare professionals must recruit all the skills of breaking bad news (e.g. right time, right place, right people, right language, right pace, right amount).

It is essential to first make sure that the question has been understood; entering into a conversation about how long a patient has to live when all they wanted to know is when they will be leaving hospital can cause unnecessary distress. Once it is clear that the patient is talking about prognosis, it is then important to find out what they already know, why they are asking now, and how much they really want to know. Patients may require gentle encouragement to sensitively explore their previous conversations with healthcare professionals. To check their understanding, consider the following questions:

- 'What have the doctors told you so far?'
- 'What has made you ask this question now?'
- 'How do you see your situation?'
- 'Would now be an okay time to talk through any concerns that you may have relating to how long you may have left?'
- 'Would you prefer me to be blunt?' 'Are you the kind of person who likes knowing everything, even the 'bad' bits?'

Patients may say they have not been told anything. Though this may be true, alternatively, subconscious denial mechanisms may have allowed them to 'forget' the bad news. Some patients may also deny knowledge in an attempt to find out more or check information. Before addressing prognosis directly, it is important to be fully aware of the patient's medical history and the pace of their clinical deterioration. Comments such as 'I believe you have not been feeling at all well recently' or 'It sounds like your life has become much more difficult over the past few weeks', or a question like 'If I'd seen you a couple of months ago, how different would you have looked then?' can open up these issues, giving you and the patient a chance to estimate prognosis. However, meaningful prognostication is difficult; studies show that health professionals tend to overestimate prognosis, particularly when they have known the patient for a long time.

Despite the uncertainty, it is important to be clear and to best answer a patient's or family's questions on prognosis. Equally, it is important to be honest about the inherent uncertainty, clarifying that we cannot predict the exact number of days, weeks, or months that a patient may expect to

live. It is more helpful to talk in terms of open-ended, short or long days, weeks, months, or years, rather than give a precise number. This will reduce situations where patients are counting down the time to a presumed date, which often only adds to the anxiety of a poor prognosis. It is also important to say that even within these broad terms, we will still be inaccurate. Discussing the pace of deterioration can help, highlighting that the illness trajectory may worsen, improve, or stabilize. In order to manage the inherent uncertainty, it is important to arm patients and families with coping strategies, e.g. rolling horizons (where the time frame and expectations continually move forward, and concertina up and down as the trajectory changes), and to hope for the best, while planning for the worst.

Times have changed: truth telling and prognosis

Conceal most things from the patient … revealing nothing of the patient's future or present condition. For many patients … have taken a turn for the worst … by forecast of what is to come.

Hippocrates

When you do it [break bad news] badly, they'll never forgive you—and when you do it well, they'll never forget you.

Dr Rob Buckman

Historically, paternalistic attitudes within medicine and society meant that bad news may have been withheld from patients, seemingly for their 'own good'. Shifts in societal views (towards individualism) mean such well-meaning but misplaced overprotectiveness has been superseded in Western medicine by the prioritization of patient autonomy. Healthcare professionals are now required to share information openly and honestly with patients. This offers patients the best opportunity to engage with and lead clinical decisions, and to plan their own future.

Full disclosure allows patients to set realistic, relevant, and achievable ambitions; to focus on important life goals; and to address unfinished business (e.g. writing a will, seeing religious advisers, spending quality time with family, having key conversations).

While some patients may not want to be told everything, most patients and families do want to be fully informed of any information relating to their care (e.g. treatment options, prognosis). Some patients may want to write an advance decision to refuse treatment (ADRT), which provides a clear, formal record of their wishes to allow informed decision-making should they lose capacity. Patients may not find it easy to discuss these issues, even with close family members, and may need some help to do so.

Background

Epidemiological literature on prognosis is available, especially in cancer populations. For a patient presenting with a defined cancer type, stage, grade, and histology, median five-year survival rates are available and often quoted to patients. However, a median is of little help to an individual (as half the patients will do better, the other half worse!). Many other factors have been studied in an attempt to categorize patients into prognostic

groups, and this can be helpful in broad terms. However, in practice it is not possible to accurately predict the prognosis of an individual, because in addition to biomedical variability, there are many other factors, including psychosocial, emotional, and existential issues, all of which defy quantitative measurement.

Sadly, it is still relatively common for a precise-sounding prognosis—e.g. 'six months' or 'won't make Christmas'—to be given, and despite the implicit inaccuracy, patients and families can understandably take this literally. If the patient dies before the given time frame, the family can feel cheated of time that they would otherwise have spent differently had they known that time was so short. If the patient survives longer, both patient and family may take some comfort that they have defeated the odds. However, the 'burden' on patients of living on borrowed time is high, and if the family have altered their lifestyles—e.g. giving up work, and salary, to look after a patient who has not deteriorated as told—tensions inevitably build up alongside all the normal feelings of guilt and anger.

Key considerations for questions on prognosis

- Approach this question as you would any breaking-bad-news scenario.
- Before addressing prognosis, confirm what actually is being asked.
- Explore the patient's knowledge, understanding, and the amount of information that they want to know.
- Be prepared; be familiar with the typical course of the patient's illness and know their specific rate of deterioration.
- Be honest about the difficulties in predicting prognosis.
- Talk in terms of days/weeks, weeks/months, months/years; avoid any precise dates or numbers.
- Offer strategies to deal with uncertainties; rolling horizons and hope for best/plan for worst, while reassuring that all necessary care and support will be available.

Scenario 3: 'Don't tell my mother the diagnosis. I know her better than you'.

Ethical issues

- **beneficence**: what will be the benefits of not telling this patient their diagnosis or prognosis in favour of collusion with the family?
- **non-maleficence**: what will be the harms of not telling this patient their diagnosis or prognosis in favour of collusion with the family?
- **justice**: are the necessary resources already in place (e.g. trained staff, time, space, administrative support), to not tell this patient their diagnosis or prognosis in favour of collusion with the family, as an explicit part of the service we provide (and adequately manage any 'fallout')?
- **autonomy**: what is the patient's informed, deliberated, competent opinion on the current appropriateness of not being told their diagnosis or prognosis in favour of collusion with the family?

Historically, it was not unusual for family members to be told a relative's diagnosis and prognosis instead of the patient. As Western healthcare moved from a paternalistic, restricted truth-telling culture to fully sharing information with patients, a parallel reduction in collusion with families has followed. The once-common scenario of being stopped in the hospital corridor by anxious relatives, who have been told that their relative has cancer, insisting that this information is not given to the patient, is now less common. As patient confidentiality requires that clinical information can only be shared with the patient's explicit consent, a situation of collusion with the family should seldom arise. Once a patient with capacity has been told all the information they want, they can then consent to the sharing of none, some, all, or more of the details with family members.

However, if you encounter a relative who has been told or suspects the diagnosis before the patient is aware, and demands non-disclosure to the patient, the negotiation on sharing such information is more complex. Some families may feel, particularly if no treatments are being offered, that it would be kinder to withhold the diagnosis, to save the patient the distress of unhelpful bad news. It is important to acknowledge the value of family concerns (knowing their relative best) with a willingness to take this into account, confirming the need for sensitivity and individualized content in all discussions. Equally, it is important to refuse to collude with family members, as there's an obligation to at least offer the patient a chance to consider the clinical information that is directly relevant to their decision-making and autonomy.

Timeliness in information sharing is central. To maximize understanding and minimize distress for all stakeholders, it may be appropriate to delay discussions or release information in stages. However, when treatment decisions are needed, if patients appear distressed as possibly feeling 'shut out', or if the patient asks direct questions, as professionals we must be honest. Similarly, the family should be advised not to lie. Families tend to be reassured that before we disclose the diagnosis with the patient, we will try to find out what the patient understands of their illness and whether or not

they would really like more information (i.e. the bad news as well as the good news). Having a family member present at these discussions can be very useful for all concerned. The family can also be reassured that family tensions generally reduce considerably following open discussions about a diagnosis, in contrast to the counterproductive impact generated by maintaining deceit, which typically outweighs any well-meaning perceived benefits of non-disclosure.

Key considerations in truth-telling

- Patient confidentiality requires that healthcare professionals are only able to share clinical information with family or friends with the patient's consent.
- If families request non-disclosure of bad news to patients, fully acknowledge their concerns as well meaning and helpful, while reassuring them of the benefits of well-timed, sensitive but frank discussions and the need to avoid lies and false reassurances.
- Patients need to be fully informed in order to make autonomous decisions regarding their care. They may have important things to say or do (e.g. visit people or places, or make financial arrangements such as wills and gifts) or choices to make (both medical and after-death decisions) that may be missed if they are not adequately informed.
- Patients may be comforted by a label for their illness or deteriorating condition—even if 'cancer'—because it explains why they have been feeling so unwell.
- Patients are not always frightened of death itself, but may be most concerned by the uncertainties leading to it, over which they will have greater awareness and control if fully informed.
- Many patients will have already worked out their diagnosis, picking up non-verbal clues from professionals (and relatives), and are not unduly surprised when it is confirmed.
- Patients often want to protect the family by denying that they know anything. At the same time, the family may be trying to protect the patient from the same information that they all already know.
- Families need to know that concealing the truth from a patient is impractical; it becomes more difficult over time, with more professionals, family members, and friends being required to keep the secret. With increasing opportunities, the truth can slip out; the patient can then lose all trust and confidence in their family and professionals and predictably be angry that they were lied to.
- It is important for professionals and family not to lie; however, an insensitive, poorly timed truth may be no better. Even if a patient starts to ask direct questions, it is important to check what is actually meant and how much truth is wanted at that time, and then provide the right amount of detail, in the right way and with the right support.

Scenario 4: 'I want full resuscitation if my heart or lungs fail'.

Ethical issues

- **beneficence**: what will be the benefits of cardiopulmonary resuscitation (CPR) in this patient?
- **non-maleficence**: what will be the harms of CPR in this patient?
- **justice**: are the necessary resources already in place (e.g. trained staff, time, drugs, equipment, hospital care, ambulance) to provide CPR to this patient as an explicit part of the service we provide?
- **autonomy**: what is the patient's informed, deliberated, competent opinion on the current appropriateness of CPR?

Background

There is heightened public and patient awareness of the issues surrounding CPR decisions. This follows increasingly explicit discussions in advance care planning and when admitted to hospital as well as media scrutiny of a high-profile legal case that detailed the use of 'do not attempt cardiopulmonary resuscitation' (DNACPR) orders (see Box 1.1).

Despite increased awareness, there remains confusion regarding the ethical, legal, and clinical decision-making processes for CPR among the public, in the media, and among many healthcare professionals. Increasing public expectations around exercising autonomy in healthcare decisions can mislead. It is a common misconception that patients, relatives, and some professionals believe the decision regarding CPR lies with the patient or family. It is very important to remember that patients, families, and professionals are on the same side: if CPR would work, it will be on offer—if not able to help, then nothing is being 'withheld'. While patients and families have the right to ask for whatever treatment they want, equally, medical and nursing staff are professionally obliged *not* to initiate a treatment that meets any of the following criteria:

Box 1.1 Communicating CPR decisions

The Royal Courts of Justice judgement relating to Janet Tracey (The Royal Courts of Justice, 2014) has reinforced GMC advice that doctors cannot be required to start a treatment, in this case CPR, if sufficiently viewed to be futile/no prospect of success, irrespective of any patient or family demands, though they do need to be able to professionally defend such decisions. Equally, the case highlighted the need for wider communication; the patient is entitled to know whether a clinical decision not to attempt CPR has been taken, even if CPR is futile and the discussion could be distressing. Senior staff need to discuss CPR decisions with the patient and, where appropriate, their family; it is only acceptable not to if it is felt that the conversation will cause the patient genuine 'harm' (and not just 'distress'). This need for openness in ceiling-of-care decisions emphasizes the importance of highly skilled communication that should be standard medical practice within all clinical decision-making.

- They believe it would not be of overall benefit to the patient (i.e. it would cause more harm than good, or no net gain).
- It doesn't have the resources available sufficient to offer that treatment at that time (i.e. it is not considered cost-effective).
- It has an informed refusal of that treatment by the patient, which is valid and applicable.

The process of discussing and documenting the resuscitation status of patients can be stressful, particularly when the patient or family remain in disagreement with their healthcare team, or each other, about the resuscitation status. The fear of litigation is ever-present in healthcare, and this can cause an unnecessary strain on staff when trying to make the right decision. Good practice would dictate that such matters are best addressed by the whole MPT, although the most senior professional available, often the patient's consultant, has the ultimate responsibility for the decision.[2]

Factors complicating CPR discussions

- Patient and family expectations of the likely success following CPR are much greater than the reality.
- Patients and families often lack a full understanding of what CPR entails, including the potential complications if successful.
- Many professionals have surprisingly patchy knowledge of the likely outcomes following CPR across different scenarios (see Table 1.1), leading to misleading and mixed messages, which do not always reflect the evidence base.
- Professionals usually have a biomedical approach to judging 'success' from CPR—i.e. 'survival to discharge', despite the more realistic chances of broader benefit in terms of initial recovery and peace of mind (before and after death).

Table 1.1 CPR chances of survival

Approximate chances of survival to discharge following CPR according to staging/performance status in cancer patients in hospital	
Unselected cases	6.2%
Localized disease	9.5%
ECOG score = 0–2	17.5%
ECOG score = 3–4	2.3%
Approximate chances of survival to discharge following CPR in different settings for all patients	
In hospital	15%
In community	5%
In hospice	1%

2 Willard C (2000) Cardiopulmonary resuscitation for palliative care patients: a discussion of ethical issues. *Palliative Medicine*, **14**: 308–12.

Decisions relating to Cardiopulmonary Resuscitation. Guidance from the BMA, Resuscitation Council (UK), and the Royal College of Nursing. 3rd edn (2016).

- Successful CPR, in contrast to unsuccessful CPR, can be particularly resource heavy, and thus requires complex and uncomfortable cost-benefit analyses in a rationed health service.
- Futile CPR is a most distressing and demoralizing intervention for healthcare professionals to 'impose'.
- Patients and families often fear that you will 'give up' on them if you are not offering CPR, and that all other active treatments will be withheld too.
- Patients and families may lack the understanding or be unable to accept the natural process of dying, so fail to see the incongruity of CPR under these circumstances.
- CPR conversations need to be approached with honesty, taking the time to explain the underpinning decision-making. It is a mistake to frame CPR conversations as if it is a decision for the patient or family to make ('Would you want CPR?'). This will cause problems, particularly when the decision may need to be taken that CPR cannot be offered (as no net gain or inadequate resources).
- DNACPR decisions and forms are not legally binding, but they do provide an invaluable guide, if valid and applicable, should the 'right' clinical action be unclear at the time of an arrest.
- DNACPR forms are binary (a limited, blanket 'yes/no') and do not allow for contextual and clinical complexities, e.g. '*Yes* now', if I have a witnessed, reversible event, but '*No* later' should I slip gradually into multi-organ failure and die.

The diversity of patients seen by specialist palliative care teams has changed, with an increased ratio of non-malignant conditions and more patients at earlier stages of their cancer. Even in advanced cancer patients, increasingly, many have ongoing or potential oncological treatment options. Patients receiving aggressive active treatment may understandably and appropriately feel that they would want CPR in the event of a sudden cardiac or respiratory collapse. A parallel cultural shift in the acceptability of CPR within palliative care means the role of basic CPR with emergency transfer to hospital is considered for hospice inpatients. This should reassure all concerned; only clinically appropriate and explicitly desired CPR should be performed. By contrast, the presumptive, blanket 'no resuscitation' previously seen in most UK hospices more than 20 years ago is now not defendable, particularly given the statistical uncertainties (even though the odds are never 'good'), the heterogeneous inpatient population, and the diverse understandings of 'benefit' and patients' and families' potentially legitimate demands. Moreover, the clinical picture is more complex than is often acknowledged—the nature and setting of an arrest carries a significant influence on any chance of success. To appreciate the variability of arrests, consider an acute reversible event, leading to a witnessed arrest, with a shockable rhythm in hospital—and then compare that to an unwitnessed arrest, with a non-shockable rhythm, in a patient with multi-organ failure as part of a progressive global deterioration/dying at home.

Key considerations behind CPR decisions and discussions

- The clinical decision on CPR must be case by case—individualized to that patient, in that setting, at that time. Following patient assessment and involvement, it should be made and owned by the MPT and evidence-based. Use the 'three-question' sequence: Will CPR help? Is CPR available? Is CPR wanted?
- If CPR is of overall benefit and available, it must be offered to patients. Conversely, if CPR is not of overall benefit, it cannot be offered. However, clinical uncertainties and differing perceptions of 'benefit' can leave differences of opinion.
- The ultimate responsibility for a DNACPR decision rests with the most senior professional responsible for that patient that is available. This decision needs to be reviewed for ongoing applicability at appropriate intervals.
- Patients' or relatives' wishes do not entitle them to receive any treatment, including CPR, which has been deemed not to provide overall benefit.
- Merely being a 'palliative care patient' does not automatically mean CPR is inappropriate.
- Patients are legally entitled to know when a clinical decision on DNACPR has been taken.
- Good communication with patients and their relatives about the reasons behind a DNACPR decision is essential.
- When explaining a DNACPR decision, it should not be framed as a decision that the patient or family must make, but instead approached as a conversation to impart clinical information, explaining why, unfortunately, CPR is no longer an option, as not now of benefit. It's not a choice for patients, families, or even professionals, but simply a consequence of the patient's disease that dictates whether CPR could offer meaningful benefit (within available resources).

Competence, capacity, and consent

Although ethical frameworks can add value to many complex or contentious clinical decisions, they are particularly useful when making decisions on behalf of patients who lack capacity.

If a patient has sufficient *capacity* to make an informed decision (e.g. consent to treatment), they are deemed to be *competent* to make that decision. Despite some differences (i.e. a clinical spectrum vs a legal all-or-none test), the terms capacity and competence are frequently used interchangeably in clinical practice. The guidance for assessing capacity in England and Wales is set out in the 2005 *Mental Capacity Act* (MCA 2005) and accompanying professional literature.[3] The MCA 2005 stresses a presumption of capacity, the need to support individuals to make their own decisions, their right to make seemingly unwise or eccentric decisions, and a requirement to act in patients' best interests and to pursue the least restrictive option. The MCA 2005 helpfully identified the four steps needed to confirm someone's capacity:

1. **understand** the information they are given
2. **retain** this information long enough to make a decision
3. **weigh up** the consequences of their particular choices
4. **communicate** their wishes

Capacity judgements can only relate to a single decision at that particular time. Consequently, a patient may be competent to make certain choices, such as deciding what clothes to wear, but not able to make more complex decisions (e.g. deciding between moderate-risk or high-risk cytotoxic chemotherapy). Additionally, capacity may fluctuate: a patient may not be competent to consent initially, but if the decision is delayed, they could make a competent choice later.

The MCA applies in England and Wales; the *Adults with Incapacity (Scotland) Act* 2000 governs decision-making in Scotland. In Northern Ireland, there is no legislation currently in place. Common law governs decision-making for patients without capacity, requiring decisions to be made in a patient's best interests.

Importantly, across the UK, it is presumed that all patients have capacity unless proven otherwise. Someone cannot be deemed to lack capacity without first providing all necessary support to maximize their capacity. This includes making sure hearing aids are working, optimizing medication, treating reversible causes of confusion, and reassessing capacity at different times of day.

If you have presumed or determined that your patient has capacity (understands the information, retained it to make a decision, having weighed the consequences, and then communicated it), then you must accept the decision they make (even if you do not think it appears to be the 'best' option).

A medical decision for a patient lacking capacity should be taken in their 'best interests'. The MCA 2005 sets out best practice. Even when a patient lacks capacity, they still need to be involved in discussions regarding their medical care as far as possible. Similarly, all stakeholders must be involved in 'best-interests' discussions, as far as is practical; typically this means at least the wider MPT and any key contactable family. Family should be consulted

3 Brazier M, Cave E (2011) *Medicine, Patients and the Law*, 5th edn, UK: Penguin, pp.145–6.

to help find out any views the patient had expressed on such matters. Asking 'What do you think your mother would say, given this situation?' may focus the minds of a distressed family. However, family members cannot make decisions for incompetent patients in the absence of appropriate legal documentation; even as a registered lasting power of attorney (LPA) for health and welfare, they still have to act in the patient's 'best interests'.

Specific situations

Not uncommonly, palliative medicine doctors are asked to assess a patient's capacity in order that they may complete legal paperwork (e.g. a will, an LPA, or an ADRT).

Making a will

When it is feared that a patient writing or changing a will could have their capacity later called into question, a solicitor may ask for formal confirmation of their client's testamentary capacity. Importantly, whenever a doctor agrees even 'just' to witness a will, establishing the specific capacity for that will is a professional prerequisite. The testator must demonstrate understanding of the nature and effect of making a will; the extent of their estate; and the claims of those who might expect to benefit from the will (both those included and those excluded). There must also be no influence from a psychiatric disorder. Because this assessment can feel overly complex and 'intrusive', and as only occasionally necessary, a number of hospice policies advise that, wherever possible, clinical staff should not agree to witness the signing of a will. If clinical involvement is required, testamentary capacity should be assessed and documented by the most well-placed staff member, probably a medical consultant.

Lasting power of attorney and advance decisions to refuse treatment

Similarly, doctors witnessing the signing of LPAs and ADRTs should ensure and document that the patient has the required capacity to make these decisions (see Chapter 34).

Key considerations in assessing capacity

- You must presume that your patient has capacity until proven otherwise.
- You must provide all measures to enhance capacity by managing the environment: e.g. optimize the senses (glasses or hearing aids), ensure a comfortable familiar environment (good lighting and heating), bring an advocate to the meeting, provide writing materials, and, if required, bring an interpreter, etc.
- Patients with capacity are entitled to make seemingly unwise treatment decisions.
- Patients may have capacity even if they have advanced mental illness, dementia, or other end-stage disease—never make assumptions.
- Patients lacking capacity may have lucid intervals during which it is important to reassess capacity to then allow appropriate, competent, patient-led decisions.

Euthanasia

> I will give no deadly medicine to any one if asked, nor suggest any such counsel.
>
> The Hippocratic Oath

Euthanasia is an emotive topic that typically generates a polarized debate, with well-meaning, strongly held views on both sides. Some clinicians may see euthanasia as a potentially beneficial intervention, empathizing with and respecting the requests of distressed, dying patients—i.e. a 'mercy killing'—while others see killing patients as the antithesis of good care that cannot be 'safely' legalized (risking acceptance of 'death on demand'), and even if legalized, should never involve clinicians.

As with any contentious ethical dilemma, the use of emotive language can easily cloud the arguments on both sides of the debate. It is therefore important to be able to distinguish between the various forms of euthanasia and bring clarity to the discussion. The term *euthanasia* derives from the Greek words '*eu*', meaning good, and '*thanatos*', meaning death, thus a 'good death'. However, this literal meaning is not helpful. Confusion follows, because euthanasia is a broad term, which spans both controversial and uncontroversial practices. Moreover, the debate misleadingly shifts from a philosophical moral debate (could it ever be 'right'?), to a technical legal debate (can meaningful and safe legislation be drafted?), to a clinical debate (are clinicians required or best excluded?).

In the UK, euthanasia is regarded legally as manslaughter or murder, with a maximum punishment of up to life imprisonment. Similarly, assisted suicide is also illegal, with punishment of up to 14 years' imprisonment, though in 2010 guidance on non-prosecution was drafted.

Proponents of euthanasia argue that there is a moral distinction between murder and euthanasia; in contrast to murder, euthanasia involves hastening death for a perceived benefit as voiced by the individual asking to be killed.

'Euthanasia' within healthcare is most helpfully defined by the World Health Organization as 'a doctor intentionally killing a person by the administration of drugs, at that person's voluntary and competent request'. However, this definition is not universally or even commonly adhered to by either the lay or medical press. Misunderstanding is common, as the overarching euthanasia can be divided into two contrasting categories, 'active' and 'passive', that are ethically distinct:

Active euthanasia describes bringing about the death of a person through a direct action, such as giving a lethal injection. Importantly, the medical cause of death is the act of euthanasia, not any underlying disease.

Passive euthanasia describes not attempting to prolong the life of a person, by the withholding or withdrawing of seemingly life-prolonging medication. Importantly, in passive euthanasia the medical cause of death is the underlying disease, e.g. an infection or a cancer, not the omission of medication, e.g. antibiotics or chemotherapy. Indeed, there may be no impact on an individual's prognosis, following a patient's request for conservative management (an understandable but potentially incorrect presumption). In patients with end-stage disease, life-prolonging treatments

may no longer be able to offer any meaningful benefit. Moreover, when nature is allowed to take its course, a number of hospice patients will live longer without (toxic) treatments. This is obviously reliant on the patient's dependency on that treatment and realizing that not all life-threatening scenarios will subsequently prove to be fatal.

In parallel, there is a further complexity linked to consent, with classification into 'voluntary', 'non-voluntary', and 'involuntary euthanasia'. Again, each is ethically distinct:

- **voluntary euthanasia**: the person requests to be killed and gives their fully informed consent
- **involuntary euthanasia**: the person has not requested to be killed, has not been consulted, or both
- **non-voluntary euthanasia**: the person cannot request to be killed, as they lack capacity and are thus not competent to consent
- **physician-assisted suicide** (PAS) has to be included in any ethical consideration of euthanasia. In PAS, a person has independently and willingly used lethal means to directly cause their own death, having needed explicit support from a doctor to access the necessary drugs or the information on doses needed. PAS provides an illusion of 'personal' comfort for doctors, with an apparent shift of responsibility to the patient. However, in terms of professional responsibility and accountability, PAS is inseparable from euthanasia, and only supporting PAS (but not euthanasia) is clinically irrational, as many of those 'most in need', and when the ethical 'risks' may be less, will be too unwell to pursue PAS when desired. Consequently, there is the inevitable consequence, in jurisdictions where only PAS is legal (e.g. Oregon), that staff perform euthanasia (administering medication for patients who are too frail).

Background

Public support for euthanasia and PAS is reportedly as high as 70–80% in a number of UK polls. However, the strength of conviction within this support and the degree of clarity behind the responses—realizing the bewildering spectrum that is covered within euthanasia and PAS—are far from clear.

The moral question 'Are euthanasia and PAS right or wrong?' is unanswerable. Instead, there are more vexing legal questions being asked of society: 'Are euthanasia and PAS healthcare priorities?' 'Would society be safe if it was a doctor's role to kill vulnerable, distressed patients on request?'

Patient support appears paradoxically less than public support, and uptake is lower still: where euthanasia and PAS are legal, only 1–3% of people actually choose it, yet all patients and doctors are exposed to the potential risks.

Following a ballot in 2014, the Association for Palliative Medicine of Great Britain and Ireland remained opposed to any change in the law concerning PAS. A majority (82%) of members were against a change in the law to allow PAS. The same proportion thought that if assisted suicide were legalized, it should be wholly outside the province of medicine, perhaps within family courts. Only 4% were prepared to be involved personally in assisting suicide.

Euthanasia and PAS remain illegal across the majority of the world's jurisdictions, though there has been a notable increase in legalization over

the last 20 years. Euthanasia is currently legal in the Netherlands, Belgium, Colombia, Canada, and Luxembourg. PAS is legal in Albania, Germany, Japan, Switzerland, and in the American states of Washington, Oregon, California, Vermont, and part of New Mexico, while it is supported by case law in Montana.

Clinical arguments in favour of legalizing euthanasia

- To respect patients' right to autonomy over their own life and follow their decision-making regarding the time and place of their death.
- It is an act of compassion, preventing the prolongation of ill health and predictable reductions in quality of life for patients.
- Currently, patients wanting legal euthanasia must travel abroad to countries where it has been legalized.
- The emotional as well as the financial cost of care for patients who would prefer to be dead appears a misuse of 'precious' healthcare resources.

Clinical arguments against legalizing euthanasia

- The medical priority is a duty of care; though not always enough and possibly not wanted, there are always health and social care options that could help, at least to make a scenario less bad, if unable to make it 'good'.
- Palliative care aims to manage physical, psychosocial, and spiritual distress in order to help patients, families, and carers feel better, do more, and cope with death and dying in order that life may feel more bearable at that time.
- Patient autonomy is not absolute; both individually and as a profession, doctors cannot be expected to end the life of patients just because it has been requested. The right to life as declared in the universal declaration of human rights does not confer a right to die at the hands of doctors.
- Though a person is able to judge that their own life is no longer worth living, a doctor should never judge another person's life as not worth living, even if they are able to identify and empathize with a fellow human's suffering.
- Safe medical boundaries are impossible; doctors all too frequently encounter patients unable to face living across various clinical settings; a meaningful distinction cannot be drawn between competent requests to be killed on the basis of diagnosis; prognosis; duration/permanency of request; perceived degree, nature, or irreversibility of suffering, etc.
- When dealing with patients contemplating suicide or asking to be killed, it is vital to consistently provide optimal medical and social care, and attempt to redress the desperate situations that can lead someone to want to end their life.
- Ending patients' lives does not require medical training.
- The irreversibility of euthanasia and PAS in inherently vulnerable patients risks hasty or inappropriate action; this generates concerns where patients could be misdiagnosed or given an inaccurate prognosis, or present with transient requests, but then inappropriately pursue euthanasia or PAS.

- Once doctors are 'expected' to kill patients as part of good care, this 'irreversibly' introduces the risk of well-meaning misuse or even abuse. This slippery-slope argument proposes that once voluntary active euthanasia is legalized, it will open the door to involuntary or non-voluntary euthanasia, as has already been demonstrated in the Netherlands.
- Patients already have the legal means to exercise autonomy and shorten their lives; they can refuse to start or to stop any medical treatment for any reason, by a competent refusal or an ADRT, including refusal of life-sustaining treatments and the voluntary refusal of food and fluids. Though legal, these pose similar ethical issues to euthanasia and PAS for professionals, needing to be handled sensitively, but ultimately respected (i.e. professionally agree to disagree even if personally might agree). The current UK legal options do not appear adequate or palatable for the pro-euthanasia lobby.
- Euthanasia and PAS are not necessarily pleasant; clinically, the mechanism of death is far from straightforward, with serious complications and notable failure rates. Deliberately inducing respiratory arrest incurs acute, hypoxic brain damage (in effect, 'suffocation').

Responding to requests for euthanasia

Questions about euthanasia and PAS, although rare, can be daunting and difficult to handle. It is important to first clarify what has prompted your patient's request. If it relates to uncontrolled physical, psychological, social, or spiritual issues, then it is your duty to seek to address these and aim to improve on the patient's quality of life. In parallel, you can still show respect for patients' and families' right to hold personal views on euthanasia and PAS, reassuring that you will always provide care without judgement in a non-discriminatory way. You can acknowledge that individuals are best placed to judge what is best for their own health and well-being, and only they can determine what is truly in their own best interests. However, it is important to remind your patients of your ongoing duty of care, stressing what you can do, rather than what cannot be done as a clinician. However, sometimes reflecting on the illegal consequences of euthanasia and PAS in the UK may remove any confusion or unrealistic expectations some patients with persisting requests for euthanasia and PAS may have.

The doctrine of double effect

The doctrine of double effect (DDE) is used when arguing the acceptability of actions that may have both good and bad effects. It states that if a morally good action is carried out with intended good effect, even though it has foreseen negative or harmful effects, the good effect can morally outweigh the bad effect provided certain provisions are met:

- Every effort to minimize the bad effect is made.
- The good result must be achieved independently of the bad one.
- The bad side effect must not be intended, even if predictably it could happen.

- The action taken must be applicable and proportionate to the medical issue—e.g. if treating pain, it must be an appropriate analgesic at an appropriate dose.

As a result of historical, but still common, misunderstandings, the DDE has inappropriately been used to justify the acceptability of administering the potentially high doses of opioids that may be needed to relieve pain in a dying patient, incorrectly believing such doses will, as a secondary effect, reduce respiratory drive to potentially hasten death (barring any historical excessive opioid use, well meaning or not). Crucially, there are no circumstances in which the correct dose of opioid necessary to control suffering could be lethal, and thus there is no need to invoke the DDE in opioid prescribing.

The DDE has limited applicability, if any, to modern, safe palliative care, given the following:

- Palliative care experience and research has shown that it is possible to control pain, distress, and other end-of-life symptoms safely.
- Opioids can be used safely, titrating as needed for each patient without hastening death.[4]
- Sedative use at the end of life has been seen to require the DDE. However, the convention to label symptom-control drugs that have sedation as a side effect as 'sedatives' in patients' final days is illogical and misleading. When used appropriately, titrating to the lowest effective dose, such 'sedatives' will not hasten death and not even cause detectable sedation. Thus, despite the common label 'sedation', the appropriate use of symptom-control drugs with sedative side effects is morally and clinically distinct from the practice of deep, ongoing 'palliative sedation' described in the literature from countries outside of the UK and Ireland.
- If patients do experience side effects from symptom-control medication (e.g. sedation or respiratory depression), actions must be taken to alleviate these (e.g. antidotes, dose reductions, or switching to other, hopefully safer, drugs, followed by an even more careful titration).
- Paradoxically, though the DDE would apply should a palliative care patient die from neutropenic sepsis or an NSAID-related haemorrhage, the doctrine is rarely, if ever, evoked in these circumstances.
- A flawed argument, based on the misapplication of the DDE, suggests that as doctors currently hasten death when relieving suffering, this equates to euthanasia. All the evidence and experience show this to be incorrect. Of note, nearly every person who dies in a hospice will have had a final dose of one symptom-control drug or another, but it is clearly misguided to blame that for their death.

Key considerations regarding euthanasia and PAS

- Euthanasia and PAS are highly emotive topics, which are gaining increasing public, professional, and media attention.
- Euthanasia and PAS are beyond a simple 'right/wrong' distinction, with multiple conflicting moral, legal, social, and clinical aspects.

4 Anderson S (1998) The double effect of pain medication: separating myth from reality. *Journal of Palliative Medicine*, **1**(4): 315–28.

- Confusion hampers discussion, with ethically distinct divisions of active and passive euthanasia and the further complexity of divisions into voluntary, involuntary, and non-voluntary euthanasia.
- Though PAS can appear morally distinct from euthanasia, professionally they share the same clinical responsibilities and accountabilities, so need to be considered together ethically.
- The medical duty of care remains the constant priority in all patients who say they would rather be dead; despite inevitable limitations, healthcare must attempt to redress the desperate situations that can lead someone to want to end their life.
- It is important to explore the reasons behind patients' requests for euthanasia, as these will often be due to unmet physical, psychological, social, or spiritual needs.
- The majority (82%) of Association for Palliative Medicine members were against a change in the law to allow PAS in 2014.

Further reading

Borasio GD, Jox R Gamondi C (2019) Regulation of assisted suicide limits the number of assisted deaths. *Lancet* https://doi.org/10.1016/S0140-6736(18)32554-6.

The person in the patient

Dying patients derive self-respect from a sense that others value them for what they have done and who they are. Bodies do not suffer. People do.

Dr Eric J Cassell

Person-centred care

Many would assume that medicine, and certainly palliative care, is person-centred. However, in reality, much care is now organ-centred or organization-centred! Somewhere between the organ and the organization, the person and their suffering and concerns can be lost.

As medicine has become more specialized, there are experts in every organ and disease, and yet many people in the West in the twenty-first century are dying slowly of multiple illnesses often affecting several organs. Single-site, disease-centred care leads to multiple silos with expert teams rarely coordinating or communicating with each other in a meaningful way. Medication gets added by each team, leading to polypharmacy with multiple exhausting clinic appointments. Important conversations are often omitted or left to another team. What we need are co-morbidity clinics where a person is seen, for example, by a diabetic nurse, a heart failure doctor, a physiotherapist, a pharmacist, and a palliative care nurse.

A patient-centred clinic model

Organizations are designed around resources, rather than what might suit patients – e.g. services that can't admit patients after 4 p.m., have no available parking, can't give advice overnight, or insist on monthly visits when intermittent phone calls might be enough.

If the patient agenda, the organizational agenda, and the medical agenda overlapped, then we would achieve high value medicine at lower cost.

So what is person-centred care?

There are numerous definitions of person-centred care, but by its nature it looks different for each person, and is therefore difficult to define. Essentially, it is about redressing the power balance between the person and the health system, ensuring that the person is an equal player in their care, not a passive recipient. There are some underpinning principles defined by the Health Foundation:[5]

- personalization: focusing on the person's goals and values
- enablement: promoting the ability to self-manage and be as independent as possible
- shared decision-making: explaining all options, in a non-coercive way
- coordination of care: harnessing multiple teams to communicate with each other, keeping the person at the heart of planning

5 Health Foundation: Person Centred Care ℞ http://www.health.org.uk/theme/person-centred-care

Why does person-centred care matter?

Discovering what matters to people, sharing decisions, and setting achievable goals is likely to lead to greater satisfaction, probably less time in hospital, and more meaningful, less costly care. Person-centred care is about new conversations, and putting the person at the heart of decisions and discussions.

It is hard to know why we have lost the ability to ask authentic questions. It is interesting, however, that trust in the medical profession has been dropping since the latter part of the twentieth century. Perhaps it is not a coincidence that medicine has become less relational and more technical over the same time period.

A more relational way of working requires a different stance from the doctor—a stance that sits more easily with person-centred care.

Michael Balint said, 'You are the medicine'!

We know from research that patients trust doctors who share something of themselves, who connect with humour and authenticity.[6] How can we do this in the chaotic and busy systems in which we work?

> Quacks are the greatest liars in the world except their patients.
>
> Attributed Benjamin Franklin (1706–90)

Seeing the person in the patient

To understand the person, it is necessary to get to know them. How can we get to know someone quickly in the context of overbooked clinics and ward rounds?

Biographical questions, such as simply knowing the job someone does, start to bring the person into focus. Use cues at the bedside, such as asking about the photos brought into the hospital, the books they are reading. This so-called small talk builds rapport, and starts to build a picture of the person. In turn, self-esteem can rise and dignity be restored.

Dr Kieran Sweeney had a dreadful time during his mesothelioma illness. As a physician, he became acutely aware that person-centredness was missing from his care, in terms of decision-making and communication. His BMJ article makes salutary reading.[7]

> *The relational aspects of care lacked strong leadership and at key moments were characterized by a hesitation to be brave.*
>
> Dr Kieran Sweeney, K. Mesothelioma, BMJ 2009;339:b2862

What matters to you?

'What matters to you?' seems such an obvious question, but it is rarely asked, and often too late. The US surgeon and writer Atul Gawande exposed this line of questioning as pivotal in his narratives published in his

6 Wright EB, Holcombe C, Salmon P (2004). Doctors' communication of trust, care, and respect in breast cancer: qualitative study. *BMJ*, **328**(7444): 864.

7 Sweeney, K.K (2009). Mesothelioma. *BMJ*, **339**: b2862.

famous book *Being Mortal*. Discovering people's hopes and goals leads to a change in direction of care. A system of questioning has been developed by his research team (see Fig 1.1): the Serious Illness Conversation Guide, which is now being evaluated in the UK.[8]

> The question to ask is not 'What's the matter?', but 'What matters to you?'
>
> Maureen Bisognano, Institute for Healthcare Improvement Boston

Who matters to you?

Palliative care, perhaps more than other specialties, allows for more time for the consultation, and it is therefore imperative that we don't spend the whole time seeking answers to the biological, when the psychological and social are at the forefront of people's concerns. The skills that are paramount are close listening, contemplation, asking new questions, and noting cues.

Many hospices have long traditions of drawing family trees—an amazing collaborative and often therapeutic tool—to discover not just what matters to people, but who. This could be modernized to construct a 'social map'—who in your world will support you as your illness progresses? This might be the neighbour, the drinking partner, or the work colleague as well as various family members and friends. Understanding everyone's role and potential tasks will make planning for the future that much easier.

People want us to connect their social world and professional world, and it is within palliative care that this becomes obligatory rather than optional. These two circles of support are often very separate, but there will be greater synergy if they overlap.

Several smartphone apps (e.g. Jointly and Rally Round) allow friends and carers to connect and communicate, keeping the person they are all supporting in touch and informed. Much of palliative care is family-centred or even network-centred care rather than person-centred, and, increasingly, digital connection can promote this.

Person-centred tools

There are many aids to support person-centred care. Excellent tools to discover what matters to people have been developed by Helen Sanderson Associates.[9] These include one-page profiles—simple templates to record the following:

- what is important to them
- what people appreciate about them
- how best to support them

This is really useful, for instance, in a care-home setting.

8 Bernacki R, Gawande A, Block S, et al. (2015) Development of the Serious Illness Care Program: a randomised controlled trial of a palliative care communication intervention. BMJ Open, **5**: 10 http://bmjopen.bmj.com/content/5/10/e009032

9 Helen Sanderson Associates http://helensandersonassociates.co.uk

Serious Illness Conversation Guide

CLINICIAN STEPS

☐ **Set up**
- Thinking in advance
- Is this okay?
- Combined approach
- Benefit to patient/ family
- No decisions today

☐ **Guide** (right column)

☐ **Summarize and confirm**

☐ **Act**
- Affirm commitment
- Make recommendations to patient
- Document conversation
- Provide patient with Family Communication Guide

CONVERSATION GUIDE

Understanding	What is your understanding now of where you are with your illness?
Information preferences	How much information about what is likely to be ahead with your illness would you like from me? FOR EXAMPLE: Some patients like to know about time, others like to know what to expect, others like to know both.
Prognosis	***Share prognosis, tailored to information preferences***
Goals	If your health situation worsens, what are your most important goals?
Fears/ Worries	What are your biggest fears and worries about the future with your health?
Function	What abilities are so critical to your life that you can't imagine living without them?
Trade-offs	If you become sicker, how much are you willing to go through for the possibility of gaining more time?
Family	How much does your family know about your priorities and wishes? (Suggest bringing family and/or health care agent to next visit to discuss together)

Fig 1.1 Serious illness conversation guide. Reproduced from Bernacki R, Gawande A, Block S et al. Development of the Serious Illness Care Program: a randomised controlled trial of a palliative care communication intervention. BMJ Open. 2015; 5:10 http://bmjopen.bmj.com/content/5/10/e009032 with permission from the BMJ Publishing group.

Tools to support self-management, including goal-setting, have been developed by the Health Foundation.[10] These strategies are suited to long-term conditions—but also when time is short. Shifting the locus of control back to the person and those close to them—e.g. by coaching the family in moving and handling techniques, ensuring the family know who to call in a crisis, and what to do while they are waiting—will instil confidence.

Person-centred questions

Questions need to be asked in an atmosphere of authentic engagement, not detached concern. It needs to be recognized that people have a past, a present, and a future—however short that future may be. Doctors need to be truth-hearers as well as truth-tellers!

The following questions are examples to try:

- What would a good day look like?
- What lifts your spirit?
- What do I need to know about you to support you?
- If I asked your son, what would he say? (an example of a useful circular question)
- If time is short, what would you like to focus on?
- Who are all the people who can play a role in helping you to stay at home?

How much suffering in this world comes about by leaving things unsaid?

The barriers to asking person-centred questions need to be overcome.

Barriers include the following:

- fear of attachment
- fear of intrusion
- lack of confidence
- too little time
- professionalism: 'it's not my role'

Histories

Histories is a novella of hospital life, exploring relationships of care with poetic clarity, humour, and poignancy.

'Everyone knows she's dying, vacillating across the grey line of it, but still they won't stop all this. It's like they can't'.

'As long as her words were unspoken, the possibilities they held remained undisturbed and locked safely away'.[11]

Dr Sam Guglani

10 A practical guide to self-management support. Health Foundation. http://www.health.org.uk/publication/practical-guide-self-management-support

11 Guglani S. *Histories* (2017). London: Quercus Press.

Case history—two scenarios

Who is the person?

A 74-year-old widowed clergyman, Rev G, with bladder cancer and deteriorating renal failure. He lives with his cat, and his closest family is his niece 70 miles away. He has an amazing supportive church community.

Following progression of his cancer through several chemotherapies, he is now being offered a trial of immunotherapy with a 5% chance of complete response and 30% chance of partial response, but with a 50% chance of significant side effects. He is feeling weak and has pain on walking.

His goals and values

Percentages are difficult to understand, but what Rev G was clear about was that he was at peace with his future, was not frightened of dying, wanted to be pain-free, and see particular people before he died. He wanted no more heroic treatment for infections, hypercalcaemia, or advancing renal failure. He also expressed a horror of needing intimate personal care. These expressed values and preferences should have made his care very easy.

Scenario 1: a disease-centred approach

Rev G was persuaded to go on the immunotherapy trial, as the 30% chance of response sounded appealing in the way it was presented. It was suggested that his pain would deteriorate if he didn't have more treatment—the option of palliation alone was not discussed. He was not asked what mattered to him, and the decision-making did not present all options equally. He was not asked about his goals of care or what mattered to him, his cat, and his niece.

He developed severe autoimmune colitis after the second immunotherapy course, with incapacitating diarrhoea, this led to several episodes of faecal incontinence and the need for personal care at home, which he dreaded. Demoralization set in.

Eventually, with high-dose steroids, the colitis and diarrhoea settled, but the steroids caused severe muscle wasting, insomnia, and restlessness.

Following a fall, Rev G went back into hospital—the hospice option was not discussed with him. The renal failure continued to progress, and, as the pattern had been for active treatment, he was admitted to the intensive care unit to manage his failing kidneys. He died four days later with seven tubes in various bodily orifices to support his kidneys, his heart, and his lungs, all to no avail.

He died alone. This was not the death he wanted.

Scenario 2: a person-centred approach

The oncologists explored his wishes, stopped the oral chemotherapy, which was worsening the fatigue, and respected his wish to decline immunotherapy.

The palliative care team in the community started to visit more often to control his bone pain. His church community did the shopping, cooked for him, and kept him entertained with stories and gossip.

He was admitted to hospital with a crisis of pain following further spinal collapse. Despite escalation of opioids, the only thing that helped was an NSAID, which of course was not good for his kidneys. Doses of opioids and

NSAIDs were negotiated with Rev G as the goal was to achieve pain-free consciousness, even if the analgesia upset his kidneys. In hospital, he was able to continue seeing his visitors and conclude several important conversations.

His renal failure worsened (it would have done even without an NSAID), and at his request, he was transferred to his local hospice, where he already knew several of the staff. A neighbour brought in his cat! He died five days later, with his nausea and pain well controlled, conscious till 24 hours before he died—a death in accordance with his wishes and goals.

The right person-centred conversations at the right time can change the direction of care and promote a very different outcome

Further reading

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Chapter 2

Communication in palliative care

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Introduction

Effective communication is essential in all clinical interactions. Although some clinicians have innate communication skills, most of us can improve our ability to give and receive information. There is good evidence that unlike many clinical skills that improve with experience, communication ability does not reliably improve unless specific educational effort is made.

> Effective symptom control is impossible without effective communication.
>
> Buckman, 2001

Reproduced from Buckman, R. (2001) Communication skills in palliative care: a practical guide. *Neurologic Clinics* 19(4):989–1004, with permission from Elsevier.

Communication is fundamental to good palliative care, but difficulties can arise that need to be understood and addressed. It is always a two-way activity, requiring sensitivity, empathy, and 'active listening'.

Society's attitudes towards death and dying can hinder open communication. Health professionals may be uneasy with issues of death and dying: they may wish to protect themselves and others, or feel a sense of discomfort with strong emotions.

It is easy for the busy health professional to use a variety of blocking tactics which inhibit communication, such as hiding behind task-focused practice. An additional hazard may arise if the setting is not conducive to privacy with space and time to listen.

Information-giving can take the place of hearing the underlying feelings and emotions. The essence of good communication is not what we say, but how we listen. The quality of listening empathically to patients should not be underestimated if patients are to feel understood and cared for.

Communication in palliative care is necessary to achieve an accurate assessment of patients' physical, emotional, and psychosocial needs. If we are to be able to find ways of supporting patients and families facing change and uncertainty, we as health professionals need to find out about the patients' expectations and goals. Effective communication and shared decision-making are highly valued by patients and families.[1]

Enabling people to make informed choices and to make future plans involves careful listening and sensitive responses. Attending to cultural and language issues and helping people face some of the strong emotions aroused by their situation—such as anger, denial, depression, and fear—are essential in providing holistic palliative care.

1 Virdun, C, Luckett, T, Davidson, PM, Phillips, J. Dying in the hospital setting: a systematic review of quantitative studies identifying the elements of end-of-life care that patients and their families rank as being most important. *Palliat Med*. 2015 Oct; 29(9): 774–96.

- Communication is not just 'being nice', but produces a more effective consultation for both patient and healthcare professional (HCP).
- Effective communication significantly improves:
  - accuracy, efficiency, and supportiveness
  - health outcomes for patients
  - satisfaction for both patient and HCP
  - the therapeutic relationship.
- Communication bridges the gap between evidence-based medicine and working with individual patients.

Adapted from Silverman J et al. (2013) *Skills for Communicating with Patients* (3rd edn). Oxford: Radcliffe Press.

It is intellectual and communication skills which will become the most crucial competency in health care.

R J Lifford Professor of Public Health,
Birmingham (Journal Royal Society of Medicine 94:560 2001)

Barriers to effective communication

There are various barriers which prevent or inhibit communication.

Healthcare professional-led barriers

Four factors are known to impact on communication behaviour: fears, beliefs, inadequate skills, and lack of support.

Fears

- of unleashing strong emotions
- of upsetting the patient
- of causing more harm than good
- of being asked unanswerable and difficult questions (e.g. Why me?)
- of saying the wrong thing and getting into trouble with the HCP hierarchy
- of taking up too much time
- of dealing with patients' emotional reactions

Beliefs

- that emotional problems are inevitable in patients with serious disease and that nothing can be done about them
- that it is not my role to discuss certain things—they should be discussed with senior team members
- that there is no point talking about fears when we have no answers
- that talking about concerns that cannot be resolved falsely raises expectations

Inadequate skills

- not knowing how to assess knowledge and perceptions
- not being able to integrate medical, psychological, social, and spiritual agendas
- not knowing how to move both into and out of feelings safely
- being uncertain how to handle specific communication situations such as breaking bad news, difficult questions, collusion, handling anger, and denial

Lack of support

- feeling that there was no support for the patient if problems were identified
- feeling that no support would be available for the HCP
- conflict within the team

Patient-led barriers

There is evidence that patients disclose as few as 40% of their concerns,[2] and that those who are most anxious or most distressed disclose least.

Reasons for non-disclosure by patients are similar to the professional-led barriers: fears, beliefs, and other difficulties.

2 Heaven C., Maguire P. (2008) Communication issues. In *Psychosocial Issues in Palliative Care* (ed. M. Lloyd Williams), Oxford: Oxford University Press.

Fears

- of admitting inability to cope
- of breaking down/losing control in front of strangers
- of stigmatization by admitting psychological problems
- of having their worst fears confirmed
- of trying to protect staff from their distress

Beliefs

- that healthcare professionals are too busy
- that the HCP is only concerned with certain aspects of care, e.g. nurses with physical care, doctors with disease and treatment-related worries
- that talking about concerns will increase the burden for the HCP
- that life depends on treatment and complaining about treatment will lead to its withdrawal: 'I mustn't alienate or upset the doctor'
- that their worries are insignificant

Other difficulties

- unable to express how they feel; they may be overawed by the consultation and might forget to mention their foremost concern
- unable to find the right words; they may be unfamiliar with both the technical language and the concepts of disease evolution and spread
- when they have tried to express their concerns to healthcare professionals, cues are met with distancing
- do not have a good enough command of the language and no independent or any interpreter is available to help
- the relevant questions are not asked by the professional

Specific communication issues

Here are various examples of communication issues which frequently require careful thought and handling.

I have received two wonderful graces. First, I have been given time to prepare for a new future. Secondly, I find myself—uncharacteristically—calm and at peace.

Cardinal Basil Hume, breaking the news of his imminent death from cancer to the priests of the Westminster diocese, 16 April 1999

Reprinted from the Oxford Dictionary of Modern Quotations (3rd edition) Ed: Elizabeth Knowles (2008), with permission from Oxford University Press.

Breaking bad news

Breaking bad news is such a fundamental aspect of communication in palliative care because it requires an understanding of so many other aspects of the healthcare professional/patient relationship. It is unusual for patients not to voice difficult or awkward questions, and strong emotions are likely to be elicited. The steps required for the successful breaking of bad news can act as a template for most other communication problems encountered.

Patients and relatives need time to absorb information and to adapt to bad news. Breaking bad news takes time, and issues often need to be discussed further and clarified as more information is imparted.

There is increasing evidence that most patients want to know about their illness. Many patients who have been denied this knowledge have difficulty in understanding why they are becoming weaker and are then relieved and grateful to be told the truth. They may be angry with the family, who have known about the illness all along and have not thought it right to tell them.

Professionals often become involved unwittingly in a potential conspiracy of silence when the family demand information before the patient has been apprised of the situation. The family might say, 'Do not tell him the diagnosis/prognosis because he will not be able to cope with it. We know him better than you do'. The family need to know that their concerns of not wanting to cause any more hurt to the patient have been heard. They also need to be aware that the bad news may be more painful for them than for the patient. The family need to know that it would be unwise for clinical staff to be untruthful if the patient appeared to want to know the truth and was asking direct questions, because of the inevitable breakdown in trust that this could cause.

Advising patients and families with regard to prognosis is important since they may want (and often need) to organize their affairs and plan for the time that is left. However, it is *not possible to be accurate with prognosis*. Overestimating or underestimating the time that someone has to live can cause untold anguish. It is therefore more sensible to talk in terms of days/weeks, weeks/months, and months/years, as appropriate.

There is a balance to be made between fully informing the patient about their disease and prognosis, completely overwhelming them with facts and figures, or providing only minimal and inadequate information.

While it is important to avoid being patronizing, it is also important not to cause distress by information overload.

It is important to be aware that people have divergent attitudes to receiving bad news, and that this needs sensitive handling. Patients and families respond badly to being told bad news in a hurried, brusque, and unsympathetic manner with no time to collect their thoughts and ask questions. However sensitively bad news is imparted, patients and families are naturally devastated, and the impact of the news can obliterate a great deal of the communication that took place. Patients may either not remember or misinterpret what has been said, particularly if they use denial as a coping technique.

A strategy for breaking bad news

> Nothing is more terrible than to see ignorance in action.
>
> Goethe: *Maxims and reflections (1748–1832)*

Outlining a strategy for breaking bad news is difficult because it turns a process which should be natural and unforced into something which seems constrained and awkward. The following advice encompasses the techniques that health professionals have found, through trial and error, to be helpful. It can be used as a guide to develop an individual's personal confidence and skills in breaking bad news.

The goals of breaking bad news

The process of breaking bad news needs to be specifically tailored to the needs of the individual concerned, for every human being will have a different history and collection of fears and concerns. The goal of breaking bad news is to do so in a way that facilitates acceptance and understanding, and reduces the risk of destructive responses.

The ability to break bad news well involves skills which need to be coveted and trained for, audited, and kept up to date with as much objective determination as that shown by a surgeon in acquiring and maintaining surgical skills. The consequences of performing the process badly may have immediate and long-term damaging effects for all involved, every bit as catastrophic as surgery going wrong. For example, patients and families may lose trust. Having awareness of strategies to complete the process well is vital, but breaking bad news must never become so routine that patients or their families detect little individual caring compassion.

> If we do it (break bad news) badly, the patients or family members may never forgive us; if we do it well, they will never forget us.

Prepare to tell bad news

Acquire all the information possible about the patient and their family. (A genogram is particularly useful in quickly assimilating the important people in the patient's life, and the web of relationships within the family.)

Read the patient's notes

For the following information:

- diagnosis
- test results

- an understanding of the patient's clinical history
- the support system for the individual
- background knowledge of the patient's life—making basic mistakes will undermine the patient's confidence
- the patient's understanding of spoken language, e.g. English (if not, arrange for an interpreter to be present)

Discuss with other members of the team, and then select the most appropriate team member to break the bad news. Decide which other member of the team should be present during the interview. Ensure there is an interpreter or advocate present for those with special needs or language difficulties.

Check

That you have the following:

- a place of privacy where there will be no interruptions; unplug the telephone and switch off the mobile phone, etc.
- tissues, a jug of water, and drinking glasses
- time to carry out the process
- your own emotional energy to do so—this job is better done earlier in the day than late
- pressing tasks are completed so that there will be minimal interruptions

Plan

Prepare a rough plan in your mind of what you want to achieve in the communication, and what you want to avoid communicating. Having a rough goal will bring structure to the communication, though it is important to avoid imposing your agenda on that of the patient.

Set the context

- Invite the patient to the place of privacy.
- Introduce yourself clearly.
- Let the patient know that they have your attention and how long you have.
- Ensure that the patient is comfortable and not distracted by pain, a full bladder, etc.
- Give a 'warning-shot' indication that this is not a social or routine encounter.
- Sit at the same eye level as each other and within easy reach.

A *warning shot* is concerned with preparing a patient that bad news is coming. This allows them to be more receptive than if it comes 'out of the blue'. An example would be, 'I'm sorry to say that the results were not as good as we had hoped'.

Assess

- how much the patient knows already
- how much the patient wants to know
- how the patient expresses themself and what words and ways they use to understand the situation

'Are you the sort of person that likes to know everything?'

Acquire empathy with the patient

- What would it be like to be the patient?
- How is the patient feeling?
- Is there anything that is concerning the patient which they are not verbalizing?
- What mechanisms has the patient used in the past to deal with bad news?
- Does the patient have a particular outlook on life or cultural understanding which underpins their approach to dealing with the situation?
- Who are the important people in the patient's life?

Respond to non-verbal as well as verbal clues

- Encourage the patient to speak by listening carefully and responding appropriately.

Share information

- Having spent time listening, use the patient's words to recap the story of the journey so far, checking regularly with the patient that you have heard the story correctly.

'Would you mind if I repeated back to you what I have heard you tell me to make sure I have understood things correctly?'

- Slowly and gradually draw out the information from the patient while regularly checking that they are not misunderstanding what you are saying.
- Use the warning-shot technique to preface bad news to help the patient prepare themselves.
- Use diagrams to help understanding and retention of information if appropriate and acceptable to the patient.
- Avoid jargon and acronyms which are easily misunderstood.
- Do not bluff: it is acceptable to say 'I do not know, and I will try to get an answer for you for our next meeting'.

Remember

- Does the patient understand the implications of what you are saying?
- Is the patient in control of the speed at which information is being imparted?
- Does the patient see that you are being empathic to their emotional response? It can be very appropriate to say something like, 'Being told something like this can seem overwhelming'.
- Have you addressed the patient's real concerns, which may be very different from what you expected them to be?
- Have you offered a record of the consultation (e.g. a tape recording or short written notes) if appropriate?

Response

- Respond to the patient's feelings and response to the news.
- Acknowledge the patient's feelings.
- Be prepared to work through the patient's emotional response to the bad news with them.

It can be very distressing to get bad news, and it is not unusual to feel very angry, or lonely, or sad on hearing such news.
Let the patient speak first.

Use open questions

- How are you feeling today?
- Can you tell me how this all came about?
- How do you see things going from here?

Make concrete plans for the next step

Your appointment to see Dr Brown the oncologist is provisionally booked for next Thursday at 2 o'clock. How would that fit in with your other arrangements?

Immediate plans

- What are you doing now?
- How are you getting home?
- Who will you tell?
- How will you tell them?
- What will you say?
- How will they cope?

Such questions can help the patient to start formulating the answers that they will need for their family or friends.

Summarize

- for the patient: try to get the patient to repeat the key points to ensure they have understood
- for other healthcare professionals
- clearly record details of the conversation in the patient's notes
- convey information quickly to those who need to know—most importantly, the patient's GP

Deception is not as creative as truth. We do best in life if we look at it with clear eyes, and I think that applies to coming up to death as well.
Cicely Saunders, in *Time* 5 September 1988

Deal with questions

- Are there any questions which you would like me to deal with at this point?

Contract for the future

> I know the news today was not what you were hoping for, but you are not going to go through this on your own. We are there for you, your family is there for you, and we are going to go through this together. Dr Brown will be seeing you next Thursday and I'll see you back here on Monday morning.

- If the patient did not have a support person with them, invite them to bring such a person with them to the next appointment if they wish.
- Closing remarks should identify support networks, including contact telephone numbers and times of easy access.
- Be fairly concrete about the next meeting but also allow the patient the option to postpone if they do not feel able to attend.

Handling difficult questions

'Is it cancer?'; 'Am I dying?'; 'What is going to happen to me?'

Key points

- Find out the patient's perceptions as to what makes them ask the question: 'What makes you feel it may be cancer or you are dying?'.
- After obtaining a response, repeat the question if necessary by asking if there are any other reasons for the patient feeling this way.

If the patient gives no other reason or changes the subject

You might say, 'You asked about the diagnosis—is that something you would like to talk about?' If the patient says, 'No—leave it there', they are probably not ready to have the truth confirmed.

If the patient gives other reasons

Confirm the patient's thoughts if they are correct. You should invite the patient to express their emotions and provide support if appropriate. Pause to see whether the patient spontaneously raises any concerns. If not, invite the patient to voice their concerns. It is sensible to address only the concerns that the patient raises. However, you should answer realistically and avoid rushing in with premature or false reassurances.

- Invite further questions.
- Offer to provide information (written or verbal) that may be relevant. Drawings are sometimes helpful if conceptualization is difficult. Just the name of the disease or complication written legibly is useful for patients to take away with them. They are likely to consult friends and the Internet.
- Assure continuity of care. This will include the offer of further access for discussion, as when breaking bad news. It may also include a contingency plan for the near future.

Collusion

This may occur when a healthcare professional is approached and pressured by, for example, a relative to withhold medical information from the patient. The HCP is being invited to collude with the relative in constructing or maintaining a conspiracy of either silence or falsehood concerning the seriousness of the patient's illness. The stated rationale is often that the relative knows the patient extremely well and that 'they would just turn their face to the wall'. Alternatively, they would be unable to cope with the truth about the situation, and that there is no reason, in the view of the relative, for the patient to be bothered or alarmed by unpleasant news.

Key points

Focus on:

- the relative's feelings
- the relative's reasons for not wanting to be truthful
- acknowledging the relative's motives, e.g. protecting the patient from distress
- the strain placed on the relative/patient relationship by not being truthful with someone who they are usually very close to emotionally
- the relative's perception of the patient's understanding—seek to identify any evidence that the patient might already suspect the truth

Then:

- offer to assess the patient's understanding of their illness directly
- reassure the relative that information will not be forced on the patient if such information is not explicitly requested or wanted

Such a strategy often results in the patient disclosing to the HCP that they are fully or partially aware of the true nature of the situation. In the majority of instances, this information will be seen as a great relief to both the relative and the patient. Communication is thereby considerably enhanced by resisting the initial pressure to withhold the truth. There are occasions, however, when a relative has invested so much energy over a long period in fostering a false picture of the true nature of the patient's diagnosis and prognosis that they are quite unable to contemplate dismantling the barrier created by the collusion. In this case, the HCP must think very carefully about what action on their part is in the best interests of the patient, or, alternatively, how the patient's confidence and trust in their relative and the HCP might be compromised by unrequested and unexpected disclosure.

Dealing with anger

Key points

The following strategies help to diffuse anger:

- Acknowledge the anger: 'You seem to be very angry', which may have the effect of increasing the person's anger temporarily; this is especially the case if their anger is displaced onto you—however, the anger will not subside if there has been no chance to articulate it.
- Invite the patient/relative to explain the cause of the anger: 'Can you help me understand what is making you so angry?'.
- Listen to their story to get as much information as possible.
- Try not to be defensive, even if the anger seems to be misdirected; once anger has been expressed, the angry person often realizes that displacement was unjust.
- Focus on the individual's stress/feelings.
- Apologize if appropriate, but there is no point in apologizing for something which is clearly not your fault or responsibility.
- Clarify the situation if appropriate, e.g. 'It must be very difficult for you to see your husband in pain'.
- If possible, negotiate a mutually acceptable solution; this may include agreement that a particular situation is quite unacceptable and helping the person to look to the correct place to register a complaint.

Exploration of feelings (e.g. anxiety)

Key points

See Table 2.1.

The foregoing steps will usually need to be taken before the most appropriate intervention can be suggested. The shortcut of prescribing sedative medication is likely to fail to relieve the anxiety unless there has been some understanding and insight on the part of the patient. Medication is nearly always going to be an adjunct to discussion and alteration in coping strategies with the stress of a difficult set of problems.

Table 2.1 Key points in exploring feelings such as anxiety

Recognition	Non-verbal/verbal evidence
Acknowledgement	'I can see you are anxious'
Permission	'It's OK to be anxious'
Understanding	'I want to find out what is making you anxious'
Empathic acceptance	'You are anxious because … '
Assessment	Severity and effects of anxiety
Alteration (if appropriate)	Removal of stress, cognitive challenge, boosting coping strategies, medication

Patients who do not want to talk

The key task is to assess what is making the patient reluctant to talk:

- denial—of the facts or of unacceptable feelings
- ignorance—low IQ/incorrect information
- depression
- dementia
- disengagement
- talking to someone else
- previously dealt with—'wanting to forget'

Handling denial

Denial occurs when a patient maintains a positive outlook on their illness or prognosis in spite of medical information given to the contrary. Denial is a coping mechanism: its function is to protect oneself against distress that could be intolerable and lead to psychological disorganization. Health professionals may explore the denial to determine whether it is an absolute barrier to understanding, but forcing through it could lead to severe psychological problems.

Key points in exploring denial

Look for any evidence that denial is not absolute (a window), e.g.:

- **Now**: 'How do you feel things are going at the moment?'
- **Past**: 'Has there ever been a moment when you thought things weren't going to work out?'
- **Future**: 'How do you see your illness affecting your future?'

If there is no evidence of awareness, leave the situation as it is. However, you should ensure regular follow-up to reassess the denial. It may well become much less absolute, especially in light of the changing clinical situation and increasingly unpleasant symptoms.

Unrealistic expectations

When patients or relatives appear to be unrealistic in their beliefs about the possible outcomes of the illness or treatment, or length of prognosis, there may be several reasons why this is the case:

- They have never been properly informed.
- They have misunderstood the meaning of the information they have been given. Explanations may have been overly technical or incomprehensible because of jargon. There may have been ambiguous or conflicting information given resulting from an uncertain clinical situation.
- Clarification may not have been sought because no real opportunities were offered.
- They are clinging to false hope, which may have been the result of false reassurance at the time of breaking bad news.
- They are in true denial. As mentioned earlier, this is usually an effective defence mechanism.

The key to dealing with unrealistic expectations is to establish *why* patients believe what they do.

Key points

- Use the patient's cues to explore their perception of their situation: 'You say you have had quite a bit more pain recently. What do you think is causing the problem?'.
- Using negotiation, test out whether they really believe what they are saying, or whether they are simply trying to cling onto false hope.
- Gently challenge unrealistic beliefs about outcomes by confronting any inconsistencies in the story.
- Look for windows of worry by asking whether the patient ever worries about the possible outcomes. Worry usually indicates that denial is not absolute and that the patient has allowed themself to look at realistic scenarios on occasions.
- Establish whether the patient is ill-informed and needs to be told bad news, or is in absolute denial.

It is important that all healthcare professionals work to accurately elicit patients' problems and concerns, but at the same time are able to recognize their professional limitations. They need to be able to identify when patients or carers have needs that are best met by other people (e.g. counsellors or mental health professionals with specialist skills in 'speaking to children', psychologists, psychiatrists). In such instances, healthcare professionals need to be aware of the specialists and services that exist locally, and how they can refer to these services.

Working with ethnically diverse patients

Useful strategies

Greeting

- Check with the patient that you are pronouncing his or her name properly. Our names are very important to our sense of self.
- Welcome the patient in a friendly manner, in terms of verbal and non-verbal communication. If patients are unwell *and* worried about understanding you *and* unsure they can make themselves understood, they will already feel under pressure, and anything which makes them feel more relaxed can only help the interaction.

Language style

- Speak in short, clear, grammatical sentences.
- Deal with one point at a time.
- Do not ask more than one question before waiting for an answer.
- Avoid clinical terms unless you are going to explain them (some explanation of key terms can be empowering for patients).
- Beware of using idioms—words and phrases that can be puzzling to a non-native speaker (e.g. 'Have you been feeling down in the dumps?').
- Try not to use euphemisms (e.g. 'passing away' for dying).
- Do not use local dialect terms unless you know the patient understands them.
- Break down instructions into short, clear steps.
- Summarize important points at the end of the interaction.

Paralinguistic features (tone, pitch, etc.)

- Speak loudly enough, but don't shout. Non-native speakers often find that people shout as if it was their hearing that was a problem.
- Speak in an unhurried way, but not so slowly that it interferes with the flow.
- Emphasize important words and phrases.
- Look at the patient when you are talking.

Understanding the patient

- Give adequate time for answers. These may take longer to formulate if English is not the patient's first language.
- Ask the patient to explain any words or phrases of which they are unsure.
- Double-check with the patient that you have understood them correctly.

Checking the patient understands you

- Check understanding at regular intervals throughout the interaction.
- For important points, ask the patient to tell you what they understand about what you have said.
- Do not assume that a nod or a 'yes' indicates understanding—these gestures are sometimes just to show politeness or deference. Some Asian cultures use shaking of the head to mean 'yes', whereas this would indicate the opposite to a native English speaker.
- If understanding seems poor, ask whether they would prefer an interpreter to be present and explain how you can organize this (otherwise they might think *they* have to both organize and pay for one).

Backing up

- Use pictures or diagrams where they will clarify meaning.
- Write down important points for the patient to take away with them. Even if their English reading ability is limited, someone else in the family might be able to help.
- In some cases where there is important information to transmit, an audio recording can be made and given to the patient.

Strategies for working with an interpreter

- Check that the interpreter and the patient speak the same language and the same dialect.
- Allow time for pre-interview discussion with the interpreter in order to talk about the contents of the interview and the way in which you will work together.
- Ask the interpreter to teach you how to pronounce the patient's name correctly.
- Allow time for the interpreter to introduce themself to the patient and explain their role.
- Explain that the interview will be kept confidential.
- Check whether the interpreter is acceptable to the patient.
- Introduce yourself and your role to the patient.
- Encourage the interpreter to interrupt and intervene during the consultation as necessary.
- Use straightforward language and avoid jargon.
- Actively listen to the interpreter and the patient.
- Allow enough time for the consultation (perhaps double the time used for an English-speaking patient).
- At the end of the interview, check that the patient has understood everything or whether they want to ask anything else.
- Have a post-interview discussion with the interpreter.

Things to remember

- The pressure is on the interpreter.
- The responsibility for the interview is yours as the health professional.
- It is your responsibility as a healthcare professional
  - to show patience and compassion in a demanding situation
  - to be aware of your own attitudes towards those who are different from you, including awareness of racism
  - to be aware of your own shortcomings, for example not being able to speak the patient's language
  - to show respect for the interpreter and their skills.

Points to check if things seem to be going wrong in the consultation

- Does the interpreter speak English and the patient's language fluently?
- Is the interpreter acceptable to the patient (e.g. same sex and similar age)?
- Is the patient prevented from telling you things because of their relationship to the interpreter? An interpreter who is a family member, especially if they are a child of the patient, is likely to act as a barrier to effective communication.

- Are you creating as good a relationship as possible with your patient?
- Is the interpreter translating exactly what you and your patient are saying or are they advancing their own views and opinions?
- Does the interpreter understand the purpose of the interview and their role?
- Have you given the interpreter time to meet the patient and explain what is going on?
- Does the interpreter feel free to interrupt you as necessary to indicate problems or seek clarification?
- Are you using simple, jargon-free English?
- Is the interpreter ashamed or embarrassed by the patient or the subject of the consultation?
- Are you allowing the interpreter enough time?
- Are you maintaining as good a relationship as you can with the interpreter? (e.g. by showing respect for their skills and maintaining an awareness that the interpreter is probably under pressure).

Adapted from PROCEED: Professionals responding to ethnic diversity and cancer (ed. J. Kai): Cancer Research UK, 2005. Copyright © University of Nottingham.

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Chapter 3

Research in palliative care

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Introduction

> The principal method and goal of investigations is recognition of truth.
> Theodore Billroth (1829–94) Professor of Surgery, Vienna

The origins of palliative care research in the modern UK hospice movement date from the founding of St Christopher's Hospice in 1967. Dame Cicely Saunders advocated scientific observation and systematic research as an essential component of the specialty.

To ensure that patients are managed in the most appropriate way, a solid body of knowledge must be developed. However, this can only be done on the basis of good research, which some would say is an absolute moral imperative.

In the palliative care setting, the effectiveness of many treatments has not yet been proven through rigorous clinical trials. The use of treatments is often based on evidence from less robust evidence with different patient populations, anecdotal evidence, and doctor preference. For instance, nebulized morphine was in vogue for many years within the palliative care setting, but it has since been shown to be only as effective as normal saline in helping with breathlessness. However, it is not practicable or ethical to remove all treatments from use in clinical practice because they have yet to be tested in clinical trials. The practice of many other specialties would be equally decimated by the application of such an approach.

In recent times, research has been expanding in the area of palliative medicine with good quality, well-designed trials being carried out and published. This is a huge step forward for the field. It will ultimately improve patient care in the future through the use of evidence-based practice being integrated into day-to-day clinical work.

The overarching ethical dilemma is in balancing the needs of the individual patient you are treating, who may be approaching the end of life, with those of future populations for whom we should endeavour to improve our evidence base to optimize their care. Without striving to develop a body of evidence for the treatments we are using in clinical practice, we risk doing our future patients a disservice.

The Declaration of Helsinki was drawn up by the World Medical Association in 1964 in response to the need for a code of ethics on human experimentation. This is particularly pertinent in the field of palliative care where the core practice is looking after the dying and there is a clear need for guidance for the physician caught in the conflict between patients' best interests and the necessity to advance knowledge for society as a whole.

Some people feel that palliative care research in dying patients is not appropriate—an affront to dignity and an expression of disrespect for the emotional and physical state of people who are terminally ill. Others feel that precious time—which is limited by disease and growing physical incapacity—should not be taken from patients or their families by conducting 'research', particularly when patients may be emotionally vulnerable

and may feel easily coerced into studies in order to maintain the level of care that they need from staff.

Research has shown, however, that patients are often keen to participate even when it is clear that such research will have no immediate benefit for them.[1] They may not share the concerns of others about the difficulties and hazards of research. However, if they are not given the opportunity to decide for themselves about whether they wish to participate in research because of the concerns of well-meaning others, an important opportunity for both patient autonomy and research will be lost.

Patient-identified reasons for being involved in research:

- altruism
- enhancement of a sense of personal value
- autonomy
- supporting the commitment of doctors in optimizing care

Thus the methodological, ethical, and practical difficulties encountered in conducting palliative care studies need to be looked at clearly, and strategies devised which are sensitive both to the needs of this particular group of patients as well as to the needs of similar patients in the future in terms of having access to improved care.

1 White C, Hardy J (2008) Gatekeeping from palliative care research trials. *Progress in Palliative Care*, **16**(4): 167–71.

Methodological difficulties

Evidence-supported clinical decision-making

Evidence-supported practice is graded according to a system that attributes high evidence to the 'gold standard' research method of the randomized controlled trial (RCT) and lower evidence to studies of a more descriptive nature (Table 3.1). However, it is worth noting that RCTs cannot be used to answer all research questions, and therefore are not always the correct methodology to use.

> Evidence-based practice is the conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients.
>
> Reprinted from Sackett D. L., et al. (1996) Evidence based medicine: what it is and what it isn't. British Medical Journal, 312(7023): 71–2 with permission from the BMJ

RCTs have not traditionally been used a great deal within the field of palliative care, although they are becoming more commonplace. There are different possible explanations for this, but the nature of palliative care itself may sometimes fit more readily with research methodologies such as qualitative and descriptive studies. Although tools are available to investigate issues such as quality of life and emotional distress as part of quantitative trials, qualitative research may better assess patient experience (Table 3.2).

Qualitative research

Qualitative research techniques incorporate the subjective experience that cannot be measured so easily within a mathematical framework. Evidence from qualitative research studies has not been bestowed with the weight of evidence attributed to quantitative research. If a qualitative study is well designed and carried out, it can glean as much useful, but different, information as that of an equally well-designed quantitative study. Specific aims (generic goals) and objectives (ends or outcomes), precision, and clarity are important whether the methodology, data collection, and analysis are qualitative or quantitative.

Table 3.1 Five strengths of research evidence

Type	Strength of evidence
I	Strong evidence from at least one systematic review of multiple well-designed RCTs
II	Strong evidence from at least one properly designed RCT of appropriate size
III	Evidence for well-designed trials without randomization, single group pre-post, cohort, time series, or matched case-control studies
IV	Evidence from well-designed non-experimental studies from more than one centre or research group
V	Opinions of respected authorities, based on clinical evidence, descriptive studies, or reports of expert committees

Reproduced from Watson et. al. (2016) Palliative Adult Network Guidelines Fourth Edition with permission from Max Watson

Table 3.2 Differences between quantitative and qualitative research

Quantitative research	Qualitative research
Tests theories	Develops theories
Rigid methods	Flexible methods
Experiments	In-depth interviews
Surveys	Observation
Large samples	Small samples
Numbers	Words
Statistics	Meaning

Qualitative research takes account of ways in which the research subject makes sense of his/her individual experience. Ideas and concepts develop as the research progresses, which may then be redirected back to further inform the research findings. Words are used as opposed to numerical data. Although hotly challenged by enthusiasts of quantitative methodology, qualitative research—which often uses the imaginative expression of language—may have the power to disrupt existing assumptions and to challenge what has been considered as reliable, factual material.

Qualitative and quantitative research methods can be combined to bring a different perspective and to enhance knowledge in a more holistic way.

A range of techniques, guided by set principles, exists. Techniques include the following:

- **Observation**: Researchers are involved in a fieldwork setting within, for instance, a ward, recording conversations, encounters, non-verbal communication, spatial arrangements, and physical environment. Aspects such as the quality of care of patients can be explored in this way.
- **Participant observation**: Researchers become an active subject within the study group. For instance, they may join in with practical tasks in a ward or day hospice setting with the sole purpose of observing and not influencing.
- **Interviews**: This is the most widely adopted method within qualitative research. Interviews may be interactive, with opportunities to develop or deepen the discussion according to the subject in question. Bereavement research may usefully be conducted in this way.
- **Focus groups**: Group interviews have the capacity to generate large amounts of data. Tape-recorded transcripts may be analysed. A number of computer packages exist to sort and code items for analysis, which facilitates the handling of large volumes of data. The researcher acts as the facilitator, usually for a group of about eight people. Ideas and experiences can be explored. For instance, a multidisciplinary group of healthcare professionals might explore issues surrounding attitudes to such issues as organ donation at the end of life.

Difficulties in defining study populations

Palliative care covers a very wide range of patients with different morbidities. Such patients may include patients with slow-growing metastatic cancer, who may have many months or even years to live, to others with end-stage heart failure and only a few days to live.

For research to be clinically applicable, it is important that the research is carried out in relevant patient groups rather than extrapolated from studies, which, although superficially similar, may include patients with widely varying characteristics.

Further, many patients with palliative care needs will have significant co-morbidities in addition to their primary illness, which can make defining a uniform palliative study population very difficult.

Levels of morbidity

A significant proportion of patients with palliative care needs will be unable to adequately report their symptoms or complete questionnaires, either because they are too ill or too fatigued, or have cognitive impairment. This raises issues of the validity of consent to participate in research. Setting appropriate eligibility criteria is crucial, and trial design needs to take account of these issues at the outset.

End points and outcomes

Setting appropriate end points in palliative care studies can be very difficult. If these end points are not specific enough, then outcomes will be hard to evaluate. If the end points are too specific, then the trial will be at risk of irrelevance to the complexity of the clinical situation encountered by patients at the end of life. It is very difficult to isolate a single variable and monitor its change over time, particularly in the palliative care population, which is commonly frail and elderly. Furthermore, patients are often receiving multiple interventions for several co-morbid conditions and facing the emotional and spiritual demands of confronting mortality. A more complex approach is necessary to take account of these different factors and to view interventions in the context of the patient's overall disease journey.

Recruitment, attrition, and compliance

Recruiting patients to trials is difficult for many reasons. They are often 'protected' by their families and also by clinical staff, who see them as being vulnerable and in need of protection against unnecessary burdens. There may be only limited opportunities to approach such patients to discuss trial involvement since rapidly changing clinical and emotional situations may make recruitment inappropriate. The recruitment to trials is therefore often much slower than anticipated.

Once patients are enrolled into studies, sample attrition rates up to 60% have been recorded on account of rapidly changing physical and emotional conditions, and sometimes death, during the course of the study.

Compliance can become a particular issue as the disease progresses, in terms of completing questionnaires or taking oral medication, for instance. In designing trials that extend into the last weeks of life, this needs to be anticipated, and other simpler methods of evaluation built into the study from the outset.

Research, audit, or service evaluation

There is often much confusion as to the differences between research, audit, and service evaluation (Table 3.3), and in particular whether ethical approval is required.

For example, if palliative care patients are interviewed as part of a service evaluation, questions are often raised as to whether ethical approval is required.

Many clinicians will often approach an ethics committee for clarification.

Table 3.3 Differentiating audit, service evaluation, and research

Research	Clinical audit	Service evaluation
The attempt to derive generalizable new knowledge, including studies that aim to generate hypotheses, as well as studies that aim to test them	Designed and conducted to produce information to inform delivery of best care	Designed and conducted solely to define or judge current care
Quantitative research—designed to test a hypothesis Qualitative research—identifies/explores themes following established methodology	Designed to answer the question, 'Does this service reach a predetermined standard?'	Designed to answer the question, 'What standard does this service achieve?'
Addresses clearly defined questions, aims, and objectives	Measures against a standard	Measures current service without reference to a standard
Quantitative research—may involve evaluating or comparing interventions, particularly new ones Qualitative research—usually involves studying how interventions and relationships are experienced	Involves an intervention in use *only* (the choice of treatment is that of the clinician and patient according to guidance, professional standards, and/or patient preference)	Involves an intervention in use *only* (the choice of treatment is that of the clinician and patient according to guidance, professional standards, and/or patient preference)
Usually involves collecting data that are additional to those for routine care, but may include data collected routinely May involve treatments, samples, or investigations additional to routine care.	Usually involves analysis of existing data, but may include administration of a simple interview or questionnaire	Usually involves analysis of existing data, but may include administration of a simple interview or questionnaire
Quantitative research—study design may involve allocating patients to intervention groups Qualitative research uses a clearly defined sampling framework underpinned by conceptual or theoretical justifications	No allocation to intervention groups: the healthcare professional and patient have chosen intervention before clinical audit	No allocation to intervention groups: the healthcare professional and patient have chosen intervention before service evaluation
May involve randomization	No randomization	No randomization
Although any of these three may raise ethical issues, under current guidance:		
Research requires REC review	**Audit does not require REC review**	**Service evaluation does not require REC review**

If in doubt, it is worth consulting your local ethics committee to ensure that your project does not need ethical approval.

Ethical difficulties

The need for equipoise in studies

Palliative care patients are considered a vulnerable group; they include those with dementia and learning difficulties, as well as children. Their vulnerability makes it difficult to allocate such patients to any form of care that could be deemed in any way less optimal than another.

Thus, randomized trials, which are understood by many to offer the best opportunity to minimize bias, should only involve patients with palliative care needs if there is a high degree of demonstrable equipoise between the interventions being studied. There should not knowingly be disadvantage or morbidity associated with trial participation. However, the commonest intention of clinical research is to determine the most effective intervention or treatment, and the only way to discover this is through trials.

European Trials Directive

The European Trials Directive, introduced in 2004, brought with it increased protection for vulnerable patient groups. It has brought increased scrutiny from ethical and sponsorship committees.

With the implementation of the directive, the length of time required to bring a trial through the process has increased considerably, adversely affecting cost and the practical administrative process. This difficulty has been addressed, in part, with the setting up of two national palliative care support collaboratives, SuPaC and COMPASS, and through organizations like the National Cancer Research Institute and other supportive and palliative care initiatives, which promote appropriately funded and supported multicentre studies.

Funding for palliative care research is limited, especially in comparison with many other specialties (e.g. oncology). The infrastructure necessary to conduct palliative care research and to gather the teams of people together who have the requisite skills and knowledge is therefore difficult.

Consent

As previously discussed, matters of competence and consent are particularly important issues in relation to running studies on patients with palliative care needs, especially when their condition is deteriorating. Researchers are currently devising methods of facilitating consent from patients to enable recruitment into a specific study in the future should the patient become incompetent before that time.

Practical difficulties

Finance

In the UK, government funding for hospice services is still less than 50% of the total running costs. Given a choice between a research programme and clinical services, most hospice directors will be obliged to maintain the latter. There are, however, many examples of small, unfunded studies taking place in hospices. Larger, more comprehensive and time-consuming studies need funding either from industry (e.g. pharmaceutical), or other sources, such as research charities.

The need for sponsorship and trial insurance is a major issue for palliative care units in the UK, two-thirds of which are charities without access to NHS research governance.

Lack of research centres

Most of those involved in palliative care research are heavily involved in clinical work without specific time dedicated to research, although internationally this is changing. The need to collaborate with other research teams, with logistical and administrative support, therefore becomes very important.

The difficulties in conducting palliative care research are many, but this does not reduce its importance or its potential to make a real difference to the lives of the growing number of patients who will need palliative care in the years to come. Collaboration, finance, new methodologies, new research tools, and new ways of studying clinically complex patients will make future palliative care research more robust.

The models of research inherited from oncology may not all be appropriate, and as the specialty becomes more involved with patients who do not have cancer, new and distinctive ways of conducting clinical trials amongst the palliative care population are needed. Studies must be of the highest standard and yet practical, with the promise to produce significant outcomes. Examples include N of 1 studies, which are trials in which patients are repeatedly treated with the same treatment in order to compare their usefulness on an individual basis.

Differentiating audit, service evaluation, and research

It is important to differentiate between research, audit, and service evaluation (Table 3.3) as the methodologies are different. They assess different parameters, and the ethical approval requirements also differ. It is important that the correct method is selected based on the aim of the project.

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Website

National Research Ethics Service information Available at http://www.nres.npsa.nns.uk (accessed October 2017)

Chapter 4

Quality of life

Quality of life assessment in healthcare *64*
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Quality of life assessment in healthcare

> The highest quality of life attainable for any normal person is the achievement of optimal function, resulting in using all of the assets that each person has.
>
> Frederick Kottke (b. 1920) Professor of Physical Medicine and Rehabilitation

Pressure to improve the cost-effectiveness of care, as well as an epidemiological shift from dealing with predominantly acute to predominantly chronic conditions, has highlighted the need to supplement traditional outcomes such as morbidity and mortality with subjective measures that focus on patients' experiences. A further factor has been the emergence of a post-modern society in which the values of equality, empowerment, and autonomy have challenged the traditional paternalism of professions.

Researchers and clinicians have developed and tested hundreds of measures of patient experiences across a wide variety of conditions. These measures are known variously as 'health status measures', 'health-related quality of life (HRQoL) measures', or simply 'quality of life measures'. Increasingly, the term 'patient-reported outcomes' (PROs) is used to refer to all subjective measures generated from patients. These measures occupy a continuum from highly standardized econometric methods, such as time-trade off and standard gamble, to individualized global measures. Each has its supporters, each involves different assumptions about the nature and interpretation of HRQoL, and each has advantages and disadvantages. The research literature is now so vast and the available measures so numerous that it can be very confusing for anyone new to the field.

HRQoL measures

The development of HRQoL measures has been influenced by the World Health Organization's (WHO) definition of health as 'a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'. Most researchers (but not all) accept that there is a subcomponent of quality of life that is influenced by health, and it is this we should concern ourselves with in healthcare. One widely used definition is that of Patrick and Erickson, who defined HRQoL as 'the value assigned to the duration of life as modified by the social opportunities, perceptions, functional states, and impairments that are influenced by disease, injuries, treatments, or policy'.

Most HRQoL measures are multidimensional and usually assess symptoms, physical functioning, psychological well-being, and social functioning (Table 4.1). The most common elements include:

- physical symptoms such as nausea, vomiting, fatigue, and pain
- functional ability
- sexuality, intimacy, and bodily perception
- emotional symptoms such as worry, anxiety, and depression
- social functioning
- work life
- family situation
- hope for the future, future planning
- general life satisfaction

Rigorously designed questionnaires such as the EORTC measure or the SF36 are available and meet the requirements of reliability, validity, sensitivity, and applicability. The aim is to collect standardized information, often for use in clinical trials or epidemiological studies. However, the routine use of such scales in clinical practice, especially in palliative care, presents a number of problems. Much of the confusion in the HRQoL literature arises from the failure to distinguish between levels of care. The *micro* level is concerned with individual patients in clinical situations; the *meso* level is concerned with groups of patients as, for example, in a clinical trial or an institutional policy; and the *macro* level is the level of decision-making that affects large communities. Selecting an appropriate measure of HRQoL depends on the level of analysis.

Table 4.1 Uses of HRQoL assessments in oncology

1	To measure the impact of specific cancers and to describe the nature and extent of functional and psychosocial problems at various stages of the disease trajectory
2	To establish norms for psychological and social complications in specific patient populations
3	To screen individual patients for possible behavioural and/or pharmacological interventions
4	To monitor the quality of care in order to improve delivery
5	To evaluate the efficacy of competing medical, surgical, and psychological interventions

Quality of life and palliative care

It is widely accepted that the essence of palliative care is maintaining and improving the quality of life of patients and their families. The WHO defines palliative care precisely in these terms. Therefore, the best strategy for dealing with patients in palliative care settings is simply to measure their quality of life and make sure that they receive integrated care to maximize it. However, that is easier said than done. Much of the research on quality of life in healthcare has been driven by experts in measurement and scale construction, and many of the studies have had an epidemiological or clinical-trials focus rather than a focus on day-to-day clinical applications.

Challenges in measuring quality of life in palliative care

- What is the definition of quality of life, and how does it differ from health-related quality of life or health status?
- How should informed consent be obtained?
- To what extent is it acceptable to burden the patient and the family?
- Given the need for research in palliative medicine, how should a doctor balance being overly protective (paternalistic) with being overly demanding?
- Given multisystem problems, limited survival, and polypharmacy, what outcome measures, timing, and study design should be used, and how can compliance be maximized?
- How can studies deal with patient attrition?
- How can measures be designed to cope with 'floor' and 'ceiling' effects?
- What is the clinical significance of changes in the measures?

Quality of life measures in palliative care

There are many good measures now available for measuring health-related quality of life in cancer patients (see Box 4.1), but most of these have been developed for assessing the impact of the disease and its treatment in the 'pre-palliative' phases of the illness.

A number of measures have been designed specifically for palliative care settings, some of which are discussed below.

EORTC QLQ-C15-PAL

The EORTC QLQ-C30 was developed by the European Organization for Research and Treatment of Cancer Quality of Life for assessing HRQoL in clinical trials. It consists of 30 questions organized into five scales measuring function, one global health/overall quality of life scale, three scales measuring symptoms (fatigue, nausea and vomiting, pain), and six single questions on symptoms and financial difficulties. A shortened version of the measure, the EORTC QLQ-C15-PAL, has recently been developed for use in palliative care.[1] Derived from interviews with 41 patients and 66 healthcare professionals in palliative care, the measure consists of scales measuring pain, physical function, emotional function, fatigue, global health status/quality of life, nausea/vomiting, appetite, dyspnoea, constipation, and sleep.

Box 4.1 Health-related quality-of-life scales commonly used in oncology and palliative care research

Instrument

Generic health status measures

- Short Form Health Survey (SF36)
- Sickness Impact Profile
- Spitzer Quality of Life Index (QLI)
- Visual analogue scales

Cancer-specific measures

- EORTC—QLQ-C30
- EORTC—Site-specific modules
- Functional Assessment of Cancer Therapy (FACT-G)
- Cancer Rehabilitation Evaluation System (CARES)
- Functional Living Index Cancer (FLIC)
- Quality of Life Index-Cancer

Palliative measures

- EORTC QLQ-C15-PAL
- McGill Quality of Life Questionnaire (MQOL)
- Missoula-VITAS Quality of Life Index
- Edmonton Symptom Assessment Schedule
- Hospice Quality of Life Index (HQLI)

1 Groenvold M. et al. for the EORTC Quality of Life Group (2006) The development of the EORTC QLQ-C15-PAL: a shortened questionnaire for cancer patients in palliative care. *European Journal of Cancer* 42: 55–64.

The McGill Quality of Life Questionnaire (MQOL)

This scale was developed at McGill University specifically for use in all phases of the disease trajectory for people with a life-threatening illness. The questionnaire differs from most others in three ways: the existential domain is measured; the physical domain is important but not predominant; positive contributions to quality of life are measured. The scale generates scores on four subscales: physical symptoms, psychological symptoms, outlook on life, and meaningful existence.

Missoula-VITAS Quality of Life Index

This is a 25-item scale for seriously ill patients aimed at measuring adaptation to and integration of their physical decline, as well as attainment of life tasks and life closure. The measure addresses five quality of life domains that are relevant to end-of-life care: symptom control, function, interpersonal issues, well-being, and transcendence.

Individualized measures of quality of life

Questionnaire approaches to the measurement of quality of life provide important information. However, such measures have one particularly important limitation: they impose a predetermined external value system on the respondent. Someone other than the respondent has decided which questions to ask, which areas of life to explore, and what weights to assign to the respondent's answers to obtain a summary score. The weights are standardized and fixed and are generally derived from grouped data. Although these measures may be reliable, they may not be relevant to an individual's present life situation. Apparently similar behaviours do not have the same relevance or importance for all individuals. Furthermore, the relevance or importance of particular behaviours or events is unlikely to remain static for a given individual with the passage of time or over the course of an illness.

In assessing quality of life in a clinical situation, one needs to know, at a given time, what particular issues are of most concern to the patient. Individuals, even when seriously ill, are active agents, engaged in an unfolding life cycle, involved in a continuous search for meaning, and constantly striving towards the goal of self-actualization. Only individuals can judge their own experiences, and they do so in the context of their own expectations, hopes, fears, values, and beliefs. To quote the psychotherapist Carl Rogers, 'The best vantage point for understanding behaviour is from the internal frame of reference of the individual himself'. In order to obtain a valid measurement of quality of life, as opposed to health status, a measure is needed that evaluates each individual on the basis of the areas of life that they consider to be most important, that quantifies current functioning in each of these personally nominated life areas, and that weights their relative importance for that individual at that particular time. A life area that is going badly for an individual but is of little importance to them clearly has less implication for that individual's quality of life than a life area that is going badly but is of great importance. HRQoL measures can be supplemented by individualized QoL measures. Much is to be gained in the clinical situation from finding out what areas of life are important to the patient, the relative importance of each, and the level of functioning or satisfaction with each.

Individualized measures of QoL

Schedule for Evaluation of Individual Quality of Life (SEIQoL)

The SEIQoL was developed based on the argument that quality of life can be defined only by the individual whose life is being assessed. In a semi-structured interview, respondents are asked to nominate the five areas (cues) of their lives most important to their overall quality of life. They then rate their level of satisfaction with each on a 100 mm visual analogue scale. Finally, they are asked to judge the overall quality of life they would associate with 30 scenarios incorporating their own cues. This provides a measure of the relative importance or weight of each cue.

SEIQoL-DW

The elicitation of cues and levels of satisfaction is the same as that used in the full SEIQoL. The direct weighting (DW) instrument is a simple apparatus consisting of five interlocking, coloured circular discs that can be rotated around a central point to form a type of pie chart. The discs are mounted on a larger backing disc, which displays a scale from 0 to 100, and from which the relative size of each coloured segment can be read. Each segment is labelled with one cue, and the respondent adjusts the discs until the size of each coloured segment corresponds to the relative importance of the cue represented by that segment.

Patient Generated Index (PGI)

The PGI presents patients with either a list of quality of life areas (ingredients) that are most frequently mentioned by patients with the particular disease, or asks them to generate the ingredients themselves. After selecting the five most important areas, patients are asked to rate how badly affected by their condition each is. Patients are then asked to prioritize, using a fixed number of hypothetical points, the areas they would most like to improve.

Anamnestic Comparative Self-Assessment (ACSA)

This is a single scale in which the respondents rate their overall well-being on a scale ranging from +5 to –5. The anchors are defined by respondents' memories of the best and the worst period in their lives.

Proxy ratings of HRQoL

Early attempts to measure HRQoL in patients with advanced incurable disease relied heavily on proxy ratings, the underlying assumption being that those patients would not be able to make such assessments themselves. It is now well established that HRQoL is subjective, and the ratings provided by healthcare personnel and even by close family often do not tally with the ratings of patients. The consensus, based on research findings, is as follows:

- Health professionals and significant others underestimate patients' quality of life to a significant and comparable degree.
- Healthcare providers tend to underestimate pain intensity.
- Proxy ratings appear to be more accurate when the information sought is concrete and observable.
- While the ratings of significant others tend to be more accurate when they live in close proximity to the patients, ratings can be biased by the caregiving function of the rater.

These findings are hardly surprising. Health professionals evaluate patients using their own particular paradigm, and this is different from that used by the patient who is experiencing the condition. Even carers who know the patient very well may be applying a particular paradigm that, again, does not tally with that of the patient. Furthermore, patients are not passive in the face of their changing circumstances but use a wide range of coping processes. Findings such as those listed earlier highlight the importance of maintaining ongoing and excellent communication between patients, carers, and health professionals.

Adaptation and response shift

The Greek philosopher Heraclitus famously said, 'You cannot step in the same river twice … all is flux … all is becoming … both you and the river are changed'. There is now considerable interest in HRQoL research in exploring the psychological mechanisms by which patients adapt to their illness. Patients' judgements of their health may stay relatively stable despite large changes in objective measures of health, or their judgement of health may change in a situation where there is little or no objective change. This phenomenon, which is increasingly known as 'response shift', is due to the fact that patients may change the criteria they use to make their judgements. For example, a patient's judgement of their health might remain stable despite objective evidence of worsening cancer because, in the course of treatment, they may have seen others who are far worse off. Response shift can help to explain apparently paradoxical findings in the health literature, such as the following:

- Patients with chronic diseases often rate their quality of life at a level similar to that of non-patients.
- Patients tend to rate their quality of life higher than do health professionals or carers.
- There are usually marked discrepancies between objective measures of health and self-rated health or quality of life.

The important thing to remember is that patients are actively engaged in trying to cope with their condition; they will use a variety of coping mechanisms to make their journey more meaningful and more bearable. Health professionals who have the motivation and the communication skills to share the patient's world view by focusing not only on the objective indicators of disease, but also on the quality of life of the individual patient, can have the privilege of walking part of that journey with the patient. In Kierkegaard's words, they will have discovered the 'secret of caring'.

Further reading

Book

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Articles

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Ebenau A. et al. (2017) Life values of elderly people suffering from incurable cancer: a literature review. *Patient Education and Counseling*, **100**(10): 1778–6.

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Chapter 5

Principles of drug use in palliative care

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Introduction

> Some drugs have been appropriately called 'wonder-drugs' inasmuch as one wonders what they will do next.
>
> Samuel Stumpf (1918–1988) Philosopher

Drugs are not the total answer for the relief of pain and other symptoms.[1] For many symptoms, the concurrent use of non-drug measures is equally important, and sometimes more so. Further, drugs must always be used within the context of a systematic approach to symptom management, namely:

- evaluation of the impact of the illness on the patient and family, and of the causes of the patient's symptoms (often multifactorial)
- explanation to the patient before starting treatment about what is going on and what is the most appropriate course of action
- management: correct the correctable; non-drug treatment; drug treatment
- monitoring: frequent review of the impact of treatment; optimizing the doses of symptom-relief drugs to maximize benefit and minimize undesirable effects
- attention to detail: do not make unwarranted assumptions; listen actively to the patient, responding to non-verbal and verbal cues

In palliative care, the axiom 'diagnosis before treatment' still holds true. A particular symptom may have different causes; for example, in lung cancer, vomiting may be caused by hypercalcaemia or by raised intracranial pressure. The treatment indicated will vary according to the cause. Attention to detail includes *precision in taking a drug history.* It is important to ascertain, as precisely as possible, the drug being taken, the dose, and the dose frequency, and to confirm that the drug alleviates the symptom. It is good practice and strongly recommended that a patient's drug history is taken from a minimum of two sources, such as the GP record, repeat prescription, recent hospital discharge letter, the patient's own prescribed drugs, the patient's carer, a family member, or the patient's chemist. Asking specifically about the use of eye, ear, or nasal drops, sprays, patches, inhalers, injections, creams, ointments, and herbal supplements will minimize the risk of something being missed. The use of illicit substances should also be considered.

It should not be assumed that a patient is taking their medicines as intended by the prescriber. Medication non-concordance occurs as a result of numerous factors, including misunderstanding of the indication, misinterpretation of instructions, side effects, and tablet burden. As the patient becomes weaker and less well, they may become less able to swallow large numbers of tablets; this will also lead to less than optimal symptom control.

1 General guidance about the use of drugs in palliative care (www.palliativedrugs.com).

Attention to detail also means *providing clear written instructions for drug regimens.* The medication regimen should be written out in full for the patient and their family to work from. This should be in an ordered and logical way, e.g. analgesics, anti-emetics, laxatives, followed by other drugs. The drug name, times to be taken, reason for use ('for pain', 'for bowels', etc.), and dose (x mg, y tablets) should all be stated. It is important that the patient and their family understand the process of obtaining further prescriptions from their GP and chemist.

Medication optimization

The use of medicines should always be evidence-based and cost-effective, ensuring that the right patient gets the right medication for their symptom at the right time. When prescribing a drug, consider the following:

- What is the treatment goal?
- What are the likely side effects?
- How can it be monitored?
- What is the risk of drug interactions?
- Is it possible to stop any of the current medications?
- Will the drug be readily available via the usual supply chain?

Safe prescribing is a skill crucial to success in symptom management. The use of decimal points in prescription should be avoided where possible, as decimal points are often a source of drug errors. In some cases, however, it makes practical sense to include a decimal point.

For example, levomepromazine injection is a 25mg/mL ampoule, therefore 12.5mg equates to 0.5mL, a dose easily drawn up into a syringe. When prescribing opioids, it is good practice to always avoid decimal points and annotate the dose in words beside the prescribed figure to avoid ambiguity.

Consideration should be given to the size, shape, and taste of tablets and solutions. Where clinically appropriate, avoid awkward doses which result in the following:

- patients taking more tablets than necessary if doses were 'rounded up' to a more convenient tablet size; for example, it may be better to prescribe m/r morphine 60mg (a single tablet) rather than 55mg (3 tablets: 30mg + 15mg + 10mg)
- nurses spending more time than necessary refilling a continuous subcutaneous infusion (CSCI); for example, in the UK, it might be appropriate to prescribe diamorphine 100mg (a single 100mg ampoule) instead of 95mg (3 × 30mg ampoule + 5mg ampoule)

Many drugs used for symptom control require cautious dose titration supervised by the palliative care specialist. On discharge from hospital or hospice, arrangements for clinical review and adjustment of drugs within the community setting must be made.

The drugs mentioned in this text are listed alphabetically in the Formulary and are based on evidence as robust as is currently available. Many of these drugs are used outside their current marketing authorization (see the following).

Use of drugs outside marketing authorization (MA)

By law in the UK, a medication must be given a MA (formerly, a product licence) by the Medicines and Healthcare Products Regulatory Agency (MHRA). The MA specifies the indication, dose, route, and patient populations for which the drug can be marketed. Drugs can be used legally in clinical situations that fall outside the remit of the MA, referred to as 'off-label' (e.g. a different indication, dose, route, or method of administration than that specified in the MA). The off-label use of drugs in palliative care is routine, with the responsibility for prescribing under such circumstances lying with the prescriber. The prescriber must be fully informed about the actions and uses of the medicinal product and should provide information on the benefits and risks of off-licence prescribing to the patient (or their proxy) to facilitate an informed decision regarding treatment options. Note the drug's patient information leaflet (PIL) and summary of product characteristics (SPC) will not contain information relevant to off-label use.

Drug interactions in palliative care

> It may seem a strange principle to enunciate as the very first requirement in a hospital that it should do the sick no harm.
>
> Florence Nightingale, *Notes on Hospitals*, 1863

Owing to polypharmacy, the potential for drug interactions is high in palliative care. However, many drug interactions are harmless, and many that are potentially harmful only occur in a small proportion of people. Drugs with a narrow therapeutic ratio and those requiring careful control of dosage are often involved.

Resources for checking drug interactions

- The *British National Formulary* (BNF) Appendix 1 contains an alphabetical list of drugs and their interactions. The • symbol denotes a potentially serious interaction, where the concomitant administration of the drugs should be avoided. Available in text and via http://www.medicinescomplete.com.
- Stockley's Drug Interactions is an international reference of drug interactions, their mechanisms, clinical importance, and management. Available in text and via http://www.medicinescomplete.com.
- The SPC for a drug contains a description of its properties and conditions attached to its use, and lists known interactions. Available via http://www.medicines.org.uk.
- University of Liverpool HIV drug interaction checker. Available online via http://www.hiv-druginteractions.org/.

Cytochrome P450 isoenzyme

Metabolism of drugs in the liver principally involves oxidation or conjugation. There are several types of oxidation reactions, each catalysed by a group of enzymes called cytochrome P450. The most important isoenzymes are CYP3A4 and CYP2D6. Most drugs that are metabolized by the liver are metabolized via several pathways, usually including the cytochrome P450 isoenzyme 3A4. Some drugs such as erythromycin and clarithromycin, some SSRIs, cimetidine, grapefruit juice, high-strength fluconazole, amiodarone, and itraconazole inhibit CYP3A4, and therefore slow down the metabolism of any other drugs that are metabolized by CYP3A4, which can increase the effects of these other drugs. Drugs metabolized by CYP3A4 include methadone, domperidone, alfentanil, fentanyl, oxycodone, and amitriptyline.

The following are some selected drug interactions which are pertinent to palliative care prescribing.

Anticonvulsants

The management of patients with cerebral tumours on anticonvulsants should be closely monitored, as anticonvulsants interact with a number of different drugs indicated for symptom control in palliative care. The potential for drug interactions should always be checked prior to prescribing a new drug to a patient taking an anticonvulsant.

Antifungal drugs

- Fluconazole increases phenytoin levels.
- Fluconazole increases the effect of sulfonylureas, e.g. gliclazide, glibenclamide (risk of hypoglycaemia).
- Fluconazole inhibits the metabolism of alfentanil and methadone.
- Itraconazole and fluconazole increase sedation with midazolam.
- Fluconazole and itraconazole enhance the anticoagulation effect of warfarin.

Proton pump inhibitors (PPIs)

- Omeprazole may increase blood diazepam levels (increase in sedation).
- Omeprazole may enhance the anticoagulation effect of warfarin.

Metronidazole

- disulfiram-like reaction with alcohol
- enhances anticoagulation with warfarin
- increases phenytoin blood levels (toxicity)

SSRI antidepressants

- antagonize anticonvulsant effects of common antiepileptics and lower seizure threshold
- care with drugs that can stimulate the CNS, e.g. tramadol
- interact with cytochrome P450 enzymes
- serious reaction with MAOIs, e.g. selegiline (serotonin syndrome)
- increased serotonergic effects with St John's wort (avoid)

St John's wort

- increased serotonergic effects with SSRIs (avoid)
- reduced plasma concentration of amitriptyline
- reduced anticoagulant effect of warfarin
- reduced plasma levels of carbamazepine, phenytoin, phenobarbital (seizure risk)
- reduced plasma levels of digoxin

Torsades de pointes

Drugs commonly prescribed within palliative care with a known risk of causing a prolonged QT interval and torsades de pointes (a serious ventricular tachycardia) include clarithromycin, domperidone, erythromycin, fluconazole, haloperidol, levomepromazine, erythromycin, methadone, ondansetron, quinolones, and SSRIs. An awareness of this phenomenon is especially important when considering treatment options for patients with cardiac disease. A register of drugs that cause QT prolongation is available via http://www.crediblemeds.org.

Points to consider

- Where possible, avoid concurrent use of more than one QT-prolonging drug.
- Use the lowest effective dose of the QT-prolonging drug.
- Consider torsades de pointes as a possible cause of palpitations.
- Explain the risks involved and rationale for using the drug in question to both the patient and family.

- ECG monitoring is recommended if prescribing methadone in a patient who has additional risk factors for QT prolongation (see SPC for methadone).
- Avoid, where possible, QT-prolonging drugs in patients with cardiac disease.

Polypharmacy and the high prevalence of metabolic disturbance within palliative care patients can potentially place them at a higher risk of a prolonged QT interval. A pragmatic approach, however, should prevail when the benefit of certain drugs used in the last days of life is likely to far outweigh any risk.

Cannabinoids

There has been a reported increase in the number of patients taking commercial cannabinoid preparations for symptom control. These come in a variety of forms, including cannabis oil capsules, vapours, and drops, and hemp oil, and are often sourced over the internet. The cannabis plant contains about 60 cannabinoids, of which the main active constituent is Δ^9-tetrahydrocannabinol (Δ^9-THC), responsible for the psychoactive effects, and cannabidiol (CBD), the main non-psychoactive component. These cannabinoids are thought to play a role in therapies for pain and inflammation, and clinical trials are ongoing into their effects for a number of indications, including epilepsy. The legality of these products depends on the concentration of THC present, with < 0.2% being classified as legal. The unregulated nature of these products means that the content of the active constituent cannot be guaranteed, and there is potential for variation between products. There is also potential for interaction with other drugs. Cannabinoids inhibit numerous CYP450 enzymes, and caution is advised. Practitioners should consider enquiring whether patients are taking cannabinoid substances prior to prescribing, as careful monitoring and adjustment of prescribed drugs may be needed.

Corticosteroids

Corticosteroids have been shown to be effective for a variety of uses in the palliative care setting. Traditionally they have been used to reduce oedema and to promote appetite and well-being. They are also used in specific disease processes, and in emergency situations such as spinal cord compression, where their use can buy time until a more definitive treatment can be instituted.

Corticosteroids are produced by the adrenal gland, and have a number of physiological roles, including catabolic effects on protein, carbohydrate, and fat metabolism, as well as anti-inflammatory effects. They influence water and electrolyte balance and suppress immunity. Dexamethasone is the corticosteroid of choice in palliative care (Table 5.1).

Side effects of corticosteroids

- increase in blood sugar (in both diabetic and non-diabetic patients)
- increased susceptibility to infection (including oral thrush)
- weight gain
- thinning of the skin and bruising
- cushingoid features
- proximal myopathy (consider switching to prednisolone)
- increased risk of osteoporosis and fractures (risk rapidly escalated within first three months of treatment—consider calcium and vitamin D supplements)

Approximate equivalent anti-inflammatory doses of steroids

See Table 5.2.

Table 5.1 Indications and daily doses of dexamethasone

Indication for use	Daily dose of dexamethasone
Anorexia	2–4mg
Weakness	
General well-being/ improved mood	
Neuropathic pain/liver pain/ bone pain	4–8mg
Nausea	
Dyspnoea	
Post-radiation inflammation	
Raised intracranial pressure (brain primary or metastases)	12–16mg
Superior vena cava obstruction/ GI obstruction	
Carcinomatosa lymphangitis	
Spinal cord compression	

Table 5.2 Approximate equivalent anti-inflammatory doses of steroids

Prednisolone	5mg
Hydrocortisone	20mg
Methylprednisolone	4mg
Dexamethasone	750micrograms
Cortisone acetate	25mg
Betamethasone	750micrograms
Triamcinolone	4mg

Points to consider

- Corticosteroids can be given as a single daily dose in the morning.
- Tablet burden: dexamethasone comes in a 2mg and 500microgram tablet.
- Parenteral doses are given subcutaneously (SC) rather than by intravenously/intramuscularly.
- P.o. to SC/IV ratio of 1:1 (see UK dexamethasone formulations following).
- Practitioners traditionally avoid doses after 2 pm to reduce the risk of corticosteroid-induced insomnia (unless given in an emergency situation).
- Prophylactic gastric mucosal protection.
- Switch from dexamethasone to prednisolone if myopathy develops.
- The possibility that steroids may be masking the clinical signs of perforation of an abdominal viscus or sepsis.
- Carefully weigh the burden/benefit of continuing steroids subcutaneously should the patient become unable to swallow.
- Check blood glucose before initiating steroids and at regular intervals during treatment.

Always:

- Keep the maintenance dose as low as possible to minimize risk of side effects.
- Review treatment regularly, stopping within 5–7 days if no benefit; ensure any co-prescribed medicines are also stopped at this point.
- Reduce the dose slowly every few days if the patient has taken steroids for longer than 3 weeks or has been taking an equivalent dose of >6mg dexamethasone daily.
- Counsel all patients about their steroid treatment and side effects.
- Issue a steroid card to patients who are likely to be taking steroids for >3 weeks.

In the terminal care situation, the patient's inability to swallow oral medication is often the provoking factor which leads to stopping steroids. Continuation of steroids by injection (usually SC) should be considered on an individual basis.

Withdrawing systemic corticosteroid therapy

Abrupt withdrawal

Systemic corticosteroids may be stopped abruptly in those whose disease or symptoms are unlikely to relapse and are not in the groups that follow.

Gradual withdrawal

Advisable in patients who have

- received >3 weeks' treatment
- received dexamethasone >6mg/24 hours or equivalent
- taken doses in the evening
- received repeated courses
- taken a short course within a year of stopping long-term treatment
- other possible causes of adrenal suppression

Reduction recommendation

Corticosteroid therapy may be reduced rapidly (halving the dose daily) to a physiological dose (dexamethasone ~1mg or equivalent). Thereafter, the dose should be cautiously weaned as tolerated by the patient.

Corticosteroids in the last days of life

Unless achieving good symptom control, it is appropriate to discontinue corticosteroids in the dying phase.

UK dexamethasone formulations

Dexamethasone comes in the form of both a sodium phosphate and a base, with dosing advice and prescribing always expressed in the latter. Recent changes to the labelling of dexamethasone injection have resulted in confusion about parenteral dosing. In the UK, dexamethasone injection is manufactured in a 3.3mg/mL (Hospira and Hameln) and a 3.8mg/mL (Aspen) amp. These injectable formulations are formulated as the sodium phosphate but labelled as the base. Oral tablets and solution are formulated and labelled as the base. A pragmatic approach is recommended when converting between p.o. and SC/IV routes such that 3.3mg/3.8mg of dexamethasone base injection can be considered approximately equivalent to dexamethasone 4mg base orally.

Liver disease

The liver is the site of metabolism for many drugs, which makes prescribing for patients with liver disease particularly difficult. Unlike renal impairment, there is not one parameter which indicates the extent to which drug clearance will be affected by hepatic impairment. In palliative care, liver metastases, chronic liver disease, alcohol, and drugs are responsible for most instances of hepatic impairment. At the end of life, the potential analgesic benefit of prescribing drugs may outweigh the potential risk, and so a pragmatic approach should be adopted. General prescribing guidance is to start at low dose, with extended dosing interval, and titrate cautiously.

Analgesics (non-opioid)

Paracetamol (oral) must be dose-reduced to 1g t.d.s. in patients <50kg or those with severe liver failure. Dose intervals should be extended in acute liver failure. IV paracetamol should be avoided. NSAIDs increase the risk of GI bleeding and should therefore be avoided.

Analgesics (opioid)

Codeine and tramadol are both activated by hepatic metabolism and should therefore be avoided in liver impairment.

Morphine is the recommended first-line strong opioid

- oxycodone is the second-line strong opioid, but should be avoided in severe hepatic impairment
- fentanyl is considered to be the first-line injectable/transdermal strong opioid in severe liver impairment, though the transdermal route should only be used for stable pain; volume in CSCI may limit its use for higher dose
- preparation: fentanyl 50 micrograms/mL solution for injection (2mL and 10mL amp)
- alfentanil half-life is increased in severe hepatic impairment and should be avoided
- buprenorphine should be avoided in severe impairment
- hydromorphone is contraindicated in hepatic impairment (SPC)

Adjuvant analgesics (slow titration advised)

Gabapentin and pregabalin are not affected by liver impairment.

Sedatives (when prescribing, reduce dose and increase interval)

- clonazepam should be avoided; may have a use in terminal care for neuropathic pain/seizure control
- diazepam should be avoided owing to increased half-life; consider p.r.n. if necessary
- lorazepam is the first-line recommended sedative drug, with midazolam second-line
- temazepam considered generally safe; no change in dose required
- zopiclone should be used with caution; note its half-life is increased in severe impairment

Anti-emetics (all used with caution)

- cyclizine; no dose change required; however, should be avoided in severe liver disease
- domperidone dose should be reduced by 50% to maximum of 10mg t.d.s.; avoid prolonged use
- metoclopramide dose should be reduced in severe hepatic impairment/cirrhosis to maximum of 10mg b.d.
- ondansetron recommended maximum daily dose is 8mg in moderate-to-severe impairment

Antipsychotics (also used for anti-emetic effects)

Haloperidol and levomepromazine should both be prescribed at a reduced dose with increased interval, titrating cautiously.

Antidepressants (start at low dose and cautiously titrate)

- amitriptyline: half-life unchanged, but use with caution
- citalopram: increased half-life; maximum dose of 20mg daily; increased bleeding risk; avoid if possible, although may be preferable to sertraline
- sertraline: increased half-life; avoid in severe cases; use with caution in mild/moderate liver failure
- mirtazapine: use with caution; max dose 30mg daily

Anti-pruritic agents

- chlorphenamine: avoid in severe liver failure
- loratadine: use with caution in severe liver failure and consider alternate-day dosing
- rifampicin: use with caution

Renal disease

➔see Chapter 18.

Further reading

Peng J-K *et al* (2019) Symptom and prevalence and quality of life of patients with end-stage liver disease: a systematic review and meta-analysis. *Palliative Medicine: London* **33**(1):24036.

Syringe drivers (or syringe pumps)

A syringe driver is an ambulatory battery-powered infusion device used to administer drugs by continuous subcutaneous infusion (CSCI) usually over 24 hours. It is suitable for patient use both in hospital and at home. The administration of drugs by CSCI is common in palliative care in the UK. It is vital to fully discuss the option of using a syringe driver with both the patient and their family prior to initiating. Many people associate syringe drivers with imminent death, so it is important to alleviate this misconception and gain patient consent. For some patients, there may be an option to revert back to oral medication once symptom control has been achieved.

Indications for use

- intractable nausea and vomiting
- dysphagia
- patient too weak to swallow oral drugs
- bowel obstruction
- reduced consciousness (last days of life)
- malabsorption
- poor patient concordance with oral medication
- refractory symptoms, where a trial switch to the subcutaneous route may result in a better clinical response

Compatibility of drugs in a syringe driver

Drug combinations may be compatible at certain concentrations but not at others; thus the concentration of each drug in the solution should be compared, not the drug itself. The following factors affect stability and compatibility: brand, formulation, strength of drug used, temperature, light exposure, order of mixing, and delivery system. Thus regular close monitoring of all CSCI drug combinations is essential. All combinations must be checked prior to mixing. Resources include the following:

- Syringe Driver Survey Database from PCF available via https://www.palliativedrugs.com
- *The Syringe Driver: Continuous Subcutaneous Infusions in Palliative Care* Dickman et al. (4th edition), November 2016

Drugs that may be mixed with morphine or diamorphine

- cyclizine
- haloperidol
- hyoscine hydrobromide
- metoclopramide
- octreotide
- granisetron
- glycopyrronium
- hyoscine butylbromide
- levomepromazine
- midazolam
- ondansetron

Drugs not suitable for subcutaneous usage

- diazepam
- chlorpromazine
- prochlorperazine

Use a separate syringe driver for

- dexamethasone in doses >1mg
- phenobarbital
- diclofenac
- levetiracetam
- ketorolac
- parecoxib

Conversion of oral morphine (or oral morphine equivalent) to parenteral morphine

See Fig 5.1.

Morphine conversion

Diamorphine can be administered subcutaneously in a smaller volume than the equivalent dose of morphine. In countries where diamorphine is available, it is the preparation of first choice for parenteral use.

When converting from opioids other than morphine, calculate the equivalent dose of oral morphine over 24h and continue as per Fig 5.1.

General principles

- Combining two or more licensed drugs in a syringe results in a new unlicensed product. Doctors and independent prescribers can mix and direct others to mix drugs for administration to a particular patient.
- In the UK, it is common to administer two to three different drugs in the same infusion device. No more than four drugs should be prescribed for infusion in one syringe.
- If the combinations of drugs required are not compatible in one driver, a second, and in some instances a third, syringe driver can be prescribed.
- Water for injection or sodium chloride 0.9% are the two options used as a diluent. Care must be taken to ensure that the drug is compatible with the diluent. For example, cyclizine will crystallize with sodium chloride, so should always be diluted with water for injection.

Infusion devices

In the UK, the CME McKinley T34 is the most frequently used syringe driver (see Fig 5.2). Following safety concerns, the older Graseby MS16A and MS26 syringe driver devices were removed from UK practice in 2015.

morphine 10mg p.o. = morphine 5mg sc

Method: add the total daily oral dose of morphine (or oral morphine equivalent) and divide by two. Take into account the number of PRN doses the patient has been taking within the previous 24 hours.

e.g. morphine 10mg p.o. 4h
or
MST® 30mg b.d.
} = morphine 60mg p.o. 24h

morphine 60mg p.o. 24h = morphine 30mg sc 24h

Local conversion guidelines should always be referred to.

Fig 5.1 Conversions of oral to parenteral morphine.



Fig 5.2 The CME McKinley T34 syringe pump.

Setting up the syringe driver (SD) pump

Refer to the manufacturer's instruction manual for full instructions and local protocols for monitoring information. Syringe drivers should only be used by those who have received the appropriate training.

Practice points

- Fill a Luer lock syringe with the prescribed drugs and dilute the contents to the maximum fill volume (see Table 5.3), using a suitable diluent.
- Ensure adequate mixing has occurred and the solution is clear and free from discolouration/crystals, and precipitate.
- Label the syringe, taking care not to completely obscure the solution. The label should contain the patient's details, the name and dose of each drug, and the diluent.
- Insert a battery into the syringe driver.
- Attach the syringe to an infusion line and prime manually (this uses ~0.3mL) and note the remaining volume.
- Take the syringe driver and primed line with the attached syringe to the specific patient.
- Choose an appropriate needle site for SD infusion (➔see pp. 87–8).
- Insert infusion cannula subcutaneously and secure with a dressing.
- Turn pump on and engage syringe on the pump.
- Follow instructions on SD screen.
- Ensure keypad is locked and secured in a locked box if appropriate (e.g. if patient is confused).
- Check the SD 30 minutes following initial loading of pump and 4 hourly thereafter.

Skin sites for CSCI

Skin areas to avoid

- oedematous areas
- skinfolds

Table 5.3 Syringe sizes and fill volumes

Size of syringe	Maximum fill volume
20mL	17mL
30mL	23mL

- breast
- broken, inflamed, or infected skin
- recently irradiated sites
- cutaneous tumour sites
- bony prominences
- near a joint
- anterior chest wall in cachectic patients
- scarring

Preferred sites

- anterior chest wall
- anterolateral aspects of upper arms

Alternative sites

- anterior abdominal wall
- anterior surface of the thighs

Problems

For problems that can occur with the SD, see Table 5.4.

Table 5.4 Problems that can occur with the SD and possible reasons

Site reaction	Cyclizine and levomepromazine cause site reactions most commonly. Firmness or swelling is not necessarily a problem, but the needle site should be changed if there is pain or obvious inflammation. Ensure patient is not allergic to the dressing. Dexamethasone 0.5mg–1mg can be added to the drug mixture for site issues.
Precipitation	Check compatibility of drugs. Check solution regularly for precipitation and discolouration and discard if it occurs. Cyclizine may precipitate at high doses, particularly in combination with high doses of diamorphine. Other combinations may also cause cloudiness in the syringe.
Light flashing	Light will flash to show pump is infusing.
Alarm	This always sounds when the battery is inserted. The alarm also sounds for 15sec when the syringe driver stops. It can be silenced by pressing the Start/Test button. Check for empty syringe, kinked tube, blocked needle/tubing, jammed plunger.

Further reading

Book

Dickman A., Schneider J., Varga J. (2016) *The Syringe Driver: Continuous Subcutaneous Infusions in Palliative Care*, 4th edn. Oxford: Oxford University Press.

Articles

Pickard J. (2008) Syringe driver site reactions: a review of the literature. *European Journal of Palliative Care*, **15**(3): 125–31.

Scottish Intercollegiate Guidelines Network, (2000) *Control of Pain in Patients with Cancer: A National Clinical Guideline*. Edinburgh: SIGN.

Dickman A et al. (2017) Identification of drug combinations administered by continuous subcutaneous infusion that require analysis for compatibility and stability. *BMC Palliative Care*. **16**: 22.

Antibiotics in palliative care

The decision to initiate antibiotics in a palliative patient is often complex and dependent on a number of factors, including ceiling of care, impact of symptoms, and stage of disease. Decisions need to be made on an individual basis considering the best interests of the patient by weighing up the benefits of treatment against the risk of prolonging dying. The increased level of antimicrobial resistance in recent years necessitates that the principles of prudent prescribing and antimicrobial stewardship should be adhered to at all times. Antibiotic choice should be guided by local guidelines and based on cultures and sensitivities where possible. Microbiology advice should be sought when there is any doubt or if there is no improvement 24–48 hours after commencing initial regimen.

The BNF contains extensive antimicrobial information for both prophylactic and therapeutic regimens, and should be consulted for dosing guidance. It is imperative to always check allergy status before prescribing.

General considerations

- Infections are common in palliative care patients who may have been immunosuppressed by either the disease or treatment.
- Chest and urinary infections are the most common in the palliative setting.
- Antibacterials often need to be dose-reduced in renal impairment.
- Corticosteroids may need to be boosted during an infection.
- Antibiotic therapy comes with added tablet burden, side effects, and potential interactions.

Aim of antibiotic therapy within the hospice

- life prolongation without prolonging dying
- symptom control (pyrexia, pain, bleeding, delirium, dyspnoea, odour reduction)

Infection-related pain

Infection around things like a skin metastasis or oral tumour can cause severe pain which is unresponsive to titration of strong opioids, and it may be associated with fever and malaise, and complicated by delirium. Antibacterial therapy can be very useful; treatment options include piperacillin/tazobactam 4.5g IV t.d.s. For penicillin-allergic patients, consult a medical microbiologist.

Respiratory tract infection

Death rattle in the imminently dying is occasionally associated with profuse sputum from a chest infection. In this case, the broad spectrum antibiotic ceftriaxone is indicated to reduce the copious purulent malodorous discharge from the mouth. Ceftriaxone has a long duration of action allowing for single dose of 1–2g administered via the SC, IV, or IM route. Administration via daily injection is an option. A decision to continue with treatment (or not) should be taken as appropriate to the individual clinical situation.

Fungating tumours

Metronidazole, to cover anaerobic infections, is indicated for malodour caused by fungating cancers, and can be administered via oral, intravenous, and topical routes of application. Complete control of malodour is reported in 50% of patients, with improvement generally seen within 2 days, but can take up to 1 month.

- Systemic treatment: metronidazole (p.o.) 200–400mg t.d.s. for 2 weeks, re-treating for a further 2 weeks if malodour recurs. If deemed necessary to continue treatment indefinitely, the recommended dose is 200mg BD; metronidazole (IV) 500mg t.d.s.
- Topical treatment: metronidazole 0.75% gel is an option when the fungating cancer is relatively small or poorly vascularized, or systemic treatment is not an option. The wound should be cleansed and the gel applied liberally, and covered with a non-adherent and then an absorbent dressing. Topical application is usually OD to BD. Consider timely administration of analgesia before dressing change.

Conversations with patients and their relatives regarding the futility of treatment in the terminal phase, or regarding the decision to stop antibacterial treatment, may prove emotive and challenging. Considered explanations will often be required from the healthcare professional.

Cultures

- If antibiotic treatment is deemed necessary, then the use of cultures can help direct therapy. However, in the palliative context, the opportunity to culture may not be available. Directed antibiotic therapy gives better outcomes, with fewer adverse effects.
- There is no point in taking samples for microbiological culture and leaving them sitting at room temperature overnight for a morning collection. This will increase the chance of having false-positive and false-negative results.
- Swabs and urine samples can be stored overnight at 4°C.
- Blood cultures must be kept at body temperature.
- Bacteriuria is common, so samples are unnecessary unless the patient is symptomatic.
- The context in which antibiotics are considered in the palliative setting is of major importance, and will determine the antibiotic choice, route of administration, and goals of treatment.

Other important considerations

- It is important to know whether the patient has a history of drug allergies.
- If the infection is severe, then the first 24 hours of antibiotics should be given intravenously (IV).
- Parenteral antibiotics IV or occasionally IM may need to be used for a prolonged course if the patient cannot swallow tablets or absorb them from the gastrointestinal tract. In this case, the reason should be clearly documented in the medical notes.
- Cross-reaction occurs in 15–20% of people between penicillin and the cephalosporins, carbapenems, and monobactam.

Deprescribing in palliative care

As a result of the increased tablet burden required for symptom control, polypharmacy is high in the palliative care setting when compared to the non-palliative setting. Deprescribing is the tapering or ceasing of inappropriate medicines. Several tools exist to guide deprescribing, including STOPP/START and Beers criteria; these however are not specific to palliative care. Deprescribing should therefore be based on clinical judgement and shared decision-making, taking into account the stage of the patient's illness. Careful consideration should be given to stopping long-term prophylactic medication such as statins, antihypertensives, anticoagulants, and oral hypoglycaemics.

Medication at the end of life

As patients approach death, swallowing often becomes increasingly difficult. It is important to ensure that the necessary drugs are prescribed by alternative routes. In the UK, when the oral route is unavailable, the SC route is the preferred method of drug administration. The marketing authorization for many of the injectable drugs used in palliative care does not cover SC administration, but this route is supported by clinical experience.

Anticipatory prescribing

See also Chapter 30, The terminal phase.

Anticipatory medications should be prescribed p.r.n. or 'when required' to ensure adequate symptom control for common symptoms at the end of life. Pre-emptive prescribing should include specific drugs for the following symptoms:

- nausea and vomiting
- pain
- agitation
- breathlessness
- respiratory secretions

The dose and recommended frequency of each drug will vary depending on the patient's background medication and care setting. In the inpatient setting, it is common to prescribe a range of permitted doses, allowing nurses to increase the amount given on their own initiative. If the patient is requiring the dose at the top end of the range at intervals of the maximum frequency stated, this should prompt a clinical review, as alternative background medication may need to be considered.

Pharmacological toxicity

Opioid toxicity

There is wide individual variation in the dose of opioid that causes symptoms of toxicity. Signs and symptoms include the following:

- drowsiness
- respiratory depression
- muscle twitching/myoclonic jerks
- vivid dreams or hallucinations
- pinpoint pupils

Common scenarios that lead to toxicity include:

- rapid dose titration of opioid
- switching from other opioids
- infection
- renal/hepatic impairment
- dehydration

Management of opioid toxicity for patients on long-term opioids

Management will depend on whether opioid toxicity is mild, moderate, or severe. The opioid antagonist naloxone (400micrograms/mL injection) is indicated for the reversal of severe opioid-induced respiratory depression indicated by the following:

- a low respiratory rate <8 respirations/minute
- oxygen saturation <85%
- patient cyanosed

If less severe toxicity:

- omit next regular dose of opioid
- review current analgesia
- monitor the patient closely; maintain hydration and oxygenation

NHS England recently highlighted the risk associated with inappropriate use of naloxone for patients receiving opioids for analgesia. A careful dose titration using lower doses of naloxone (e.g. 20–100micrograms) is recommended for these patients to avoid precipitating a severe acute withdrawal syndrome, severe pain, and hyperalgesia.

Naloxone dose and administration

There is a wide range in the initial bolus of naloxone recommended in the literature. Local guidelines should be consulted where possible. Scottish palliative care guidelines suggest the following:

- Dilute 400micrograms to 10mL with sodium chloride 0.9%.
- Administer 80micrograms (2mL diluted naloxone) as a slow IV bolus every two minutes until the patient's respiratory status is satisfactory.
- The cannula should be flushed with sodium chloride 0.8% between naloxone doses.
- Patients usually respond after 80micrograms (2mL) to 160micrograms (4mL) of diluted naloxone.

If repeat doses of naloxone are required, a continuous infusion may be necessary. Expert advice should be sought.

Benzodiazepine overdose

Fatal iatrogenic overdoses of midazolam have occurred, and it is therefore recommended that flumazenil is available for emergency use wherever midazolam is available clinically. For dosing guidance, the flumazenil SPC or the BNF should be consulted. The SPC is available via http://www.medicines.org.uk

Specialist drugs in palliative care

Cocaine 2% mouthwash

Cocaine mouthwash has an important role to play in the management of oral pain in the palliative setting. There is no evidence to support the use of cocaine mouthwash for radiation-induced oral mucositis, and it should never be used in the management of acute radiation-induced mucositis in head and neck patients. The analgesic dose used is 5–10mL q.d.s., swirled around the mouth, and spat out. This provides localized pain relief for up to 30 minutes. User experience varies: some patients report great benefit whilst others do not find it to be effective or find that it stings too much. There is potential for systemic absorption, and patients should be monitored for subsequent systemic side effects.

Preparation

- cocaine 2% mouthwash 200mL
- available from Guy's and St Thomas' (T) 020 71884992
- 6-month shelf life

Ketamine

Ketamine is a short-acting anaesthetic with analgesic properties at low doses. It is used particularly for neuropathic pain, ischaemic limb pain, and refractory cancer pain, and as an adjunct to opioid therapy. Ketamine for these indications is unlicensed and should only be initiated by a palliative medicine specialist, who should then transfer care to the patient's GP, per a local shared-care agreement. Ketamine can be given orally by SC injection p.r.n. and via CSCI.

Preparations

- oral ketamine (50mg/5mL) is the standard strength that must be used
- available from local wholesalers and Rosemont Pharmaceuticals (0800 919312) and Martindale Pharmaceuticals (0800 137627)
- ketamine injection (Ketalar®) 50mg/mL (10mL vial) and 10mg/mL (20mL vial) available from Pfizer (0845 6088866) and local wholesalers

Levetiracetam

Levetiracetam has been administered off-label via CSCI for palliative patients at the end of life requiring seizure control when the oral route is no longer feasible and IV administration is not an option. An oral:parenteral ratio of 1:1 has been used; however, the maximum dose feasible will be limited by the volume that can fit into the syringe driver. There is currently no compatibility data for it in a driver with other drugs. Sodium chloride 0.9% should be used as the diluent.

Preparation

- available from local wholesalers
- Keppra® injection (500mg/5mL vial)

Methadone

Methadone is a strong opioid used in palliative care for pain refractory to other opioids. Methadone has a long half-life and wide person-to-person variability in its pharmacokinetics; as such, it should only be initiated under specialist palliative supervision. Methadone can be prescribed as the single

opioid used, or used as an adjuvant alongside other opioids. Methadone is metabolized by the CYP enzyme system, and therefore caution must be taken when initiating or stopping other drugs metabolized by this route. Information on the use of methadone and monitoring requirements should be transferred from the palliative specialist to the patient's GP.

Preparations

- available from local wholesalers
- tablet: 5mg
- oral solution: 1mg/mL
- injection: 10mg/mL, 25mg/mL, 50mg/mL

Octreotide

Octreotide is an analogue of the natural hypothalamic release-inhibiting hormone somatostatin. Its use in palliative medicine is frequently off-label. Indications include the following:

- malignant bowel obstruction/high volume vomiting
- severe discharge from rectal carcinoma
- intractable non-infective diarrhoea
- high output GI fistula
- malignant ascites

Octreotide is administered via CSCI using sodium chloride 0.9% as the diluent. Dose varies according to indication and clinical response.

Preparations

- available from local wholesalers
- Note: store in fridge at 2–8°C
- 50micrograms/mL
- 100micrograms/mL
- 200micrograms/mL
- 500micrograms/mL

Parecoxib

Parecoxib is a COX2 inhibitor used in palliative care off-label for bone or musculoskeletal pain. Parecoxib can be given as subcutaneous injection 10–40mg p.r.n. or via CSCI over 24 hours. Maximum recommended dose of 80mg/24 hours, but occasionally higher doses up to 120mg/24 hours, have been used under close clinical supervision. Doses should be halved in the elderly and in those with low body weight. As with all NSAIDs, caution is required, as there is an increased risk of cardiovascular and thrombotic events. Renal function should be closely monitored, and consideration given to gastric protection with a PPI. Administer in a separate syringe driver diluted with sodium chloride 0.9%.

Ranitidine

Ranitidine is administered via CSCI at a dose of 200mg/24 hours to reduce the volume of gastric secretions in bowel obstruction; it has been shown to be more effective than PPIs for this indication. Furthermore, it is compatible for mixing with other drugs, making administration via CSCI more convenient.

Preparation

- available from local wholesalers
- ranitidine 50mg/2mL injection

Drugs and driving

> Every nectar is poison if taken to excess.
>
> Hindu Proverb

Patients should be advised that taking prescription drugs such as strong opioids and benzodiazepines may impair their ability to drive. It is an offence to drive if your driving has been impaired by drugs, whether prescribed or illicit. It is good practice for patients to inform their insurance company if they are taking prescribed medication and intending to continue driving. For further information, see https://www.gov.uk/drug-driving-law.

Travelling abroad with controlled drugs

Note: may change depending on the result of a no-deal Brexit—check regulations before confirming

Consider the regulations for both UK Customs *and* any countries being visited. If travelling for **less than 3 months**, patients can carry a supply of controlled drugs through UK Customs without the need for a specific Home Office licence. This is regardless of the controlled drug or the amount being carried.

- This applies for Schedule 2 medicines, e.g. diamorphine, ketamine; Schedule 3, e.g. buprenorphine, midazolam, temazepam; Schedule 4, e.g. diazepam, lorazepam; and Schedule 5, e.g. Oramorph 10mg/5mg oral solution.
- The controlled drugs should be carried in their original labelled packaging, i.e. not in unmarked multi-compartment boxes or unlabelled bottles.
- They should be in the passenger's hand luggage (100mL restriction on liquid medicines applies—contact the airline if greater quantities are required).
- Each patient should carry an up-to-date letter issued by the prescribing doctor containing:
  - the patient's name, address, and date of birth
  - the outward and return dates of travel and countries being visited
  - the names, forms, strengths, dosages, and total amounts of the controlled drugs being carried

Check whether any restrictions apply in the countries to be visited (including stopovers/transit). A letter from the prescribing doctors may only be valid for passage through UK customs. A list of embassies and contact details is available here: https://www.gov.uk/travelling-controlled-drugs

- Some medicines available in the UK are illegal in other countries, e.g. diamorphine, or even over-the-counter medicines such as co-codamol.

Patients wishing to travel with controlled drugs for a **period greater than 3 months** will need to apply for Home Office personal export licence. A personal licence has no legal standing outside the UK and is intended to assist travellers passing through UK Customs. Application can be downloaded at: https://www.gov.uk/travelling-controlled-drugs

Further reading

UK Civil Aviation Authority
British Airways Guidelines

Swallowing difficulties and feeding tubes

Swallowing difficulties

Liquids are the preferred formulation for patients with swallowing difficulties. Where possible, a licensed liquid preparation should be obtained. Liquid medications must be drawn up and given using an enteral syringe. Unlicensed 'special' liquids are occasionally available to order; cost, however, should be considered, especially for long-term treatment, as they are often expensive. Crushing standard tablets to aid administration is almost always outside the market authorization and may be unpalatable. Furthermore, the crushed tablet may have an anaesthetic effect on the oral mucosa, putting the patient at risk of burns. Film-coated tablets are usually suitable for crushing, but may have an unpleasant taste.

❗The following preparations must not be crushed: buccal and sublingual, cytotoxic, enteric-coated, and modified release.

Some capsules can be opened and the contents mixed with water for administration, including Palladone SR® (hydromorphone).

Enteral feeding tubes (EFTs)

Speech and language therapists should be consulted to understand the degree of swallowing impairment and to perform a risk assessment. Depending on the placement of the tube, the drug's pharmacokinetics could be altered. Pharmacists can give advice on changing formulations and giving drugs via enteral feeding tubes, and should be consulted when possible.

General information on EFT drug administration

- Bulk-forming laxatives should not be administered via EFT, owing to risk of blockage.
- Drugs should never be added to enteral feeds.
- Malnutrition may alter the drug pharmacokinetics.
- Where possible, rationalize the drug regimen to once or twice daily.
- Select an appropriate formulation (see NEWT guidelines).
- Ensure effective flushing of the tube before and after drug administration.
- In the inpatient setting, ensure the route of administration is correctly annotated on Kardex as RIG/NG, etc.
- Strong opioids—MST® suspension, hydromorphone capsules—can be opened (off-label) and mixed with sterile water prior to administration.
- Note modified-release oxycodone currently does not come in a formulation suitable for administration via EFT.

Further resources

The NEWT Guidelines: A Comprehensive Database on Administration of Medication to Patients with Enteral Feeding Tubes or Swallowing Difficulties. Accessed via http://www.newtguidelines.com

Handbook of Drug Administration via Enteral Feeding Tubes. Accessed via http://www.medicinescomplete.com

Rosemount Pharmaceuticals specialize in medication management for patients with swallowing difficulties; (T) 0800 919312.

Non-medical prescribing

Non-medical prescribing (NMP) is the prescribing of medicines by suitably trained healthcare professionals other than doctors to improve patient care across a range of healthcare settings, including palliative care. There have been extensive changes in NMP over the years; of note is the legislative change in 2012 allowing non-medical professionals to prescribe controlled drugs such as morphine. This legislative change gave non-medical prescribers in palliative care access to the majority of medications required to support them to manage patients' symptoms. Evaluations of NMP have been favourable, with patients and doctors being generally positive about the concept.[2] The majority of nurse prescribers feel strongly that prescribing has had a positive impact on quality of patient care and improved access to medicines. Nurses have also reported that the training to be a non-medical prescriber has enhanced their knowledge about medication and increased their confidence to engage in prescribing decisions.[3] With end-of-life care and choice of place of care being key principles of palliative care, NMP continues to play an important role.

2 Latter S. et al. (2005) *An Evaluation of Extended Formulary Independent Nurse Prescribing: Final Report*. London: Department of Health.

3 Bradley E., Nolan P. (2007) Impact of nurse prescribing: a qualitative study. *Journal of Advanced Nursing*, **59**(2): 120–8.

Formulary

Drugs **in bold** can be given in a syringe driver. ➔See Table 5.3, p. 87. The dose regimens of medication used in palliative care are constantly changing, and are subject to review. The responsibility for prescribing decisions must rest ultimately with the prescribing clinician.

Drug	Route	Dose	Frequency	Indications/Side effects (SE)/Remarks
Alfentanil	CSCI	**Titrate**	**24h**	Synthetic opioid working on similar opioid receptors to fentanyl. Alternative opioid for patients unable to tolerate morphine, e.g. in renal failure. Half-life is short; only provides analgesia for about 30 min as a single injection. If a longer action is required, consider oxycodone. Alfentanil spray 5mg/5mL is available as an 'unlicensed special' for nasal or buccal use. ➔See opioid equivalence table (p. 284).
Amitriptyline	p.o.	10–150mg	Nocte	Neuropathic pain. Start at 10–25mg. Faster effect at lower doses than for depression. Sialorrhoea (e.g. in MND), bladder spasms, and nocturnal enuresis. SE: blurred vision, dry mouth, hypotension, sedation, bladder spasms, and nocturnal enuresis. Reduce dose in renal/hepatic impairment. Caution if cardiac disease, frail elderly, or history of urinary retention.
Artificial saliva	Spray, gel, pastilles		As required	Many available products contain mucin, an animal product not suitable for some religions. Exceptions include Glandosane, Saliveze, SST, Xerotin.
Baclofen	p.o.	5–10mg max 100mg/day	t.d.s.	Spasticity, i.e. in MND, MS. Increase dose slowly SE: sedation, nausea, ataxia.

Benzydamine	0.15% oral mouthwash/ spray	15mL (4–8 sprays)	1.5–3h	Local analgesic. Dilute with water if stings.
Bethanechol	p.o.	25mg	t.d.s.	Dry mouth. Give dose 30min before meals.
Bicalutamide	p.o.	150mg	OD	Anti-androgen for prostate cancer. 50mg p.o. OD with combination therapy. With gonadorelin therapy, start 3 days beforehand. SE: nausea, vomiting, depression, loss of libido, hot flushes.
Bisacodyl	p.o. PR	5–20mg 10–20mg	Nocte OD	Stimulant laxative. 5mg tabs: action 6–12h. 10mg supps: action 20–60min. Avoid in intestinal obstruction.
Bupivacaine	Neb.	5mL 0.25%	6h	Useful for persistent dry cough, not breathlessness. Beware reflex bronchospasm. (Pretreat with nebulized salbutamol.) No food for 1h after treatment because of pharyngeal anaesthesia. (Injection is the only available preparation.)
Buprenorphine	Transdermal matrix patch	35, 52.5, 70 micrograms/hr	96h	Maximum dose: 140micrograms/hr.
Buprenorphine (e.g. Butec)	Transdermal Matrix patch	5, 10, 20 micrograms/hr	Every 7 days	5micrograms/hr patch is approximately equivalent to 12mg/24h p.o. morphine.
Buscopan® see Hyoscine butylbromide				
Capsaicin	Topical	0.075% cream 0.025% cream	t.d.s.–QDS	Neuropathic pain/post-herpetic neuralgia. Initially painful on application: patient counselling needed. Wear gloves to administer. Avoid contact with eyes and broken skin.

(*Continued*)

Drug	Route	Dose	Frequency	Indications/Side effects/Remarks
Carbamazepine	p.o. PR	100–600mg 125–250mg	OD–BD OD–QDS	Generalized tonic-clonic seizures; neuropathic pain (not 1st-line). Build up dose slowly. Can measure serum levels. Watch drug interactions. Tabs/chewtab/liquid/supps. SE: ataxia and blood, hepatic, and skin disorders.
Carbocisteine	p.o.	750mg	t.d.s.	Reduce to BD when satisfactory reduction in cough and sputum production. Reduces sputum viscosity and increases expectoration. SE: gastric irritant. Avoid if peptic ulceration.
Celecoxib	p.o.	100–200mg	OD–BD	NSAID Cox-2 inhibitor. Increased risk of myocardial infarction/stroke. Lower risk of serious upper GI side effects than with non-selective NSAIDs.
Chlorpromazine	p.o. PR	25–50mg 100mg	OD–t.d.s. t.d.s.–QDS	Alternative to levomepromazine in countries where this is not available. Consider low dose for tenesmus or hiccups. Significant interaction profile. SE: sedative/hypotensive. Half dose in elderly. 100mg PR = 20–25mg. IM = 40–50mg p.o.
Citalopram	p.o.	10–40mg (max 20mg in elderly)	OD	SSRI for depression, panic disorder. Caution in epilepsy, cardiac disease, and GI bleeding. 10mg tab = 8mg oral drops. Avoid with drugs known to prolong QT interval.
Clonazepam	p.o. CSCI	0.5–2mg **1–4mg**	Nocte or BD **24h**	Anticonvulsant, neuropathic pain, terminal agitation. For CSCI use non-PVC tubing (e.g. IVAC) or give as bolus. Injection available by special order. SE: sedation. Max 8mg/24h for terminal agitation.

Co-codamol	p.o.	1–2 tabs	4–6h Max 8 in 24h	Codeine phosphate 8mg, 15mg or 30mg + paracetamol 500mg. Soluble preparations available. There is no evidence that 'weak' co-codamol is any more efficacious in pain control than paracetamol alone.
Co-danthramer	p.o.	5–10mL	OD–BD	Stimulant (dantron) + softener (poloxamer). Useful for drug-induced constipation. Capsules discontinued 2015. Liquid high cost. SE: may colour urine red. Do not use if incontinent, as is associated with burning of perineal skin and excoriation. Not licensed for patients with non-malignant disease, as dantron is a potential carcinogen.
Co-danthrusate	p.o.	5–15mL 1–3 caps	Nocte Nocte	Stimulant (dantron) + softener (docusate). See co-danthramer.
Co-dydramol	p.o.	1–2	4–6h Max 8 in 24h	Dihydrocodeine 10mg + paracetamol 500mg. There are also combined preparations containing dihydrocodeine 20mg and 30mg.
Cyproterone acetate	p.o.	200–300mg/24h	Divided doses	Anti-androgen. Long-term palliative treatment of prostate cancer when orchidectomy or gonadorelin therapy are contraindicated. Covers flare of initial gonadorelin therapy. Watch for hepatotoxicity.
Cyclizine	p.o. SC CSCI	50mg 50mg **100–150mg**	BD–t.d.s. t.d.s. **24h**	**Antihistamine.** Useful for vomiting of GI cause, or raised intracranial pressure. SC route may cause skin reaction. Usual max dose of 200mg p.o. 24h and CSCI. Avoid in severe CHF. Use water as CSCI diluent.
Dexamethasone	p.o. IM/SC	Up to 16mg Up to 16mg	24h 24h	2–4mg OD. for appetite 8–16mg daily for raised intracranial pressure, SVCO, bowel obstruction, spinal cord compression. 2–6mg for prevention of chemotherapy emesis. Give a.m. to avoid excitation. Review regularly and reduce dose ASAP to minimum effective dose. Watch glucose and proximal myopathy. Consider PPI prophylaxis in patients at risk of peptic ulceration.

(*Continued*)

Drug	Route	Dose	Frequency	Indications/Side effects/Remarks
	IV	Up to 16mg	24h	0.5–1mg CSCI to reduce skin site reactions. Separate syringe pump for doses >1mg
	CSCI	Up to 16mg	24h	Note. Different strengths of dexamethasone injection are available. To avoid confusion use local guidelines and agreed injection formulation.
Diamorphine	SC	Titrated	4h	Strong opioid analgesic. Higher solubility than morphine allows for larger doses in a syringe pump. SC diamorphine is three times as potent as oral morphine. Modify dose in elderly patients and in patients with renal failure. SE: ➔see Chapter 8, Pain management.
	CSCI	**Titrated**	**24h**	
	Topical	10mg		Can be mixed in Intrasite gel (unlicensed).
Diazepam	p.o.	2–10mg	OD–t.d.s.	Anxiety; agitation; night sedation; convulsions. Alternative is SC midazolam, which is shorter-acting. Caution in chronic respiratory disease.
	PR	5–10mg	p.r.n. (supps or soln)	SE: drowsiness, confusion, paradoxical increase in agitation.
Diclofenac	p.o.	25–50mg	t.d.s.	Bone pain and other inflammatory conditions if paracetamol and weak opioids found to be ineffective.
	p.o.	75mg (m/r)	BD	
	IM	75mg	Stat	May enhance the anticoagulant effect of warfarin. Caution required in patients with asthma. Increased risk of thrombotic events.
	PR	50mg	OD–t.d.s.	
	CSCI	**up to 150mg**	**24h**	If ineffective, try another NSAID. Contraindicated with active peptic ulcer, GI bleeding, or renal failure. Consider PPI prophylaxis in patients at risk of peptic ulceration. Use separate syringe pump.
				SE: local irritation.
Dihydrocodeine	p.o.	30–60mg	4–6h	Moderate pain. Similar efficacy to codeine orally—one-tenth as potent as morphine. Increased risk of toxicity in renal failure, requires dose reduction to 8h. Anticipate constipation.
	p.o. (m/r)	60–120mg	BD	

Disodium pamidronate	IV	30–90mg	Minimum 60mg per 250mL sodium chloride 0.9%	**Hypercalcaemia.** Rehydrate first. Max rate: 1mg/min or 20mg/h if renal impairment. Repeat after one week gap if poor initial response. Bone pain (especially breast cancer and multiple myeloma). Takes 7 days to produce maximal effect, which lasts for 2–3 weeks. Give 60–90mg every 3–4 weeks and monitor efficacy. Risk of osteonecrosis of jaw. Dental checkup before start of non-emergency treatment.
Docusate sodium	p.o.	100–200mg	OD–t.d.s.	Softens stool. Weak stimulant. May help constipation in presence of partial bowel obstruction. Acts in 12–72h.
Domperidone	p.o. PR	10mg 30mg	8–12h 8–12h	Anti-emetic, bowel motility stimulant. Beware intestinal obstruction as may cause colic. BD dosing may be adequate, 30mg PR = 10mg p.o., less extrapyramidal problems than with metoclopramide. Avoid if other risk factors for QT interval prolongation.
Duloxetine	p.o.	30–120mg	OD	Depression/ diabetic neuropathy. Multiple drug interactions. Avoid in hypertension, renal/hepatic impairment. SE: nausea.
Etamsylate	p.o.	500mg	QDS	Useful for capillary bleeding in presence of normal platelet numbers. Discontinued in UK but unlicensed product is available.

(*Continued*)

Drug	Route	Dose	Frequency	Indications/Side effects/Remarks
Fentanyl	Transdermal	12, 25, 37.5, 50, 75, 100 micrograms/h	72h	Strong opioid for severe pain. Owing to slow onset of action, patients may need extra analgesia for up to 24h after fentanyl patch is started. Laxatives may be reduced, as causes less constipation than other opioids. On removal of patch, it may take 17h or more for plasma levels to drop by 50%. Unsuitable for unstable pain owing to slow onset of action.

Equivalent Conversion:

Daily oral morphine	Fentanyl patch mg. micrograms/h
30–59	12
60–89	25
90–119	37.5
120–149	50
150–179	62.5
180–239	75
240–299	100

Caution: when changing from transdermal fentanyl to morphine, use lower equivalent than calculated morphine dose.

To avoid confusion between available products, it may be safer to prescribe using brand name.

Some evidence that patients on anticonvulsants may need increased doses.

Fentanyl	Oral transmucosal	50–1600 micrograms	For breakthrough pain (max QDS)	There are several transmucosal fast-acting fentanyl products. See pp. 269–75. Products are not interchangeable—prescribe by brand. Breakthrough doses are not related to background analgesia doses. Should only be initiated when patient is on at least 60mg oral morphine or other strong opioid equivalent.
Fluconazole	p.o.	50mg	OD	Oral candidiasis. Give 7–14 day course. Multiple drug interactions. Higher doses if immunocompromised. 150mg stat for vaginal candidiasis.
Fluoxetine	p.o.	20–60mg	Mane	SSRI antidepressant. Long half-life. SE: anxiety. GI symptoms usually settle within a few days. Check drug interactions.
Gabapentin	p.o.	Starting dose100–300mg Max 1.2g p.o. t.d.s.	Initially nocte, then t.d.s.	Neuropathic pain. Anticonvulsant. First-line choice for neuropathic pain. Use lower dosing in elderly and if renal failure present. Avoid in psychotic illness. Slow titration over several weeks is advisable in debilitated, elderly patients and those with renal impairment or receiving CNS depressant drugs. Avoid abrupt withdrawal. (Withdraw over 1 week.) SE: drowsiness, fatigue, ataxia. Used off-label for uraemic itch, sweats, and hiccups.
Gliclazide	p.o. (i/r) p.o. (m/r)	40–80mg 30mg (equivalent to 80mg i/r)	OD OD max120mg/24h	Sulfonylurea. SE: weight gain, hypoglycaemia, GI upset.
Glycopyrronium	p.o. CSCI SC	0.2–2mg 0.6–1.2mg **200–400 micrograms**	t.d.s. 24h **t.d.s.**	Reduces secretions in terminal phase and sialorrhoea, e.g. MND. Also used for antispasmodic, e.g. in inoperable bowel obstruction. Probably less central and/or cardiac side effects than atropine or hyoscine hydrobromide.

(*Continued*)

Drug	Route	Dose	Frequency	Indications/Side effects/Remarks
Granisetron	p.o. transdermal	1–2mg 3.1mg/24hr	OD Up to 7 days	Serotonin (5HT3) antagonist. Nausea/vomiting especially post RT or C/T. SE: constipation.
Haloperidol	p.o. SC CSCI	0.5–5mg 1–2.5mg **1.5–10mg**	Nocte–BD p.r.n. up to t.d.s. **24h**	Anti-emetic. Small doses (e.g. 1.5mg–3mg nocte) for nausea, particularly drug- or metabolic-induced. CSCI concentration dependent on compatibility with 0.9% NaCl. Higher doses in psychosis and agitation. The management of delirium or psychosis should be distinguished from the long-term treatment of behavioural disturbance in dementia for which antipsychotics should be regarded as the last resort. Beware extrapyramidal side effects and avoid in Parkinson's disease.
Hydromorphone i/r	p.o.	Titrated	4h	Alternative strong opioid. Caps i/r 1.3, 2.6mg × 7.5 potency of morphine
Hydromorphone m/r	p.o.	Titrated	BD	Caps m/r 2, 4, 8, 16, 24mg (12h) hydromorphone (mg) — morphine (mg) 1.3 — 10 2 — 15 4 — 30 8 — 60 16 — 120
Hydromorphone	CSCI SC	**Titrated**	**24h** 4h	10mg in 1mL, 20mg in 1mL, 50mg/1mL amps. Available only as 'unlicensed special'. When converting hydromorphone from p.o. to SC, use half the p.o. dose.

Hyoscine butylbromide	CSCI	**60–180mg (intestinal obstruction)**	**24h**	Antimuscarinic, anticholinergic. Less sedating than hyoscine hydrobromide as does not cross blood–brain barrier.
	CSCI	20–120mg (noisy respiratory secretions)	**24h**	Uses: intestinal colic, reduces GI and bronchial secretions. Very short half-life. **Poor oral bioavailability**
	SC	20-80mg	4h p.r.n.	
	p.o.	10–20mg	QDS	
Hyoscine **hydrobromide**	SC	200–400 micrograms	4–8h	Antimuscarinic, anticholinergic. Anti-emetic for refractory nausea. Dries respiratory and GI secretions.
	CSCI	**1.2–2.4mg**	**24h**	
	SL	300 micrograms	6h p.r.n.	SE: sedation, confusion, paradoxical agitation.
	patch	1 patch behind ear (1mg)	Change every 72h	
Ibandronic acid	p.o.	50mg	OD	Reduction of bone damage in bone metastases.
	IV	6mg	3–4 weekly	Hypercalcaemia. Only bisphosphonate authorized for use in severe renal impairment.
	IV	2–4mg	Stat	Dental checkup before start of treatment. Monitor for osteonecrosis of jaw with all bisphosphonates.
				SE: oesophagitis with tablets; swallow whole with plenty of water 30min before food or other meds.
Ibuprofen	p.o.	200–800mg	t.d.s.	First-line NSAID. Lower risk of side effects than with other commonly used NSAIDs.
				Topical preparations available. See diclofenac for contraindications.
Ipratropium bromide	Neb	250–500 micrograms	t.d.s.–QDS	Reversible airways obstruction, particularly if COPD present. Drying effect on secretions. Mouthpiece preferable to minimize nebulized solution affecting eyes.

(*Continued*)

Drug	Route	Dose	Frequency	Indications/Side effects/Remarks
Ketamine	p.o.	10–100mg	t.d.s.–QDS	Under specialist supervision only. Neuropathic pain; build up dose slowly. May need prophylactic oral haloperidol or a benzodiazepine to cover psychotomimetic side effects. Oral solution available as an 'unlicensed special'.
	CSCI	**75–300mg** (higher doses have been reported)	**24h**	Opioid sparing. May need to reduce opioids by 50%. Dilute SC with 0.9% sodium chloride to reduce skin irritation. ❗Caution: epilepsy, raised BP, heart disease. Potential for urinary tract, hepatobiliary, and neuropsychiatric toxicity.
Ketorolac	p.o.	10mg	4–6h (elderly 6–8h)	Bone pain and other inflammatory conditions. Max 40mg p.o. daily. Max 90mg SC daily.
	SC	**10–30mg**	t.d.s.	See diclofenac warnings and cautions. Beware gastric bleeding.Use separate syringe pump.
	CSCI	**60–90mg**	24h	High risk of gastric side effects; use gastric protection (PPI).
Lactulose	p.o.	15–30mL	BD	Osmotic laxative. May cause abdominal bloating and wind. Requires a good fluid intake. May take 48h for full effect.
Lansoprazole	p.o.	15–30mg	OD	Proton pump inhibitor. Gastric and duodenal ulcer and oesophagitis Prophylaxis with NSAIDs and corticosteroids. Orodispersible tablet available.
Levomepromazine	p.o.	6–25mg	OD–BD	**Nausea and vomiting.** Broad-spectrum anti-emetic. 25mg tabs; 6mg tablets available (unlicensed). SE: sedation.
	SC	5–12.5mg	4–8h (max 25mg/24h)	

	CSCI	**5–25mg**	**24h**	SC route may cause skin reaction. Dilute with sodium chloride 0.9%.
Levomepromazine	p.o.	25–200mg	OD	**Psychosis or severe agitation.** Can use for terminal sedation. SE: May cause anticholinergic side effects, hypotension, and extrapyramidal symptoms. Avoid in dementia or use lowest effective dose if necessary. May lower seizure threshold. Avoid in Parkinson's disease.
				SC 5–25mg 48h
	CSCI	**5–150mg**	**24h**	SC route may cause skin reaction. With long half-life, can be given as intermittent SC injections 1–3 times/24h. Dilute with sodium chloride 0.9%.
Lidocaine (lignocaine)	Topical	5% ointment 5% plaster		Topical analgesia. Neuropathic pain. Apply 1–3 patches for 12h, on-off basis. Avoid broken/irritated skin. Can cut patch to desired size.
Loperamide	p.o.	2–4mg max 16mg/24h	p.r.n. after each loose stool or up to QDS	Useful for diarrhoea and the pain of bowel colic. Max of 64mg/day for stoma output reduction. No CNS effects. Ensure diarrhoea not secondary to faecal impaction.
Lorazepam	p.o./SL	0.5–2mg	BD	Anxiety/panic attacks. Shorter duration of action than diazepam. Useful sublingually in acute anxiety and breathlessness.
	IV	4mg	Stat (slowly)	Acute treatment of seizures.
	SC	1–2mg	6h-8h	Terminal agitation. Generally used with an antipsychotic.
Macrogols (polyethylene glycols) (e.g. Movicol)	p.o.	Dissolve sachet in125mL water	1–3 sachets/day up to 8 sachets/day for faecal impaction	Osmotic laxative. Effect seen within 1–3 days. Requires 5–10 times more oral fluid volume than lactulose, which may be unacceptable for many seriously ill patients. Licensed for faecal impaction. Check taste/volume acceptable to patients.

(*Continued*)

Drug	Route	Dose	Frequency	Indications/Side effects/Remarks
Medroxyprogesterone acetate	p.o. p.o.	400mg 5–20mg	OD–BD BD–QDS	Appetite stimulation in anorexia. Increase in body mass likely due to fluid retention and increase in body fat. Effect enhanced with concurrent NSAID. Takes 2–3 weeks to produce maximal effect. Hot flushes after surgical or chemical castration. SE: weight gain, thromboembolic events, male impotence.
Megestrol acetate	p.o.	40–160mg	OM	See medroxyprogesterone acetate.
Methadone	p.o. SC CSCI	Titrated Titrated **Titrated**	BD–t.d.s. BD–t.d.s. **24h**	Alternative strong opioid analgesic for patients who fail to respond to/tolerate morphine. Nociceptive and neuropathic pain. Specialist use only: widely variable half-life, multiple interactions, and complicated dose titration. Avoid concurrent use with drugs that prolong QT interval. Subcutaneously, use 50–70% oral dose. Can be used in renal failure. Prescribed differently from morphine, ➔see Chapter 8, Pain management. SE: Long half-life can lead to overdosing.
Methotrimeprazine, see levomepromazine				
Methylnaltrexone	SC	8–12mg depending on weight		Peripheral opioid antagonist for reversal of constipation. Bowel action 30–60min after dose. Alternate days or stat. SE: abdominal discomfort. Avoid in mechanical GI obstruction.
Methylphenidate	p.o.	2.5mg–10mg	OD–BD	Similar to dexamfetamine but less potent and shorter half-life. Uses: cancer-related fatigue, depression in terminal illness. Monitor BP. Last dose no later than 2 p.m. SE: restlessness, confusion, sleep disturbance.

Metoclopramide	p.o. SC CSCI	10mg 10mg **30–100mg**	t.d.s. t.d.s. **24h**	Anti-emetic. Increases gut motility and gastric emptying. Use cautiously in GI obstruction. Stop if makes GI cramps or diarrhoea worse. SE: extrapyramidal (reversible with procyclidine).
Metronidazole	p.o. Topical IV PR	400mg 0.75% gel 500mg 1g	t.d.s. t.d.s. t.d.s. t.d.s.	Antibiotic for anaerobic infections. Topically useful for fungating, odorous wounds. Reduce dose in elderly/hepatic impairment. SE: nausea. Avoid alcohol.
Midazolam	SC/ buccal CSCI	2–10mg **10–60mg**	p.r.n. **24h**	**Benzodiazepine.** Shorter duration of action than diazepam. Buccal liquid available. Single doses useful for quick, uncomfortable procedures, anxiety, and agitation. Used in the management of terminal agitation. A dose of 20–30mg/24h needed to replace oral anticonvulsants. IM/IV for crisis dose, e.g. in terminal bleeds, may be needed.
Mirtazapine	p.o.	15–45mg titrate	Nocte	Noradrenergic and specific serotoninergic antidepressant (NaSSA). Some evidence of faster onset of action and promotion of appetite and sleep than other newer antidepressants (lower doses more sedating than higher, enervating doses).
Morphine (i/r)	p.o. PR	Titrated Titrated	4h 4h	Pain/breathlessness. Morphine is first-line strong opioid of choice. Oramorph 10mg/5mL, 100mg/5mL. Sevredol tabs: 10mg, 20mg, 50mg. Supps: 10, 15, 20, 30mg Topical gel can be made up. SE: constipation, N&V, drowsiness, myoclonic jerks, etc.

(*Continued*)

Drug	Route	Dose	Frequency	Indications/Side effects/Remarks
Morphine (m/r)	p.o.	Titrated	12h	Various preparations available, induding tablets (MST®, Morphgesic®, Filnarine® SR), sachets containing m/r granules (MST® sachets), and capsules containing m/r granules (Zomorph®). Where possible, keep individual patients on the same m/r brand to minimize confusion and improve safety.
Morphine (m/r)	p.o.	Titrated	24h	MXL® 30, 60, 90, 120, 150, 200mg (OD). Capsules containing m/r granules
Morphine inj				
	SC	Titrated	4h	10mg, 15mg, 20mg, 30mg/mL–1mL and 2mL amps.
	CSCI	**Titrated**	**24h**	Conversion: p.o. to SC 2:1.
Nabilone	p.o.	0.25mg–1mg	BD	Cannabinoid for nausea, spasticity, and refractory pain. SE: sedation/dysphoria may occur with higher doses. Unsuitable in atrial fibrillation, heart failure, and psychosis.
Naloxegol	p.o.	25mg	OD Pre-breakfast	Treatment of opioid-induced constipation in adults whose constipation has not adequately responded to laxatives. Avoid if risk of GI perforation. Contraindicated in underlying malignancies of gastrointestinal tract or peritoneum, recurrent or advanced ovarian cancer
Naloxone	IV IM/SC	20 micrograms–100 micrograms (Dilute 1mL amp of 400 micrograms naloxone to 10mL with NaCl 0.9%)	Every 2 min or according to response	Reversal of respiratory depression caused by medicinal use of opioids. Titrate small doses based on respiratory rate. Use caution: larger than recommended naloxone doses can reverse analgesia, leading to intense pain/distress. They may result in hypertension, arrhythmias, pulmonary oedema, and cardiac arrest. Follow local/BNF guidance. Be aware that treating opioid-induced respiratory depression may require repeated dosing and close monitoring for several hours. NB: These doses are lower than referenced doses for acute opioid overdose (0.4mg–2mg).

Naproxen	p.o.	250–500mg	BD	Bone pain and other inflammatory conditions. If ineffective, try another NSAID. Beware with warfarin and in patients who are asthmatic. Contraindicated with active peptic ulcer or GI bleeding. See diclofenac for warnings and cautions. No increase in thrombotic events compared with other commonly used NSAIDs.
Nifedipine	p.o. p.o. SL	5–10mg 10–20mg m/r 5mg	t.d.s. BD t.d.s.	Smooth muscle relaxant; useful for hiccups, oesophageal spasm, and tenesmus. SE: hypotension, peripheral oedema, headache. Patients with angina should not bite into or use a normal release capsule.
Nystatin	p.o.	1–5mL 100,000 u/mL	QDS	Oral candidiasis. Swirl round mouth and teeth for 1 min and then swallow.
Octreotide Sandostatin LAR Lanreotide Somatuline autogel	SC CSCI Depot IM Depot IM Depot SC	50–200 micrograms **100–600 micrograms** 10–30mg/month 30mg/2 weeks 60–120mg/4 weeks	t.d.s. **24h**	Use on specialist advice only. Somatostatin analogue. Uses: hormone-secreting tumours, intestinal obstruction, intractable diarrhoea, ascites. Dose varies according to indication. Expensive; use when other treatments have failed. Use with caution if patient has diabetes mellitus. **Higher doses may be recommended by specialists**
Olanzapine	p.o.	2.5–10mg	Nocte	New-generation antipsychotic. Moderate-to-severe mania and nausea (off-label). Starting dose for nausea 2.5mg. SE: drowsiness, weight gain. Less movement-related disorders than older antipsychotics. Caution: Parkinson's disease, hyperglycaemia. Avoid if any cerebrovascular risk.
Omeprazole	p.o. IV	10–40mg 40mg	OD OD	Proton pump inhibitor (PPI). Gastric/duodenal ulcers, reflux oesophagitis, and NSAID-associated peptic ulcer disease. Dispersible tabs available.

(*Continued*)

Drug	Route	Dose	Frequency	Indications/Side effects/Remarks
Ondansetron	p.o./SC/IV PR CSCI	8mg 16mg **8–24mg**	BD–t.d.s. OD **24h**	Serotonin ($5HT_3$) antagonist. Uses: vomiting caused by RT or C/T, intestinal obstruction, hepatic cholestatic itch. Max 8mg daily in severe hepatic failure. SE: constipation, headache. Can prolong QT interval. Avoid high IV doses in patients aged over 65 yrs. Melt forms and syrup available.
Oxycodone m/r	p.o.	Titrated	12h	Modified release tabs 5mg, 10mg, 20mg, 40mg, 80mg, 120mg 12h. Available in combination with naloxone (Targinact). May be of benefit if upward titration of laxatives is ineffective. See SPC for details.
Oxycodone i/r	p.o. PR	Titrated Titrated	4–6h 8h	Moderate-to-severe pain. 5mg, 10mg, 20mg caps. Liquid 5mg/5mL, 10mg/mL. 20mg Oral morphine equivalent to 10mg oxycodone. Oxycodone 30mg supps available (longer-acting than morphine supps).
Oxycodone inj	SC CSCI	1.25–10mg **Titrated**	4h **24h**	10mg/mL, 1mL/2mL amps, 50mg/mL high-strength 1mL amp (may be useful where high doses cause volume difficulties for CSCI). Twice as potent as oral oxycodone; e.g. 20mg of oral oxycodone is equivalent to 10mg of injectable oxycodone.
Pamidronate (see Disodium pamidronate)				
Pancreatin	p.o.	Dose titrated with meals		Steatorrhoea caused by biliary and/or pancreatic obstruction. Several products available; e.g. Creon® 10,000 units, 1–2 capsules with meals. Preparations containing higher doses of lipase and amylase available.

Paracetamol	p.o. PR IV	0.5–1g 0.5–1g 1g (if weight <50kg reduce dose to 15mg/kg)	4–6h 4–6h 4–6h	Analgesic. Antipyretic. Max 4g in 24h. Available as tabs, caps, caplets, susp, dispersible, suppositories, and IV. Reduce dose in renal/hepatic impairment.
Parecoxib	SC/IV CSCI	40mg initially then 20–40mg **40–80mg**	12 h **24h**	Cox-2 inhibitor NSAID. Less GI irritation than non-selective NSAIDs. Max 80mg/day. Half dose in elderly or low body weight. Use cautiously as increased risk of cardiovascular and thrombotic events. Use separate syringe pump.
Paroxetine	p.o.	10–40mg	OD	SSRI antidepressant/anxiolytic. Short half-life. Used for itch and sweating. Withdraw slowly. SE: Beware serotonin syndrome. Multiple drug interactions.
Phenobarbital	p.o. IM CSCI	60–180mg 50–200mg **100–600mg**	Nocte BD **24h**	Anticonvulsant. Specialist use only when used as replacement for oral anticonvulsant and in terminal agitation. Use separate syringe pump. Avoid abrupt withdrawal. Max 1600mg daily (extreme terminal agitation). Avoid SC stat doses—risk of local necrosis.
Pilocarpine	p.o.	5mg	t.d.s. with meals	Parasympathomimetic. Can also use eye drops orally; 3 drops of 4% = 6mg. Sialagogue for dry mouth.
Pregabalin	p.o.	75mg Max 300mg	BD BD	Neuropathic pain. Similar mode of action to gabapentin. Reduce dose in renal impairment. Start with 25mg in elderly or debilitated patients. Common side effects are sedation, dizziness, and headaches. Potentiated by alcohol and oxycodone.

(*Continued*)

Drug	Route	Dose	Frequency	Indications/Side effects/Remarks
Prochlorperazine	p.o.	5–10mg	t.d.s.	Neuroleptic anti-emetic.
	IM	12.5mg	t.d.s.	May be useful for metabolic/drug-induced nausea. Too irritant to be given subcutaneously.
	buccal	3–6mg	BD	
Procyclidine	p.o.	2.5–5mg	t.d.s.	For management of extrapyramidal side effects of neuroleptic drugs or dopamine antagonists. Max 30mg daily.
	IM/IV	5–10mg	p.r.n.	
Ranitidine	p.o.	300mg	Nocte	Prophylaxis and treatment of gastric or duodenal ulceration and gastric reflux. Less evidence of protection against NSAID-induced gastric ulceration than PPIs.
	p.o.	150mg	BD	
	IV/IM/SC	50mg	6–8h	
	CSCI	**150–300mg**	**24h**	
Risperidone	p.o.	0.25–2mg	BD	'Atypical' antipsychotic useful for psychoses in which both positive and negative symptoms are prominent. Extrapyramidal symptoms are less common than with traditional antipsychotics. Also licensed for aggression in Alzheimer's dementia, although use cautiously as increased risk of CVA in dementia patients. Caution in presence of cardiovascular disease or epilepsy. In elderly, start at 250 or 500 micrograms.
Salbutamol	Neb	2.5–5mg	2–4h p.r.n.	B_2 agonist for bronchospasm. Can be used p.r.n. SE: tachycardia, tremor and hypokalaemia. Multiple doses can lead to agitation and anxiety.
Saline	Neb	2.5mL	p.r.n. or QDS	May be helpful to loosen tenacious sputum.
Senna	p.o.	15–30mg	Nocte	Stimulant laxative. Acts in 8–12h. May cause bowel colic. Avoid in bowel obstruction. Max dose of 30mg QDS.
Sertraline	p.o.	50–200mg	OD	SSRI antidepressant. Considered a first-line option for depression. Caution in epilepsy as reduces seizure threshold.

				SE: GI upset (avoid if gastric bleeding). As effective as amitriptyline in treating depression with anxiety. Benefit in cholestatic pruritus.
Sodium picosulphate	p.o.	Start 5mg	o.d.	Stimulant laxative. Can be used as a single agent and titrated up as necessary. Do not use in intestinal obstruction.
Sodium valproate	p.o.	100mg (initial dose)	BD	Anticonvulsant. Some evidence for use as a neuropathic agent. Titrate every 3 days up to max of 2.5g/24h. Use equivalent dose for IV route. Tabs, m/r tabs, IV. Suppositories available by special order. SE: nausea, blood dyscrasia, liver dysfunction, pancreatitis.
Spironolactone	p.o. p.o.	100–400mg (ascites) 12.5–50mg (severe CHF)	OD OD	Potassium-sparing diuretic. Potentiates thiazide or loop diuretics. Ind: oedema, and ascites in cirrhosis of the liver, malignant ascites, CCF. (Ascites dose regimens vary considerably.) Trial with furosemide for few days. Avoid with ACE inhibitors, potassium supplements, and potassium-sparing diuretics as could cause hyperkalaemia. SE: gynaecomastia, GI disturbance.
Sucralphate	p.o. p.o.	2g 1g	BD QDS	Protects mucosa from acid-pepsin attack in gastric and duodenal ulcers (suspension). Can make topical suspension for mouth or rectal surface bleeding. SE: constipation, bezoar formation with enteral feeds. Reduces absorption of several drugs.
Tinzaparin	SC	175u/kg (units)	OD	Low molecular weight heparin (LMWH). Treatment dose DVT/PE.

(*Continued*)

Drug	Route	Dose	Frequency	Indications/Side effects/Remarks
Tizanidine	p.o.	2mg titrate, 3-day intervals, 2mg steps, max 36mg/day	OD	Muscle relaxant for spasticity associated with multiple sclerosis or spinal cord disease. Regular LFT monitoring for first 4 months. Higher doses given BD–QDS. SE: drowsiness. Avoid abrupt withdrawal.
Tramadol	p.o. (i/r) p.o. (m/r)	50–100mg 50–200mg (max 400mg/24h)	QDS BD	WHO Step 2 analgesic. May be useful for nociceptive and neuropathic pain. ➔See p. 284 for opioid conversion factors. Less constipating than codeine, but more vomiting and dizziness.
Tranexamic acid	p.o. IV	1–1.5g 15mg/kg	BD–QDS QDS	Inhibits fibrinolysis. Useful for capillary bleeding, e.g. surface bleeding from ulcerated tumours. IV amps (undiluted 50mg/5ml) can be used as a topical solution or oral rinse for local bleeding. Caution if haematuria, as may encourage clot formation and ureteric obstruction. Contraindicated: history of thromboembolism, DIC.
Venlafaxine	p.o.	Initially 37.5mg	BD	Serotonin and noradrenaline reuptake inhibitor (SNRI). Antidepressant: useful in anxiety/panic. Depression max dose = 375mg daily, anxiety/panic max dose = 225mg daily. Used also for hot flushes and neuropathic pain. Avoid abrupt withdrawal. Can prolong QT interval.
Zoledronic acid	IV 15 minutes	4mg	Stat or every 3–4 weeks	Bisphosphonate used to treat bone pain, hypercalcaemia, and in the prevention of skeletal-related events associated with osteolytic bone metastases. Use with caution in renal impairment. Monitor calcium levels if used in bone pain, as may require vit D and calcium. SE: flu-like syndrome and osteonecrosis of jaw. Dental checkup before start of treatment.

Further reading

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Chapter 6

Oncology and palliative care

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Introduction

> Cancer is a word not a sentence.
>
> John Diamond (1950–2001)

> Clinical observations, classifications, and theories of cancer extend to the dawn of medical history.
>
> Michael Shimkin (b. 1926)

Cancer is an important cause of morbidity and mortality, particularly in industrialized countries. Currently in the UK, one person in two will be diagnosed with some form of cancer during their lifetime and one in four will die of the disease.

Cancer incidence increases exponentially with age; with increasing life expectancy, cancer will become an even more common problem in the future.

Cancers may develop in all body tissues. The cells that form cancers can be differentiated from cells in normal tissues in a number of ways:

- cell division that has escaped the control of normal homeostasis
- abnormalities of cell differentiation—in general, cancer cells tend to be less well differentiated than their non-malignant counterparts
- resistance to programmed cell death
- the potential for cancerous cells to invade local tissues and metastasize

The development of cancer is associated with the accumulation of defects or 'mutations' in a number of critical genes within the cell. Many cancers are associated with mutations leading to overactivity of growth-promoting genes, commonly known as 'oncogenes'. Conversely, cancers may also be associated with mutations leading to underactivity of genes which normally act to suppress growth.

Although our understanding of the genetic abnormalities underlying cancer has grown exponentially over the last decade, the factors that cause these changes are not clear for most cancers. There is evidence that exogenous carcinogens may be closely linked to some cancers. Smoking, for example, is a causative factor in lung, cervix, and bladder cancer.

In other cancers, there is an inherited susceptibility to particular types of malignancy. In the majority of common cancers, however, the cause remains elusive. It is likely that for many of these cancers, both environmental and genetic factors are implicated.

Organization of cancer care

Optimal care of the patient with cancer requires input from a number of medical disciplines. Typically a provisional diagnosis of cancer is made by a surgeon or physician and confirmed by a pathologist following biopsy or fine-needle aspiration. After staging the cancer, a surgeon or an oncologist may then undertake definitive treatment. Support of the patient through treatment may well involve input from a wide range of surgical, medical, allied medical health, and laboratory disciplines.

Several factors facilitate this care:

- good organization of cancer services
- site specialization for doctors treating cancer
- multidisciplinary team working
- well-established links with laboratory and clinical cancer research

The disease journey

A close working relationship between oncology and palliative care professionals is important. Increasingly, the goals are shared, and closer working relationships forged at different points along the patient's disease journey (Fig 6.1).

At the time of original diagnosis

Oncological services, and specialist and generalist palliative care services, including the GP and community health team, need to share information quickly so, at this point, when the patient and their family feel particularly vulnerable, informed support can be maximized.[1]

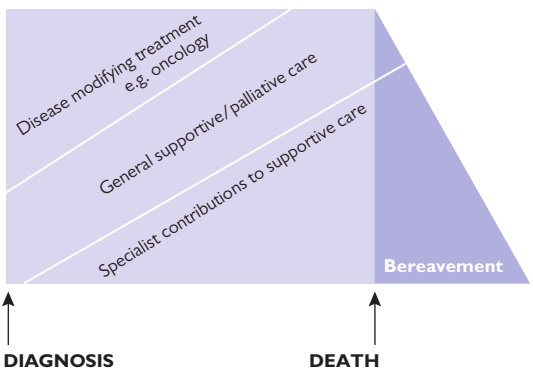


Fig 6.1 The disease journey.

1 National Council for Hospice and Specialist Palliative Care Services. (2002) Definitions of Support ive and Palliative Care. London: NCHSPCS (Briefing Bulletin 11).

Traditionally, palliative care services were only 'offered' to patients when 'there is nothing more that can be done'. Increasingly, palliative care is involved from the point of diagnosis, with increasing input as the oncology needs decrease, maximizing at the time of death, and continuing on with bereavement support.

Through the period of staging and/or surgery

This can be a time of great uncertainty for patients, when communicating the often complex prognostic and treatment information is so important. Many find the issues very difficult to grasp, so vast are the associated life implications. An understanding of these issues and of the likely treatments by all those involved in the clinical and supportive care of patient and family can help to consolidate information transfer. It is often only a few days after a crucial oncology outpatient appointment that patients become receptive to important information.

If other healthcare professionals are hesitant or contradictory in their explanations of treatment options, patient anxiety will be increased.

'When I was diagnosed with my bowel cancer I was simply devastated. You see, I had watched my father dying from lung cancer and I was sure I would go the same way. I could hardly get out of the hospital quickly enough to get my farm and affairs sorted out. The doctor said something about treatment, but I knew from watching others with cancer that treatment was pointless, so I never went back for the cancer specialist appointment.

'It was only after my own doctor came out and we had a good chat that I even thought that they could do anything for me. In the end I decided to go and see what they were offering, still never believing that they could do any good.

'I honestly believe if my own doctor hadn't taken the time to come and explain that there really was something they could do to help, I would not have been alive to enjoy these past six years'.

Through the period of treatment

While the majority of supportive care during this period tends to be linked through the oncology services, specialist and generalist palliative care teams need to be aware of the following:

- goals of treatment
- side effects of treatment
- follow-up plans

The goals of oncology treatment

Before commencing any treatment it is important that both patient and carers are aware of the goals of treatment.

It is possible, particularly if the outlook is not good, that patients will ask different members of the team, hoping to find a more optimistic prognosis. Clearly it is not in the patient's interest to hear conflicting opinions about their prognosis, and this should be avoided.

Openness regarding realistic treatment outcomes is also important in maintaining staff morale. While the death of a patient is often difficult, particularly for the nurses who are most closely involved in care, this is especially so if unrealistic expectations of treatment are fostered.

Radical oncological treatment

Radical oncological interventions are curative in intent. They may involve surgery, radiotherapy, immunotherapy, or chemotherapy (or a combination of these modalities).

Because the potential benefits of treatment are great, a relatively high incidence of side effects is more acceptable.

Providing patients with good symptom control and emotional support through radical treatment is important. They need to be encouraged to complete what is often a very demanding treatment course in order to benefit maximally. Without such encouragement, patients may miss the only opportunity they have of cure.

Increasingly, there is an appreciation that such treatments may be associated with long-term toxicities or side effects (which may be especially relevant for children). Clearly, in this potentially curative group, care must be taken to minimize the potential for cumulative dose toxicities such as cardiotoxicity caused by anthracyclines.

Adjuvant oncological treatment

Many patients suffer tumour relapse following apparently curative surgery for their primary tumour. This is believed to be due to the presence of micrometastatic disease that is not clinically apparent at the time of the primary treatment. Anticancer treatment (usually chemotherapy) given at this stage has been shown to improve long-term survival for some tumours. This approach has proven successful even for tumours where chemotherapy is not curative in the metastatic setting, and is presumably related to the increased chemosensitivity associated with microscopic volumes of disease.

The absolute gains in survival from adjuvant chemotherapy are generally small but real. At present, there are few predictive factors to identify those patients most likely to benefit from adjuvant therapy. The decision to proceed is often based on the statistical likelihood of relapse, with those at highest risk benefiting most.

The fact remains that the majority of patients will not benefit from adjuvant therapies. Such treatments should therefore have manageable acute toxicities and a low incidence of long-term toxicities.

Palliative oncological treatment

Palliative treatment is indicated when curative treatment is not possible but where treatments may have sufficient anticancer activity to improve cancer-related symptoms. In many cases, improvement of symptoms is accompanied by tumour shrinkage detectable clinically or by radiological methods such as CT scan or MRI. It is increasingly recognized that there may be a palliative benefit even in the absence of tumour shrinkage.

As the primary object of therapy is to improve quality of life, such treatments should be well tolerated with a low incidence of acute side effects. Long-term toxicities are generally not relevant.

In some cases the distinction between radical and palliative treatment may not be absolutely clear-cut. Indeed, the aims of treatment may change as the disease progresses.

Patients presenting with advanced ovarian cancer, for example, have largely incurable disease. However, the tumour is often chemosensitive, and lengthy remissions are often seen following primary chemotherapy. In such patients a relatively high incidence of acute toxicity may be acceptable,

with efforts being focused on managing chemotherapy-related symptoms. Conversely, a patient presenting with relapsed ovarian cancer following first-line chemotherapy has a low expectation of benefit from further chemotherapy. Consequently, only a low incidence of acute toxicity is acceptable with second-line chemotherapy, from which expectation of benefit is very limited.

For patients and carers who have been through radical or adjuvant therapy, the switch to palliative treatment can be difficult to accept.

In particular, the patient and carers have to be informed that the most important element of assessing palliative treatments is their overall impact on quality of life, and that emphasis will shift to a global assessment balance between toxicity and antitumour benefit.

Managing patients receiving oncology treatments

Chemotherapy, radiotherapy, and immunotherapy are now given largely on an outpatient basis. Surgical patients also spend less time in hospital than in the past. This allows patients to spend more time at home, which inevitably places an increased burden of care on those providing support in the community, particularly where the cancer centre is a long distance from home. Thus a general understanding of the particular side effects, and the appropriate treatment for such complications, is needed by healthcare professionals in the community and those providing on-call services.

It should not be assumed that a new symptom developing in a patient undergoing treatment for cancer is related to the side effects of treatment or to the cancer itself, although the high possibility of this must be considered. (Chemotherapy does not prevent patients developing appendicitis!) Thus the health professional needs to assess each new symptom independently, and be aware of the side effects of commonly used oncological treatment regimens. (➔ See Chemotherapy, pp. 138–45, and Radiotherapy, pp. 151–3.)

Supportive teams need to know the significance and *appropriate responses for individual patients* to such side effects, as with the following:

- clinical anaemia
- nausea and vomiting
- pain
- pyrexia and possible infection
  - *What are the risks of neutropenia for this patient?*
- increased drowsiness
- confusion
  - *Could this patient be opioid toxic, hypercalcaemic, or developing renal failure?*
- hair loss
- altered sensation, back pain, incontinence
  - *Could this patient be developing spinal cord compression?*
  - peripheral neurotoxicity

The appropriate response and management will differ according to what the patient and family want, the disease process, and where the patient is on their disease journey.

Treatment planning

It is important that treatment plans are communicated adequately to patients, families, and professional carers to ensure that appropriate support is given.

A basic management plan should include:

- details of proposed diagnostic and staging investigations
- proposed treatment plan for surgery, chemotherapy, and radiotherapy where appropriate. The plan should include details regarding the duration of treatment and timing of interval investigations to assess response to therapy. (Patients can be understandably anxious in the days preceding a scan aimed at assessing response to treatment.)
- changes to treatment dosages or frequency, including reasons for change
- particular side effects of treatment and specific advice on what to do if these problems develop
- clear instructions about how long treatments such as antibiotics or steroids should be administered or tailed off
- treatment goals
- details of significant conversations with patients and their carers relating to their understanding of their disease and their wishes for further treatment
- clear details of who to contact in case of treatment complications

No single set of healthcare professionals can manage the many needs that patients have on their disease journey. Holistic, patient-centred care requires a multiprofessional and multidisciplinary approach that places the patient and family at the centre.

Many centres are now using patient-held records to facilitate improvements in communication. The different professionals record their findings and management plans, thus improving the continuity of care. With the increasing demand for transparency in care from patient groups, and the importance of ongoing care, such systems may well become commonplace in the UK.

Clinical trials

Clinical research is necessary in order to improve outcomes for patients with cancer. The link between the laboratory and the clinic is developing and increasingly patients are being recruited into trials.

There are three main types of clinical trial:

Phase I

Aims

- to establish the human toxicity of a new drug through delivering carefully selected increasing doses to patients
- to establish the safe dose at which to start further trials with the drug
- to evaluate the body's handling of the drug by pharmacokinetic studies

Eligible patients

- patients who have progressive disease despite standard oncological therapy or those for whom no standard therapy exists
- patients must be aware that the primary objective of the studies is to assess toxicity—there is little expectation of benefit to themselves, with a response rate of approximately 5%
- patients recruited to Phase I trials usually have a good performance status and are highly motivated individuals, since involvement often requires intensive monitoring as an inpatient

Phase II

Aim

- to establish the antitumour activity of the drug for a particular tumour type

Eligible patients

- patients who have progressive disease despite standard chemotherapy or for whom no standard therapy exists
- patients usually have a good performance status and are highly motivated
- patients are closely monitored with toxicity and response assessments, but not as intensively as those in Phase I studies

Phase III

Aim

- to compare the new drug or drug combination with conventional therapy

Eligible patients

- patients for whom a standard therapy exists (new drugs may also be compared with 'best supportive care' where no standard therapy exists)

Important and common end points include disease-free survival (in adjuvant studies) and overall survival (in palliative studies). Increasingly, more clinically relevant end points such as improvements in pain, performance status, weight gain, and quality of life are being used in Phase III trials of palliative agents.

Typically Phase III trials are much larger than Phase I and Phase II trials, and patients require less frequent monitoring.

Aims of clinical trials

- Phase I: dose/schedule finding, typically 20–50 patients
- Phase II: disease finding, typically 50–100 patients
- Phase III: comparison of novel treatment/schedule to standard of care, typically 500–1000 patients

Some studies include Phase IV trials. These studies continue after the drug or treatment has been marketed to gather information on the drug's effect in various populations and to identify side effects associated with long-term use.

Survivorship

Overall survival rates for cancer are increasing, but sometimes at a cost. It is estimated that by 2020 there will be over 2 million people living in the UK who have received cancer treatments. This may or may not have resulted in clinical cure, but their health has nevertheless been affected. The majority will be affected in a minor way, but some will have significant severe long-term adverse effects. Cancer 'survivors' live with a significantly higher incidence of chronic illness and debility than those without a cancer diagnosis.

Traditionally, oncologists have concentrated on the management of acute rather than more chronic side effects of cancer treatment. There is no system to record severe long-term outcomes for those who have received radiotherapy or chemotherapy in the past, making it impossible for national trends to be studied or clusters of problems spotted early. This may become an increasing problem as new equipment, surgical techniques, and drugs are being introduced at an ever-increasing rate. High-profile clinical situations include radiation-induced brachial plexopathy following treatment for cancer of the breast, and pelvic morbidity following radical radiotherapy for cancer of the cervix.

The concern is that many professionals will fail to make a connection between a patient's new problem and previous cancer diagnosis and treatment. Even when late effects are recognized, the investigation and management of sometimes multiple problems require the help of a wider multiprofessional team.

There is considerable potential for improvement in the aftercare that our patients should receive. Macmillan Cancer Support has identified a number of priorities:

- a national register of severe late consequences of cancer treatment
- support to ensure that patients recognize and understand changes in health after cancer treatment, and have the information and support to manage these effectively
- increased understanding of cancer survivorship from a primary care team point of view and provision of information and support
- innovative ways to bring multidisciplinary specialist expertise to the patients with rare, severe, treatment-related chronic illness (estimated as 5–10% of survivors)

Specialists involved in the palliative care needs of patients may be in a position to help in the management of some of those patients with the severest symptoms.

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Oncological surgery

Surgery remains the modality of treatment most likely to cure patients diagnosed with solid tumours. It has most potential when the cancer is localized, although results are improving for patients with certain types of metastatic tumours.

Surgery has three main roles in cancer management:

- diagnosis and staging
- treatment with curative intent
- palliative treatment

Diagnosis and staging

In the past, many patients suspected of having cancer required surgery to confirm the diagnosis. The development of cross-sectional radiology and the ability to perform diagnostic biopsies using radiological guidance or endoscopy often allow accurate diagnosis before surgery.

Patient morbidity has significantly reduced since some surgical procedures are avoided. The number of 'open-and-close' laparotomies for unresectable cancer, for example, has reduced to <5% in recent years, largely due to these advances. The introduction of sentinel node biopsy for patients with breast cancer has been effective in reducing the number of axillary clearances with less morbidity, including pain and lymphoedema.

However, surgical staging remains important in a number of common tumours:

- Axillary lymph node dissection for patients with breast cancer, for example, allows assessment of these nodes for tumour involvement. Such information is important in determining prognosis and guiding decisions regarding adjuvant treatments.
- Ovarian cancer spreads mainly via the transperitoneal route, leading to tumour deposits in peritoneal surfaces and the omentum—sites poorly visualized on conventional imaging. A laparotomy for patients with ovarian cancer therefore allows a more accurate staging of disease than is currently possible with non-invasive means. Again, such information is vital in determining prognosis and guiding further treatment.

Curative surgery

Localized disease

Surgery is most commonly curative in intent for localized cancers, and is generally dependent on complete resection of the tumour with a margin of normal tissue.

In some tumours with a propensity to spread to lymph nodes, resection of the draining lymph nodes may improve local control (e.g. vulval tumours). In other tumours, the value of lymphadenectomy is uncertain and is the subject of ongoing clinical trials (e.g. endometrial cancer).

Unfortunately, surgery still fails to cure many patients. There are a number of reasons for this:

- Development of metastatic disease—this is due to the presence of micro-metastatic disease unidentifiable at the time of surgery. This is a common reason for failure of surgery to cure breast and bowel tumours.

- Development of local relapse—outcomes from surgery are often closely linked to the margin of normal tissue excised in continuity with the tumour. The amount of tissue that can be resected may be limited by patient-related factors (e.g. only a partial lobectomy may be possible in patients with lung cancer due to the patients' underlying poor respiratory function) or by tumour-related factors (e.g. tumour invasion of a vital structure such as the aorta).

Metastatic disease

- Although much less common, surgery may be curative in certain tumours in the metastatic setting. For those patients considered to have 'oligometastatic' disease (metastases are limited in number and organ sites) and good performance state, potentially curative surgery can be considered on a case-by-case basis. Metastasectomy can be considered for pulmonary, hepatic, adrenal, splenic, and renal metastases, as well as for isolated brain metastases, in special circumstances.

In each of these cases, best results are seen with careful patient selection according to well-defined criteria. In general terms, the best long-term results are seen in patients who relapse after a long period from initial tumour diagnosis, and who have low volume disease and a good performance status.

Palliative surgery

Surgery may provide very effective palliation in a number of situations. Given the specific problems of oncology patients in the palliative situation (limited life expectancy, poor performance status, rapid tumour progression), the decision to proceed with surgery must involve a careful weighing up of the risk/benefit of such procedures. These decisions are best made with a multidisciplinary approach by surgeons specialized in oncology and experienced in palliative management.

Bowel obstruction

Patients with colonic or ovarian cancer form the majority of patients with bowel obstruction referred for surgery. Surgery to relieve the obstruction is warranted even if the disease is incurable (e.g. due to liver metastases or locally advanced disease) as such patients may live for many months. Where possible, these patients should have the primary tumour excised and a primary anastomosis performed.

Patients with ovarian cancer commonly present with obstructive bowel symptoms. At initial presentation, debulking surgery provides excellent palliation. Patients presenting with relapsed disease and obstructive symptoms often have multiple sites of obstruction due to widespread intraperitoneal dissemination of their disease. In this instance, surgery is much less likely to be useful.

Fistulae

Fistulae may arise as a result of pelvic tumours or as a complication of radiotherapy. They are often associated with unpleasant symptoms. Optimum preoperative assessment requires imaging to delineate exactly the site of fistula formation and to guide surgical decisions. Surgery may provide excellent palliation but may not be useful in those with multiple sites of fistulae or rapidly advancing intra-abdominal disease where life expectancy is limited.

Jaundice

Obstructive jaundice due to extrinsic pressure by lymph nodes on the biliary system, or due to intrinsic lesions such as cholangiocarcinoma, is commonly well palliated by placement of stents.

The complications of stents include infection and blockage, with consequent need for replacement.

Surgical relief of obstructive jaundice (e.g. by choledocho-enterostomy) avoids problems associated with stents, and may be indicated in a small minority of patients with an excellent performance status and slow-growing disease.

Pain

Surgical debulking of large slow-growing tumours can reduce pain and is justified in patients where the expected morbidity of the procedure is low. Neurosurgical approaches (e.g. cordotomy) are only infrequently considered.

Gastrointestinal bleeding

A wide range of endoscopic techniques has been developed to stop bleeding from benign and malignant causes. This may avoid the need for more major surgery in patients who have a limited life expectancy.

Techniques include the following:

- sclerotherapy
- laser coagulation
- radiological embolization

Bone metastases

Metastases to bones can cause major palliative problems. Specific problems include pain and pathological fracture. Factors that identify patients most at risk of pathological fracture:

- site—lesions in weight-bearing bones
- extent of destruction—destruction of >50% of the cortex
- symptoms—patients complaining of pain, particularly on weight-bearing
- type of lesion—lytic lesions > blastic lesions

Such patients may benefit (both in terms of reduced pain and reduced risk of fracture) from prophylactic fixation of a long bone. The type of internal fixation used depends on the site of fracture and the patient's performance status. In all cases, internal fixation of the bone should be followed by radiotherapy to control tumour growth and to promote healing.

Techniques such as vertebroplasty are available to manage pain in vertebrae.

Further reading

Errani C *et al.* (2017) Treatment for long bone metastases based on a systematic literature review. *European Journal of Orthopaedic Surgery & Traumatology* **27**(2):205–11.

UICC TNM Classification of Malignant Tumours, 8th edn (2016) update 2018: Springer.

Chemotherapy

I am dying from the treatment of too many physicians.

Alexander the Great

Identification of agents

Chemotherapy generally refers to a group of agents used in the systemic management of cancer. Different groups are linked by having demonstrated evidence of anticancer activity and a common range of side effects.

The anticancer activity of these agents has been identified in a number of ways. For some, the discovery of antineoplastic activity was serendipitous. Cisplatin was discovered while using platinum electrodes in an antibiotic experiment.

For others, this activity was identified during screening of a wide range of natural products (e.g. paclitaxel). Some of these agents have been biochemically modified to reduce their toxicity while retaining their antineoplastic activity (e.g. carboplatin).

Mechanism of action

Chemotherapy exerts its anticancer action by a wide variety of mechanisms which are as yet incompletely understood.

For many, DNA is believed to be the most important cellular target, e.g. irinotecan inhibits the topoisomerase I enzyme, thereby causing double-strand breaks in DNA. For other agents, microtubules, particularly those involved in mitotic spindle formation, appear to be the vital target, e.g. paclitaxel promotes tubulin polymerization and so arrests cells in metaphase.

A number of factors determine the likelihood of achieving a useful response to chemotherapy. Some tumours are inherently more sensitive to chemotherapy than others. In general terms, chemotherapy tends to be most effective in tumours with fast cell turnover, such as acute leukaemia and high-grade lymphoma. Seminoma, however—a tumour with a long natural history—is also very chemosensitive. Clearly there are other factors, as yet poorly understood, that determine a tumour's chemosensitivity.

Patient-related factors are also important in determining likelihood of response. Patients with poor performance status, for example, respond less well than those with good performance status. The reasons for this are poorly understood but are probably due, at least in part, to a reduced tolerance to the acute toxicity of chemotherapy.

While chemotherapy may induce a partial or even complete response, the tumour may regrow with disease that has become chemoresistant. There is evidence in some cases that the tumour may have become more efficient at actively pumping the drug out of the cell. Increasingly it is recognized that the ability of cells either to repair or tolerate the damage inflicted by chemotherapy may lead to chemoresistance. The causes of chemoresistance and the development of agents to overcome such mechanisms are active areas of research.

Adverse effects of chemotherapy

Although the specific side-effect profile varies between agents, there are a number of side effects common to most agents.

- **Alopecia** is a common and often distressing side effect associated with many agents. Patients can be reassured that hair will regrow. On regrowth the hair may develop waves or curls and will revert towards its previous character over many months.
- **Nausea and vomiting** are common with many agents, although the degree to which this is a problem varies both between agents and between patients (Table 6.3). The development of 5-HT_3 antagonists (e.g. tropisetron, granisetron, ondansetron) as well as the neurokinin receptor antagonist aprepitant has greatly aided the management of this troublesome side effect. The efficacy of 5-HT_3 antagonists can be improved by the addition of steroids.
- **Myelosuppression** is a significant cause of morbidity associated with chemotherapy. The white cells (in particular, the neutrophils) are most commonly affected between one and two weeks following chemotherapy. Patients should be warned of the possibility of developing infection during this time and the urgency with which they should seek help, as they will require immediate treatment with broad-spectrum antibiotics. The development of granulocyte colony-stimulating growth factors has reduced this toxicity by shortening the duration of neutropenia. This has allowed higher doses of chemotherapy to be given more safely in certain situations.
- **Anxiety**—the prospect of chemotherapy is a frightening concept for many patients, not least due to the (often mistaken) view that the side effects will be difficult. It is important that the patient and their carers are fully educated about the type of side effects they are likely to encounter during treatment and how best to deal with them. Most patients are extremely anxious during this difficult time, and information may have to be repeated a number of times. It is very useful to have written information to supplement what has been said in consultations. It is also useful if a relative or friend attends with the patient—they will often be able to help the patient review the information at a later date.

Chemotherapy regimens

A wide range of chemotherapy regimens are used in the treatment of patients with cancer. The usual rationale has been to combine drugs that demonstrate antitumour activity as single agents but which do not share the same side effects.

More sophisticated techniques to examine synergy and pharmacokinetic interactions in a preclinical setting are now developing, and this will guide a logical approach to the optimal combinations of agents.

Chemotherapy may be given in the following situations:

- curative
- adjuvant
- neoadjuvant
- palliative

Curative

A small number of solid malignancies are curable by chemotherapy alone—for instance, germ-cell tumours, lymphomas, and certain childhood tumours.

Chemotherapy regimens used in the treatment of these diseases tend to be intensive and associated with a high incidence of acute toxicity. It is important that patients receive chemotherapy on schedule as there is evidence that dose reductions and prolonging treatment times may adversely affect outcome. Consequently, treatment can exact a high physical and psychological toll on patients and their relatives.

Given that the long-term aim of treatment is cure, patients and their carers need encouragement to persevere, which will be easier if physical symptoms are optimally managed. The palliative care team can provide expert assistance at this stage of the patient's management.

Increasingly it is becoming clear that patients who are cured following chemotherapy are at risk of long-term toxicity from their treatment. Such problems include secondary leukaemias and solid tumours, fatigue, infertility, and cardiomyopathy. These problems have only become appreciated in recent times. Undoubtedly, as more people become long-term survivors of cancer, more problems will emerge. For this reason it is important that long-term survivors of cancer remain on long-term follow-up.

Adjuvant

Many patients presenting with apparently localized cancer are known to be at high risk of developing metastatic disease. This is presumed to be due to the presence of micrometastases not apparent by current imaging modalities. Chemotherapy given following successful primary treatment for apparently localized cancer may reduce the risk of developing clinical metastatic disease.

Cancers where adjuvant chemotherapy is commonly used include breast and colorectal cancer where large, multicentre, randomized controlled trials and subsequent meta-analysis have confirmed the survival gain.

At an individual level, these gains are small, but at a population level, this represents a large number of lives saved in diseases as common as breast and bowel cancer.

Presently, surrogate markers such as tumour size, grade, and lymph node involvement are commonly used to assess risk of disease relapse and thereby identify those most likely to benefit from adjuvant therapy. Much current research is directed at developing predictive markers to identify more precisely those most likely to benefit.

Given that the majority of patients treated will not benefit from treatment as their disease will relapse anyway, or because primary treatment has been curative, adjuvant regimens must be well tolerated with a low incidence of serious acute side effects and long-term side effects.

Again, as with treatment in the curative setting, positive outcomes from treatment are closely linked to dose intensity and to avoiding delays in chemotherapy. Where acute toxicities are a problem, involvement of the palliative care team may improve symptom management and facilitate delivery of treatment on schedule.

Neoadjuvant

Chemotherapy may be used 'up front' in non-metastatic tumours prior to definitive treatment (usually surgery) for the tumour. This may be employed for a large inoperable primary tumour to shrink the tumour and facilitate surgery. Such an approach is standard practice in very large primary breast tumours or those with skin involvement.

Increasingly, neoadjuvant therapy is being utilized for tumours that are operable. Potential advantages of this approach include less extensive surgery in a tumour that has been debulked. From a research point of view, a neoadjuvant approach with biopsies before and after therapy may allow molecular markers that predict chemosensitivity to be identified.

Conversely, there are a number of potential problems with neoadjuvant chemotherapy. First, in a responding tumour there may be a loss of potentially useful prognostic information from the subsequently resected tumour specimen. There is also the risk that such an approach may allow interim tumour progression in a lesion that does not respond to chemotherapy. Finally, performing less radical surgery in a tumour that has responded to chemotherapy may compromise local control.

This approach is being examined with particular interest in a number of tumours including oesophageal, gastric, and breast tumours.

Palliative

The majority of solid cancers are not curable in the metastatic setting. Chemotherapy, however, may have a valuable role to play in the palliative treatment of such patients. Clinical trials now include end points such as quality of life and toxicity, which are more clinically relevant in this setting than assessing overall survival as a sole entity.

Given that improvement or maintenance of quality of life is the aim of palliative chemotherapy, acute toxicities must be easily managed and tolerable.

Optimally, a patient is best managed when chemotherapy is administered *in conjunction with* input from the palliative care team. Such input also facilitates the gradual handing over of care to the palliative care team as the patient's disease progresses. Such a team-based approach reduces problems of patients feeling neglected by their oncologist when chemotherapy is no longer useful.

Indications for palliative chemotherapy

Treatment decisions need to be based on consideration of the balance between the benefits expected and the toxicity and risks of chemotherapy which will differ for each patient.

- Maintaining or improving quality of life: the most important aim of palliative chemotherapy. Chemotherapy may alleviate specific symptoms such as dyspnoea or chest pain in a patient with lung cancer. It may also improve or maintain general well-being with improvements in such factors as appetite and energy. The development of quality-of-life assessment tools, especially those with disease-specific elements, has greatly facilitated the assessment of the effect of chemotherapy on quality of life.

- Improving survival: while a secondary objective in most cases, it is quite clear that chemotherapy given with palliative intent frequently prolongs survival. The extent to which it is expected that survival may be prolonged varies between diseases. Chemotherapy in pancreatic cancer is associated with an improvement in survival of only a few weeks or months, whereas patients receiving chemotherapy for ovarian cancer may have improved survival of many months or even years.
- In emergency situations: potentially life-threatening tumour-related emergencies, such as spinal cord compression or superior vena cava compression, may be treated with chemotherapy where the primary tumour is chemosensitive. Such tumours include lymphoma and small-cell lung cancer.

Chemotherapy within the palliative setting is increasingly common because of:

Earlier referral for palliative care services

Chemotherapeutic services and palliative care services can be enhanced by a close working relationship with good lines of communication and early referral. The journey from diagnosis to death, with different interventions is governed not by the passage of time but by a patient's particular needs. With an integrated service and earlier referral patterns, there will be an ever-increasing number of patients in the palliative care setting who have just had, are having, or are just about to have, chemotherapy. In many cancer centres, patients will be introduced to the palliative care team as part of their initial contact with 'the cancer service'.

Increasing indications for chemotherapy

Over the last decade there has been a large increase in the number of drugs available to treat cancer patients, and clinical trials have confirmed that these agents may provide palliative benefit in those for whom no treatment would have been available 20 years ago.

Patients undergoing clinical trials

Patients who have relapsed from their initial chemotherapy may well be involved in clinical trials of other agents if their overall fitness and clinical condition permit. As trials often involve treatments where conventional regimens have failed, such patients may have advanced disease, and need increasing palliative care input.

When is chemotherapy offered in the palliative care setting?

The decision to use chemotherapy with palliative intent is often complex, and a number of factors must be taken into consideration:

- **Patient fitness**: Generally patients with an ECOG performance status (➔ see Table I.2, p. xxxiv) >2 tolerate chemotherapy very poorly—chemotherapy is generally contraindicated in such patients. Possible exceptions include those patients with very chemosensitive tumours who may be expected to respond quickly, such as small-cell lung cancer and lymphoma.

- **Patient symptoms**: Chemotherapy in the palliative setting is usually delayed until the patient develops symptoms. The potential danger with this approach is that the patient may rapidly develop symptoms which render them unfit for chemotherapy. In some cases, therefore, oncologists may choose to monitor disease and institute treatment when there is evidence that disease, although asymptomatic, is progressing.
- **Disease sites**: Generally, large volume disease at life-threatening sites, e.g. the liver, requires urgent chemotherapy even when disease-related symptoms are absent, as patients are likely to become symptomatic very quickly.
- **Appropriateness**: Close relationships may build up between doctors and patients over many years. It may be difficult for doctors to withdraw toxic oncological treatment from a patient who continues to demand it, even if it has now become clearly inappropriate. Thus clear and open discussion with patients and their families about the potential benefits and risks of chemotherapy, the aims of treatment, and, in particular, agreed criteria for stopping treatment, is important. The palliative care team can support the oncology team in these discussions.

> I would like to remind those responsible for the treatment of tuberculosis that Keats wrote his best poems while dying of this disease. In my opinion he would never have done so under the influence of modern chemotherapy.
>
> Arthur Walker (1896–1955)

How will chemotherapy affect the patient and family?

Each individual patient and family will have their own particular response to chemotherapy in the palliative care setting. Certain themes may be common to many such individuals. The following are some of the scenarios encountered in GP surgeries, oncology services, and palliative care units.

- *'We've got to keep on trying'.* Having endured the rigours of their disease and its management, some patients reach the palliative setting protesting their capacity as 'fighters'. (There is now evidence that psychological disposition has no bearing on disease outcome.) They have coped with their disease by trusting in the system and in being 'active' in fighting their cancer. It is very hard to wean such patients off chemotherapy or to stop active treatment, as to do so seems, in their eyes, to admit defeat. Such patients will ask to be put into trials, and see their role as patients as being fulfilled only so long as they are participating in active treatment.
- *'It was not half as bad as I thought it was going to be'.* Increasingly, owing to improved symptom control measures and a more holistic approach, patients may be pleasantly surprised by their tolerance of chemotherapy. Most people have had a previous contact with someone

going through chemotherapy, and their expectations are often adversely affected by this.

- *'He has suffered enough'.* Other families come through their disease journey with very ambivalent attitudes towards the system and to chemotherapy. They arrive in the palliative care setting determined that further suffering should be kept to a minimum. They can be reluctant to consider any intervention at all, other than the administration of pain-controlling medications. For such a family, the prospect of chemotherapy entering into the palliative setting is anathema, and time may need to be taken to explain the benefits in certain situations, if appropriate.
- *'Her hair fell out, then she died'.* Many patients and families come with memories and histories of relatives who have received chemotherapy in the past. Memories seldom show clearly the distinction between problems caused by the illness itself and problems caused by side effects. The two merge into a mess of suffering, leaving the patient and the family convinced that there is only one thing worse than dying with cancer—and that is dying from cancer with the side effects of chemotherapy. Doctors and nurses are not immune from such emotional responses.
- *'Whatever you say, doctor'.* Another group of patients cope with their disease by investing their trust in 'the doctor' looking after them. Such an approach runs contrary to non-patronizing modern trends, but is still present, particularly among older patients. To present such patients with a meta-analysis of the benefits of one form of chemotherapy or another and to ask the patient which one they want to choose would be inappropriate.
- *'What about Mexican dog weed?'* Some patients and relatives may come into the palliative care setting clutching reams of printouts from the internet about treatments from clinics around the world. They will often be very articulate and questioning of every intervention. Some will have an alternative medicine approach and be very sceptical of Western medicine. Honest communication needs to include how health professionals interpret the clinical research literature and what they would be prepared to do in terms of agreeing to provide a treatment that is controversial, unproven, and unlicensed. Boundaries need to be set and unrealistic expectations dispelled, alongside not removing hope that a reasonable quality of life can still be achieved.
- *'I've had a good life'.* A section of patients come into the palliative setting without illness at the centre of their lives. Instead they are focused on their living and their dying, with its important stages and goodbyes. Such patients have accepted the inevitability of their death and have moved on to preparing for it. They have things that they want to do. When it comes to the possibility of chemotherapy for such people, their main concern is, 'Will it interfere with what I still have to do?'. They are strangely neutral about chemotherapy; it is almost as if they are humouring the professionals by agreeing to it, while they get on with the real business of living.

- *'I just can't face it'.* Some patients have been so worn down by their disease and treatment that the prospect of any more chemotherapy fills them with fear and dread. Sometimes the fears are justified and sometimes they are not. Sometimes their expression of fear about chemotherapy is a way of verbalizing fears about other matters which should be explored. They face the dilemma of risks and fears whether or not they accept chemotherapy and will need a lot of support in reaching a treatment decision.

Anticancer agents

see Tables 6.1–6.3.

Table 6.1 Classification of anticancer agents

Class of agent		Mode of action	Examples in common usage
Cytotoxics	Alkylating agents	Damage DNA by addition of an alkyl group	Cyclophosphamide, ifosfamide, melphalan, busulphan
	Platinum agents	Damage DNA by addition of platinum adducts	Cisplatin, carboplatin, oxaliplatin
	Antimetabolites	Inhibit production of pyrimidine and purine metabolites	Fluorouracil, methotrexate, capecitabine, mercaptopurine, gemcitabine
	Antitumour antibiotics	Variable	Doxorubicin, epirubicin, mitoxantrone, bleomycin
	Vinca alkaloids	Bind to tubulin-blocking microtubules and therefore spindle formation at metaphase	Vincristine, vinorelbine, vinblastine
	Taxanes	Promote tubulin polymerization and arrest cells at metaphase	Paclitaxel, docetaxel
	Topoisomerase I inhibitors	Inhibit topoisomerase I, leading to DNA damage	Irinotecan, topotecan
Hormonal agents	Selective oestrogen receptor modulators (SERMs)	Partial antagonists of the oestrogen receptor	Tamoxifen, fulvestrant
	Aromatase inhibitors	Inhibit extragonadal oestrogen production	Anastrozole, letrozole, exemestane
	Gonadorelin analogues	Inhibit gonadal production of oestrogen and testosterone	Leuprorelin
	Anti-androgens	Testosterone receptor antagonists	Cyproterone acetate
Immunomodulatory	Interferon		
'Novel' agents	Antibodies	Opsonization, interrupt growth stimulatory pathways	Rituximab, trastuzumab
	Signal transduction inhibitors	Interrupt growth stimulatory pathways	Imatinib, erlotinib, gefitinib, bortezomib, sunitinib, sorafenib, lapatinib
	Vascular targeting agents	Target 'new' vessels associated with tumours—not in use with a clinical trial	Bevacizumab, sunitinib, sorafenib, thalidomide

Hormone therapy

Hormone therapy is a treatment that uses medicines to block or lower the amount of hormones in the body to slow down or stop the growth of cancer. Hormones are commonly used in cancers of the breast (e.g. aromatase inhibitors) and cancers of the prostate (anti-androgens, e.g. bicalutamide).

Table 6.2 Hormone and antihormone drugs

Drug	Administration	Side effects	Comments
SERMs	p.o.	Menopausal symptoms	Used first-line in adjuvant treatment of ER/PR +ve breast cancer
Tamoxifen	IM	Thromboembolic event	
Fulvestrant		Endometrial hyperplasia and cancer	Post-menopausal ER/PR +ve breast cancer
Anti-androgens			Used in prostatic cancer sometimes in combination with gonadorelin analogues
Bicalutamide	p.o.		
Enzalutamide	p.o.	Hepatotoxicity	
Abiraterone	p.o.	Gynaecomastia	
Aromatase inhibitors	p.o.	Menopausal symptoms	Used in post-menopausal breast cancer
Anastrozole		Increased fractures	
Letrozole			
Exemestane			
GNRH analogues*			
Buserelin	SC and intranasal	Gynaecomastia; impotence; nausea; fluid retention	Prostate cancer
Goserelin	Implant		Breast cancer
Leuprorelin	IM	Menopausal symptoms	

* GnRH (gonadotrophin-releasing hormone): Beware initial flare-up of symptoms on initial use in men with prostate cancer. This should be 'covered' with the concomitant use of anti-androgens for the first few weeks of therapy.

Immunotherapy

Monoclonal antibodies

These biological response modifying agents can be added to chemotherapy and have been shown to improve response rates and survival in a number of malignancies.

- **Trastuzumab**—a monoclonal antibody to human epidermal growth factor receptor 2 (HER2)—a member of the epidermal growth-factor (EGF) receptors overexpressed in approximately 25% of all breast cancers and associated with a poor prognosis. Trastuzumab has demonstrated activity in HER2 overexpressing breast tumours both alone and in combination with chemotherapy in the adjuvant and palliative settings. It has also shown improvements for HER2-positive gastric cancers.
- **Rituximab**—a monoclonal antibody to CD-20, a protein expressed in some lymphomas. Again, rituximab is active both alone and in combination with chemotherapy.
- **Bevacizumab**—inhibits angiogenesis by binding to circulating vascular endothelial growth factor (VEGF). Bevacizumab increases the efficacy of chemotherapy in patients with cancers such as colorectal and ovarian.
- **Cetuximab**—attaches itself to the extracellular portion of the EGF receptor, preventing the receptor from being activated. It has been combined with chemotherapy and radiotherapy, and it is used in the treatment of colorectal and head and neck cancers.

Small-molecule inhibitors of tyrosine kinases

Small-molecule tyrosine kinase inhibitors, which include selective and multikinase inhibitors, have demonstrated activity in a variety of malignancies by targeting specific molecular pathways involved in angiogenesis and in the proliferation of malignant cells. Examples include the following:

- **Gefitinib and erlotinib**—inhibit the tyrosine kinase activity of the epidermal growth factor receptor (EGFR). Activity is demonstrated in non-small-cell lung cancer. Common side effects include diarrhoea and skin rashes.
- **Imatinib**—inhibits the tyrosine kinase activity of the cKIT proteins found in gastrointestinal stromal tumours and also of the Bcr/Abl fusion protein found in chronic myeloid leukaemia.
- **Bortezomib**—inhibits the proteosome, the mechanism by which cells dispose of intracellular peptides. It causes a delay in tumour growth; it is used in the treatment of multiple myeloma.
- **Sorafenib**—a small-molecule inhibitor of Raf kinase, PDGF (platelet-derived growth factor), VEGF receptor-2 and -3 kinases, and cKit. It is used in the treatment of renal-cell cancer.
- **Sunitinib**—a small-molecule, multitargeted receptor tyrosine kinase inhibitor which is used in the treatment of renal-cell cancer and imatinib-resistant gastrointestinal stromal tumour (GIST).
- **Lapatinib**—EGFR and HER2 dual tyrosine kinase inhibitor, which is used in the treatment of HER2 positive metastatic breast cancer in combination with capecitabine.

In recent years, there have been significant developments in the area of immunotherapy. Cancer immunotherapy aims to augment recognition of cancer as foreign, stimulate immune responsiveness, and relieve inhibition of the immune system that allows tolerance of tumour survival and growth.

The greatest advances have been in the development of immune checkpoint inhibitors, specifically to PD-1 (programmed cell death 1), PD-L1 (programmed cell death ligand 1), and CTLA-4 (cytotoxic T-lymphocyte associated protein 4).

Table 6.3 Emetic risk of common chemotherapy drugs

Cytotoxic agent	Risk
Cisplatin*	High
Cyclophosphamide >1000mg/m^2*	
Ifosfamide*	
Melphalan*	
Actinomycin	Moderate
Amsacrine	
Busulfan	
Carboplatin*	
Chlorambucil	
Cladribine	
Cyclophosphamide <1000mg/m^2	
Cytarabine >150mg/m^2	
Dacarbazine	
Daunorubicin	
Daunorubicin liposomal	
Doxorubicin	
Epirubicin	
Lomustine	
Methotrexate >1g/m^2	
Mitoxantrone	
Procarbazine	
Bleomycin	Low
Cyclophosphamide <300mg/m^2	
Cytarabine <150mg/m^2	
Etoposide	
Fludarabine	
Mercaptopurine	
Methotrexate <1g/m^2	
Tioguanine	
Thiotepa	
Vinblastine	
Vincristine	

*Delayed emesis risk.

PD-1 is an inhibitory molecule on immune cells that binds to PD-L1 on tumour cells and effectively 'puts the brakes' on the immune response. Nivolumab and pembrolizumab are two antibodies to PD-1 that are showing promise in a number of malignancies.

CTLA-4 is a negative regulator of T-cell activation and the anti-CTLA-4 antibody, ipilimumab, has become well established in the treatment of melanoma.

Checkpoint inhibition is now a treatment modality in advanced melanoma and non-small-cell lung cancer; clinical trials are ongoing to assess response in other malignancies. It is likely there will be significant progress in this field in the years to come.

Further reading

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Davis M.P., Panikkar R. (2019) Sarcopenia associated with chemotherapy and targeted agents for cancer therapy. *Annals of Palliative Medicine*, **8**(1):86–101.

Radiotherapy

Radiotherapy is the most important type of non-surgical treatment for patients with common cancers. The proportion of these treated by radiotherapy at some time during their illness has risen steadily and is now well over 50%.

Professor Jeffrey Tobias, UCL

Radiotherapy as a therapeutic modality developed shortly after the discovery of X-rays in 1895. Clinical and technological advances subsequently have made it one of the most successful modalities in the treatment of patients with cancer, both in the curative and palliative settings.

Mechanism of action

Radiotherapy is the therapeutic use of ionizing radiation to destroy cancerous cells. The critical cellular target is, in common with chemotherapy, nuclear DNA. Double-stranded breaks in the DNA molecule are the key lesion responsible for cell death. Not all double-stranded DNA breaks, however, result in cell death; indeed, most are repaired by the cell's DNA repair enzyme apparatus (Fig 6.2). The success or otherwise of the repair process determines the fate of the cell. Malignant cells are less able to repair double-stranded DNA breaks than normal tissues; therefore radiotherapy preferentially targets malignant cells.

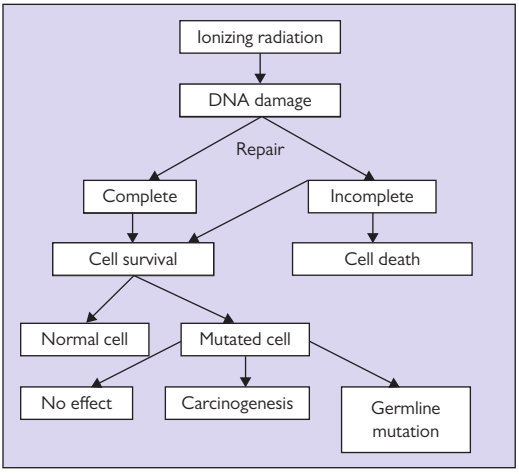


Fig 6.2 The cell repair process after radiotherapy.

Response of normal tissues to radiation

Different types of normal tissue respond differently to radiation. Homeostatic mechanisms control cell populations by balancing cell death with new cell growth through the proliferation of stem cells. If a proportion of these stem cells are destroyed by radiation, the rate of renewal of normal cells will be reduced. The time of appearance of this tissue damage is determined by the lifespan of the mature cells within that tissue. For certain tissues, such as skin and mucosa, this lifespan is short, as cells are quickly lost by desquamation, and hence tissue damage is manifest during the radiation course. For other tissues, cell turnover is much slower, and radiation damage will only become apparent many months or years after radiation exposure. This gives rise to the distinction between the acute and late effects of irradiation. In general, cells that are rapidly proliferating tend to display acute response to irradiation, whilst cells that proliferate slowly tend to display late responses to irradiation. The balance between the probability of tumour control and the risk of normal tissue complications is a measure of the therapy ratio. An improved therapeutic ratio represents a more favourable trade-off between tumour control and toxicity.

Acute effects of radiation

Acute effects refer to the normal tissue reactions during a course of radiotherapy. The mucosa and haemopoietic system—i.e. tissues with a fast normal cellular turnover—display the effects of irradiation the earliest. For example, patients receiving radiotherapy to the head and neck area may develop severe oral mucositis, while those receiving radiotherapy to significant volumes of bone marrow may develop bone marrow suppression.

Acute reactions are usually observed during the course of conventionally fractionated radiotherapy (1.8–2Gy per fraction five times a week).

Late effects of radiation

These occur predominantly in slowly proliferating tissues (lung fibrosis, kidney, heart, liver, and CNS). By definition, late reactions occur more than 90 days after commencing a course of radiation.

In addition, some of the tissues which develop their effects early can also demonstrate late effects, such as fibrosis or telangiectasia in the skin. This reflects the differing populations of cells (fibroblasts, endothelium, etc.) which exist within a single organ.

Normal tissue tolerance

Not only do different tissues respond at different rates to irradiation, they also vary in their sensitivity. Certain tissues, e.g. the lens, exhibit damage at very low doses, while other tissues demonstrate marked resistance to the effects of radiation, e.g. uterine cervix. The situation is analogous among cancers. Lymphomas and seminomas show sensitivity to radiation, while renal-cell carcinomas and melanomas are radio-resistant.

A number of treatment and patient factors influence tissue tolerance to radiation:

- total radiation dose given: higher doses are more toxic
- fraction size: late-responding tissues are more sensitive to large fractions
- overall longer treatment time: better tolerated by normal tissues

- treatment volume: larger volumes are generally more toxic
- quality of the radiation: neutrons are more damaging than photons or electrons
- concomitant therapy: concurrent chemotherapy reduces tolerance

Patient factors adversely influencing tissue tolerance:

- older age
- haemoglobin level
- smoking
- diabetes mellitus
- connective tissue disorders
- genetic syndromes (e.g. ataxia-telangiectasia)

Tolerance doses for specific tissues

The following tissues suffer a 5% incidence of toxicity at 5 years when conventional radiotherapy is given in dose sizes of 1.8–2Gy per fraction at the doses stated for each tissue type (Tables 6.4 and 6.5).

Re-treatment

Traditional teaching precluded re-treating areas that had already received a maximal radiation dose. Recent studies have shown some tissues and organs have a greater capacity to recover from subclinical radiation injury than was previously thought. For example, the large capacity of long-term regeneration of the CNS allows new possibilities for re-treating recurrent neurological tumours with irradiation.

Table 6.4 Normal tissue tolerance

Tissue	Injury	Tolerance
Brain	Necrosis	60Gy
Spinal cord	Myelopathy	45Gy (<1% incidence)
Lens*	Cataract	10Gy
Small intestine	Ulceration/perforation	45–50Gy
Kidney*	Clinical nephritis	23Gy
Lung*	Pneumonitis	18–20Gy
Heart*	Pericarditis	40Gy
Ovary	Sterilization	2Gy
Testis	Sterilization	1Gy

* Whole organ

Table 6.5 Radiation effects within specific tissues (following standard radical doses)

Skin	*Acute* reaction—erythema begins week 3–4; dry or moist desquamation later	Reaction settles within 2–4 weeks of completion of therapy
	Late reaction—fibrosis, atrophy, telangiectasia	
Oral mucosa	*Acute* reaction—erythema/oedema from week 2–4	Reaction settles within 2–4 weeks of completion of therapy
	Late reaction—patchy followed by confluent mucositis	
Gastrointestinal tract	*Acute* reaction—mucositis causes nausea, anorexia, cramps, and diarrhoea	Reaction settles within 2–4 weeks of completion of therapy; treat symptomatically
	Late reaction—ulceration and fibrosis leading to strictures, fistulae, and malabsorption	Usually >6 months post RT
Brain	*Acute* reaction—lethargy common; occasionally cerebral oedema	
	Late reaction—somnolence syndrome at 1–3 months post RT; brain necrosis at 6 months to 3 years	Resolves spontaneously with/without help of steroids; indistinguishable clinically from recurrent tumour
Spinal cord	*Late* reaction—Lhermitte's syndrome 2–18 months after RT; radiation myelopathy at 6–12 months	Resolves spontaneously. Does not progress to myelopathy. Irreversible
Lung	Early/intermediate reaction—pneumonitis at 1–3 months; results in pulmonary fibrosis	Classical straight-edged appearance on chest X-ray if opposed radiotherapy fields used
Kidney	*Late* reaction—proteinuria, hypertension, renal failure	May take up to 10 years to develop
Heart	*Late* reaction—pericarditis/effusion; most within 6 months of RT; cardiomyopathy; coronary artery disease	Most resolve spontaneously; may develop into a constrictive process 10–20 years post RT

NB Patients undergoing radiotherapy usually experience lethargy as a *general* side effect.

Types of radiation therapy

There are two main types of radiation therapy:

- **external beam radiotherapy**—delivered by radiotherapy machines
- **brachytherapy**— delivered by radiation sources within the body cavity in one of two ways:
  - sealed sources or implants (e.g. prostate brachytherapy seed implants)
  - unsealed source or radioisotope therapy—given by mouth, intravenously, or into tissue spaces (e.g. radioactive iodine treatment for thyroid cancer)

External beam radiotherapy

External beam radiation consists of different energies, as shown in Table 6.6.

Superficial X-rays

Relatively low-energy X-ray photons in the range 80–150kV. These X-rays are relatively non-penetrating, depositing the majority of their energy in the most superficial few millimetres of skin. Therefore, they deliver a high dose to the skin with rapid fall-off with increasing depth, and are thus appropriate for the treatment of superficial skin lesions such as skin metastases.

Orthovoltage energy X-rays

Orthovoltage X-rays are slightly more penetrating, and deliver sufficient dose at depth to treat adequately thicker skin or subcutaneous lesions, such as rib metastases. (Both superficial and orthovoltage X-rays suffer the disadvantage of delivering a higher absorbed dose to bone compared to soft tissue, thus increasing the risk of osteoradionecrosis if a lesion is positioned too close to underlying bony tissue.)

Megavoltage X-ray

Photons possess energies 50–200 times those of superficial X-rays (1–20MV). In contrast to superficial and orthovoltage X-rays, megavoltage

Table 6.6 External beam radiation

Type of radiation	Energy	Use
Superficial X-rays	80–150kV	Skin tumours
Orthovoltage X-rays (DXT)	200–400kV	Thick skin tumours Superficial tumours, e.g. ribs
Megavoltage X-rays		
γ-rays—cobalt 60	1.25MV (mean)	Deep tumours
X-rays—linear accelerator	4–25MV	Deep tumours
Electrons	4–20MeV	Skin tumours Superficial tumours/skin or breast treatments
Particle beam therapy	1–250MeV	All tumour types (but currently CNS and paediatric)
Protons	290–400 MeV	
Carbon-ion therapy		Largely experimental

photons are produced by the acceleration of electrons along a linear tube (wave guide) before striking a target. This is done within a machine called a 'linear accelerator'. The interaction of these high-energy electrons with the target material generates high-energy X-rays.

High-energy X-rays are very penetrating and give a much higher dose at a given depth within a tissue than superficial X-rays.

Megavoltage X-rays possess the advantage of relative sparing of the superficial skin tissues, as the maximum absorbed dose occurs up to several centimetres below the skin surface. There is also no increased absorption of dose in tissues containing elements of high atomic mass, such as bone.

Electron therapy

Electrons may be generated using a linear accelerator. In this situation the accelerated electron beam exits the linear accelerator without striking the target. Electron therapy is used to treat superficial tumours, most often of the skin. It is their characteristic deposition of dose with depth which makes electrons ideal for this purpose: >90% of the dose is deposited in the first few centimetres of tissue with very rapid dose fall-off thereafter, thus sparing underlying structures.

Particle beam therapy and protons

Particle beam therapy describes the use of accelerated atomic particles or ions (instead of photons), delivered in a similar manner to megavoltage radiotherapy to treat cancer. Proton therapy is the most widely available, and this is available in a few specialized centres in the UK. Protons have a finite range of penetration and sharper cut-off than X-rays. This enables a more precise distribution of radiation dose to the tumour, sparing normal tissues optimally. The therapeutic ratio is thus increased, leading to better tumour control and fewer side effects. Clinical trials of proton therapy vs photon therapy are awaited to see whether protons offer patients a distinct clinical advantage.

Treatment planning for external beam radiation

This is the essential prerequisite step before treatment delivery. During the process of treatment planning, questions such as 'Where to treat?', 'What to treat?', 'What not to treat?', and 'How to treat and how much to treat?' are addressed. It is essentially an iterative process with changes being made at various stages to facilitate the design of an optimal treatment schedule. There are several rungs in the planning ladder (Fig 6.3).

The complexity of treatment planning depends upon the tumour and the intent of therapy. Radical plans are generally more complicated and time-consuming than those with palliative intent.

Immobilization is relatively more important for tumours positioned close to sensitive normal tissue structures and for radical, high-dose treatments.

The tumour is **localized** either by clinical examination, e.g. skin tumours, or by imaging, most commonly fluoroscopy or CT scanning. Newer technology permits the fusing of various imaging modalities, e.g. CT/MRI images, PET/CT images.

Once the tumour is localized, the **gross tumour volume** is defined. This encompasses all visible tumour on inspection or on available imaging. A margin is added to allow for microscopic tumour extension—the so-called

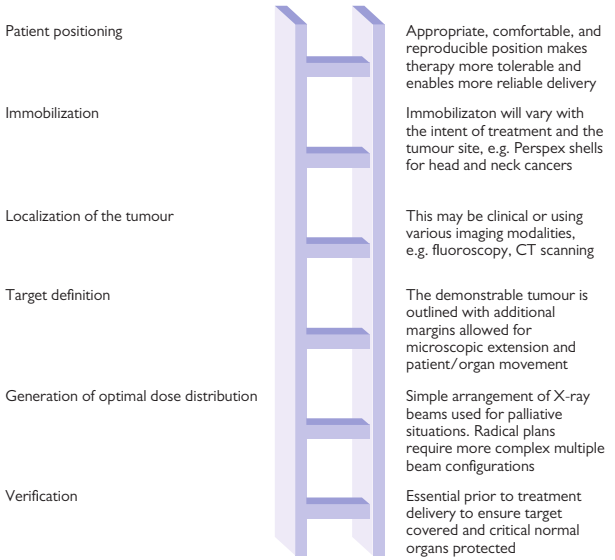


Fig 6.3 Treatment planning ladder.

clinical target volume. Additionally, a margin known as the **planning target volume** is added in order to accommodate movements in the organ containing the tumour, and to cover any uncertainties inherent in the treatment delivery system.

After the target has been delineated, differing beam arrangements are generated. The arrangement is chosen which best covers the target volume (planning target volume) and most successfully spares the normal tissue structures (also known as the **organs at risk**).

The final step in treatment planning is **verification**. This is an essential step to ensure that a plan generated on a planning computer actually fits the patient, i.e. the tumour is accurately targeted and critical structures such as the spinal cord are adequately spared. The verification process continues through treatment with dose measurements confirming appropriate dose delivery.

Radiotherapy dose prescription

Once the final treatment plan is decided upon, the radiation dose must be prescribed. There are several constituents that together make up the prescription:

- total dose
- number of fractions (fraction size)
- overall treatment time

Total dose/number of fractions

Rather than deliver the entire dose of radiation in a single treatment, the dose is divided up into smaller quanta. This is the process of fractionation, each treatment dose being known as a 'fraction'. Fractionation is performed to permit repair of normal tissue radiation damage. Fractionation will also permit repair to occur within tumour tissue, although this is relatively less efficient. In consequence, when a treatment course is fractionated, the total dose of radiation must be increased. Early studies showed that changing from a single dose to a 6-week fractionated course of therapy required an increase in the total dose by a factor of three in order to achieve the same biological effect.

The relationship between total dose and number of fractions is, however, complex; mathematical models are used to help predict and compare the biological effects.

Small numbers of fractions are convenient for the patient, as travelling is kept to a minimum. However, the fraction size is in consequence larger; this increases the biological effectiveness of each fraction, resulting in more severe damage to late-responding tissues. The total dose in such hypofractionated courses must be reduced to maintain an acceptable level of late-tissue damage.

Hypofractionated treatment courses are often employed in the palliative setting because of their convenience for patients and the relative unimportance of adverse long-term radiation effects in patients with limited life expectancy. Hypofractionated radiotherapy is increasingly being used in high-precision, potentially curative treatments such as stereotactic radiotherapy to the brain or lung. Hypofractionated external beam radiation is being used in breast and prostate cancer with promising results.

Overall treatment time

Standard radical fractionation schedules involve treating once per day, Monday to Friday, for 4–7 weeks. As treatment generally extends beyond 4 weeks, tumour cell repopulation may become a problem.

As the number of tumour stem cells and mature functional tumour cells are depleted as a result of radiotherapy, the remaining stem cells sense this loss and begin to replicate actively to counteract this deficit. This is known as **tumour repopulation**. It appears that there is a lag period of approximately 3–4 weeks before this phenomenon occurs. Each fraction of radiotherapy delivered after the onset of repopulation is therefore relatively less effective, since part of the fraction must counteract this increase in the number of tumour cells resulting from repopulation.

A means of circumventing this effect of tumour repopulation is to accelerate the radiotherapy course so that the dose is delivered over a shorter period, preferably less than the 3–4 weeks required for the onset of repopulation.

Brachytherapy—sealed and unsealed source therapy

In brachytherapy, the radiation source is closely applied to the tumour (literally, therapy at a short distance, from the Greek *brachys*, meaning 'short').

The underlying principle is the inverse square law, which states that the intensity of radiation, *R*, at a given distance, *D*, from a radioactive source—and therefore the absorbed dose—is inversely proportional to the square of that distance. Put simply, doubling the distance between the radiation source and the tissue reduces the dose absorbed by the tissue by a factor of 4 (rather than a factor of 2, as might be expected if the relationship was linear):

$$R \propto 1 / D^2$$

The beauty of brachytherapy lies in the ability to administer high doses of radiation to the tumour with relative sparing of neighbouring normal tissue because of rapid fall-off of absorbed dose with distance.

Sealed source therapy is so called because the radioactive substance (often a metal), e.g. iridium-192, is usually encased or sealed within a metal casing such that the radioactive substance does not actually physically touch the tissue even when inserted directly into the tumour (see the following).

Sealed source brachytherapy takes three main forms:

- **interstitial**: the radioactive source is inserted directly into the tumour tissue
- **intracavitary**: the radioactive source is inserted into a body cavity such as the uterus or the vagina when treating endometrial or cervical cancer
- **intraluminal**: the radioactive source is positioned in the lumen of a hollow viscus, e.g. bronchus, oesophagus

Brachytherapy, because it involves the placing of radioactive sources in close proximity to the patient, must of necessity make staff vulnerable to the risk of radiation exposure.

Decreasing the time during which exposure might occur, maximizing the shielding between the source and staff, and, most importantly, increasing the distance from source to personnel all help to diminish risk.

In practice, the oncologist places hollow tubes into the tumour, cavity, or lumen, through which the source may subsequently be driven mechanically. This remote afterloading allows the radioactive source to be brought into very close proximity to the tumour without exposing staff to any significant radiation exposure.

Unsealed source therapy involves administering radioactive substances directly into the patient, either in the form of liquids for ingestion or solutions for intravenous administration.

Unsealed source therapy may be used as a palliative manoeuvre, as an adjuvant to curative surgery (e.g. ^{131}I for thyroid cancer), as a curative treatment alone (e.g. ^{131}I for thyroid cancer), or in the treatment of benign conditions such as thyrotoxicosis (^{131}I) and polycythaemia vera (^{32}P).

Radiation protection is important as patients emit radiation for a variable period after administration of the radioisotope, depending on the half-life of the isotope. They are carefully instructed regarding the precautions necessary to prevent excess exposure to others, most notably family members. Such precautions include double flushing of the toilet after micturition, refraining from close contact with children, and avoiding places of entertainment or work for a specified period post-treatment.

A number of radioisotopes are commonly used:

- **Strontium-89 (^{89}Sr):** used for the relief of bone pain due to metastatic bone disease. A disadvantage is the relatively long half-life which poses radiation protection problems, especially if the patient dies within a short period after treatment. Some patients experience a flare-up in their bone pain within a few days of treatment. This usually settles with appropriate analgesia. As strontium is absorbed into bone tissue, bone marrow toxicity may occasionally occur, and regular blood count monitoring after treatment is advised.
- **Samarium-153 (^{153}Sm):** used less commonly than ^{89}Sr but indicated likewise for the relief of pain from bony metastatic disease. It has the advantages of a shorter half-life and the production of photons as part of its decay pathway. These photons permit scintigraphy and thus bone scan images may be obtained. The propensity to pain flare up and marrow toxicity pertain as for strontium-89.
- **Iodine-131 (^{131}I):** Both normal thyroid and well-differentiated thyroid cancer (papillary and follicular variants) selectively take up and concentrate iodine. This can be exploited therapeutically using ^{131}I. Owing to this concentrating effect within thyroid tissue, high doses can be selectively delivered to the normal or malignant thyroid tissue, leading to its destruction. In the case of normal thyroid tissue, hyperthyroid patients may be rendered euthyroid with a relatively low dose of ^{131}I; in the case of malignancy, ^{131}I is used as an adjuvant treatment following surgery to ablate the remaining normal thyroid tissue and any potential microscopic residual tumour.
- **Phosphorus-32 (^{32}P):** This has proved useful in the treatment of polycythaemia vera, although, because it may increase the risk of subsequent development of leukaemia, it is generally reserved for patients over 70 years of age.
- **Radium-223 (^{223}Ra):** is a mildly radioactive form of the metal radium, also known as Alpharadin, which emits alpha particles. Radium-223 is used in the treatment of bone metastases from prostatic carcinoma in a similar manner to that in which strontium-89 and samarium-153 have been used.

Radiation therapy

> Radiotherapy is used for about half of the 200,000 patients who develop cancer in the UK each year. It has a curative [or adjuvant] role in two-thirds, and a palliative role in the remainder.
>
> Alan Horwich, Institute of Cancer Research, London

Radiotherapy may be administered in differing clinical situations and with varying intents.

Treatment can be:

- **radical**—curative intent
- **adjuvant**—post-operative
- **palliative**—symptom control

Radical radiotherapy

Radiotherapy may be administered with the intent of cure either as the preferred primary therapy (e.g. early-stage Hodgkin's disease), or as an alternative to surgery.

In the latter situation, it has the advantage of preserving normal anatomy (e.g. anal canal cancer, bladder cancer). Additionally, acute morbidity is often less severe. However, because no surgical specimen is obtained, there can be no pathological data to permit accurate staging. Stage must therefore be assessed by clinical or radiological methods. Late effects of radiation, such as fibrosis, may also make subsequent assessment of the tumour site for local recurrence difficult.

Radical radiation is reserved for tumours which can be encompassed within a reasonable radiation treatment volume, i.e. localized, as opposed to widely metastatic disease; this presupposes accurate staging investigations.

Treatment is often complex, with effort given to rigid immobilization and the use of complicated beam arrangements to obtain a uniform dose distribution confined to the tumour, with preservation of normal surrounding structures. A high dose of radiation is necessary for all but the most radiosensitive of tumours, and treatment is delivered in conventional (small) fraction sizes in order to reduce the late adverse effects of radiation.

Examples of radical radiotherapy include:

- **Head and neck tumours:** Many squamous-cell tumours of the head and neck region can be cured by radical radiotherapy (often combined with synchronous chemotherapy), e.g. early-stage cancers of the larynx are frequently cured with preservation of good-quality voice.
- **Anal canal cancer:** A radical approach using concurrent chemo-radiotherapy has been shown to be effective management for epidermoid anal canal cancer. Additionally, 60–70% of patients retain a functioning anal sphincter after treatment. A common alternative to such an approach is primary abdominoperineal excision of the rectum and anal canal, which results in a permanent colostomy.
- **Lung cancer:** Radical radiotherapy can be employed as a second-best option in the management of lung cancer. Although the patients selected for such treatment may not be sufficiently fit to undergo radical surgery,

they may be fit for radiation treatment, with a cure rate of 15–20% for standard dose radiation but with local control rates of 70–90% following high-precision stereotactic radiation of Stage I lung cancer.

Adjuvant radiotherapy

Radiotherapy is administered as an adjunct to potentially curative treatment, i.e. surgery or chemotherapy. The principle underpinning such treatment is the hope that microscopic loco-regional residual disease, either within the tumour bed, lymphatic channels, or regional lymph node drainage, ought to be eradicated by the radiotherapy, thereby reducing the rate of local relapse and improving overall survival.

Examples of adjuvant radiotherapy:

- **Breast cancer**: This is perhaps the best example and is certainly the most common exemplar of adjuvant radiation. Up to 50% of the workload of many UK radiotherapy centres is devoted to adjuvant breast irradiation. Local relapse rates following partial mastectomy may reach 30%. Post-operative breast irradiation can reduce this figure by three- to four-fold. Local control rates then conform to those achieved after mastectomy, but with a superior cosmetic outcome.
- **Head and neck cancer**: Surgery for squamous tumours of the head and neck is complex. Owing to the close proximity of tumours to important structures, surgical margins may often be inadequate because compromise must be made to retain acceptable functional and cosmetic outcomes. Adjuvant irradiation is employed if margins are unsatisfactory, or if radical neck surgery reveals multiple involved lymph nodes. Classically, adjuvant radiotherapy is administered after surgery has been performed.

However, in some situations, although surgery remains the mainstay of treatment, radiotherapy may be delivered as a prelude to a surgical procedure.

True **neoadjuvant radiation** is administered in order to reduce the risk of relapse after surgery. However, **induction radiation** may be used to shrink or downstage the tumour, thus facilitating subsequent surgery. In this case, time must elapse between irradiation and surgery to allow tumour reduction. An illustration of this technique is preoperative rectal radiotherapy for tethered or fixed rectal adenocarcinoma. Treatment is delivered over 4–5 weeks, after which there is a gap of about 6 weeks during which tumour shrinkage occurs. This facilitates radical surgery in patients who were initially regarded as technically inoperable.

Short-course neoadjuvant preoperative rectal radiotherapy, by contrast, is delivered over the week immediately prior to surgery. No time is permitted for tumour shrinkage. Trials have, however, confirmed a significant improvement in local control and overall survival with this approach.

Adjuvant radiation treatment courses typically extend over 3–6 weeks. The general principles applied to radical radiotherapy also hold for the adjuvant setting, as treatment intent is curative: i.e. immobilization, careful avoidance of critical organs at risk, and low dose per fraction. Total doses tend to be slightly lower since the target is microscopic residual disease. It must, however, be remembered that following surgery the vascular supply to tissues is disrupted, resulting in areas of tissue hypoxia. **Radiation is relatively less effective in an environment that is poorly oxygenated.**

Palliative radiotherapy

When radiotherapy is administered in the palliative setting, the aim is the control of distressing symptoms. The disease is, by definition, incurable. These factors impact upon treatment in a variety of ways:

- symptomatic sites of disease are targeted
- sites at high risk of producing symptoms may receive prophylactic treatment
- fractionation regimens are kept short
- moderate doses of radiation are employed
- palliative benefit must outweigh treatment-related toxicity

Palliative radiotherapy may produce prolongation of survival, but this is not its primary aim; rather, it is the quality of that survival which is the goal. Palliative radiotherapy often produces significant symptomatic gain.

There are several clinical scenarios in which palliative radiotherapy commonly proves useful.

Pain

Bone metastases and pain due to nerve compression or soft tissue infiltration will usually respond to radiation treatment. They respond to a single fraction of radiotherapy as effectively as more prolonged treatment schedules.

A single fraction is more patient-friendly and may be repeated if necessary. If pain is diffuse, affecting many different sites within the skeleton, wide field—or **hemibody**—irradiation often produces relief. An alternative is radioisotope therapy with ^{89}Sr, ^{153}Sm, or ^{223}Ra.

Osteolytic tumour deposits in weight-bearing bones are at risk of fracture and are best fixed prophylactically by orthopaedic intervention. This is often followed by post-operative irradiation, although good evidence of benefit is lacking. Rarely, radiation is given without prophylactic surgical intervention.

Haemorrhage

Haemoptysis, haematuria, haematemesis, and rectal bleeding all respond to radiation. A hypofractionated treatment course often produces prompt sustained benefit (at least 70% in carcinoma of the bronchus).

Obstruction

Any hollow viscus may become obstructed caused by a malignant process. Several organs may commonly be obstructed by cancer:

- superior vena cava (SVC)
- upper airways, i.e. trachea, bronchus
- oesophagus

Prompt, if not immediate, relief is frequently afforded by insertion of a stent under the care of the interventional radiologists for SVC or oesophageal obstruction. There is a role for palliative radiotherapy in some patients who are unsuitable for such procedures, or in the case of stent overgrowth by tumour.

Radiotherapy is most often used for bronchial obstruction due to lung cancer; laser resection or stent insertion are less commonly employed alternatives.

Chemotherapy is also used for SVC obstruction caused by chemosensitive tumours, e.g. small-cell lung cancer.

Neurological symptoms

- spinal cord compression
- brain metastases
- cranial or peripheral nerve compression
- malignant meningitis
- choroidal or orbital metastases

Radiotherapy is used in treating spinal cord compression. There are a number of important indications for surgical as opposed to radiotherapeutic intervention (e.g. uncertain pathology, unstable spine).

Radiotherapy often improves pain associated with the compression, but neurological recovery is less predictable and mainly depends on the degree of weakness prior to therapy and the particular histological tumour type.

Brain metastases are increasing in incidence; as many chemotherapy agents cross the blood-brain barrier poorly, and as oncological management improves, patients survive long enough to develop relapse within the brain. Steroids can produce significant benefit if the effects are due to oedema or compression rather than tissue destruction. However, their beneficial effects tend to be short-lived. Prolongation of symptom control and a small gain in survival (1–2 months) can additionally be obtained with cranial irradiation, usually at the cost of alopecia and lethargy. A recent study in patients with lung cancer showed no survival or symptomatic benefit following cranial irradiation in patients with brain metastases.[2] Thus, there is uncertainty regarding the role of cranial irradiation for those with widespread brain metastasis. It is suggested that those patients with good pretreatment neurological function and sensitive tumours stand to gain the most from cranial irradation.

Stereotactic radiosurgery (SRS) is increasingly being used to treat patients with one to three brain oligo-metastases. SRS describes high-precision radiotherapy delivered with the patient's skull immobilized in a stereotactic frame. Treatment is usually given in a single large-dose fraction (21Gy); subsequent control rates at the site of treatment are good. For patients with one to three brain metastases alone and no disease elsewhere, SRS may lead to long-term control or 'cure'.

Cranial or peripheral nerve compression most often occurs with breast or prostate neoplasms. Pain is often improved, but nerve palsies seldom show significant recovery.

Fungating tumours

Locally advanced breast tumours, skin tumours, and metastatic skin or lymph node deposits can all lead to fungation. If surgical intervention is not possible or felt to be inappropriate, radiotherapy can reduce the tumour mass and serous ooze or haemorrhage, and promote healing.

2 Mulvenna, P., et al. (2016). Dexamethasone and supportive care with or without whole brain radiotherapy in treating patients with non-small cell lung cancer with brain metastases unsuitable for resection or stereotactic radiotherapy (QUARTZ): results from a phase 3, non-inferiority, randomised trial. *Lancet (London, England), 388*(10055), 2004–14.

Managing the side effects of radiotherapy

Skin

General advice

- Skin reactions tend to be worse in the skin folds, i.e. inframammary fold, axilla, groin, and perineum.
- Aftershave lotions or astringent cosmetics should be avoided.
- Mild soaps are permitted, and washing should be gentle (no vigorous rubbing) and the area patted dry.
- Care must be taken not to remove skin markings delineating the treatment fields.

Mild reactions

- Skin pink or slightly red.
- Apply emollient cream frequently.

Moderate reactions

- Skin red, dry, and scaly; some pruritus/tingling.
- Apply emollient cream frequently and consider using an emollient ointment.
- If itch is problematic, 1% hydrocortisone cream b.d. is useful.

Severe reactions

- Skin is inflamed with patchy areas of moist desquamation.
- Epidermis may blister and slough, exposing the dermis, leading to pain and serous ooze with an increased risk of infection.
- Hydrogel or alginate dressing can be applied to moist areas; apply emollient ointment to the intact epidermis.
- Swab if there is evidence of infection.

Mouth and throat care

This is particularly important for patients receiving radiotherapy for head and neck cancer.

General advice

- The patient needs a dental assessment and any dental treatment should be carried out before radiotherapy begins.
- A good fluid and nutritional intake is very important and nutritional support by NG feeding is indicated if >10% weight loss occurs.
- Cessation of smoking should be strongly encouraged.
- Alcohol and spicy foods should be avoided.
- The voice should be rested as the radiotherapy reaction becomes established.

Treatment of mucositis

- Normal saline or bicarbonate mouth washes often help.
- Antiseptic mouthwashes, e.g. chlorhexidine, keep the mouth clean but can cause pain owing to their alcohol content.
- Oropharyngeal Candida infection should be actively sought and treated.
- Local analgesics include:
  - Aspirin (which may be gargled).
  - Paracetamol (which may be gargled).

- benzydamine
- local anaesthetics
- topical steroids (hydrocortisone oromucosal tablets)
- coating agents (sucralfate, Gelclair®)

Dysphagia

Thoracic radiotherapy can lead to oesophagitis, which needs explanation and symptomatic treatment. Smoking should be strongly discouraged; spirits and spicy food should be avoided.

An antacid, soluble paracetamol, or aspirin may all help. An NSAID, either orally or by suppository, may be used. The oesophagus can be coated with some effect by sucralfate.

Nausea and vomiting

Radiotherapy to the abdomen often causes nausea due to serotonin release. All patients should thus be considered for prophylactic anti-emetic therapy, e.g. 5-HT_3 antagonist.

Diarrhoea

This side effect frequently accompanies radiotherapy to the abdomen or pelvis. Dietary modification, i.e. reduction in dietary roughage, may sometimes relieve the diarrhoea. Antidiarrhoeal drugs (e.g. loperamide) should be provided to all patients with clear instructions of when and how they should be taken. Proctitis often accompanies rectal or prostatic irradiation and should be treated with rectal steroids either by suppository or enema.

Pneumonitis

Acute radiotherapy-induced pneumonitis can develop 1–3 months after treatment and is associated with a fever, dry cough, and breathlessness. The main differential diagnosis is pneumonia, and this should be excluded where possible. The diagnosis can be confirmed by a CXR, which shows lung infiltration confined within the treatment volume. Treatment is with a reducing course of steroids, i.e. a starting dose of prednisolone 40mg.

Cerebral oedema

Cerebral oedema can occur during or after cranial irradiation, particularly if no surgical decompression of the brain tumour or metastasis has been undertaken. Oedema usually responds to an increase in the dose of oral steroids (e.g. dexamethasone 4mg twice daily).

Somnolence syndrome

Somnolence syndrome occurs within a few weeks of the completion of brain irradiation and may manifest itself with nausea, vomiting, anorexia, dysarthria, ataxia, and profound lethargy. Recovery occurs spontaneously but can be accelerated with steroids.

Further reading

Jain V., Berman A. (2018) Radiation pneumonitis: old problem, new tricks. *Cancers*, **10**(7):222.

New developments

Radiotherapy has advanced markedly since the early days of the twentieth century. Progress is still being made to improve the quality and effectiveness of treatment for patients.

There are a number of areas of development.

Defining tumour volume

Improvements in imaging have enabled tumours to be targeted more accurately. This reduces the risk of missing the tumour, and also allows the treatment volume to encompass the tumour more closely. The dose of radiation can therefore be higher (giving improved tumour control) without risking additional toxicity to normal tissues.

Imaging

Refinements in CT scanning technology have led to the advent of the multislice CT scanner, which provides multiple high-quality images rapidly, from which tumour volumes may be defined not only in two but also in three and four dimensions (tracking a tumour during respiratory motion).

Images can now be fused from different imaging modalities, e.g. MRI/CT image fusion. The new development of co-registered CT/PET scanning combines functional data (through PET scanning) and high-quality spatial information (through CT scanning), providing opportunity for optimal target volume definition.

Conformal therapy

Imaging improvements provide the ability to identify the tumour target more accurately. This reduces the risk of missing the tumour, but it also provides the opportunity for conforming the treatment more closely to the tumour volume and thereby lessening damage to surrounding normal tissues. Taken further, conformal therapy may permit dose escalation with resulting improved tumour control rates, but without increased toxicity. Multileaf collimators within the treatment unit can automatically shape the treatment field, conforming it to the desired target shape.

Intensity-modulated radiotherapy (IMRT) takes this a step further; it is used widely and further improves the therapeutic ratio. With IMRT, the intensity of the treatment beams are modified in such a way that almost any three-dimensional volume may be generated. Even concave volumes may be created, and so targets which envelop the spinal cord, e.g. thyroid, can be treated much more satisfactorily than with conventional techniques.

During the verification stage of radiotherapy, image-guided radiotherapy (IGRT) describes how cone beam CT (CBCT) imaging can be acquired during the treatment process on the linear accelerator. This is used to ensure both the patient and tumour have been accurately positioned during radiotherapy treatment. Gross changes to the patient's anatomy (e.g. the development of a pleural effusion) can also be detected.

Fractionation/combined modality treatment

Advances in the understanding of the principles of fractionation have led to improved treatment outcomes for patients. Further research with hypo/hyperfractionation and acceleration is aimed at improving the therapeutic ratio.

Integration of chemotherapy with radiation treatment has provided benefit in a number of tumour sites, e.g. cervical cancer. Research seeks to refine this further and also to incorporate the newer molecular agents into radiation therapy.

Individualization of therapy

Two patients with ostensibly similar tumours receiving identical treatments may respond differently, one being cured and the other dying from cancer in a short time. There are clearly factors inherent within tumours which predict response to radiotherapy. If such variables were identified before treatment, the chance of response could be defined. This would help clinicians decide whether radiotherapy would be a good treatment option. Furthermore, it might be possible, knowing the particular tumour characteristics, to adapt the treatment course, perhaps by modifying the dose prescribed or the fractionation schedule, to enhance the prospect of cure. Predictive assays are being developed to realize this possibility. New microchip technology may help elucidate the genes behind the differing responses to therapy, and offer patients the possibility of treatment tailored to their individual needs.

Government funded screening (UK)

Currently in England, people are offered screening for breast, bowel, and cervical cancer on the basis that early detection and treatment will lead to improved survival. A large-scale UK study (SUMMIT) has recently been set up to detect lung cancer in those at risk (smokers and ex-smokers aged 50–77y).

Breast screening to detect early disease is offered every 3 years for all women registered with a GO who are aged 50–71y. Screening for bowel cancer is offered every 2 years to men between the ages of 60y and 74y. An additional one-off test (bowel scope screening) is being introduced at 55 years. Future screening will start at age 50. All women registered with a GP are invited every 3 years (25–49y) or 5 years (50–64y) for cervical screening. HPV primary screening is also being offered.

Further reading

Brennan P. *et al.* (2017) Intensity-modulated radiotherapy in head and neck cancer—an update for oral and maxillofacial surgeons. *The British Journal of Oral and Maxillofacial Surgery*, **55**(8):770–4.

Wegner R. *et al.* (2017) Trends in intensity-modulated radiation therapy use for rectal cancer in neoadjuvant setting: a National Cancer Database analysis. *Radiation Oncology Journal*, **36**(4):276–84.

Common cancers

Incidence

Huge variations in cancer incidences exist across the globe, reflecting the impact of environmental and genetic factors on the causes of cancer (Tables 6.7 and 6.8).

In this handbook, it is not possible to outline oncological management of all cancer types. The following cancers are the commonest, and those for which the palliative care team has a particular role to play (Figure 6.4).

Table 6.7 The eight commonest cancer types affecting men and women worldwide

Cancer type	Ratio, high:low rate	High incidence	Low incidence
Oesophagus	200:1	Kazakhstan	Holland
Skin	200:1	Australia	India
Liver	100:1	Mozambique	UK
Nasopharynx	100:1	China	Uganda
Lung	40:1	UK	Nigeria
Stomach	30:1	Japan	UK
Cervix	20:1	Hawaii	Israel
Rectum	20:1	Denmark	Nigeria

Reproduced from Souhami R.L., Tobias J.D. (2003) *Cancer and its Management* (4th edn). Oxford: Blackwell Science with permission from Wiley.

Table 6.8 The eight commonest cancer types affecting men and women in the UK, 2014

Men	Women
Prostate	Breast
Lung	Lung
Colorectal	Colorectal
Head and neck	Melanoma
Kidney	Ovary
Melanoma	Non-Hodgkin's lymphoma
Non-Hodgkin's lymphoma	Brain/CNS
Bladder	Pancreas

Data sourced from Cancer Research UK. http://www.cancerresearchuk.org/health-professional/cancer-statistics/incidence/common-cancers-compared#heading-One. Accessed April 2018.

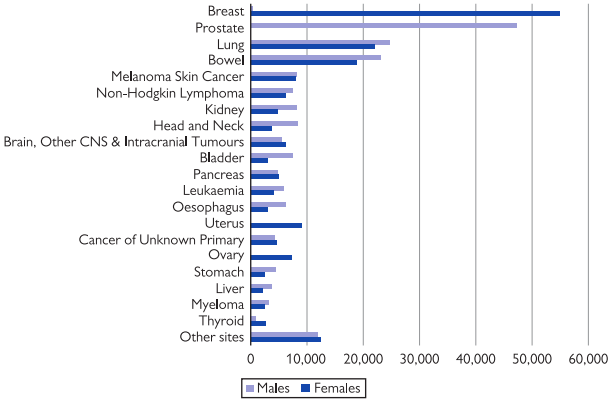


Fig 6.4 Cancer Research UK statistics from 2016 for the 20 most common cancers by sex.

Patients with lung cancer

Background

- most common cause of cancer deaths in men and women in the UK and the US
- 80–90% due to smoking
- 80% are non-small-cell subtype (squamous, adenocarcinoma, or large-cell)
- 20% are small-cell subtype

Symptoms at presentation

- cough
- haemoptysis
- chest pain
- recurrent chest infection
- hoarseness

Diagnosis and staging

Diagnosis

- CXR
- sputum cytology
- bronchoscopy with biopsy
- bronchial brushings and washings
- CT-guided biopsy

Staging

- bronchoscopy
- CT scan of chest, liver, and adrenals
- PET scanning (if available)
- mediastinoscopy
- pleural aspiration, pleural biopsy
- bone and brain scan if symptomatic

Small-cell lung carcinoma

Small-cell lung carcinoma (SCLC) is generally believed to be a systemic disease at diagnosis; thus surgery generally plays no part in the management of this disease.

Staging

- limited stage disease—disease confined to one hemithorax
- extensive stage disease—disease present beyond one hemithorax

Management

- Because of chemoresponsiveness and frequent dissemination at diagnosis, combined chemotherapy is the treatment of choice.
- Many chemotherapeutic agents have demonstrated activity in this disease. Etoposide plus cisplatin or carboplatin has been established as the best first-line treatment. Cyclophosphamide/doxorubicin/vincristine, topotecan, or taxanes can be effective second-line treatments.
- For patients with limited stage disease, thoracic irradiation in addition to chemotherapy improves local disease control and prolongs survival

when compared with chemotherapy alone. Prophylactic cranial irradiation reduces the incidence of brain metastases and improves survival in patients who have responded to chemotherapy.
- Further radiotherapy may be a useful palliative treatment for patients relapsing after or resistant to chemotherapy.

Prognosis

Approximately 80% of patients respond to chemotherapy, but the majority relapse, and only approximately 10% of patients are alive 2 years after diagnosis.

Non-small-cell lung carcinoma

Non-small-cell lung carcinoma (NSCLC) metastasizes later in its course than small-cell lung cancer, and consequently surgery offers the best chance of cure. All patients being considered for surgical treatment must be carefully staged (refer to the latest TNM staging tables) to determine tumour operability. The patient must also be carefully assessed preoperatively to assess their fitness for surgery.

Perioperative mortality rate should be less than 5%.

See Table 6.9.

Management

Surgery

Surgical resection offers the best chance of cure in this disease. The aim of surgery is to resect the primary tumour with clear lateral and bronchial margins with draining peribronchial and hilar lymph nodes. Lobectomy is the most commonly performed operation; however, a bilobectomy or pneumonectomy may be performed for more extensive tumours.

Conversely, in less fit patients with limited respiratory reserve, only a partial lobectomy may be tolerated, although the results from this surgery in terms of the risk of tumour recurrence may be inferior.

NSCLC radiation therapy

Radical radiotherapy

Selected patients with Stage I–III disease and who are technically unsuitable or medically unfit for surgery may be suitable for radical radiotherapy. Five-year survival rates of 15–20% have been reported in this highly selective patient group.

The benefit of adjuvant radiotherapy following surgery for high-risk disease is uncertain, but may reduce the risk of local disease relapse.

Table 6.9 Stage grouping

IA	$T_{1a\text{-}1b}\ N_0\ M_0$
IB	$T_{2a}\ N_0\ M_0$
IIA	$T_{1a\text{–}2a}\ N_1$ or $T_{2b}\ N_0\ M_0$
IIB	$T_{2b}\ N_1$ or $T_3\ N_0\ M_0$
IIIA	$T_{1a\text{–}2b}\ N_2$ or $T_3\ N_{1\text{–}2}$ or $T_4\ N_{0\text{-}1}\ M_0$
IIIB	$T_4\ N_2\ M_0$; or any T $N_3\ M_0$
IV	Any M_{1a} or M_{1b}

Palliative radiotherapy

Radiotherapy is a key component of symptomatic treatment for the following:

- haemoptysis
- chest pain
- dyspnoea due to bronchial occlusion
- pain from bone metastasis
- symptoms from brain metastasis

NSCLC-targeted treatments

Genetic alterations have been identified in NSCLC, with two of these—epidermal growth factor receptor (EGFR) mutation and anaplastic lymphoma kinase (ALK) rearrangement—determining specific targeted treatment pathways. EGFR mutations are predictive for response to the EGFR TKIs erlotinib, gefitinib, and afatinib. Such treatments when used first-line give better response rates, progression-free survival, tolerability, and quality of life than platinum-based chemotherapy. ALK rearrangements predict for response to the ALK TKIs crizotinib and ceritinib.

NSCLC chemotherapy

NSCLC is much less chemosensitive than SCLC. Adjuvant platinum-based chemotherapy following surgery confers a modest survival benefit. Chemotherapy may also be used in the neoadjuvant setting to downstage a tumour prior to consideration of surgery. Cisplatin- or carboplatin-based therapy has been demonstrated to improve quality of life and survival in patients with good performance status (ECOG performance scale 0–1) in the palliative setting. Commonly used regimens include combinations of carboplatin or cisplatin with paclitaxel, vinorelbine, or gemcitabine.

NSCLC immunotherapy

For those patients who progress on chemotherapy, immunotherapy using a PD-1 or PD-L1 inhibitor can be considered.

General issues

Lung cancer, because of its link with smoking, both active and passive, may be associated with emotional distress in the patient and their carers. Lung cancers often occur on top of a background of pre-existing lung disease, which may alter the patient's perception of breathlessness and cough, thereby leading to a delay in diagnosis.

Specific pain issues

- **Pleuritic pain** may be associated with the tumour itself, metastases in the ribs, or local inflammation. This type of pain responds well to NSAIDs. It may also be helped by local nerve blockade.
- **Pancoast tumour** at the lung apex can produce severe neuropathic pain by invasion of the brachial plexus; it may only be partially opioid-responsive and will need adjuvant analgesics. Early referral for specialist help should be considered.
- **Bone metastases** may occur, putting the patient at risk of pathological fractures and spinal cord compression. Management of consequent pain may be difficult, and specialist advice should be sought.

Other complications

- **Breathlessness** is common and can be very distressing for carers (➔ see Chapter 10, Respiratory symptoms). Treat reversible causes, such as anaemia and pleural effusion, where appropriate. Give clear explanations of what is happening. Ensure that practical measures such as sitting upright, opening windows, and using fans have been discussed with the family. Regular doses of short-acting oral morphine every 2–4 hours may decrease the sensation of breathlessness. Other more specialist interventions such as palliative radiotherapy, endobronchial laser therapy, and stenting may help some patients. Panic and anxiety are frequently associated with breathlessness and may be helped by simple relaxation techniques. A low dose of an anxiolytic such as diazepam may be helpful,
- **Haemoptysis** is a frightening symptom. Palliative radiotherapy may be effective if the patient is fit enough. Oral antifibrinolytics such as tranexamic acid may help. Occasionally, frequent small episodes herald a catastrophic haemoptysis. This is rare, but it is a difficult situation to manage, and early involvement of specialists should be considered. The risks of frightening a family with information about a possible risk of catastrophic haemoptysis need to be balanced against the potential distress that could be caused by leaving a patient and family unprepared.
- **Cough** can exacerbate breathlessness and pain, and affect sleep and a patient's ability to eat. Its management will depend on the cause, but it is often appropriate to try to suppress the cough pharmacologically using codeine linctus or morphine. If not responding to simple measures, refer for specialist assessment.
- **Hypercalcaemia** may occur. It should be considered in any patient with persistent nausea, thirst, altered mood, confusion (even if intermittent), worsening pain, or constipation. It should be treated with IV hydration and bisphosphonates, unless the patient is clearly dying, in which case treatment is not appropriate.
- **Cerebral metastases** are common. Decisions about investigation and management may be complex and need to be made on an individual basis. Altered behaviour and personality, as well as problems of comprehension and communication, can be very distressing for relatives. Persistent headache, worse in the mornings, and unexplained vomiting may be early signs of this diagnosis. There is a risk of seizures; prophylactic anticonvulsant medication may be appropriate.
- **Hyponatraemia** and other biochemical imbalances are particularly common in small-cell lung cancer. Management can be complex and needs specialist input.
- **Altered taste and anorexia** are common. Good oral hygiene and effective treatment of oral candidiasis may help. Carers may find it helpful to talk through different ways of encouraging the patient to eat, such as freezing supplement drinks and making frequent small meals.
- **Superior vena cava obstruction (SVCO)** can occur, particularly in patients with right upper lobe lung cancers. Management includes consideration of vascular stenting, radiotherapy, and high-dose oral steroids.

Mesothelioma

General comments

Mesothelioma usually affects the pleura but can affect other mesothelial linings, most commonly the peritoneum. It is associated with exposure to asbestos, although, unlike patients with asbestosis, the history may be difficult to elicit, as the risk of mesothelioma appears unrelated to the length of exposure to asbestos and may occur many years after such exposure. It is a relentlessly progressive tumour.

It is important that the patient is aware that they may be entitled to compensation and should consult a specialist lawyer about this.

All deaths due to mesothelioma should be discussed with the coroner, who will most probably order a post-mortem, unless the disease was clearly not related to industry. The patient, and family, to minimize distress at the time of death, should be made aware that the coroner will be contacted (regardless of any compensation claims or litigation).

Diagnosis

- CXR
- CT scan of chest
- pleural biopsy
- thoracoscopic biopsy

There is a high incidence of false-negative biopsies—in some cases these may need to be repeated a number of times to make a diagnosis.

Treatment

Surgery

Radical surgery is of uncertain value, with a high mortality and few long-term survivors reported. Palliative surgery with parietal pleurectomy and decortication of the lung may offer excellent palliation with minimal morbidity.

Radiotherapy

The tumour may grow along the track of a biopsy or drainage needle to produce a cutaneous lesion. These areas can become painful and ulcerated, and can be difficult to manage. Hence, palliative radiotherapy is given prophylactically following the biopsy. It may also be used locally for established cutaneous spread.

Chemotherapy

Upfront chemotherapy with doublet combination of cisplatin and pemetrexed has been shown to improve overall survival and time to progression. Carboplatin is an acceptable alternative to cisplatin and may be better tolerated in the elderly population. Immunotherapy with checkpoint inhibitors may offer promise for disease control, but further clinical study is required.

Specific problems in the management of mesothelioma

- **Pleural effusions** are common and frequently blood-stained, and become increasingly difficult to aspirate as the disease progresses. Surgical intervention to prevent reaccumulation of fluid may be helpful if carried out early enough.
- **Breathlessness** can be severe due to pleural disease limiting the capacity and expansion of the lung as well as the occurrence of pleural effusions. Give clear explanations of what is happening. Ensure that practical measures, such as sitting the patient up, opening windows, and using fans have been discussed with the family. Regular doses of short-acting oral morphine every 2–4 hours may decrease the sensation of breathlessness. Panic and anxiety are frequently associated with breathlessness and may be helped by simple relaxation techniques. A low dose of an anxiolytic such as diazepam may be helpful. Other treatment options are limited.
- **Ascites** occurs with peritoneal mesothelioma. The ascitic fluid is often blood-stained and becomes increasingly difficult to aspirate as the disease progresses.

Specific pain complexes

Mesotheliomas can produce severe neuropathic pain which may only be partially opioid-responsive, and may need adjuvant analgesics. Early referral for specialist help should be considered. Local nerve blockades can help in some cases.

Further reading

Sanganalmath P. *et al.* (2018) Continuous hyperfractionated accelerated radiotherapy (CHART) for non-small cell lung cancer (NSCLC): 7 years' experience from nine UK centres. *Clinical Oncology*, **30**(3):144–50.

Colorectal cancer

Background

- third-commonest cancer worldwide
- approximately 50% of tumours occur in the rectum or sigmoid colon
- dietary factors are thought to be important
- tumour often secretes carcinoembryonic antigen (CEA)
- 6–8% of cases are familial
- associated syndromes include familial adenomatous polyposis coli and hereditary non-polyposis coli (Lynch syndrome)

Common presentations

- iron deficiency anaemia
- abdominal pain
- altered bowel habit
- PR bleeding

Staging and diagnosis

- sigmoidoscopy
- colonoscopy—all patients must have a full evaluation of the colon prior to surgery
- barium enema (less useful than colonoscopy)
- CT scan of chest, abdomen, and pelvis
- MRI/endorectal ultrasound may be useful to assess local extent of tumour in the rectum

Management

Surgery for primary disease

Surgery is the mainstay of therapy for colorectal cancer.

For colonic tumours, a segment of colon with its blood supply and draining nodes is excised. Depending on the site of the tumour, this may involve a right or left hemicolectomy or a sigmoid colectomy.

Traditionally, surgery for rectal tumours has involved an abdomino-perineal approach. In the absence of radiotherapy, local relapse rates of 25–30% have been reported. Previously, radiotherapy has been used post-operatively, but increasingly a short course of radiotherapy is being used to 'sterilize' the area prior to surgery. In more advanced disease, preoperative chemoradiotherapy can downstage the disease to allow for less radical surgery and can also reduce the risk of pelvic recurrence. Surgery now typically involves the more meticulous procedure of total mesorectal excision and an anterior resection preserving the anus and reducing local relapse rates to less than 10%.

Surgery for hepatic metastases

The majority of patients develop liver metastases as the first site of disease progression following definitive first-line treatment.

A proportion of these patients may be suitable for metastasectomy. Up to a 40% five-year survival has been reported for carefully selected patients.

Chemotherapy

Adjuvant chemotherapy of colorectal cancer

Several large, randomized controlled trials have demonstrated a clear survival advantage to fluorouracil-based or capecitabine therapy following surgery for patients with Stage III disease. The addition of oxaliplatin to fluorouracil increases the benefit.

The value of adjuvant chemotherapy for patients with Stage II disease is less clear, but chemotherapy may be offered to patients with tumours that exhibit adverse prognostic features, such as lympho-vascular invasion or poorly differentiated tumour.

Chemotherapy for advanced colorectal cancer

In the last 10–15 years, there have been major advances in the treatment of metastatic colorectal cancer. Previously, fluorouracil (FU) was the sole active agent, and overall survival was approximately 11–12 months. Currently the average median survival duration is approaching 3 years, and 5-year survival rates as high as 20% are reported in some trials. These improvements have occurred on account of the availability of new active agents, which include conventional cytotoxic agents other than FU, and biological agents targeting angiogenesis and the epidermal growth factor receptor (EGFR). Doublet chemotherapy with the addition of oxaliplatin or irinotecan to FU improves survival and response rates.

Capecitabine is an orally available pro-drug of fluorouracil, which is equally effective but more convenient, and has a different side-effect profile.

Biological therapy

Bevacizumab is a monoclonal antibody that targets vascular endothelial growth factor (VEGF) and is an angiogenesis inhibitor. When added to chemotherapy regimens, time to progression and overall survival are improved. The EGFR-targeted monoclonal antibodies cetuximab and panitumumab can be added to chemotherapy regimens to improve response and survival rates for those patients whose tumours do not express activating RAS/BRAF mutations.

Immunotherapy

Immune checkpoint inhibitors are used for patients with mismatch repair-deficient, microsatellite instability-high tumours.

General comments

- **Liver metastases** often occur and may cause capsular pain. This usually responds well to NSAIDs or steroids. Liver metastases may also lead to hepatomegaly, causing squashed stomach syndrome with delayed gastric emptying and a feeling of fullness. This may respond to a prokinetic agent such as metoclopramide.
- **Perineal and pelvic pain** may be caused by advancing disease or be iatrogenic. There is nearly always a neuropathic element to the pain which will only be partially opioid-sensitive. Tenesmus is a unique type of neuropathic pain which requires specialist assessment.
- **Bowel obstruction**, unless it can be palliated surgically, should be managed medically using a syringe driver containing a mixture of analgesics, anti-emetics, and antispasmodics. Bowel obstruction at

multiple levels, which is common in relapsed disease, may make surgery inappropriate. Differentiating between a high blockage (where vomiting is a feature) and blockage lower in the bowel can be useful in targeting treatment strategies. Imaging techniques may also be helpful to delineate the level of obstruction.

- **Fistulae** between the bowel and the skin or bladder may occur. These can be very difficult to manage and require a multidisciplinary approach with specialist input.
- **Rectal discharge and bleeding** are unpleasant and difficult symptoms to manage. Referral to a clinical oncologist is appropriate, as radiotherapy may be of benefit.
- **Hypoproteinaemia** is common owing to poor oral intake and poor absorption from the bowel, and may lead to lower-limb oedema.
- **Poor appetite** is not uncommon and can be helped with the use of steroids.

Breast cancer

Background

Breast cancer is the commonest solid tumour occurring in women in Europe and the US.

- lifetime risk for females in the UK is 1 in 8
- factors which increase the risk of breast cancer include increasing age, a family history of breast cancer, nulliparity, and the use of HRT or the contraceptive pill
- incidence of breast cancer is increasing, although overall mortality has decreased by 20% in the UK since 1985
- 5-year survival rate is 80%
- male breast cancer is rare—accounting for <1% of all breast cancers

Genetics of breast cancer

5–10% of breast cancers are believed to be hereditary. Many of these cancers are due to germline mutations in the tumour-suppressor genes *BRCA1* or *BRCA2*. Prophylactic bilateral mastectomy will reduce the incidence of breast cancer by 90% in patients with proven mutations in the *BRCA1* or *BRCA2* gene.

Presentation

- breast lump (most common)
- mammographically detected lesion—increasingly common mode of presentation
- nipple inversion or discharge
- occasionally rash at nipple (Paget's disease)

Pathology

See Box 6.1.

Diagnosis and staging

Breast cancer is diagnosed by a 'triple assessment':

- clinical examination
- imaging: bilateral mammography (or ultrasound/MRI)
- biopsy: fine-needle aspiration cytology or core biopsy

Box 6.1 Pathology

Preinvasive lesions

Lobular carcinoma *in situ* (LCIS)—significance uncertain
Ductal carcinoma *in situ* (DCIS)—usually detected mammographically; may progress to invasive disease

Invasive lesions

Ductal carcinoma—not otherwise specified—accounts for approximately 80% of all tumours
Lobular carcinoma
Tubular carcinoma
Medullary carcinoma

This approach has >90% sensitivity and specificity.

All patients with proven invasive disease should have the axilla assessed as part of staging. Traditionally, this includes axillary clearance, but increasingly sentinel node biopsy is performed. Staging investigations (such as liver or bone scans) in patients without systemic symptoms rarely detect metastases and are recommended only in patients with four or more lymph nodes involved by tumour.

Prognostic factors

- axillary node involvement: most important prognostic criterion
- tumour grade
- oestrogen receptor (ER)/progesterone receptor (PR) status: more favourable prognosis if ER/PR positive
- HER2 status: *HER2* overexpression is associated with poor prognosis
- patient age: <35years is an independent adverse prognostic factor

Common problems

- **Bone pain** due to bone metastases, which may respond to radiotherapy, bisphosphonates, or systemic therapy. Prophylactic surgery may be indicated where there is a risk of fracture.
- **Pathological fractures** may occur without obvious trauma.
- **Spinal cord compression** requires prompt diagnosis, high-dose oral steroids, and urgent referral to the orthopaedic- or neurosurgeon, or oncologist. The steroids should be continued at a high dose until a definitive plan has been made.
- **Neuropathic pain** can be a problem, if there has been spread into the axilla affecting the brachial plexus.
- **Liver metastases** are common and may require steroids or NSAIDs to reduce the pain of liver capsule distension.
- **Hypercalcaemia** may occur. Treatment with IV hydration and IV bisphosphonates should be considered.
- **Lymphoedema** affecting the arm can develop at any point in the course of the disease, following surgery and/or radiotherapy. Early referral to a lymphoedema specialist provides the best chance of minimizing the morbidity and distress caused. Preventive measures include good skin care and avoiding additional trauma to the affected arm (such as taking of blood tests and BP measurement). Treatment involves bandaging, lymphatic massage, and fitting a compression sleeve.
- **Lung and pleural spread** are common causes of breathlessness and cough. These symptoms need to be investigated thoroughly. Drainage of a pleural effusion may be a useful symptomatic procedure, and pleurodesis should be considered. Systemic therapy (chemotherapy or hormone therapy) is indicated in patients with good performance status.
- **Psychosocial problems**: some of these patients will be mothers with young children for whom the trauma of disease is worsened by fears for their children. A multidisciplinary supportive approach at a pace dictated by the patient can help to reduce some of the distress for the patient and her family.

Management

See Table 6.10.

Table 6.10 Management

Non-invasive breast cancer DCIS	Simple mastectomy or partial mastectomy (lumpectomy) +/- post-operative radiotherapy. Axillary dissection not indicated.
Early breast cancer Example of treatment	**Surgery:** either simple mastectomy or partial mastectomy (lumpectomy) +/- axillary node dissection.
	Loco-regional radiotherapy: indicated for all patients with partial mastectomy and for mastectomy patients at high risk of local relapse (e.g. patients with T_3 or T_4 tumours or positive lymph nodes).
	Adjuvant endocrine therapy: should be commenced after completion of chemotherapy. Tamoxifen is indicated for all ER- or PR-positive tumours and achieves approximately 30% relative reduction in mortality. Aromatase inhibitors are preferred to tamoxifen in post-menopausal women because of improved outcomes and tolerability.
	Adjuvant chemotherapy: Combination chemotherapy reduces recurrence and improves overall survival. Anthracycline-based regimens are more effective than non-anthracycline-based regimens; incorporation of a taxane further improves efficacy. Absolute 10-year survival benefit: 7–12% <50 years; 2–6% >50 years.
	Commonly used regimens include fluorouracil/epirubicin/cyclophosphamide (FEC), docetaxel/doxorubicin/cyclophosphamide (TAC), doxorubicin/cyclophosphamide (AC), cyclophosphamide/methotrexate/fluorouracil (CMF). The benefit:risk ratio for chemotherapy must be assessed on an individual patient basis.
	Adjuvant trastuzumab: results of large clinical trials have shown significant improvements in relapse-free and overall survival with the addition of adjuvant trastuzumab in patients with tumours that overexpress HER2.
	Neoadjuvant therapy: has advantage in allowing more patients to have breast-conserving surgery and is also an option for patients with medical contraindications to undergoing surgery at the time of diagnosis, such as those women who develop breast cancer during pregnancy.
Locally advanced breast cancer *Presence of infiltration of the skin, chest wall, or fixed axillary nodes*	The presence of infiltration of the skin, chest wall, or fixed axillary nodes requires a *neoadjuvant* approach. Younger patients and those with ER/PR-negative disease may need chemotherapy. Elderly patients with ER- or PR-positive disease may be treated with hormonal therapy alone (aromatase inhibitors are superior to tamoxifen in this setting).

Metastatic breast cancer *The aim is palliation. Usual sites of metastases: lung, liver, bone, brain.* *Bone metastases often respond to hormone manipulation; such patients may survive for many years.*	**Endocrine therapy:** indicated in those patients with ER- or PR-positive disease and slowly progressive disease. Responses tend to be slower in onset (3–6 months) than with chemotherapy but also tend to be more durable. Expected response rates of 40–60% to first-line hormonal therapy in those with ER- and/or PR-positive tumours. Disease that responds to endocrine therapy and then progresses has a 25% response with second-line treatment. Response to a third hormonal agent is 10–15%. In recent years the kinase inhibitor everolimus given in combination with exemestane has been shown to improve progression-free survival.
	Chemotherapy: indicated in situations where a high response rate and rapid time to response are required. Anthracycline-based regimens are used in patients if they have not already been used in the adjuvant setting. First-line response rates are of the order of 40–60%. Taxanes are used in patients who have had prior exposure to anthracyclines with similar response rates. In patients with HER2 overexpression, addition of trastuzumab plus pertuzumab increases response rate and prolongs survival. At progression, second-line HER2-directed treatment with trastuzumab emtansine or lapatinib can be offered. In patients unfit for chemotherapy, trastuzumab may be used as a single agent. Other chemotherapy agents with activity include capecitabine, carboplatin, vinorelbine, eribulin, and liposomal doxorubicin.
	Radiotherapy: useful for palliation of painful bone metastases, brain metastases, or soft-tissue metastases causing pressure effects.
	Osteoclast inhibition: for patients with bone metastases, there are two main agents used: bisphosphonates and denosumab. Such agents have been demonstrated to reduce bone pain, skeletal events related to malignancy, and the incidence of hypercalcaemia.

Further reading

Bhattacharya I.S. *et al.* (2019) Patient-reported outcomes over 5 years of whole- or partial-breast radiotherapy. *Journal of Clinical Oncology*, **37**(4):305–17.

Sardar P. *et al.* (2017) Long term cardiovascular mortality after radiotherapy for breast cancer: a systematic review and meta-analysis. *Clinical Cardiology* **40**(2):73–81.

Prostate cancer

Background

- accounts for approximately 25% of all cancers in men in the UK
- second to lung cancer as a cause of cancer deaths in men
- increasing age is a major risk factor: 70% of men >80 years of age have some evidence of prostatic cancer
- associated with a 78% five-year survival
- appears to be linked to androgen exposure: rare in men castrated before 40 years of age
- incidence of prostate cancer is rising, owing, in part, to increased detection of early disease by PSA (prostate-specific antigen) screening
- many PSA-detected cancers are clinically unimportant; more research is needed to distinguish patients with raised PSA levels who are at risk of developing metastatic disease

Presentation

- urinary outflow symptoms
- haematuria
- symptoms of metastatic disease, e.g. back pain
- asymptomatic elevation of PSA

Diagnosis and staging

- PSA assessment: PSA >4ng/mL: clinical suspicion, requires transurethral ultrasound and needle biopsy
- PSA >50ng/mL: often distant metastases
- transurethral ultrasound and biopsy
- CT/MRI—may help to assess lymph node involvement
- isotope bone scan
- for staging, refer to the latest TNM staging tables

Management

Many prostate tumours are clinically insignificant and will not cause symptoms in the patient's lifetime. It is important, however, to recognize those patients whose tumours are likely to become clinically apparent.

Prognostic factors in patients with cancer confined to the prostate:

- tumour grade: assessed by Gleason score
- tumour stage: assessed clinically and radiologically
- patient age: younger patients are more likely to develop advanced disease than older patients

Cancer confined to prostate gland

If aged <70 and fit, consider radical localized therapy:

- prostatectomy
- radiotherapy-external beam or brachytherapy

There are currently no trials directly comparing these approaches.
In general terms, fitter patients tend to be treated with surgery rather than radiotherapy.

Complications

- prostatectomy: 50% impotence; 8–15% long-term incontinence
- radiotherapy: 40% impotence; rectal stricture/bladder irritation but no incontinence

If aged >70 years

- active surveillance policy: active process of examining patient regularly and treating if evidence of disease progression

Locally extensive disease (T_3/T_4) or Node N_1 disease

- Neoadjuvant anti-androgen therapy followed by radical radiotherapy

Metastatic disease

The natural history is highly variable, with a number of patients with metastatic bone disease living for >5 years following diagnosis.

The majority of tumours are driven by androgens. Hormonal manipulation or androgen deprivation therapy (ADT) aimed at reducing the effect of androgens (mainly testosterone) at a cellular level will produce responses in around 70% of men with bone metastases with a median response duration of 12–18 months.

Commonly used hormonal treatments:

- **Medical castration** with luteinizing hormone-releasing hormone (LHRH) agonists. (These can induce a flare-up of hormone-induced activity on initiating therapy which needs to be suppressed with anti-androgens for the initial 2 weeks.)
- **Anti-androgens** (cyproterone acetate, flutamide, bicalutamide). These may be used alone or in combination with LHRH agonists. The value of the combination is, however, uncertain.
- **Oestrogens**, such as diethylstilbestrol (stilboestrol), may be used after other hormones have failed. Diethylstilbestrol is used at lower doses than previously to minimize thromboembolic side effects.
- **Bilateral orchidectomy** is less popular owing to the availability of medical methods of castration.

The side effects of androgen suppression include the following:

- loss of libido and potency
- hot flushes
- change in fat deposition
- osteoporosis
- poor concentration
- decreased energy and drive
- metabolic syndrome

For fit patients with high-volume metastatic hormone naive disease, the addition of docetaxel chemotherapy to ADT has been shown to provide improved progression-free and overall survival rates.

Local radiotherapy may be useful as an additional palliative measure particularly for bone pain. Strontium-89 and samarium-153—bone-seeking radioisotopes—have proved effective, though expensive, treatments for reducing bone pain.

Hormone refractory prostate cancer

For patients whose disease has progressed through traditional anti-androgen therapy, there are further hormone treatment options and chemotherapy agents.

Therapeutic options at this stage include the following:

- **Anti-androgen withdrawal**: this results in a response in a small number of patients.
- **Glucocorticoids**: low-dose glucocorticoids, such as dexamethasone 1mg o.d., produce clinical benefit in some patients.
- **Enzalutamide**, a non-steroidal anti-androgen, has shown improvements in the time to disease progression and median survival rates as well as patient-reported pain and quality of life scores.
- **Abiraterone** is an androgen synthesis inhibitor used in combination with low-dose prednisolone. It has been shown to improve time to progression and overall survival. Pain palliation and PSA decline were also improved.
- **Chemotherapy**: prostate cancer is relatively chemoresistant. Docetaxel and prednisolone improve symptoms with a modest survival improvement but are appropriate only for fitter patients. For patients who progress on docetaxel and who remain fit enough for chemotherapy, cabazitaxel is available second-line.

Common palliation issues

- **Pathological fracture** may occur without obvious trauma. Orthopaedic intervention (pinning or joint replacement) and radiotherapy may be needed. Prophylactic orthopaedic intervention may also be required for bone lesions at high risk of fracture.
- **Spinal cord compression** requires prompt diagnosis and treatment with high-dose steroids and radiotherapy. A minority of cases may be suitable for surgical intervention; such patients include those with a single site of disease and those in whom there is uncertainty regarding the diagnosis. These patients should be discussed with a neurosurgeon.
- **Neuropathic pain** may be caused by local recurrence of tumour, pelvic spread, or a collapsed vertebra. Such pain is partially opioid-sensitive, and adjuvant analgesics are usually required to supplement the effect of the opioid.
- **Bone pain**: specialist advice should be sought about the appropriate use of radiotherapy and radioactive isotopes as well as nerve blockade. The RANK ligand inhibitor denosumab and bisphosphonates such as zoledronic acid help to reduce bone pain and also reduce the number of cancer-associated skeletal events and incidence of hypercalcaemia.
- **Bone marrow failure** may occur in patients with advanced disease. Typically, the patient has symptomatic anaemia and thrombocytopenia. Support with palliative blood transfusions may be appropriate initially, but ongoing appropriateness should be discussed with the patient and their family when symptomatic benefit is no longer being gained.
- **Retention of urine**: problems with micturition, including haematuria (forming blood clots), may lead to retention of urine. This may be acute and painful, or chronic and painless. If the patient is unfit for transurethral resection of the prostate (TURP), then consider a

permanent indwelling urinary catheter. Chronic urinary retention can lead to renal failure.

- **Lymphoedema** of the lower limbs and occasionally the genital area is usually due to advanced pelvic disease. It needs to be actively managed if complications are to be avoided.
- **Altered body image and sexual dysfunction** can result from the disease or any of the treatment modalities. This may be exacerbated by apathy and clinical depression. Specialist mental and psychological health strategies may be required.

Further reading

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Gynaecological cancer

Ovarian carcinoma

Background

- sixth-commonest cancer in women in the UK
- median age at diagnosis 66 years
- approximately 5% are familial
- 95% of tumours are epithelial in origin
- risk is reduced by factors that reduce the number of ovulatory cycles, e.g. pregnancy, use of oral contraceptive pill

Presentation

Ovarian cancer spreads intraperitoneally and may remain silent until late: 80% of patients present with disease which has spread beyond the pelvis.

Common presenting symptoms:

- abdominal distension
- abdominal pain
- altered bowel habit
- weight loss

Diagnosis and staging

Preoperatively, a diagnosis of ovarian cancer may be suspected if the marker CA-125 is raised (elevated in approximately 85% of patients with advanced disease) and a CT scan shows the presence of a pelvic mass or ascites.

Confirmation of the diagnosis requires histology. Adequate staging and initial disease management require total abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy, lymph node sampling, and multiple peritoneal biopsies.

Management

Radical surgery has an important role in treatment, and retrospective studies demonstrate significantly improved survival rates in patients whose disease has been optimally debulked (i.e. no tumour remaining measuring >1cm in diameter). Where optimal debulking is not possible initially, there may be a benefit to survival from performing debulking surgery after three cycles of chemotherapy—the so-called interval debulking.

First-line chemotherapy

After surgery, a platinum/taxane combination is considered by most oncologists to be the optimum treatment for ovarian cancer, the most commonly used combination being carboplatin and paclitaxel. Response rates are about 70–80%, and median survival is 2–3 years with such treatment.

Although the introduction of paclitaxel has improved the median survival in this disease, the majority of patients develop progressive disease, and 5-year survival is still less than 25%.

Bevacizumab in addition to chemotherapy can be considered for patients with suboptimally debulked disease (residual disease >1cm).

Treatment at relapse

The vast majority of patients who relapse after first-line therapy are incurable. Secondary surgical debulking may be useful in selected patients, but its value is uncertain. The choice of further chemotherapy depends on the interval between completion of previous chemotherapy and relapse.

Patients relapsing more than 6 months after the completion of platinum-based therapy are considered to have platinum-sensitive disease and should generally be rechallenged with a platinum agent. If rechallenge takes place more than 2 years from previous chemotherapy, the response rate is 60%, whereas rechallenge within 6 months rarely results in tumour response.

Patients relapsing less than 6 months after completion of platinum-based chemotherapy are considered platinum-resistant and are unlikely to respond to further platinum-based therapy. Paclitaxel, topotecan, liposomal doxorubicin, and gemcitabine have been shown to have some activity, but overall response rates remain low. Treatment of these patients should focus on quality of life and control of symptoms.

Eventually, all patients who relapse following primary chemotherapy will develop chemotherapy-resistant disease. The majority of these patients will have symptoms related to intra-abdominal disease, including abdominal pain and bowel obstruction. Management of these symptoms can be very challenging and requires a multidisciplinary approach with involvement of palliative physicians, surgeons, and oncologists.

Carcinoma of the cervix

Background

- strongly associated with human papillomavirus (HPV)-16 (and also, but less strongly, with HPV-18 and -31)
- 30–40% of patients with untreated cervical intraepithelial neoplasia progress to invasive squamous-cell carcinoma with a latent period of 10–20 years
- commonest female cancer in South-East Asia, Africa, and South America
- in the UK, incidence and mortality have fallen by approximately 40% since the 1970s; likely to fall further following initiation of the HPV vaccination programme

Presentation

- unless detected at screening, it is often asymptomatic until the disease is advanced
- postcoital bleeding
- intermenstrual bleeding
- pelvic pain
- dyspareunia

Staging

MRI plays an increasingly important role in the preoperative staging of these tumours.

Management

Management depends largely on disease stage. Patients with very early stage may be treated with simple hysterectomy or a conization procedure in patients wishing to preserve fertility.

Radical hysterectomy or pelvic radiotherapy may be used in more advanced disease; a combination of radical pelvic radiotherapy and platinum-based chemotherapy gives good results. Chemoradiotherapy may also be indicated, particularly with bulky tumours.

For patients with late stage disease, pelvic radiotherapy may be useful in palliating troublesome pelvic symptoms. Cervical cancer is only moderately chemosensitive, with responses to single agents of around 20–30%. Agents with some activity in this disease include cisplatin, ifosfamide, and paclitaxel.

Palliative issues in gynaecological cancers

- **Primary treatment** often affects sexual function, fertility, and body image, which may impact on coping strategies and need specialist counselling. Ovarian and vulval cancers often present late, and specialist palliative care input from the point of diagnosis may be appropriate. Genetic counselling should be considered for close female relatives of patients with ovarian cancer, particularly if there is also a strong family history of breast cancer.
- **Perineal and pelvic pain** is common in all three of the common gynaecological malignancies—cervical, ovarian, and vulval carcinomas. There is usually a neuropathic element to the pain which may be only partially opioid-sensitive.
- **Lymphoedema affecting one or both limbs** develops with uncontrolled pelvic disease. It can develop at any time in a patient's cancer journey and frequently affects both lower limbs. This needs to be actively managed if complications are to be avoided. Management includes good skin care, avoiding additional trauma to the affected leg(s), and appropriately fitting compression garments.
- **Ascites** is common with ovarian cancer and can be difficult to manage. Oral diuretics, particularly spironolactone in combination with a loop diuretic such as furosemide, may provide a little help. Repeated paracentesis may be needed. Consideration of a peritoneovenous shunt may be appropriate in some cases where prognosis is thought to be longer than 3 months.
- **Acute or subacute bowel obstruction** is often not amenable to surgical intervention and should be managed medically using SC medication via a syringe driver. Nasogastric tubes are rarely needed, and hydration can often be maintained orally if the nausea/vomiting are adequately controlled.
- **Renal impairment** due to bilateral ureteric obstruction can develop in any patient with advanced pelvic disease. It may be a pre-terminal event. Ureteric stenting may be appropriate, depending on the patient's perceived prognosis, the patient's wishes, and future treatment options. Renal impairment increases the risk of a patient developing opioid toxicity as renal excretion of opioid metabolites may be reduced.

- **Vaginal or vulval bleeding** may respond to antifibrinolytic agents such as tranexamic acid, radiotherapy, and/or surgery.
- **Offensive vaginal or vulval discharge** can cause considerable distress to both patient and carers. Topical or systemic metronidazole may help, as can barrier creams. Deodorizing machines may also help if the patient is confined to one room.
- **Vesicocolic and rectovaginal fistulae** need surgical assessment. These can be very difficult to manage and require a multidisciplinary approach with specialist input.

Upper gastrointestinal tract cancer

Stomach cancer

Background

- fifth-most common cancer worldwide—high incidence in Japan, Korea, South America, and Eastern Europe
- UK incidence of cancer of the distal stomach is falling, but incidence of tumours of the cardia or gastro-oesophageal junction is rising
- more common in males than females (2:1) and in those over 60 years of age
- 90–95% of gastric tumours are adenocarcinomas

Presentation

- insidious onset
- anaemia
- early satiety and anorexia
- weight loss
- dyspepsia

Diagnosis and staging

- **full staging is essential if inappropriate surgery is to be avoided**
- endoscopy and biopsy
- endoluminal ultrasound to assess depth of invasion and lymph node involvement
- CT scan to assess lymph node involvement and distant metastases
- laparoscopy: may be indicated to assess peritoneal disease if surgery is being considered

Treatment

Resectable disease

Surgery remains the only potentially curative modality of treatment. Partial or total gastrectomy (depending on tumour site and mode of spread) and regional lymphadenectomy is the most commonly performed operation. Factors determining outcome include:

- tumour location: patients with distal tumours do better than those with more proximally located tumours
- tumour extent: patients with tumours beyond the gastric wall have a worse prognosis
- extent of lymph node involvement

Following surgery, many patients remain at high risk of local and distant disease relapse. Trials have shown that such patients benefit from adjuvant chemotherapy or chemoradiation. The current standard of care is peri-operative ECF/ECX chemotherapy. Three cycles of ECF chemotherapy (epirubicin, cisplatin, and continuous fluorouracil) are given prior to surgery, followed by a further three post-operatively. Continuous fluorouracil can be replaced with capecitabine (ECX). Combined pre- and post-operative chemotherapy has been shown to increase resectability and to reduce relapse rates in patients with operable gastric cancer.

Locally advanced/metastatic disease

Palliative operations can be performed to control pain or bleeding or to relieve obstruction for patients with advanced disease. The type of operation performed depends on the status of the patient and on the anticipated disease course.

Chemotherapy, with cisplatin and fluorouracil, with or without epirubicin, has a palliative benefit for patients with locally advanced or metastatic gastric cancer, and may also improve survival by some months. Oxaliplatin in combination with fluorouracil and epirubicin has shown a further improvement in overall survival, and is often used instead of cisplatin. The addition of trastuzumab to cisplatin-fluoropyrimidine chemotherapy for patients with HER2-positive disease increases survival compared to chemotherapy alone. Endoscopic procedures such as stenting or laser coagulation may also provide palliative benefits.

Radiotherapy may provide useful palliation for bleeding from locally advanced tumours. It may also be useful in palliating pain caused by metastatic disease, e.g. bone metastases.

Treatment of the rare gastrointestinal stromal tumours (GISTs) has been revolutionized by the biological therapy imatinib, which has had dramatic impact in some patients.

Oesophageal carcinoma

Background

- ninth-most commonly occurring cancer in males in the UK
- more common in males than females (2.5:1)
- tumours in the upper two-thirds of the oesophagus are usually squamous-cell cancers
- tumours in the lower third are usually adenocarcinomas—incidence of adenocarcinoma has been steadily increasing
- adenocarcinoma often arises in a Barrett's oesophagus—endoscopic screening may reduce the incidence
- overall survival in the UK is <10% at 5 years

Symptoms

- dysphagia
- chest pain
- dyspepsia

Diagnosis and staging

- endoscopy and biopsy
- barium swallow: demonstrates tumour length
- endoluminal ultrasound: demonstrates extent of local invasion and lymph node involvement
- CT scan to assess nodal involvement and distant metastases
- laparoscopy
- bronchoscopy should be performed if tracheal involvement suspected
- PET scanning is used increasingly to detect nodes and distant metastases, with the result that fewer oesophageal resections are being performed

Treatment

Resectable disease

Surgery remains the key potentially curative modality for tumours in the lower two-thirds of the oesophagus. Unfortunately, however, owing to the tumour's tendency to spread longitudinally via the submucosa, circumferentially to other mediastinal structures, and to lymph nodes early in its course, the results are poor, with a 5-year survival of 20%. Neoadjuvant chemotherapy with cisplatin and fluorouracil improves the resectability and reduces the likelihood of local and distant relapse; it is now the standard of care in the UK.

Tumours in the upper third of the oesophagus are inoperable, but may be suitable for radical radiotherapy.

Chemoradiotherapy may also be used with radical intent in tumours in the lower two-thirds of the oesophagus in patients who are unfit for surgery.

Unresectable disease

Endoscopic placement of stents or radiotherapy may provide excellent palliation, particularly of dysphagia. Platinum-based chemotherapy may also be useful in palliating symptoms in patients who are fit.

Pancreatic carcinoma

Background

- fifth-most common cause of cancer death in the UK
- 75% arise from the head of the pancreas, 15% from the body and a 10% from the tail
- risk factors
  - smoking
  - chronic pancreatitis
  - alcohol
  - obesity
  - diabetes
- 90% are adenocarcinomas

Presentation

- insidious onset of symptoms
- jaundice
- weight loss
- pain: local invasion of the coeliac plexus by tail or body tumours may cause severe neuropathic abdominal pain radiating to the back

Investigations

- LFTs (liver function tests) may show obstructive pattern
- Tumour marker CA19–9: elevated in the majority of cancers but low specificity
- ERCP (endoscopic retrograde cholangio-pancreatography) with brushings or biopsy
- endoluminal ultrasound
- ultrasound scan or CT with FNA (fine needle aspiration) or biopsy of pancreatic mass
- CT scan to assess chest, abdomen, and pelvis

- MRI can delineate tumours, ducts, and vessels with less morbidity than ERCP
- laparoscopy: may be required to assess peritoneal involvement prior to surgery

Management

Surgery is the only potentially curative modality of treatment. Unfortunately, less than 15% of patients present with surgically resectable disease. A pancreaticoduodenectomy is the operation of choice, but even in those patients suitable for this surgery, 5-year survival is less than 10%.

The majority of patients will present with advanced unresectable disease, although surgical bypass procedures may be possible. Primary treatment is aimed at relief of jaundice, which is generally achieved by endoscopic or percutaneous transhepatic placement of a stent.

Pancreatic enzyme supplements may help with malabsorption.

Chemotherapy with gemcitabine can provide a small survival benefit, and should be considered in patients with unresectable disease and an ECOG performance status of <3. For fitter patients with ECOG <2, FOLFIRINOX (fluorouracil, leucovorin, irinotecan, and oxaliplatin) chemotherapy has shown greater efficacy than single-agent gemcitabine, with significant improvements in overall response rates and survival rates. The third option is the addition of nab-paclitaxel to gemcitabine to improve response rate and overall survival.

Palliative issues for patients with upper gastrointestinal tract cancer

Mild and non-specific symptoms often precede the onset of dysphagia for many months in oesophageal carcinoma. Stomach cancer often presents late and is frequently metastatic at presentation.

- **Liver capsular pain** due to liver metastases is common. This is only partially opioid-responsive but responds well to NSAIDs or oral steroids.
- **Oesophageal spasm** may occur and can be difficult to manage. Specialist advice from the palliative care team should be sought. It may be aggravated by oesophageal candidiasis, which needs systemic treatment with oral systemic antifungals.
- **Involvement of the coeliac plexus** causes a difficult pain syndrome with non-specific abdominal pain and mid-back pain. Blockade of the plexus using anaesthetic techniques can be useful.
- **Dysphagia** can occur in both oesophageal and stomach cancer. It may be helped by stenting. Oncological treatment of the tumour may provide temporary relief. Advice about appropriate diet and food consistency may also help. A feeding gastrostomy is sometimes used to improve functional status prior to aggressive treatment. Gastrostomy feeding can also improve nutrition and quality of life in the palliative setting, but should only be inserted after careful multidisciplinary discussion involving the patient and their family. Ethical dilemmas can arise towards the end of life when issues of avoiding the prolongation of an uncomfortable dying period (by reducing or stopping artificial feeding) may need to be discussed. There is no evidence that the insertion of feeding tubes in the dying either extends life or improves symptoms.

- **Anorexia** is frequent and often profound. There may be a fear of eating because of pain. This may bring the patient and their carer into conflict about food and the 'need to eat'. However, open and honest explanation can help to relieve anxiety and provide practical approaches to dealing with the situation.
- **Weight loss and altered body image** can be profound with these cancers and can cause distressing problems for the patient and family.
- **Nausea and vomiting** can be persistent and difficult to control. Specialist advice is often needed, and drugs may need to be given by routes other than oral. Small but frequent meals may reduce the frequency of vomiting.
- **Haematemesis** may be one of the presenting symptoms but can also occur as the tumour progresses. Where possible, external beam radiotherapy, brachytherapy, or laser treatment may be helpful. There is a risk of a major bleed. This is a difficult situation to manage, and early involvement of specialists should be considered.

Further reading

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Cancer of the bladder and ureter

Background

- accounts for 1% of all cancers
- 90% are transitional-cell carcinomas (TCC)
- Risk factors for TCC:
  - smoking
  - occupational exposure to aromatic amines and azo dyes
  - cyclophosphamide therapy
  - phenacetin-containing analgesics
- squamous-cell carcinoma of the bladder is less common, and associated with schistosomiasis, bladder calculi, and chronic irritation

Presentation

- painless haematuria in 90% of cases
- frequency
- urgency

Diagnosis and staging

- cystoscopy and biopsy
- CT/MRI

Treatment

- 70–80% of all bladder cancers are 'superficial'—that is, they do not invade the muscularis mucosa

'Superficial' tumours

- treated with transurethral resection of the tumour
- many will recur and follow-up with regular cytoscopy is required
- factors that identify patients likely to develop invasive disease:
  - high-grade tumours
  - tumours that have breached the basement membrane
  - multiple tumours

Such patients may benefit from intravesical mitomycin or bacillus Calmette-Guérin (BCG).

'Invasive' tumours

Disease which invades the muscularis mucosa of the bladder may be treated with radical cystectomy or radiotherapy. These modalities have not been directly compared; decisions regarding the choice of therapy tend to be based on performance status, with surgery reserved for younger and fitter patients.

Bladder cancer is moderately chemosensitive. Neoadjuvant chemotherapy confers a 5% benefit in 5-year survival. Patients with locally advanced or metastatic disease may benefit from palliative chemotherapy. The most commonly used regimen is cisplatin/gemcitabine.

Common problems

- **Bladder spasm** can be frequent and troublesome, leading to urinary frequency as well as pain.
- **Pelvic pain** is common in advanced disease owing to progression of the tumour. This pain can be extremely difficult to control as it is often complex and includes neuropathic elements. Anaesthetic interventions, including intrathecal and epidural procedures, may be needed to achieve pain control.
- **Recurrent haematuria** is common and may be sufficient to cause anaemia and urinary retention due to clot retention. Catheter blockage may be a problem.
- **Urinary incontinence** may occur.
- **Urinary tract infections** due to long-term indwelling catheters are common but are treated only if symptomatic.
- **Lymphoedema** of the lower limbs and genital area may occur and requires specialist management to prevent complications.
- **Vesico-cutaneous fistulae** may occur and are often suitable for surgery. If surgery is not possible, the risks of skin breakdown are high.
- **Renal failure** may occur owing to bilateral ureteric obstruction. Stenting the renal tract may be possible but may not be appropriate and needs full discussion.
- **Altered body image** and problems with sexual function are understandably common.
- **Depression** is common because of the long course of the disease, sleep disturbance, and damage to self-esteem.

Tumours of the central nervous system

Background

- Primary brain tumours account for approximately 2% of all cancers.
- Most brain tumours are metastatic from 1° sites outside the CNS.
- Primary brain tumours tend to remain localized to the CNS.

Primary brain tumours include

- Gliomas (50% of all CNS tumours):
  - Astrocytomas: account for 80% of gliomas, i.e. the most commonly occurring primary brain tumour; grade is important in determining prognosis (e.g. grade IV astocytomas are often referred to as *glioblastoma multiforme* and are the most invasive and rapidly growing astrocytomas).
  - Oligodendrogliomas: account for 10–15% of gliomas and commonly occur in the frontal lobes; longer prognosis.
  - Ependymomas: account for 5% of gliomas and tend to occur in children and young adults; may metastasize within the CNS.
- Pituitary adenomas: account for 20% of CNS tumours; treated medically for endocrine symptoms; treated with surgery or radiotherapy if there are pressure symptoms or visual field problems.
- Medulloblastomas: account for 25% of all childhood tumours.
- Cerebral lymphomas: 1–2 per million per year worldwide; are increasing in incidence partly owing to HIV-associated malignancy.

Symptoms

- Headache (especially in the morning) and vomiting if intracranial pressure is raised.
- Seizures.
- Neurological symptoms.

Investigations

- Contrast-enhanced CT scan.
- Gadolinium-enhanced MRI scan.
- Isotope scanning (PET, SPECT (single photon emission computed tomography)).
- If CSF spread is anticipated (e.g. for high-grade ependymoma) a neuroaxis MRI ± CSF cytology is required.
- Biopsy is usually required to confirm diagnosis.

Primary brain tumours

Surgery

Where possible, surgical resection for some low-grade tumours may be curative. If complete resection of a low-grade glioma is not going to be anticipated, then the timing of surgery is a matter for discussion between the neurosurgeon and patient. For higher-grade lesions, decompression of the tumour may provide palliation and facilitate post-operative radiotherapy.

Radiotherapy

For high-grade gliomas, post-operative radiotherapy adds to the effectiveness of surgery and increases median survival by 5–11 months. For tumours with a propensity for leptomeningeal spread, e.g. high-grade ependymoma or medulloblastoma, craniospinal irradiation improves prognosis.

Chemotherapy

A survival benefit has been demonstrated for patients treated with a combination of radiotherapy and temozolamide compared to radiotherapy alone in glioblastoma multiforme. Chemotherapy is the principal treatment of CNS lymphoma and is important as adjuvant therapy for medulloblastoma. Some response to temozolamide or the PCV combination—procarbazine, CCNU (lomustine), and vincristine—in recurrent disease can be expected.

Prognosis

As a general rule, in patients with brain tumours poorer prognosis is related to

- high tumour grade
- neurological deficit at presentation
- older age at presentation

Secondary brain tumours

Brain metastases

Autopsy reveals that metastases are commoner than revealed clinically: 60% in small-cell lung carcinoma and 75% in melanoma. Carcinoma of the prostate, bladder, and ovary rarely metastasize to the brain. The prognosis for brain metastases is dependent on the extent of systemic disease, the performance status of the patient, and the response to treatment.

Assessment—clinical history

Neurological examination of higher cortical function, cranial nerves, musculoskeletal system, sensation, cerebellar function, and gait.

Clinical features

Symptoms and signs can evolve over days to weeks. Multiple deposits are present in over two-thirds of patients, and clinical signs depend on the anatomical site:

- focal neurological disturbance consists of motor weakness, including hemiparesis (30%), dysphasia, and cranial nerve palsies
- seizures (15–20%)
- raised intracranial pressure, e.g. headache (50%), nausea, vomiting, and lethargy
- change in mood, cognitive function, or behaviour

Investigations

CT scan or MRI scan (better for tumours situated in the posterior fossa or brainstem) show the location of metastases, surrounding oedema, and mass effect.

Management

With a solitary metastasis—and depending on the anatomical site of the tumour—surgery may be suitable for a very small percentage of patients who are young and fit, with no disease elsewhere and a long treatment-free interval. If anatomical location is the only contraindication to surgery, then high-dose localized radiotherapy may be considered.

Patients who might benefit from radical treatment should be identified, including those with chemosensitive tumours such as the haematological malignancies and testicular cancer.

Palliative radiotherapy with corticosteroids is the most usually appropriate treatment; it may improve neurological symptoms and function in over 70% of patients (with a median survival of 5–6 months), enabling a gentle reduction and sometimes withdrawal of steroids 4–6 weeks following treatment. However, benefit may not be gained in patients with poor prognostic factors: poor performance status, over 60 years of age, non-breast primary site, multiple lobe involvement, short disease-free interval, and overt uncontrolled metastases elsewhere. As ever, decisions regarding treatment should be tailored to the problems of the individual patient.

Cranial irradiation may cause some degree of scalp and upper pinna erythema and irritation. Temporary alopecia is universal in a population whose prognosis is unlikely to allow regrowth of hair within the remaining lifespan. The start of treatment may induce an increase in cerebral oedema, which may require steroid dose readjustment. Other effects include transient somnolence, occurring within a few weeks, and longer-term impairment of memory and cognition. These are significant problems in very few people, and most patients do not survive long enough for late radiation changes in the CNS to develop.

Anti-epileptics

In patients presenting with seizures, anti-epileptic therapy is indicated. Prophylactic use of anticonvulsants is not recommended. First-generation anti-epileptics such as phenytoin and carbamazepine are strong inducers of hepatic metabolism and may interfere with other medications including chemotherapy agents. Preferable agents include levetiracetam, lamotrigine, pregabalin, and sodium valproate.

Corticosteroids

High-dose corticosteroids (dexamethasone 16mg/day initially) reduce cerebral oedema, and associated symptoms of headache and vomiting may reduce rapidly. In certain situations—particularly if metastases are in the posterior fossa—hydrocephalus may be present, in which case a ventricular shunt may be required for symptom control.

The short prognosis for most patients means that the issue of long-term side effects of steroids may not be a problem. It is best practice, however, to gradually reduce the dose to the lowest possible over a few weeks to minimize potential side effects, since difficulties may build up insidiously.

A stage may be reached when the dose necessary to control the cerebral oedema causes significant side effects. Disabling problems such as obesity (and associated problems with immobility management), body image problems, proximal myopathy, mood swings, fragile skin, and diabetes may then develop. There should be open dialogue (particularly while the patient is well enough and can join in discussions) about the ongoing use of steroids in the event that quality of life becomes adversely affected. Patients and families may view steroids as agents to control the disease and resist attempts to reduce the dose, fearing the return of symptoms of raised intracranial pressure.

On the other hand, patients may have recognized that their quality of life is deteriorating despite continuing steroids, and may then be happy for (or request) steroids to be withdrawn. This should generally be done slowly, while controlling the symptoms of raised intracranial pressure by other means.

When patients become moribund and can no longer swallow, the steroids can generally be stopped, but this may depend on the particular clinical circumstances and may need negotiation with the patient and their family. There should be adequate medication provision (subcutaneous), including analgesics, anti-emetics, anticonvulsants, and sedatives as necessary.

Multiple complex physical and psychological problems, including poor mobility, heavy care needs, swings in mood, and confusion, can completely exhaust even the most caring family, who need the expert support of an experienced multidisciplinary team.

Prognosis

Although some patients, particularly with metastases from breast cancer, may survive relatively longer, most patients with brain metastases from solid tumours have a survival in the order of a few weeks or months at best.

Metastatic disease of the leptomeninges (meningeal carcinomatosis)

Some 5% of patients with tumours may develop clinical signs and symptoms of leptomeningeal disease, although the autopsy rate is higher (10%). It is most commonly seen in lymphoma and leukaemia, although it may occur in breast cancer, small-cell lung cancer, and melanoma.

Clinical features

The presenting features may be varied and fluctuating; the diagnosis should be considered when there are any unexplained neurological symptoms in a patient with cancer. The most frequently encountered are cranial nerve problems (75%), headache (50%), radicular or back pain (40–45%), and weakness in one or more limbs (40%). Other presentations include meningism, altered consciousness, confusion, sphincter disturbance, and seizures. Abnormal physical signs are more prominent than symptoms, with lower motor neurone lesions predominating.

Investigations

- lumbar puncture if there is no evidence of raised intracranial pressure (90% will have positive cytology and increased protein on CNS analysis)
- gadolinium MRI scan of the brain and whole spine

Management

Management may include intrathecal chemotherapy (depending on the tumour type and radiotherapy). The aim is to halt the progression of disease and relieve symptoms, but is essentially palliative except for in a curable subgroup of leukaemia or lymphoma. Steroids and NSAIDs may help symptoms.

Prognosis

Without treatment, patients may survive for several months, depending on the tumour type, but with relentless progression of neurological symptoms. Even with treatment, prognosis is usually less than 6 months. It is worst in small-cell lung cancer, widespread disease, poor performance status, and where there are widespread neurological signs.

Chronic leukaemia and myeloma

Background

- Balancing opportunities for cure with impact of treatment on quality of life are crucial in assessing the appropriate interventions, which are often extremely aggressive and taxing for patients.
- Chemotherapy has led to marked improvements in survival over the past 40 years.

General comments

The clinical course tends to be highly variable, but is characterized by a protracted cycle of relapses and remissions. This can cause considerable distress as the patients and their carers have to live with uncertainty about the future. Both patient and the professionals involved in their care may find it hard to accept that the patient is entering the terminal phase.

Infection is a frequent complication of both the disease process and its treatment. It can be fatal and this makes the prognosis even more uncertain.

Chemotherapy may continue in advanced illness because of the possibility of a further remission, useful palliation, or both.

Specific pain complexes

- **Bone pain** is very common. The pain is often worse on movement or weight-bearing, which makes titration of analgesics very difficult. The pain often responds well to radiotherapy and/or oral steroids. NSAIDs may help but must be used with caution because they may interfere with platelet and renal function.
- **Pathological fractures** are particularly common in myeloma owing to the lytic bone lesions. These often require orthopaedic intervention and subsequent radiotherapy. Prophylactic pinning of long bones and/or radiotherapy should be considered to prevent fracture and to reduce the likelihood of complex pain syndromes developing.
- **Spinal cord compression** requires prompt diagnosis, high-dose oral steroids, and urgent discussion with an oncologist. The steroids should be continued at a high dose until a definitive plan has been made. They may then be titrated down in accordance with the patient's condition and symptoms.
- **Wedge and crush fractures of the vertebral column** can lead to severe back pain, which is often associated with nerve compression and neuropathic pain. Such pain is partially opioid-sensitive, but adjuvant analgesics in the form of antidepressants and/or anticonvulsant medication are usually required to supplement the effect of the opioid. Specialist advice is frequently needed to maintain symptom control.

Other complications

- **Bone marrow failure** is usual. Recurrent infections and bleeding episodes can leave the patients and carers exhausted. Patients often feel dependent on the administration of blood and platelet transfusions, unable to consider reducing the frequency of what is seen as life-sustaining treatment. Difficult decisions about reducing regular transfusions or stopping them if they are providing no further benefit may need to be faced with patients and families.

- **Night sweats and fever** are common, imposing a heavy demand on carers, particularly as several changes of night and bed-clothes may be needed. Specialist advice may help in relieving the symptoms, as there are a number of drugs that appear to be effective.
- **Hypercalcaemia** may occur, especially in myeloma. It should be considered in any patient with persistent nausea, altered mood, confusion (even if intermittent), worsening pain, or constipation. Treatment with IV hydration and IV bisphosphonates should be considered. Resistant hypercalcaemia may be a pre-terminal event, when aggressive management would be inappropriate.

Palliative care of patients with carcinomatosis of unknown primary

Background

Approximately 3–5% of patients present with metastases from an unknown primary site. For these patients, standardized diagnostic work-up often fails to identify the site of origin at the time of diagnosis. As a group, the prognosis for these patients is poor, with a median survival of 3–4 months.

Investigations

- serological tumour markers, including CA15-3, CA19-9, CEA, CA125, αFP (plasma α-fetoprotein), βhCG (β human chorionic gonadotrophin), PSA, and paraproteins
- biopsy: thorough pathological assessment with immunohistochemistry may provide clues to the primary site
- CT scan of chest, abdomen, and pelvis
- endoscopies should be guided by signs, symptoms, or laboratory abnormalities

In some instances, the site of metastatic disease may suggest a probable primary site, e.g., adenocarcinoma in axillary nodes suggests a breast primary.

Particularly in young patients, it is important to rule out the possibility of a potentially curable germ-cell tumour. This may be suggested by elevated αFP or βhCG. Chemosensitive lymphoma should also be excluded.

In a substantial number of patients, a primary site is not identified. In this instance, exhaustive investigations may not be appropriate, particularly if the patient has a poor performance status.

Treatment

In some patients where the clinical presentation suggests a primary cancer, even if a tumour cannot be detected in that organ, it may be appropriate to treat the patient as if they had the cancer in question. For example, a patient presenting with ER-positive adenocarcinoma in an axillary node could reasonably be treated as if breast cancer was the primary.

For patients in whom there is little evidence of a primary site (e.g. those presenting with liver metastases with certain histology), the choice is much more difficult. As the primary is unknown, it is impossible to give patients an idea of the likelihood of a treatment response or of how durable such a response is likely to be. Any potential benefit of treatment must be carefully balanced against possible toxicity, and a decision to proceed with chemotherapy should only be undertaken following a very full discussion with the patient and carers, outlining the uncertainties and limitations of treatment and overall limited prognosis.

Anxiety is common in this group of patients. Not knowing the site of the primary tumour causes considerable distress. Extensive investigations may raise false expectations and may exhaust the patient. Equally, patients and carers may feel cheated of the chance to have effective treatment if the primary is not looked for.

Carers may find coming to terms with the patient's death due to an 'unknown primary' difficult, and are perhaps at greater risk of an adverse bereavement reaction.

Key points

- anxiety and anger
- risk of over-investigation
- adverse bereavement reaction

Investigations

- tumour markers increasingly used to both monitor disease progression and response to treatments
- interpretation of marker results often not straightforward

See Tables 6.11 and 6.12.

Table 6.11 Tumour markers and associated conditions

Tumour marker	Associated conditions	
	Malignant	Non-malignant
CEA	GI tract cancers (particularly colorectal cancer)	Cirrhosis
		Pancreatitis
		Smoking
CA 19-9		Cholestasis
	Pancreatic cancer	
CA 15-3	Breast cancer	Cirrhosis, sarcoidosis, lupus
CA-125	Ovarian cancer	Cirrhosis
	Breast cancer	Pregnancy
	Hepatocellular cancer	Peritonitis
αFP	Hepatocellular cancer	Cirrhosis
	Germ-cell cancers (not pure seminoma)	Pregnancy
		Hepatitis
		Open neural tube defects
βhCG	Germ-cell cancers	Pregnancy
	Choriocarcinoma and hydatidiform mole	
PSA	Prostate cancer	Benign prostatic hypertrophy
		Prostatitis
		Prostate instrumentation (incl. rectal examination)
		Acute urinary retention
		Physical exercise
		Old age

Patient tip
Further information about treatment decisions:
Cancer Research UK 0808 800 4040 http://www.cancerresearchuk.org/4-about-cancer
DIPEx Patient experience database http://www.dipex.org

Table 6.12 Advantages of imaging techniques

Imaging technique	Preferred when evaluating
CT	Lungs, abdominal cavity
Spiral CT	Makes 3-D images of areas inside the body. Detects small abnormal areas better than conventional CT
MRI	Mediastinum, liver, pelvis, brain, spinal cord
PET	By using 5-FDG, which is avidly taken up by actively dividing cells, this helps to:
	• determine the functional and metabolic status of tumours
	• distinguish benign from malignant lesions
	• distinguish whether a residual mass after treatment represents fibrosis or residual tumour

Further reading

Books

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Kvale P.A. (2007) Palliative care in lung cancer: ACCP evidence-based clinical practice guidelines (2nd edn). *Chest* **132**: 368S–403S.
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Chapter 7

Palliative care and haematology

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Anaemia in chronic disorders

Anaemia is defined in adults as haemoglobin concentration of less than 13.0g/dL in men and 11.5g/dL in women. Anaemia occurs commonly in chronic renal disease, endocrine diseases, and connective tissue disorders. Various factors may contribute, and commonly more than one is present (see Table 7.1).

Anaemia is a common problem, occurring in over 50% of patients with solid tumours and in most patients with haematological malignancies such as multiple myeloma and lymphoma.

Symptoms caused by anaemia

- fatigue, weakness
- breathlessness on exertion
- impaired concentration
- low mood
- anorexia
- exacerbation of congestive cardiac failure
- chest pain
- loss of libido

Table 7.1 Causes of anaemia and indicators for diagnosis

Causes of anaemia	Diagnostic indicators
• Reduced red cell production due to bone marrow infiltration: • Multiple myeloma • Prostate cancer • Breast cancer • Leukaemia	• Full blood count—pancytopenia and reduced reticulocytes • Bone marrow examination—may show infiltration by non-haematological cells, e.g. prostatic or breast carcinoma
• Chemotherapy-induced bone marrow suppression	• Hypocellular marrow
• Malnutrition/malabsorption, e.g. post-gastrectomy • Vitamin B_{12} deficiency • Folate deficiency • Iron deficiency	• Blood film: megaloblastic anaemia • Low serum vitamin B12 • Reduced serum or red cell folate • Reduced ferritin
• Blood loss: • Gastrointestinal • Urinary tract	• Clinical—haematuria, melaena • Acute—blood count and film: normochromic normocytic anaemia, reticulocytosis, and polychromasia • Chronic—iron deficiency anaemia
• Reduced red cell survival/haemolysis: • Autoimmune haemolysis—lymphoproliferative disorders • Physical haemolysis—microangiopathic haemolytic anaemia (MAHA) in some adenocarcinomas	• Blood film: polychromasia; autoimmune—spherocytes; MAHA—red cell fragments (schistocytes); reticulocytosis • Autoimmune—positive direct Coombs test • Bilirubin—raised

There are no specific criteria for the functional assessment of anaemia. However, randomized controlled trials on managing anaemia in malignancy use validated tools in assessing its effect on quality of life (QoL), e.g.:

- Cancer Linear Analogue Scale (CLAS)
- Functional Assessment of Cancer Therapy—Anaemia (FACT—An)

The anaemia may also be due to co-morbidities—chronic renal failure or chronic disorders leading to a combination of contributors (see Table 7.2):

- suppressed erythropoietin production
- impaired transferrin production
- shortened red cell survival

Table 7.2 Differentiation between iron deficiency anaemia and anaemia of chronic disease*

	Iron deficiency anaemia	Anaemia of chronic disease
Blood film	Hypochromic microcytic	Normochromic or hypochromic
Red cell distribution width (RDW)	Increased with low MCV**	Normal (with high or low MCV)
Total iron-binding capacity (TIBC)	High	Normal/low
Plasma iron	Low	Low
Serum ferritin	Low	Normal/raised

*N.B. The two causes can coexist

** Mean corpuscular volume

Management of anaemia

Decrease bleeding risk

- Consider discontinuation of drugs that may increase risk of bleeding:
  - aspirin, NSAIDs
  - anticoagulants
  - steroids
- Consider gastro-protection using:
  - proton pump inhibitors
  - H_2-receptor antagonists
  - prostaglandin analogues, e.g. misoprostol
- Give vitamin K in liver disease-related coagulopathies as evidenced by prolonged prothrombin time (PT). Vitamin K tablets (menadiol phosphate) 10mg p.o. daily for 1 week, then recheck PT.
- Give tranexamic acid (antifibrinolytic agent) 1g p.o. t.d.s. or q.d.s. for mucosal bleeding. Tranexamic acid can also be given topically and as a mouthwash. (Use with care in bleeding from the bladder or prostate as clot formation is enhanced. Subsequent urinary retention may become a new problem.)
- Etamsylate, by improving platelet adhesion, can be useful.

Replace haematinic deficiencies

- iron deficiency: ferrous sulfate 200mg b.d. or t.d.s. (or ferrous fumarate 322mg o.d. or b.d. daily) taken whole, with a full glass of water, 1 hour before food, for 3 months
- folate deficiency: folic acid 5mg o.d.
- vitamin B_{12} deficiency: hydroxocobalamin 1mg IM every 3 months

Blood transfusion

It is common practice for patients who are becoming terminally ill to receive blood transfusions when they develop fatigue or dyspnoea, with a low Hb. It is inappropriate to decide on transfusion on the basis of the haemoglobin result alone and it is rarely indicated with values above 8.0g/dL. The decision should be made in the context of symptoms attributable directly to anaemia, which are adversely affecting quality of life. As there are currently no guidelines, the use of blood products in the terminally ill requires ethical discussions for appropriateness for the individual situation.

Blood transfusion helps about 75% of patients in terms of well-being, strength, and breathlessness.

- The aim of transfusion is to relieve symptoms.
- One unit of packed red cells (approximately 300mL) results in a rise in haemoglobin of 1g/dL. Rate of transfusion should be reduced in patients at risk of pulmonary oedema. Administration of furosemide can help reduce the preload.
- Patients should be told that the beneficial effects may not be apparent for a day or two post-transfusion.
- It is good practice to document the clinical effects of the transfusion. This will help in discussing the merits or otherwise of further transfusions.

Considerations for blood transfusion in patients with palliative care needs

- prognosis longer than 2 weeks
- functional status (i.e. not predominantly bedbound) (ECOG <3)
- presence of at least two of the following symptoms in association with Hb <9g/dL:
  - breathlessness on exertion
  - weakness
  - angina
  - postural hypotension
  - worsening cardiac failure
  - worsening fatigue

In addition to symptomatic relief, we should acknowledge the subtle support group that develops around patients who continue transfusions and the benefit derived—i.e. the regular interactions with the medical assistants, nurses, and physicians with whom they have formed strong personal connections over the course of their treatment. When patients cease to be able to receive transfusions, this network of support is also perceived as severed.

Blood transfusion reactions

The commonest reactions are febrile and mild allergic reactions. It is managed with slowing of the transfusion, and managing the fever with paracetamol. Chlorphenamine 10mg is useful for urticaria.

If allergic reactions are frequent and persistent, hydrocortisone may be used 1–2 hours prior to transfusions. Leuco-reduction of the blood product reduces the frequency of febrile reactions significantly.

Acute life-threatening transfusion reactions are rare; however, new symptoms or signs that occur during a transfusion must be taken seriously as they may herald a serious reaction. As it may not be possible to identify the cause of a severe reaction immediately, initial supportive management should generally cover all possible causes. These include:

- acute haemolytic transfusion reaction
- infusion of a bacterially contaminated unit
- severe allergic reaction or anaphylaxis
- transfusion-related acute lung injury (TRALI)

Acute haemolytic transfusion reaction

Incompatible Group A or B transfused red cells react with the patient's own anti-A or B antibodies. This results in acute renal failure, and can cause disseminated intravascular coagulation (DIC). The reaction can even occur after a few millilitres of blood have been transfused.

- **symptoms:** acute onset of pain at the venepuncture site, loins, chest
- **signs:** fever, hypotension, tachycardia, oozing from the venepuncture sites
- **action:** if a severe acute reaction is suspected:
  - Stop the transfusion, keep the IV line open with sodium chloride 0.9% infusion.
  - Monitor temperature, heart rate, BP, respiratory rate, urine output.
  - Recheck the patient's identification, the blood unit, and documentation.
  - Inform the blood bank.
  - Further management will depend on the clinical picture.

Infusion of bacterially contaminated unit

This may cause haemolysis or clots within the blood bag. For this reason, visual inspection of every unit is part of the pre-transfusion check. Symptoms and signs are identical to acute haemolytic transfusion reaction. Treat as for acute haemolytic transfusion reaction in addition to:

- taking blood cultures
- sending the blood unit to microbiology

Major allergic reactions

Rare but life-threatening complications usually occur in the early part of a transfusion. These complications are more common with plasma-containing blood components, e.g. fresh-frozen plasma (FFP) or platelets.

- **symptoms**: chest pain, breathlessness, nausea, and abdominal pain
- **signs**: hypotension, bronchospasm, periorbital and laryngeal oedema, vomiting, urticaria
- **action**:
  - stop transfusion
  - maintain IV access
  - provide high concentration O_2
  - chlorphenamine 10–20mg IV over 1–2 minutes
  - hydrocortisone 100–200mg IV
  - adrenaline 0.5–1mg (0.5–1mL of 1 in 1000) IM
  - salbutamol 2.5–5mg by nebulizer

Transfusion-related acute lung injury (TRALI)

This is usually caused by antibodies in the donor's plasma that react strongly with the patient's leucocytes.

- **symptoms**: rapid onset of breathlessness and dry cough
- **signs**: chest X-ray shows bilateral infiltrates—'white-out'
- **action**:
  - stop transfusion
  - give 100% O_2
  - seek expert advice and treat as adult respiratory distress syndrome (ARDS)

Fluid overload due to blood transfusion

More common in patients with a history of heart or renal disease, but any patient with advanced malignancy or advanced systemic disease is susceptible. In patients with systemic dysfunctions, each red cell unit should be given over 3–4 hours, and a maximum of two units may be given per day. Look out for:

- **symptoms and signs**: breathlessness with basal crepitations, raised BP, tachycardia, raised jugular venous pressure (JVP)
- **action**:
  - stop transfusion
  - provide supplemental O_2 and give furosemide 40mg IV

Contraindications to blood transfusion

- patient refusal
- no symptomatic benefit from previous transfusion
- patient moribund with life expectancy of days

Erythropoietin

- This is a hormone made by the kidney. It stimulates the production of red blood cells and is licensed for anaemia of chronic renal failure and for patients undergoing chemotherapy who are receiving platinum-containing chemotherapy (NICE guidance).
- It may also be effective in improving the chronic anaemia of cancer.
- Erythropoietin is used for severe anaemia in Jehovah's Witnesses.
- A number of erythropoiesis-stimulating agents (ESAs) are available (epoetin alpha, beta, theta and zeta; and darbepoetin alpha). There is no evidence to distinguish between ESAs in terms of efficacy.
- An injection of epoetin alpha 150–300 units/kg SC three times a week for 4–6 weeks increases the Hb significantly in 50–60% of patients with cancer. The patients most likely to benefit include those with a low erythropoietin concentration, those with an adequate bone marrow reserve, and those who have an initial good response (i.e. an increase in Hb of >1g/dL within 4 weeks of starting treatment).
- It is important to maintain hydration of the patient.
- The maximum benefit is achieved after about 2 months, which may be a factor limiting its usefulness in palliative care patients where prognosis is short.
- Patients should be given iron supplements during erythropoietin therapy to maximize the response.
- Owing to the thrombotic risk, the haemoglobin level must be monitored weekly to ensure this does not increase above 12.0g/dL.

Complications

- hypertension
- thrombosis
- iron deficiency, if not on iron supplements

Bleeding and haemorrhage

For emergency management of massive haemorrhage, see Chapter 29, Emergencies in palliative care.

Bleeding occurs in about 20% of patients with advanced cancer and may contribute to death in 5%. Bleeding may be directly related to the cancer, e.g. local bleeding from fungating tumours, or indirectly attributed to it, e.g. peptic ulceration or nosebleeds secondary to treatment with NSAIDs or thrombocytopenia.

A decline in the haematological profile may mirror the systemic deterioration in a patient's condition.

Common sites where bleeding is most obvious

- oral mucosa or gums
- nose, nasopharynx
- skin
- haemoptysis
- haematemesis
- muscle

Hidden bleeding

- gastrointestinal—melaena, tarry stools (urea may be raised)
- bronchopulmonary—worsening breathlessness, haemoptysis, pleural effusion
- urogenital—macroscopic or microscopic haematuria
- cerebral—headache, visual disturbance, change in neurological status
- gynaecological—lower abdominal, perineal pain, spotting

General management of bleeding

The sight of blood can have a profound effect on patients and their carers. Relatives and patients who have coped calmly with a full range of demanding symptoms may become deeply distressed in the event of a bleed. When the bleed is significant, there are but a few who are stoic enough not to be frightened.

Explanation of what is happening, or what happened, and providing the opportunity for the fears to be expressed and listened to, can be a very important part of professional support under these circumstances.

Where possible and when appropriate, it is important to evaluate and correct haemostatic factors that may be contributing to the bleeding.

Deficiency of factors contributing to bleeding

Platelets

Thrombocytopenia due to:

- reduced marrow production:
  - marrow infiltration
  - myelosuppression following chemotherapy

- increased consumption/utilization:
  - disseminated intravascular coagulation (DIC)
  - autoimmune
- splenic pooling: hypersplenism, abnormal function

Coagulation factors

These are deranged when there is high-level expression of tissue factors:

- extrinsic pathway activation
- thrombin generation
- consumption of clotting factors
- DIC

Disseminated intravascular coagulation

Acute DIC is uncommon. It presents as a mixed picture with both thrombosis and bleeding. The skin develops petechiae and purpura. Areas of end circulation such as the digits, nose, and ear lobes may exhibit features of gangrene. Bleeding may be seen from areas of minor trauma, such as the venipuncture sites, or as haematuria through a recently placed urinary catheter. Treatment includes platelet infusions, FFP (fresh-frozen plasma), and cryoprecipitate.

Chronic DIC (as measured by laboratory tests) is more common and may be asymptomatic, but thrombotic symptoms of deep vein thrombosis (DVT), pulmonary embolus (PE), or migratory thrombophlebitis may occur. Treatment is usually with heparin (low molecular weight).

Laboratory investigations for DIC

- **D-dimers**—are more specific than fibrin degradation products (FDPs). A significant increase in D-dimers + prolonged prothrombin time, reduced fibrinogen, and thrombocytopenia are necessary for diagnosing DIC (D-dimers are also increased in infection, impaired renal function, post-transfusion, malignancy, and with increasing age).
- **prothrombin time (PT)**—less sensitive, usually prolonged in acute DIC, but may be normal in chronic DIC
- **activated partial thromboplastin time (APTT)**—less useful, as may be normal or shortened in chronic DIC
- **platelets**—reduced or falling count found in acute DIC
- **blood film**—may show red cell fragments (schistocytes)

Thrombocytopenia

Spontaneous bleeding due to thrombocytopenia is rare with a platelet count of $>20 \times 10^9$/L. Sepsis increases the bleeding tendency. Possibility of traumatic bleeding becomes significant when the platelet count falls below 40×10^9/L. If platelet function is abnormal, bleeding may occur at higher counts.

Decision on transfusing platelets in the setting of advanced cancer should be done on a case-by-case basis, with the aim of controlling symptoms. The whole team should be involved in these decisions on maintaining regular prophylactic transfusions and also for their withdrawal.

If the count is greater than 10×10^9/L, the risk of a major bleed is small. It is important to anticipate which patients are likely to require platelet transfusions and decide on the appropriateness of transfusion prior to a crisis. A platelet transfusion may be considered, but it only raises the

platelet count for a few days; in a palliative context this should only be done when it will relieve distress and meaningfully improve QoL. Severe bleeding can occur with counts less than 5×10^9/L.

A unit of platelets of 300mL is pooled from four units of donated blood. The donor should be ABO compatible with the patient. Platelets must be kept at room temperature and transfused within 30min, using a sterile administration set or a platelet infusion set. Inline filters are not used. Occasional reactions with rigors and fever may occur. These respond to chlorphenamine 10mg IV and hydrocortisone 100mg IV.

Tranexamic acid (inhibits fibrinolysis) can be used to control mucosal bleeding due to thrombocytopenia.

- 1g orally t.d.s. or slow IV injection
- mouthwash 500mg every 6 hours for oral bleeding
- topical tranexamic acid for superficial fungating tumours with spots of bleeding

On average, it takes 2 days of therapy to slow down bleeding and 4 days for bleeding to stop. The shortened half-life of platelets limits the usefulness of their transfusions in patients with end-stage disease.

Blood products

These are less commonly used in the palliative care setting. Close liaison with the haematology department is essential when considering their administration. The list below outlines some products and their indications.

Indications for blood products

Fresh-frozen plasma (FFP)

- disseminated intravascular coagulation
- rapid correction of warfarin overdose
- liver disease
- coagulopathy due to massive blood loss

Cryoprecipitate

- in DIC when fibrinogen <1.0g/L
- for bleeding in cases of dysfibrinogenaemia

Bleeding directly related to cancer

Radiotherapy should be considered in patients with local bleeding at cancer sites, e.g. ulcerating skin tumours, lung cancer causing haemoptysis, gynaecological cancer causing vaginal bleeding, and bladder/prostate cancer causing haematuria.

Specific situations

Nosebleeds

- Most nosebleeds are venous, and when arising from the anterior septum can often be stopped by pressure.
- Silver nitrate caustic pencil may be applied to the bleeding point.
- The nose may be packed with calcium alginate rope (e.g. Kaltostat) or with ribbon gauze soaked in adrenaline (epinephrine 1:1000 1mg in 1mL).
- If the bleeding is more posterior, and continues into the nasopharynx, a Merocel nasal tampon may need to be inserted for 36 hours with antibiotic cover, or the nose packed with gauze impregnated with bismuth iodoform paraffin paste (BIPP) for 3 days. These procedures may be performed only by an experienced clinician, preferably by an ENT surgeon.
- Refer to the ENT department for further management with a balloon catheter or cauterization under local anaesthetic.

Surface bleeding

The bleeding from tumour masses responds well to radiotherapy. Other measures include the following:

Physical

- applied pressure for 10 min with gauze soaked in adrenaline (epinephrine 1:1000) or tranexamic acid 500mg in 5mL
- silver nitrate sticks applied to bleeding points
- haemostatic dressings, i.e. alginate, e.g. Kaltostat, Sorbsan

Drugs

- topical
  - sucralfate paste 2g (two 1g tablets crushed in 5mL K-Y® jelly)
  - sucralfate suspension 2g in 10mL b.d. for mouth and rectum
  - tranexamic acid 5g in 50mL (instil 50mL of 500mg/5mL injection) for rectal bleeding
- systemic
  - antifibrinolytic, e.g. tranexamic acid 1.5g p.o. stat and 0.5–1g b.d.–t.d.s. p.o. or slow IV 0.5–1g t.d.s. **Do not use if DIC suspected.**
  - haemostatic, e.g. etamsylate 500mg q.d.s. (restores platelet adhesiveness)

Haemoptysis

➔ see Chapter 29, Emergencies in palliative care.

- One-third of patients with lung cancer develop haemoptysis, although the incidence of acute fatal bleeds is only 3%, of which some occur without warning.
- An episode of massive haemoptysis can be a frightening experience for patients and families and often is heralded by a smaller episode. This gives opportunity for an element of preparedness.

Haematemesis

The incidence is 2% in patients with cancer and may be directly associated with the cancer and/or secondary to gastroduodenal irritants such as NSAIDs or aspirin. The management includes stopping NSAIDs and adding a proton pump inhibitor or H_2-receptor antagonist; a gastro-protective agent such as sucralfate may also be useful.

Major bleeds

If the patient's condition is not stable, and they have a history of major haemorrhage or ongoing bleeding:

- Consider carefully the appropriateness of transferring the patient to an acute medical/endoscopy unit. Reflect on the balance of benefit vs burden of the aggressive interventions for that patient.
- Site an IV cannula in anticipation of the need for emergency drugs.
- Treat anxiety or distress as needed
  - midazolam 2–5mg initially by slow IV titration (10mg diluted to 10mL with sodium chloride 0.9%).
- If no IV access, midazolam 5–10mg SC (give IM if shocked or vasoconstricted).

Rectal bleeding

This may be associated with local tumour (radiotherapy may be the treatment of choice to stop the bleeding) and/or radiotherapy. Pelvic radiotherapy causes acute inflammation of the recto-sigmoid mucosa, and can lead to acute onset bloody diarrhoea. This is usually self-limiting. A Predsol retention enema 20mg in 100mL o.d.–b.d. or prednisolone 5mg and sucralfate 2g in 10mL b.d. may help.

Bleeding from chronic ischaemic radiation proctitis may respond to a suspension of tranexamic acid, etamsylate or sucralfate given rectally.

Haematuria

see Chapter 11, Genitourinary problems.

This may occur with carcinoma of the bladder or prostate or as a result of chronic radiation cystitis. Urinary infection aggravates the condition. Tranexamic acid or etamsylate are useful, although there is the risk of clot formation and urinary retention. 50mL of a 1% solution of alum can be useful if retained in the bladder via a catheter for 1 hour.

Massive terminal haemorrhage

see Chapter 29, Emergencies in palliative care.

Thromboembolism

It is over 130 years since Trousseau first noticed the association between cancer and thrombosis. Patients with cancer are at high risk of developing venous thromboembolism (VTE) and the risk increases as malignancy advances. Therefore, it follows that palliative care patients are extremely thrombogenic.

Studies have suggested that the incidence of deep vein thrombosis (DVT) may be as high as 52% in palliative care, with 33% of those being bilateral.

The following list, based on **Virchow's triad**, suggests reasons for the higher risk seen in patients with cancer.

Thrombogenic risk in cancer

- **stasis**
  - immobility due to weakness, lethargy
  - compression of vessels by tumour, e.g. pelvic disease
  - extrinsic compression from oedematous legs
- **endothelial perturbation**
  - recent surgery
  - central venous access
  - direct tumour invasion of vessels
- **hypercoagulable state**
  - dehydration
  - tissue factor/tumour procoagulant release
  - increased platelet activation
  - DIC
  - cytokine-related thrombotic changes
  - prothrombotic changes from certain chemotherapeutic agents

Deep vein thrombosis (DVT)

Signs and symptoms vary, depending upon the severity of the DVT. It should be suspected in those patients with a swollen, tender, warm, erythematous leg, although it is unreliable to make a firm clinical diagnosis on the basis of these findings alone. Some are asymptomatic, whilst extreme cases may lead to vascular insufficiency and gangrene. The risk of a pulmonary embolus from a distal DVT (i.e. below knee) is low, and only about 20% of calf vein thromboses extend proximally. Clinical scores for DVT are given in Table 7.3.

Differential diagnosis

- cellulitis
- lymphoedema
- oedema due to hypoproteinaemia
- ruptured Baker's cyst

Diagnosis

It is not always practical to confirm the presence of a DVT if the patient is in the terminal stages of illness or to treat all patients with VTE. If a patient is not going to be anticoagulated, there is little point in investigating to confirm a suspected thrombus. Anticoagulation carries risks as well as benefits and these should be weighed on an individual basis before planning the direction of care.

Table 7.3 Wells' clinical score for deep venous thrombosis

	Clinical parameter	Score
1.	Active cancer or cancer treated within 6 months	+1
2.	Recently bedridden for more than 3 days or major surgery less than 4 weeks prior	+1
3.	Paralysis or recent plaster immobilization of lower extremities	+1
4.	Pitting oedema (greater than asymptomatic leg)	+1
5.	Entire leg swelling	+1
6.	Calf swelling ≥3cm compared to asymptomatic calf (measured 10cm below tibial tuberosity)	+1
7.	Collateral superficial veins (non-varicose)	+1
8.	Localized tenderness along the distribution of the deep venous system	+1
9.	Previous documented DVT	+1
10.	Alternative diagnosis (as likely or greater than that of DVT)	–2

Score of 2 or higher—DVT is 'likely'

Score of less than 2—DVT is 'unlikely'

Reprinted from Tovey and Wyatt (2003) Diagnosis, investigation, and management of deep vein thrombosis BMJ 326:1180 with permission from the British Medical Journal.

- Doppler ultrasound
  - non-invasive; no ionizing radiation
  - can be performed at the bedside
  - easily repeatable
  - bedside ultrasound for femoral DVT can be taught without the need for a specialist referral, and can be invaluable in the hospice context, i.e., the Focused Abdominal Sonography in Palliative Care (FASP) Programme
- venography
  - no longer the first-line investigation; useful when Doppler is inconclusive, e.g. in patients with large oedematous legs or with previous deep vein thrombosis
  - invasive; involves ionizing radiation; contrast media is injected into a vein on the dorsum of the foot; low risk of allergic reaction
  - gives excellent visualization of all the leg veins
- light reflection rheography
  - non-invasive and can be done at bedside
  - high sensitivity but poor specificity
  - cannot localize thrombus or distinguish intrinsic from extrinsic compression
  - not very useful in clinical practice
- D-dimers
  - high false-positive rate in malignancy limits its use in cancer patients
  - negative values are useful in ruling out DVT
- magnetic resonance angiography
  - non-invasive imaging of leg vessels
  - use in palliative care patients is yet to be evaluated

Pulmonary embolus (PE)

Venous thromboembolism is a significant concern throughout the cancer trajectory—from pre-diagnosis, through diagnosis, treatment, palliation, and until death.

Most PEs occur as a complication of DVT in the legs or pelvis. Evidence from post-mortem studies suggests under-diagnosis of PE in the palliative care setting.

This may be due to several factors:

- breathlessness attributed to co-morbid causes
- patient not well enough for investigation
- other lung pathologies making radiological diagnosis problematic
- concerns over anticoagulation in some patients

The risk of PE from untreated DVT is estimated at 50% and the mortality rate of untreated PE at 30–40%. Most deaths from PE occur in the first hour.

Signs and symptoms

Pulmonary emboli may go unnoticed, causing mild breathlessness, whilst in more severe cases, sudden cardiovascular collapse and death occur. The symptoms and signs vary depending upon the extent of the thrombus, the general condition of the patient, and respiratory/cardiovascular co-morbidities, and also on whether the PE occurs as an acute or protracted event.

Features suggestive of pulmonary emboli include:

- breathlessness and cough
- haemoptysis
- palpitations
- chest pain

Clinical signs may vary and are useful if present. Likewise, many of the signs could be accounted for by other co-morbidities. Signs include:

- tachycardia
- tachypnoea
- irregular pulse
- raised jugular venous pressure
- hypotension
- loud P_2 heart sound
- cyanosis
- syncope

If there is a strong clinical suspicion, absence of signs should not exclude the diagnosis.

Investigations

It is important to decide whether an investigation is going to alter management and, if so, which test would be the most appropriate and best tolerated by the patient. Consider a balance between the test most likely to confirm the diagnosis and that with the least disruption/burden to the patient. Several tests done by protocol for suspected PE in the acute-care setting may be most inappropriate if done near the end of life.

- arterial blood gases
  - invasive, painful procedure; unlikely to provide useful information in the presence of coexisting lung disease
- pulse oximeter—O_2 saturation
  - non-invasive information available at the bedside
- ECG
  - usually normal; or may show sinus tachycardia
  - $S_1Q_3T_3$ phenomenon rare
  - atrial fibrillation may be present
- D-dimers
  - negative result helpful in excluding the diagnosis of thromboembolism
  - positive result does not confirm the diagnosis in the presence of malignancy, infection, increasing age, or impaired renal function
- chest X-ray
  - to evaluate other causes of breathlessness besides PE

Objective testing for PE

All imaging techniques have their limitations and add to the burden on the patient:

- **spiral CT**
  - first-line investigation
  - requires large volume of IV contrast
  - gives assessment of pulmonary veins
  - other chest pathologies may be identified
  - can be used to assess lower limb veins and inferior vena cava (IVC) at the same time
- **ventilation/perfusion (V/Q) scan**
  - usually well-tolerated procedure
  - less preferred than CT and pulmonary angiography
- **pulmonary angiography**
  - 'gold standard' investigation
  - invasive
  - complication rate 0.5%, mortality 0.1%
  - limited use in palliative care population
  - with the advent of CT and pulmonary angiography, it is rarely used
- **magnetic resonance angiography**
  - under evaluation
  - limited use in the palliative population

Chronic venous thrombosis

Patients with hypercoagulability related to disseminated malignancy or with cancers obstructing veins may have chronic venous thrombosis requiring warfarin and/or low molecular weight heparin (LMWH). Migratory thrombophlebitis affecting superficial veins, associated commonly with disseminated bronchogenic adenocarcinoma, may also cause venous and arterial clotting.

Palliative treatment of venous thromboembolism (VTE)

The treatment is planned as a fine balance between handling thrombotic complications and haemorrhagic complications, any of which may predominate at a given time. In the first few weeks to months after the diagnosis, the risk of haemorrhage outweighs the thromboembolic risk.

Palliative treatment goals would be to decrease symptoms and distress (leg swelling and pain, chest pain, shortness of breath), and prevent the clot burden.

DVT

- consider leg elevation
- analgesia for swelling and tenderness (NSAIDs may interfere with the international normalized ratio (INR))
- compression stockings if tolerated to ease the symptoms of venous hypertension
- anticoagulation in a patient with advanced malignancy requires a well-considered decision; if chosen, use intravenous (IV) unfractionated heparin (UFH) or subcutaneous (SC) low-molecular-weight heparin (LMWH)

PE

- oxygen
- opioids ± benzodiazepines for breathlessness and panic
- anticoagulation as appropriate
- venocaval filters may be used to prevent PE if DVTs are recurrent despite anticoagulation measures

Evidence now suggests that anticoagulation with LMWH reduces the recurrence of VTE by 50% without significant bleeding complications. Within the palliative care setting, long-term LMWH should be the first-line anticoagulant of choice.

►Important! Never commence anticoagulant therapy without first checking the INR or platelet count.

Warfarin in patients with cancer

Although the mainstay of long-term anticoagulation for VTE, extreme caution should be used when recommending warfarin. Several studies have demonstrated significant increases in rates of bleeding amongst cancer patients on warfarin (in the order of 20%).

Palliative care patients are particularly at risk of haemorrhage for several reasons:

- presence of DIC
- consumption of clotting factors
- platelet dysfunction/thrombocytopenia
- vascularity of tumours
- liver dysfunction due to metastases

More frequent monitoring of the international normalized ratio (INR) is often needed in patients with cancer (i.e. every 2–3 days) to reduce the risk of bleeding (see Table 7.4).

Problems when using warfarin in patients with advanced cancer

- high risk of bleeding—even higher if thrombocytopenia or liver metastases present
- unpredictable metabolism of warfarin
- interaction with other drugs
- difficulty maintaining INR in therapeutic range
- burden of repeated INR checks to optimize safety
- progression of thrombus despite therapeutic INR in a proportion of patients

Rapid reversal of warfarin

Give 12–15mL/kg FFP; usually 3–4 units of fresh plasma and 10mg vitamin K by slow IV injection.

Low molecular weight heparin (LMWH) in patients with cancer

Although the mainstay of treatment of VTE in patients with cancer has been long-term anticoagulation with warfarin, this is likely to change.

There is evidence comparing long-term LMWH with warfarin in this patient group (level 1a). LMWH has been shown to reduce the recurrence of VTE from 17% to 9% with no statistical difference in bleeding when

Table 7.4 Target INR

Target INR	Indication
2.0–2.5	DVT prophylaxis
2.5	Treatment of DVT and PE (or recurrence in patients not on warfarin)
3.5	Recurrent DVT and PE in patients receiving warfarin Mechanical prosthetic heart valves

compared with warfarin. LMWH may be of particular benefit in palliative care, since concerns regarding monitoring the INR, as well as drug interactions, are reduced.

Considerations before using long-term LMWH

- The once-daily injection of LMWH could be felt as too invasive and burdensome, and may lower the patient's quality of life. This should be weighed against the burden of alternate-day INR checks that may be required to minimize the risk of warfarin-related haemorrhage.
- LMWH is costly. This needs comparing with the costs of repeated blood monitoring and the length of hospital stay whilst loading warfarin to therapeutic levels.

Potential benefits of LMWH

- reliable pharmacokinetics
- anticoagulant effect not altered by diet or concomitant drug use
- fast onset of action
- repeated blood test monitoring not required

There are no guidelines at present to clearly define which patients should receive LMWH for long-term anticoagulation. Anticoagulation with LMWH may be preferred over warfarin in the following patient categories:

- continued thrombosis despite maintaining INR within therapeutic range
- ongoing chemotherapy
- liver metastases
- symptoms of thrombosis that are difficult to control
- regular INR checks considered too great a burden
- poor venous access for blood testing

Direct oral anticoagulants (DOACs) or novel oral anticoagulants (NOACs)

These drugs are increasingly replacing warfarin therapy for ensuring anticoagulation in non-palliative patients. This group, which includes apixaban, rivaroxaban, dabigatran, and edoxaban, do not require regular monitoring of anticoagulation and have standard dosing regimens. However, with a lack of safety and efficacy data in palliative care, their use requires caution. Other areas of concern include significant drug interactions, potential accumulation in renal impairment, and the limited availability of antidotes.

VTE and brain metastases

The management of VTE in those patients with brain metastases is complicated. Studies comparing the use of vena caval filters with anticoagulation show that 40% of patients with filters may experience further thrombotic events, and 7% of those anticoagulated may develop neurological deterioration from intracerebral bleeding. There is no evidence yet for a beneficial role of LMWH in these patients.

Length of anticoagulation

A patient should remain anticoagulated as long as the prothrombotic risk persists. In cancer, as the risk increases as the disease advances, anticoagulation should in theory continue indefinitely. However, as the disease progresses, the bleeding tendency also increases. Hence, stopping anticoagulation may be the lesser of the two evils. The decision should be made, after taking into account the patient's views, impact of treatment and its withdrawal, logistics of treatment, and the complications.

Prophylaxis for VTE

VTE is associated with advanced cancer. In hospitals, patients with VTE are routinely prescribed anticoagulants. Recent evidence has questioned the need for this in patients admitted to a specialist palliative care unit.

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Palliative care in patients with haematological malignancy

Haematological malignancies are unique, as the benefit from aggressive active haematological intervention, in terms of symptom control and prolongation of life, continues even with advanced stages of the disease. Studies indicate that patients with haematological malignancies are significantly less likely to receive palliative care services than patients with solid tumours. The focus on cure often precludes the involvement of palliative care specialists. Efforts to integrate palliative care must therefore move farther upstream and operate independently of any requirement to predict advanced or terminal stages.

The disease-modifying treatment remains aggressive, and younger patients with haematological malignancies have significantly higher rates of emergency room visits, hospitalizations, ICU admissions, and chemotherapy use in the last 30 days of life, than patients with advanced solid tumours.

Improving integration of palliative care services into the care of patients with haematological malignancies

In order to provide the best possible care and awareness of all the choices for patients with late-stage and end-stage haematological disease, palliative care teams need to build close working relationships with colleagues in haematology. A few barriers (in italics) and ways to overcome them are as follows:

- *I shall refer to the palliative care team during the terminal stage*s. There may be a misperception that palliative care teams provide terminal care and therefore referrals should be made when the patient is 'actively dying'. Yet, when such a patient is nearing death, it is often too late to provide meaningful palliative care. This barrier would disappear once the role of palliative care—especially regarding the team approach to all dimensions of the person, with core values centred on quality of life—is understood by haematology colleagues.
- *Palliative care is required for patients with solid tumours*. Given the comparable or even increased physical and psychological symptom burden in patients with haematological malignancies, it is very likely that patients with haematological malignancies will significantly benefit from involvement of the palliative care team.
- '*Palliative' care may be seen by the patient as giving up*. This is often a concern more of the oncologist than of the patients. This barrier may be overcome when the scope of palliative care is understood. Clarity would lead to early and appropriate introductions to the team members, and involvement in shared discussions.
- *I don't want to take away hope*. Studies show that patients prefer open, honest disclosure of prognosis, even when the news is bad. Involving the palliative care team can, in fact, facilitate this difficult task without

leading to more anxiety or depression. It is important to acknowledge that oncology and palliative care are not an either/or option.

- *I want to prioritize on the required haematological interventions for my patient.* Prognostication is very challenging in patients with haematological malignancies. During treatment and as the disease progresses, haematology patients can become very ill, very quickly. It is important for the palliative care team to understand that this may not be the terminal stage, as patients often respond to active support with antibiotics, fluids, and blood products. It is also important for oncologists to appreciate that the chances of the patient completing their prescribed oncological treatment would be higher with integration of palliative care.
- *I do the required palliative care for my patients*. The general palliative care needs are best taken care of by the primary team, be they supportive care interventions, symptom control measures, or proactive discussions on prognosis. Involving palliative care specialists in the care of patients is not to replace this, but to enhance it when the complexities require specialized care.
- *I am not sure whether the palliative care team can handle the care of my patient*. The treating team may doubt the competency levels of palliative care team members to manage the care of haematology patients. Expertise of each team is different, essential, and complementary. Working together helps understanding and respect, enhances the skills in caring for both teams, and improves the overall quality of care and the quality of life for the patient.
- *Involving another clinical team may be disruptive to the overall care*. The comprehensive approaches adopted by the palliative care team and the limited role expected by the treating oncology team may cause difficulties. The palliative care team may explore the patient's knowledge and understanding of their illness and attitude to continuation of treatment. This may be seen as undermining the planned haematological treatment or as pushing patients towards DNR (do not resuscitate) decisions. Yet, experience with integration suggests that patients maintain strong relationships with their oncologists and do not perceive their care as being fragmented. Both teams can work amicably with mutual consensus on goals of care, negotiating treatment plans together. Discussions and regular communications help build the trust required to provide the most appropriate care.

Palliative care is valuable for patients with haematological malignancies in the following situations:

- distressing symptoms of the disease or cancer-directed therapies
- significant psychological concerns and communication needs
- during the period of allogeneic stem cell transplantation
- complex family and social needs; difficulty in coping with the illness
- misperceptions and conflicts about illness trajectory and overall prognosis
- uncertain or poor prognosis, with limited life expectancy
- high symptom burden or refractory symptoms of advanced disease
- end-of-life care and bereavement

Symptoms in patients with haematological malignancies

Mucositis

Cytotoxic mucosal injuries of most anti-neoplastic drugs used in treating haematological malignancies cause severe pain and difficulty with chewing, swallowing, and speech. Mucositis is worsened by the occurrence of candidiasis secondary to reduced immunity and/or superimposed herpes simplex infection. The damage to the mucosal barriers can be severe enough to cause septicaemia.

Good oral and dental hygiene and regular mouthwashes with salt-soda water or normal saline are helpful in preventing chemotherapy-related oral complications. Details of managing mucositis are described in Mucositis,p. 444

Symptoms due to splenomegaly and hypersplenism

Symptomatic splenomegaly is common with haematological malignancies—in particular, chronic granulocytic leukaemia and certain types of non-Hodgkin's lymphoma. It is also a feature of myelodysplasia. The symptoms are:

- pain and discomfort—due to local bulk
- anaemia and coagulopathy/hypersplenism leading to consumption of red cells and platelets

Splenic infarction can develop in patients with long-standing myeloproliferative diseases and splenomegaly. This results in left upper quadrant pain that is continuous with exacerbations of stabbing pain. The patient has difficulty sitting or bending owing to the bulk and pain.

Surgical removal of the spleen could be a good option for patients with a good functional status. Local irradiation is used for palliating symptoms in patients with poor performance status. The radiation dose is chosen very carefully for control of hypersplenism, as high doses may precipitate pancytopenia. It is usually given as single doses of 1Gy or less per week with total dose adjusted to between 3Gy and 10Gy. The effect on the peripheral blood count and the degree of splenic shrinkage is evaluated weekly, prior to each treatment.

Symptoms due to thrombocytopenia

Thrombocytopenia results in easy bruising. Spontaneous bleeding can occur at a platelet count of less than 20×10^9, and fatal intracranial haemorrhage can occur at a platelet count of less than 5×10^9. Indications for the transfusion of platelets in patients with advanced haematological malignancies include:

- continuous bleeding from the mouth and gums
- overt haemorrhage (gastrointestinal tract, gynaecological, urinary)
- extensive and painful haematoma
- recent onset disturbance in vision (in the setting of thrombocytopenia)
- severe and recent onset headache (in the setting of thrombocytopenia)
- severe anaemia (and thrombocytopenia)

A general approach to this issue is given in the earlier sections, but managing bleeding in patients with haematological malignancies is complex and requires the expertise of haematological oncologists. Approaches using infusion of desmopressin (0.4micrograms/kg diluted in 100mL saline) and infused

over 30 min have been effective in controlling bleeding in patients with various haematological malignancies and thrombocytopenia.

Pain

Besides the mucositis and swollen spleen, rapid enlargement of lymph nodes causes pain. Lymphadenopathy was the most common cause of visceral pain in a study of patients with haematological malignancies. Enlarged retroperitoneal lymphadenopathy can cause focal or diffuse back pain. This pain syndrome is most prevalent among those with lymphomas or germ cell tumours. Patients with lymphomas may experience a flare-up of pain related to enlarged lymph nodes after drinking alcohol.

Pain is managed per the WHO analgesic ladder guidelines.

Symptoms due to hypercalcaemia

In patients with haematological malignancies, hypercalcaemia does not always indicate poor prognosis. Onset of malaise, thirst, nausea, and constipation may herald hypercalcaemia. Later, neurological or cardiological symptoms may appear. Management is based on the mainstays rehydration and administration of calcium-lowering agents. Unlike in other malignancies, hypercalcaemia of haematological malignancies responds well to the cytostatic effects of corticosteroids. It takes 4–10 days for oral prednisolone 40–100mg/day to lower the serum calcium.

Delirium

Studies indicate a high prevalence of hypoactive type of delirium in patients with haematological malignancies. This diagnosis may be missed easily unless specifically screened for. For details of evaluation and management, see Chapter 20, Dementia and frailty.

End-of-life care for patients with haematological malignancies

In patients with haematological malignancies, the gap between the acute care bed and home-based palliative care is wide, and interspersed with transfusions of platelets and blood products. Standard home-based end-of-life (EOL) services do not meet the unique needs of patients with haematological malignancies.

It is important for the palliative care team to fully appreciate the fact that the haematology team may have looked after their patient through several near-death crises, and that the patients may have responded to previous treatments in extremis. Offering further chemotherapy may be totally appropriate even when the disease is in advanced stages.

Ironically, the gap between acute care and end-of-life care could be very marginal. The aim of involvement would be to enhance the quality care available to these patients by identifying and addressing those concerns which are reversible and by assisting in transitioning care goals in those situations which are irreversible.

Haematological malignancy-specific quality measures for terminal care would hence have to be developed jointly by haematologist-oncologists together with palliative physicians based on precise criteria, such as response to earlier therapies, pre-morbid physical status, and the benefit and burden of continuing disease-directed therapies, and by defining criteria for discontinuing interventions such as transfusions of platelets or blood products.

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Chapter 8

Pain management

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Introduction

Theories of pain

> Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.
>
> International Association for the Study of Pain

Pain is a complex phenomenon and an important clinical problem. New therapeutic approaches have developed from research and from novel theoretical perspectives. Although the physiology of pain has been little understood until relatively recently, our understanding of pain and its management continues to develop rapidly.[1]

The **specificity theory** of pain proposed by René Descartes in the sixteenth century stated that pain intensity relates directly to the amount of associated tissue injury. This unidimensional approach to pain implied that pain has a predominantly physical basis and is treatable by analgesics.

The limitations of this theory were increasingly recognized during the early twentieth century. During the Second World War, Dr Henry Beecher observed that only one out of three soldiers carried into a combat hospital complained of enough pain to require morphine. He inferred that clinical pain was a compound of physical sensation and cognitive and affective elements.[2]

In 1965, the psychologist Ronald Melzack and the physiologist Patrick Wall published the classic **gate control** theory of pain, proposing a spinal cord mechanism which regulates the transmission of pain sensations between the periphery and the brain.[3, 4] This theory shifted attention away from the peripheral source of injury towards the neural mechanisms responsible for the experience of pain. It provided the first physiological mechanism for psychological interventions to minimize pain. The theory stimulated discussion amongst clinicians and pain researchers, and provided momentum to scientific investigation into the nature of pain. The first clinical trials of oral morphine began in the 1970s; the International Association for the Study of Pain took shape in 1973; and the World Health Organization began developing the analgesic ladder for the management of pain in 1982. Following on from this work, an increasingly multidimensional and multidisciplinary approach to pain has been adopted.

It is now recognized that pain perception is governed by a multitude of factors—the **neuromatrix theory** of pain).[4]

> I think the simplest and probably the best definition of pain is what the patient says hurts. I think that they may be expressing a very multi-faceted thing. They may have physical, psychological, family, social and spiritual things all wound up in this one whole experience. But I think we should believe people and once you believe somebody you can begin to understand, and perhaps tease out the various elements that are making up the pain.
>
> Cicely Saunders

Total pain

Dame Cicely Saunders recognized that many important factors can influence the pain experience. In parallel with the work of others, she developed the concept of **total pain** from her understanding that the origins of pain may be:

- physical
- social
- psychological
- spiritual

The concept of total pain has become a central tenet of palliative care practice. It recognizes that cancer pain is often a complex, chronic pain with multiple, coexisting causes. Effective management of cancer pain requires a multidisciplinary approach that addresses the patient's concerns and fears, as well as treating the physical aspects of pain. As a result, the provision of analgesics should be combined with the provision of emotional, social, and spiritual supports.

> One patient in particular, a lady whose name should be recorded, a Mrs Hinson, there were days that I remember saying to her, 'Tell me about your pain', and without any more prompting from me, she went on to say, 'Well doctor, it began in my back, but now it seems that all of me is wrong'. And she gave a description about her symptoms. And then she went on to say, 'I could have cried for the pills and the injections, but I knew that I mustn't, the world seemed to be against me, nobody seemed to understand how I felt. My husband and son were marvellous, but they were having to stay off work and lose their money, but it's so wonderful to begin to feel safe again'. So really, she's talked about physical pain, she's talked about emotional pain of feeling shut away and all the emotional burden that she couldn't share. She was talking about social pain, financial in that case, but the impact on her family. And then the spiritual need, I think it is spiritual, of the security, the safety, to look at herself and who she was and just be herself. And then the concept of what I called total pain, and really started to lecture about, really comes from there.
>
> Cicely Saunders

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Pain in the palliative care setting

Pain is a common and feared symptom of cancer and certain other life-limiting, non-malignant conditions (Table 8.1). Despite the availability of effective methods of controlling pain, significant numbers continue to receive inadequate pain relief.

Some examples of pain relating to non-cancer causes include lower limb oedema in chronic heart failure, neuritic pains in HIV/AIDS, musculoskeletal pain related to the work of breathing in chronic obstructive pulmonary disease, and generalized pain secondary to cachexia and immobility in advanced dementia.

Table 8.1 Causes of cancer-related pain

The cancer itself	Bony/visceral/soft tissue involvement, nerve compression or infiltration, muscle spasm, ulceration, raised intracranial pressure, etc.
Complications of the cancer	Pressure sores, constipation, post-herpetic neuralgia, candidiasis, lymphoedema, deep vein thrombosis, etc.
Treatment of the cancer	Neuropathy caused by chemotherapy, mucositis caused by radiotherapy, post-operative pain, etc.
Co-morbidities	Angina, diabetic neuropathy, arthritis, etc.

Prevalence of cancer pain

Estimates indicate that 59–90% of patients with cancer experience pain at some stage.[1]

- one-quarter of patients do not experience pain
- one-third of those with pain have a single pain
- one-third have two pains
- one-third have three or more pains

Impact of cancer pain

Pain is increasingly understood as a multidimensional construct with implications on patients' affect, cognition, behaviour, social relations, spirituality, function, and overall quality of life. A strong correlation has been demonstrated between cancer pain and psychological distress.[2]

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Classification of pain

See Table 8.2.

Cancer pain may be **acute** or **chronic**. **Background pain** is a persistent baseline pain. Background pain is managed by the regular administration of analgesics. **Breakthrough pain** is a transitory exacerbation of pain experienced by the patient with stable and adequately controlled background pain. Breakthrough pain is usually related to the background pain, rapid in onset, severe in intensity, and self-limiting, with an average duration of 30 min.[1]

Table 8.2 Definition of pain terms

Nociceptor	A receptor preferentially sensitive to a noxious stimulus or to a stimulus which would become noxious if prolonged
Nociceptive pain	Pain which is transmitted by an undamaged nervous system and is usually opioid-responsive
Neuropathy	A disturbance of function or pathological change in a nerve
Neuropathic pain	Pain which is transmitted by a damaged nervous system, and which is usually only partially opioid-sensitive
Pain threshold	The least experience of pain which a subject can recognize
Pain tolerance level	The greatest level of pain which a subject is prepared to tolerate
Allodynia	Pain caused by a stimulus which does not normally provoke pain
Analgesia	Absence of pain in response to stimulation which would normally be painful
Causalgia	A syndrome of sustained burning pain, allodynia, and hyperpathia after a traumatic nerve lesion, often combined with vasomotor dysfunction and later trophic changes
Neuralgia	Pain in the distribution of a nerve
Central pain	Pain associated with a lesion in the central nervous system (brain and spinal cord)
Dysaesthesia	An unpleasant abnormal sensation which can be either spontaneous or provoked
Hyperaesthesia	An increased sensitivity to stimulation
Hyperalgesia	An increased response to a stimulus that is normally painful
Hyperpathia	A painful syndrome characterized by an increased reaction to a stimulus, especially a repetitive stimulus, and an increased threshold

Data sourced from Merskey H, Bogduk N. Classification of Chronic Pain 2nd ed. Seattle: IASP Press, 1994.

Chronic pain may be further subdivided

Nociceptive and neuropathic pain

Two main types of pain may be identified on the basis of the mechanism of the pain: **nociceptive** and **neuropathic**. Different types of pain respond with varying degrees of effectiveness to different types of intervention, so it is important that clinicians determine what type of pain a patient is experiencing in order to prescribe the most appropriate analgesic. Many patients with cancer have **mixed-pain syndromes**, and therefore require combination therapy.[1]

Nociceptive pain may result from injury to somatic structures (somatic pain) or injury to visceral structures (visceral pain) (Fig 8.1):

- **Somatic pain** results from the stimulation of skin, muscle, or bone receptors. The neural pathways involved are normal and intact and the pain is typically well localized, and may be felt in the superficial cutaneous areas (e.g. cellulitis) or deeper musculoskeletal areas (e.g. bone pain). It may be described as aching, stabbing, throbbing, or pressure.
- **Visceral pain** results from infiltration, compression, or the distension of thoracic or abdominal viscera. It is often poorly localized and may be described as gnawing, cramping, aching, or sharp. It may be referred to cutaneous sites (e.g. shoulder-tip pain from diaphragmatic irritation due to liver capsule distension), and the cutaneous site may be tender. The mechanism of action of referred pain is poorly understood.[2]

Neuropathic pain is caused by injury to the peripheral and/or central nervous system (Fig 8.2). The underlying mechanisms of neuropathic pain are poorly understood, but broadly speaking, pain occurs because the injured nerves either react abnormally to stimuli or discharge spontaneously. Typically, pain that arises from damage to the peripheral nervous system is termed 'deafferentation' pain, while pain that arises from injury to the spinal cord or brain is termed 'central' pain.

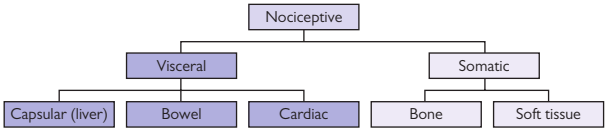


Fig 8.1 Somatic pain.

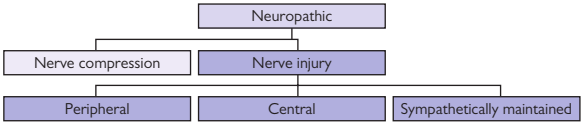


Fig 8.2 Neuropathic pain.

Neuropathic pain is typically described as being different in character to nociceptive pain. Patients may describe having a dull ache with a 'vice-like' quality, or burning, tingling, shooting, or electric shock–like sensations. It may be associated with hyperalgesia and allodynia.

Mixed pain has components of both neuropathic and nociceptive elements.

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Assessment of pain

> What we were aiming at as we started to work together in St Joseph's, was a patient who was alert and themselves and free of pain. For the great majority of patients that isn't that difficult with drugs that are available to anybody in a method that is simple. But it does include the very important careful analysis and assessment at the beginning.
>
> Cicely Saunders

Failure to assess pain is a critical barrier to good pain management.

- Pain is a subjective experience, and so **patient self-report** is the gold standard of pain assessment.
- Evaluation and treatment of pain are best achieved by a **team approach.**
- It has been shown that patient education and involvement in the management of their own pain can result in a significant decrease in pain intensity.[1]
- Many patients will have more than one type of pain, and **each pain should be assessed separately.**
- Patients should be **re-assessed at regular intervals** following initiation of treatment, and also at each report of new or altered pain.

Principles of pain assessment

A comprehensive assessment of pain should consider the following domains:

- physical effects and manifestations of the pain
- functional effects of the pain
- psychosocial and spiritual factors influencing the pain
- potential modulators of pain expression including substance use and delirium.

Key components of a pain assessment

- description of the onset and duration of the pain
- description of the pain, e.g. location, quality, pattern, character
- rating of pain intensity (including a current pain rating, and ratings when pain is worst and least)
- description of aggravating and relieving factors
- description of associated symptoms and signs
- description of the effects of pain on functioning and quality of life
- description of current pain management regimen and assessment of effectiveness
- summary of the past history of pain management
- identification of the patient's goals of treatment
- physical examination
- diagnostic testing, where appropriate

Pain assessment tools

Pain scales can be useful tools in the systematic assessment of symptoms, during both initial and ongoing assessments. Not only can they encourage

patient communication and facilitate the professional's understanding of the patient's experience, but they can also be used to chart the trend of the patient's response to therapy. However, tools should never be seen as substitutes for a complete pain assessment, and may need to be tailored to the needs of specific populations. Pain assessment should be carried out in the context of an overall psychosocial and spiritual assessment using appropriate tools.

There is no consensus at present regarding the gold standard pain assessment tool, but ideal qualities of a pain assessment tool include the following:

- ease of administration
- validity and reliability
- sensitivity to treatment effect

Pain assessment tools may be **unidimensional** or **multidimensional**:

- unidimensional tools provide information about the intensity of the pain experienced by the patient, and take the form of visual analogue scales, verbal rating scales, and numeric rating scales
- multidimensional pain measuring tools provide information about additional aspects of the pain such as history, location, affective component, and quality of the pain; examples include the McGill Pain Questionnaire and the Brief Pain Inventory (Fig 8.3)

The visual analogue scale (VAS)

The VAS is a line with extremes marked as 'no pain' and 'worst pain'. Patients are asked to mark the point in the line that best describes their pain.

No pain_____Worst pain

The categorical verbal rating scale (VRS)

This involves a sequence of words describing different levels of pain intensity, e.g.

None_____Mild_____Moderate_____Severe

The categorical numerical rating scale (NRS)

This uses numbers or gradations that indicate the severity of the pain experience:

0___1___2___3___4___5___6___7___8___9___10

No pain_____Worst pain

Assessing pain in people with dementia and cognitive impairment

Pain is under-reported and under-treated in cognitively impaired people. Particularly at the end of life, it has been shown that people with dementia often receive suboptimal management of physical and psychological symptoms in comparison to the general population—one group of the so-called disadvantaged dying.[2]

As dementia progresses, and cognitive function and the ability to communicate verbally declines, it becomes increasingly more difficult to ascertain accurately wishes and needs and, consequently, people with dementia often have painful conditions that go unnoticed. This loss of language communication presents a major challenge in assessing pain in this group, as self-reporting is required for most pain assessment tools.

Brief Pain Inventory

Date: /___/

Name:_____ _____ _____

Last First Middle Initial

Phone: (____)_____ Sex: ☐ Female ☐ Male

Date of Birth: /___/

1) Marital Status (at present)

1. ☐ Single 3. ☐ Widowed
2. ☐ Married 4. ☐ Separated/Divorced

2) Education (Circle only the highest grade or degree completed)

Grade 0 1 2 3 4 5 6 7 8 9
10 11 12 13 14 15 16 M.A./M.S.

Professional degree (please specify)_____

3) Current occupation _____
(specify titles; if you are not working, tell us your previous occupation)

4) Spouse's Occupation _____

5) Which of the following best describes your current job status?

☐ 1. Employed outside the home, full-lime
☐ 2. Employed outside the home, part-time
☐ 3. Homemaker
☐ 4. Retired
☐ 5. Unemployed
☐ 6. Other

5) How long has it been since you first learned your diagnosis? _____months

7) Have you ever had pain due to your present disease?

1. ☐ Yes 2. ☐ No 3. ☐ Uncertain

8) When you first received your diagnosis, was pain one ol your symptoms?

1. ☐ Yes 2. ☐ No 3. ☐ Uncertain

9) Have you had surgery in the past month? 1. ☐ Yes 2. ☐ No

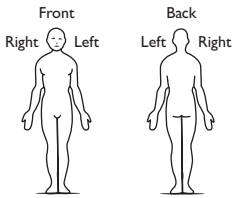
10) Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain during lhe last week?

1. ☐ Yes 2. ☐ No

IF YOU ANSWERED YES TO THE LAST QUESTION, PLEASE GO ON TO QUESTION 11 AND FINISH THIS QUESTIONNAIRE IF NO YOU ARE FINISHED WITH THE QUESTIONNAIRE. THANK YOU.

Fig 8.3 Brief pain inventory. Reproduced with permission from Doyle et al. (eds) (2004) *The Oxford Textbook of Palliative Medicine* (3rd edn). Oxford: with permission from Oxford University Press.

11) On the diagram, shade in the areas where you feel pain. Pul an X on the area that hurts the most



12) Please rate your pain by circling the one number that best describes your pain at its worst in the last week.

01	2	3	4	5	6	7	8	9	10
No Pain								Pain as bad as you can imagine	

13) Please rate your pain by circling the one number that best describes your pain at its least in Ihe last week.

01	2	3	4	5	6	7	8	9	10
No Pain								Pain as bad as you can imagine	

14) Please rate your pain by circling the one number that best describes your pain on the average

01	2	3	4	5	6	7	8	9	10
No Pain								Pain as bad as you can imagine	

Fig 8.3 Brief pain inventory. Reproduced with permission from Doyle et al. (eds) (2004) *The Oxford Textbook of Palliative Medicine* (3rd edn). Oxford: with permission from Oxford University Press.

15) Please rate your pain by circling the one number that tells how much pain you have right now.

0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

16) What kinds of things make your pain feel better (for example, head, medicine, rest)?

_____

_____

17) What kinds of things make your pain worse (tor example, walking, standing, lifting)?

_____

_____

18) What treatments or medications are you receiving for your pain?

_____

_____

19) In the last week, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0%	10%	20%	30%	40%	-50%	60%	70%	60%	90%	100%
No Relief										Complete Relief

20) If you take pain medication, how many hours does it take before the pain returns?

☐1. Pain medication doesn't help at all
☐ 2. One hour
☐ 3. Two hours
☐ 4. Three hours
☐ 5. Four hours
☐ 6. Five to twelve hours
☐ 7. More than twelve hours
☐ 8. I do not take pain medication

21) Circle the appropriate answer for each item. I believe my pain is due to:

☐ Yes ☐ No 1. The effects of treatment (for example, medication, surgery, radiation, prosthetic device).
☐ Yes ☐ No 2. My primary disease (meaning the disease currently being treated and evaluated).
☐ Yes ☐ No 3. A medical condition unrelated to primary disease (for example, arthritis).

Fig 8.3 Brief pain inventory. Reproduced with permission from Doyle et al. (eds) (2004) *The Oxford Textbook of Palliative Medicine* (3rd edn). Oxford: with permission from Oxford University Press.

22) For each of the following words, check yes or no it that adjective applies to your pain.

Aching	☐ Yes	☐ No	Exhausting	☐ Yes	☐ No
Throbbing	☐ Yes	☐ No	Tiring	☐ Yes	☐ No
Shooting	☐ Yes	☐ No	Penetrating	☐ Yes	☐ No
Slabbing	☐ Yes	☐ No	Nagging	☐ Yes	☐ No
Gnawing	☐ Yes	☐ No	Numb	☐ Yes	☐ No
Sharp	☐ Yes	☐ No	Miserable	☐ Yes	☐ No
Tender	☐ Yes	☐ No	Unbearable	☐ Yes	☐ No
Burning	☐ Yes	☐ No			

23) Circle the one number that describes how, during the past week, pain has interfered with your:

A. General Activity

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

B. Mood

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

C. Walking ability

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

D. Normal work (includes both work outside the home and housework)

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

E. Relations with other people

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

F. Sleep

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

G. Enjoyment of life

0 1 2 3 4 5 6 7 8 9 10
Does not Interfere — Completely interferes

Pain Research Group, Department of Neurology, University of Wisconsin-Madison

Fig 8.3 Brief pain inventory. Reproduced with permission from Doyle et al. (eds) (2004) *The Oxford Textbook of Palliative Medicine* (3rd edn). Oxford: with permission from Oxford University Press.

In the absence of verbal self-report, nurses and carers are forced to rely increasingly on non-verbal and behavioural cues of physical and emotional pain. They need to use a combination of indicators to determine levels of pain, e.g. crying, facial grimacing, etc. Using observation skills rather than relying on verbal responses is essential, as is consideration that any sign of agitated behaviour may be emotional and not a result of pain.

Behaviour commonly associated with pain may be absent or difficult to interpret; for example, extrapyramidal signs in people with dementia syndromes may mislead the healthcare professional, who may interpret the movements as an indication of pain. There is no agreed physiological or biological chemical marker of pain, and in people who are unable to communicate, there is no benchmark that can be used to allow a definitive diagnosis of pain.[3]

A number of pain assessment tools have been developed for use in people with dementia.[4, 5] However, it remains a complex area of clinical assessment practice. It is important to select a scale that matches the person's abilities; even their pre-dementia educational level and pre-existing abilities influence their ability to use pain scales.[6, 7]

Enlisting the assistance of a carer or family member who is familiar with the usual behaviours and responses of the person with dementia is also essential in identifying behaviour changes that may indicate pain or discomfort.

The Abbey Pain Scale is an assessment tool that is presented in a form suitable for clinical use and is both easy and quick to administer. It was developed with care-home residents with end- or late-stage dementia, using a combination of quantitative and qualitative data collection and analysis processes.[8] The Abbey Pain Scale has been shown to be most useful as an aid to intervention where the scale is used to assess changes prior to and following the administration of analgesia (Fig 8.4).

Many of the principles of assessing and managing pain in people with dementia also apply to people with learning disabilities when providing end-of-life care. The Disability Distress Assessment Tool (DisDAT),[9] developed to aid in the assessment of distress in people with learning disabilities, may also be of use in guiding practitioners in assessing distress in the dementia group.

Use of the Abbey Pain Scale:

A pain scale is best used as part of an overall pain management plan.

Objective

The pain scale is an instrument designed to assist in the assessment of pain in residents who are unable to clearly articulate their needs.

Ongoing assessment

The scale does not differentiate between distress and pain, therefore measuring the effectiveness of pain relieving interventions is essential.

The Australian Pain Society recommends that the Abbey pain scale be used as a movement based assessment.

The staff recording the scale should, therefore, observe and record on the scale while the resident is being moved eg, during pressure area care, while showering etc.

Record results in the resident's notes. Include the time of completion of the scale, the score, staff member's signature and action taken in response to results of the assessment.

A second evaluation should be conducted 1 hour after the intervention taken in response to the first assessment, to determine the effectiveness of any pain relieving intervention.

If, at this assessment, the score on the pain scale is the same, or worse, undertake a comprehensive assessment of all facets of the resident's care, monitor closely over a 24 hour period, including any further interventions undertaken, and, if there is no improvement, notify the medical practitioner

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Further details re original validation can be found : Jennifer Abbey. Neil Piller. AnitaDe Bellis, Adrian Esterman, Deborah Parker. Lynne; Giles and Belinda Lowcay (2004) The Abbey pain scale: a 1-mmute numerical indicator for people with end-stage dementia. *International Journal of Palliative Nursing*, Vol 10. No 1pp 6–13.

Abbey Pain Scale

For measurement of pain in people with dementia who cannot verbalise

How to use scale: While observing the resident, score questions 1 to 6.

Name of resident: .....

Name and designation of person completing the scale : .....

Date : .....Time : .....

Latest pain relief given was.....at.....hrs.

Q1. **Vocalisation**
eg whimpering, groaning, crying Q1 ☐
Absent 0 Mild 1 Moderate 2 Severe 3

Q2. **Facial expression**
eg looking tense, frowning, grimacing, looking frightened Q2 ☐
Absent 0 Mild 1 Moderate 2 Severe 3

Q3. **Change in body language**
eg fidgeting, rocking, guarding part of body, withdrawn Q3 ☐
Absent 0 Mild 1 Moderate 2 Severe 3

Q4. **Behavioural Change**
eg increased confusion, refusing to eat, alteration in usual patterns Q4 ☐
Absent 0 Mild 1 Moderate 2 Severe 3

Q5. **Physiological change**
eg temperature, pulse or blood pressure outside normal limits, perspiring, flushing or pallor Q5 ☐
Absent 0 Mild Moderate 2 Severe 3

Q6. **Physical changes**
eg skin tears, pressure areas, arthritis, contractures, previous injuries Q6 ☐
Absent 0 Mild 1 Moderate 2 Severe 3

Add scores for 1 - 6 and record here ⟹ Total Pain Score ☐

Now tick the box that matches the Total Pain Score

0-2 No pain	3-7 Mild	8-13 Moderate	14+ Severe

Finally, tick the box which matches the type of pain

Chronic	Acute	Acute on Chronic

Abbey. J. DeBellis. A. Piller, N., Esterman. A., Giles, L, Parker. D and Lowcay. B.
Funded by the JH&JD Gunn Medical Research Foundation 1998-2002
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Fig 8.4 Use of the Abbey Pain Scale.

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Breakthrough pain

Breakthrough pain is a transient increase in pain intensity over and above the background pain. Breakthrough pain typically is of rapid onset, severe in intensity, and self-limiting, with an average duration of 30 min. Breakthrough pain affects over 50% of patients with cancer. It is a poor prognostic indicator and may lead to anxiety, depression, decreased functioning, and prolonged stays in hospital.[1-3] Every patient on an opioid should have access to breakthrough analgesia in order to ensure optimal pain control.

Three types of breakthrough pain

- **incident pain:** pain is related to movement (either voluntary or involuntary)
- **idiopathic/spontaneous pain:** no identifiable cause; lasts longer than incident pain
- **end-of-dose failure:** prior to scheduled dose of analgesia; gradual onset; this is not regarded as a true breakthrough pain

Management of breakthrough pain

- **Non-pharmacological management:**[4] if possible, treat the underlying cause (e.g. surgery, chemotherapy, radiotherapy); avoid precipitating factors (if possible), physical therapy, education about limitations and exacerbating factors, and patient counselling to reduce anxiety.
- **Optimize around-the-clock medication.**
- **Specific pharmacological interventions:** it is generally appropriate to use a **short-acting opioid at a dose of one-sixth of the total 24-hour dose of opioid**. However, it is recognized that the relationship between the 24-hour dose of opioid and the breakthrough dose is not fixed, and some patients may require individual titration of the breakthrough dose to control their incident pain.

Newer analgesics are available that offer more rapid onset and offset of analgesia than traditional short-acting opioids. These rapid-onset opioids offer certain advantages over traditional short-acting opioids because of their favourable pharmacokinetic profile. Examples include fentanyl as an oral transmucosal lozenge, a sublingual tablet, an effervescent buccal tablet, and an intranasal spray. Given the relative lack of comparative studies, factors such as disease characteristics, patients' preference, ease of administration, and cost are determinants in deciding the most appropriate formulation for individual patients.

Pharmacological management should be tailored to the type of breakthrough pain:

- **incident pain:** pre-emptive use of a short-acting opioid at an appropriate interval before activity (if predictable)
- **idiopathic/spontaneous:** use of a short-acting opioid when pain occurs
- **end-of-dose failure:** alter the around-the-clock medication to increase the dose or shorten the dosing interval

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Principles of pain management

The right dose of an analgesic is the dose that relieves pain without causing unmanageable side effects.

The WHO analgesic ladder

First published in 1986 by the World Health Organization (WHO), *Cancer Pain Relief* is a book which sets out the principles of cancer pain management, including the use of the three-step analgesic ladder.[1] The WHO ladder indicates that a structured yet flexible approach to the management of cancer pain—one that is simple for the patient to follow—is important. The steps of the ladder illustrate that the process of selecting analgesics should be dependent on an assessment of the intensity of pain experienced by the patient, rather than the aetiology of the pain or stage of the disease.

The WHO method can be summarized in five phrases

- by the mouth
- by the clock
- by the ladder
- for the individual
- attention to detail

The oral route is the preferred route for all analgesics, including morphine. For persistent pain, analgesics should be taken at regular time intervals and not 'as needed'. Adjuvant drugs may be needed.

Each patient should be regularly reassessed in order to determine response to treatment and to ensure that they experience maximum benefit with as few adverse effects as possible. Pain relief can be achieved for the majority of patients by adopting the basic principles of 'by the mouth, by the ladder, and by the clock'.[2]

The WHO analgesic ladder has been extensively validated[3] and the principles are widely accepted. The approach has had significant clinical and educational impact across the globe.[4]

Classification of analgesics

The three classes of analgesics referred to in the WHO analgesic ladder are: non-opioids, opioids, and adjuvants (co-analgesics) (Fig 8.5).

Mild pain refers to pain assessed as 1–2 on a numerical rating scale of 0–10; mild-to-moderate pain refers to pain assessed as 3–6/10; and severe pain refers to pain assessed as 7–10/10.[5]

Non-opioids

Non-opioids are analgesic drugs that mediate their effect through receptors other than opioid receptors. Examples of non-opioids are aspirin, paracetamol, and NSAIDs.

Step 1: Non-opioid ± adjuvants

Patients with mild pain should be treated with a non-opioid analgesic, and if a specific indication exists, the use of the non-opioid analgesic may be combined with that of an adjuvant analgesic.

For example, a patient with mild neuropathic pain may be prescribed paracetamol 500mg–1g q6–8h regularly (max daily dose 4g) in combination with amitriptyline 25–75mg o.d.

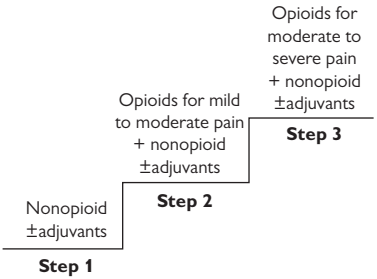


Fig 8.5 The analgesic ladder. Reproduced from WHO Cancer Pain Relief (1986) Geneva, WHO. With permission from the World Health Organization.

Opioids

Opioids are drugs that are agonists at opioid receptor sites. There are at least three types of opioid receptor (mu, kappa, and delta), which are found in many areas of the brain, throughout the spinal cord, and in other tissues. Stimulation of opioid receptors results in a variety of responses, including analgesia, respiratory depression, myosis, reduced gastrointestinal motility, and euphoria. Differences between opioids relate, in part, to differences in receptor affinity.

Step 2: Opioids for mild-to-moderate pain + non-opioid ± adjuvants

Patients who fail to achieve adequate relief after a trial of a non-opioid analgesic, or who present with moderate pain, should be treated with an opioid conventionally used for the treatment of mild-to-moderate pain. The opioid may be combined with a non-opioid in order to achieve an additive analgesic effect. Adjuvant drugs may also be used as required.

For example, a patient with moderate neuropathic pain may be prescribed codeine 30–60mg q6h in combination with paracetamol 1g q6h and amitriptyline 25–75mg o.d.

The clinical usefulness of step 2 of the ladder has been questioned. The WHO now recommends the use of a two-step analgesic ladder for the management of cancer pain in children.[6] One systematic review demonstrated that opioids for mild–moderate pain, either alone or in combination with non-opioids, were no better than full doses of NSAIDs alone.[7] A meta-analysis of four clinical trials found that it was impossible to assess the risks and benefits of a two-step vs a three-step approach.[8] However, subsequent to this meta-analysis, an open-label randomized controlled trial demonstrated that low-dose morphine provided earlier and more adequate analgesia for moderate cancer pain than traditional step 2 opioids, and was well tolerated.[9]

Combination preparations of opioids and non-opioids are available for use at step 2, and are some of the most widely used medicines in the community, e.g. co-codamol.

Step 3: Opioids for moderate-to-severe pain + non-opioid ± adjuvants

Patients who fail to achieve adequate relief despite appropriate prescription of step 2 drugs, or for whom a clinical decision is made to start treatment with a low dose of a step 3 opioid, or who present with moderate-to-severe

pain should be treated with a strong opioid conventionally. Adjuvant drugs may also be used.

Opioids for moderate-to-severe pain are available as immediate release and modified release preparations. Immediate-release (i/r) opioids typically reach peak plasma concentrations within one hour of ingestion and have a duration of action of 1–4h, depending on formulation. Modified-release (m/r) opioids typically reach their peak plasma concentrations 2–6h after ingestion, and the plasma levels are sustained over a period of 12–24h, depending on formulation.

Adjuvant analgesics

These are drugs which do not function primarily as analgesics but can relieve pain in specific circumstances. The choice of adjuvant drug is generally guided by the nature of the underlying pain (i.e. nociceptive or neuropathic). Examples of adjuvant analgesics are listed in Table 8.3 (see Choice of analgesic: adjuvant agents, p. 289).

Table 8.3 Adjuvant analgesics

Adjuvant analgesic	Use
Antidepressant	Neuropathic pain
Anticonvulsant	Neuropathic pain
Antispasmodic	Pain due to colic
Bisphosphonate	Pain due to bone metastases
Antibiotics	Pain due to infection
Corticosteroid	Pain due to oedema or nerve compression
Muscle relaxant	Pain due to muscle spasm or cramp
NMDA-receptor blocker	Neuropathic pain

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Choice of analgesic: non-opioid analgesics

Paracetamol and NSAIDs are the step-one analgesics of choice. The choice between paracetamol and NSAIDs should be based on a risk/benefit analysis for each patient.

Paracetamol

Paracetamol is well-established as an effective and well-tolerated agent for mild-to-moderate pain, both as a single agent and in combination with more potent analgesics, including codeine.[1] It has minimal toxicity in adults at recommended doses, but at higher doses can cause fatal hepatotoxicity and renal damage. The recommended maximum daily dose is 4g/24h; however, one manufacturer in the United States has changed its recommendation to 3g/24h (McNeil Consumer Healthcare). The risk of toxicity increases in patients with pre-existing hepatic impairment, low body weight, or nutritional compromise. There is insufficient evidence to support routine continuation of paracetamol in patients on high doses of strong opioids.[2]

Non-steroidal anti-inflammatory drugs (NSAIDs)

There is a body of evidence supporting the use of NSAIDs in the management of cancer pain, both as an initial non-opioid for use at step 1 of the WHO analgesic ladder, and throughout a patient's escalating pain trajectory.[3]

NSAIDs are a heterogeneous group of drugs, which produce their analgesic effect through inhibition of one or both of the isoenzymes of cyclooxygenase: COX-1 or COX-2. Selective COX inhibitors, such as aspirin, ibuprofen, and diclofenac, inhibit both isoenzymes, but their use is associated with a number of adverse effects, including gastrointestinal (GI) complications and renal toxicity. Selective COX-2 inhibitors (such as celecoxib) are associated with reduced GI side effects. All NSAIDs may provoke or worsen renal failure. Evidence has linked NSAID use to cardiovascular risk.[4]

There is no clear evidence to support the superior safety or efficacy of one NSAID over another. The lowest effective dose should be used for the shortest duration required to control symptoms, and the need for ongoing treatment should be reviewed regularly.[5] Risk stratification and identification of the individual cardiovascular and GI risk factors should inform the decision regarding choice of NSAID. There appears to be reduced cardiovascular risk for low-dose ibuprofen (<1.2g/24h) or naproxen. For patients who are at high risk of GI complications (see Table 8.4), the choice can be made between traditional NSAID with a proton pump inhibitor (PPI), a double-dose H2-receptor antagonist, or a COX-2 inhibitor.

Topical NSAIDs in the forms of gel or patches have been shown to provide effective analgesia in acute musculoskeletal conditions such as sprains.[6] There is insufficient data to allow comparisons between preparations, or between topical and oral formulations of the same NSAID.[7]

Tables 8.4 and 8.5 provide guides to NSAID selection and dosages, respectively, in palliative care practice.

Table 8.4 NSAID selection

	No or low NSAID GI risk factors*	NSAID GI risk factors*
No CVD	Non-selective NSAID ± PPI	COX-2 inhibitor ± PPI, or non-selective NSAID + PPI
CVD	Consider alternative analgesia first (e.g. paracetamol ± tramadol) then a non-selective NSAID ± PPI (cautiously)	Consider alternative analgesia first (e.g. paracetamol ± tramadol) then a non-selective NSAID ± PPI (cautiously)

*Gastrointestinal (GI) risk factors include age >65yrs, previous history of peptic ulcer disease, concurrent medication, e.g. aspirin, warfarin, selective serotonin reuptake inhibitors (SSRIs).

Abbreviations: NSAID, non-steroidal anti-inflammatory drug; CVD, cardiovascular disease; PPI, proton pump inhibitor; COX-2, cyclo-oxygenase inhibitor-2.

Table 8.5 NSAID dosages—oral

Ibuprofen	**200–400mg t.d.s. p.o.**
Diclofenac	50mg t.d.s. (can be used p.o., SC, or PR)
Celecoxib	up to 200mg b.d. p.o.
Naproxen	250–500mg b.d. (p.o.)
Ketorolac	10–30mg SC every 4–6h p.r.n.; max 90mg daily (max 60mg for elderly); max duration 2 days
Parecoxib	10–20mg 4h p.r.n. SC or 20–80mg CSCI/24h.; max 80mg daily (max 40mg for elderly)

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Choice of analgesic: opioids for mild-to-moderate pain

Codeine is metabolized by the hepatic cytochrome enzyme CYP2D6 to morphine. Codeine is a much weaker agonist at mu receptors than morphine, and the analgesic effect is highly dependent on the production of its active metabolite, morphine, by the CYP2D6 system.

Some 7% of Caucasians and 1–3% of Asian people are CYP2D6 poor metabolizers, and do not experience effective analgesia with codeine. CYP2D6 activity may also be inhibited by antipsychotic agents (haloperidol, levomepromazine, and thioridazine) and antidepressants (amitriptyline, fluoxetine, and paroxetine).

Codeine may provide good levels of pain relief for some adults with cancer pain. While it is not generally a first-line drug in this context in many countries, it is an inexpensive and widely available drug with well-known adverse effects.

Codeine is available in tablet and syrup formulations. Doses of 30–60mg p.o. q4h to a maximum dose of 240mg in 24 hours are prescribed, as doses in excess of this are associated with an increased side-effect profile. It is also available in preparations in combination with a non-opioid. The compound preparations may contain either low-dose (8mg) or high-dose (30mg) codeine, and so it is important to stipulate the dose of codeine required in the preparation, e.g. 'paracetamol 500mg/codeine 30mg'. There is evidence for the efficacy of combinations of codeine 30mg and paracetamol over paracetamol alone; however, there is no evidence available to support the superiority of codeine 8mg and paracetamol combinations over paracetamol alone in the management of cancer-related pain.[1]

Tramadol

Tramadol displays weak opioid activity and it is also a noradrenaline and selective serotonin reuptake inhibitor (SSRI). It is metabolized by both CYP2D6 to the active metabolite, and additionally by CYP3A4. Like codeine, CYP2D6 inhibitors can reduce its analgesic effect. CYP3A4 inducers (e.g. carbamazepine) can also reduce analgesia.

There is some disagreement as to which step of the ladder tramadol should be prescribed. But, traditionally, it has proved suitable as a step 2 analgesic because, at therapeutic doses, its analgesic effect is similar to that of an opioid for mild-to-moderate pain in combination with a non-opioid.

Tramadol is available in both oral and injectable forms (for preparations, see Table 8.6). It is recommended that, except in special clinical circumstances, doses of 400mg a day should not be exceeded, as at doses above this the risk of convulsions may be increased.

In 2014, tramadol was reclassified in the UK to a schedule 3 controlled drug. Controlled drug prescription requirements will apply, but it is exempt from safe custody requirements.

Adverse effects

- Adverse effects include nausea, vomiting, dizziness, and drowsiness. Hallucinations and confusion, as well as rare cases of drug dependence

Table 8.6 Tramadol preparations

Caps: 50mg	Sol. Tabs: 50mg	Sachets effervescent powder: 50mg
Tabs: m/r (12h)	75mg, 100mg, 150mg, 200mg	
Caps: m/r (12h)	50mg, 100mg, 150mg, 200mg	
Tabs: m/r (24h)	150mg, 200mg, 300mg, 400mg	
Inj.	100mg/2mL	
Starting dose	50mg q.d.s. p.o. or 100mg b.d. p.o. (12h m/r)	

and withdrawal symptoms, have also been reported. Seizures may occur with use, and appear to be most likely in people taking drugs that lower the seizure threshold, or who have a history of seizures.

- Tramadol has the potential for serious drug interactions, and may cause serotonin syndrome (particularly when combined with other serotonergic drugs, such as most antidepressants).

Tapentadol

Tapentadol is a mu-opioid receptor agonist and noradrenaline reuptake inhibitor. It is available in immediate and modified release formulations (see Table 8.7). A randomized controlled trial has demonstrated that tapentadol is effective compared to placebo for the management of moderate-to-severe cancer-related pain,[2] and has a comparable efficacy to that of morphine sulphate.

At present there is insufficient evidence to support the use of either tramadol or tapentadol in preference to codeine/paracetamol combinations for the management of mild-to-moderate cancer pain.[3]

Table 8.7 Tapentadol preparations

Palexia® IR	50, 75mg
Palexia® oral solution	20mg/mL
Palexia® SR (12 hour):	50, 100, 150, 200, 250mg

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Opioids for severe pain

Principles of use of opioids for severe pain

Opioids are safe, effective, and appropriate drugs for the management of cancer pain, provided that

- appropriate starting doses and titration are observed
- the properties and relative potencies of different opioids are understood
- opioid-related adverse effects are monitored and managed
- prescribers are aware that some types of pain are poorly responsive to opioids and require other types of analgesics (adjuvant analgesics)

The choice of strong opioid should take into account efficacy, safety, and flexibility of dosing.[1] Although morphine sulphate has traditionally been the strong opioid of choice owing to well-established efficacy and safety data, it has been shown that the efficacy and tolerability of morphine sulfate, oxycodone, hydromorphone, and methadone are equivalent, and that these agents all represent valid choices as first- and subsequent-line opioids for moderate-to-severe cancer pain. Methadone should only be used under specialist supervision. Transdermal opioids such as fentanyl and buprenorphine are valid alternatives in selected patients, e.g. renal impairment patients, or where compliance is a concern.[2]

Introducing and titrating opioids for severe pain

See Fig 8.6.

The starting dose of analgesia will depend on the severity of pain, previous or current opioid-related side effects experienced, and the amount of analgesia required by the patient previously.

Titration is a systematic process of incremental dose adjustment based on the patient's needs and responses. The goal of titration is to use the smallest dose that provides satisfactory pain relief with the fewest side effects.

The need for dose adjustment is based on reported severity of pain and frequency of need for breakthrough doses: 'titrating to effect'. Titration may be upward (a.k.a. 'dose escalation') or downward (tapering), depending on the individual response. Dose adjustments are calculated based on a percentage of the total dose of breakthrough analgesia required in the previous 24-hour period (most commonly an increase or decrease of 25–30%).

- Opioids for severe pain may be titrated using either oral immediate release (i/r) or oral modified release (m/r) preparations of the opioid of choice.[3]
- An i/r opioid regimen gives greatest flexibility for initial dose titration, but it may be appropriate to start some patients directly on m/r opioid, e.g.
  - patients who are already taking step 2 opioids
  - patients with less severe pain
  - patients who have difficulties with compliance
  - outpatients
- Using an m/r opioid for initial dose titration may be less cumbersome for patients and this may improve compliance.

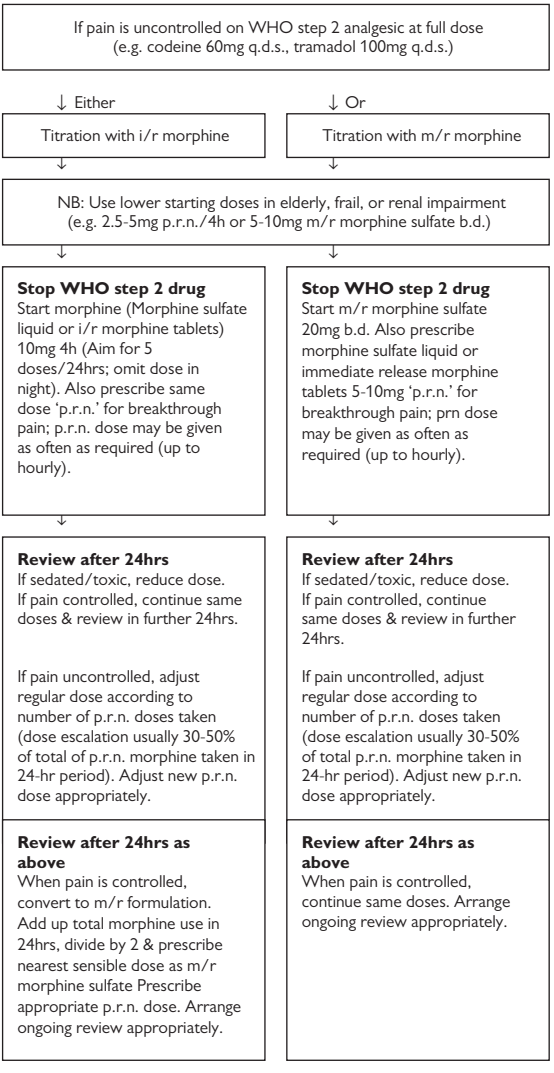


Fig 8.6 Starting morphine. Flowchart adapted from Cancer Care Alliance of Teeside, Durham and North Yorkshire Network Supportive and Palliative Care Guidelines 2006.

Combination opioid therapy

Combination opioid therapy refers to the use of two strong opioids simultaneously. There is presently insufficient evidence to support the use of such an approach.[4]

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Choice of opioid

Morphine sulfate

The effects of morphine sulfate and the other strong opioids are mediated through opioid receptors found in the central and peripheral nervous systems. Morphine sulfate appears to have no clinically relevant ceiling effect to analgesia, and there is wide inter-individual variability in the clinically effective dose required.

Morphine sulfate is primarily metabolized in the liver into two main active metabolites: morphine-3-glucuronide (M3G) and morphine-6-glucuronide (M6G). M6G is believed to be a more potent analgesic than morphine itself, while M3G plays a role in mediating opioid-related side effects.

Morphine metabolism can be affected by a variety of medications

Enzyme inducers, including carbamazepine, phenobarbital, phenytoin, and rifampicin accelerate the clearance of morphine. Enzyme inhibitors, including phenothiazines, tricyclic antidepressants, and cimetidine—and certain benzodiazepines, including lorazepam—interfere with morphine metabolism and increase its effects.

The products of morphine metabolism are eliminated by the kidney; as a result, patients with renal impairment are at an increased risk of accumulating metabolites and developing adverse effects.

Administration

Morphine can be administered via oral, rectal, SC, IV, topical, epidural, and intrathecal routes. The oral route is favoured for reasons of patient acceptability; however, if this is not possible, the subcutaneous route is preferred. The relative potency of morphine varies according to the route of administration. In general, opioids administered via the subcutaneous or intravenous routes are twice as potent as opioids administered via the oral route.

Formulation

Oral morphine sulfate is available in two formulations: immediate-release (i/r; also known as 'normal release') and modified-release (m/r, also known as 'slow release', SR) (see Table 8.8). Peak plasma concentrations of i/r preparations usually occur within the first hour after oral administration, and the analgesic effect lasts for about 4h. In contrast, m/r preparations produce a delayed peak plasma concentration after 2–6h, and analgesia lasts for 12 or 24h.

Dosage

Best current evidence demonstrates that an initial oral morphine dose of 30mg/24 hours for opioid-naive patients with normal renal function, and up to 60mg/24 hours in patients rotating from step 2 analgesia, is safe and effective. However, it is important to remember that care should always be taken to consider the individual circumstances of each patient and appropriate adjustments should be made.

Table 8.8 Morphine preparations

Morphine i/r (4h)	
Oral solution	10mg/5mL; 20mg/1mL
Tablets	10, 20, 50mg scored tabs
Morphine suppositories	10, 15, 20, 30mg
(Equianalgesic dose by oral and rectal routes)	
Morphine m/r (12h)	
MST® and Zomorph® can be used interchangeably	
MST® Continuous®	5, 10, 15, 30, 60, 100, 200mg tabs
Morphgesic® SR	10, 30, 60, 100mg tabs
Zomorph®	10, 30, 60, 100, 200mg caps (can be opened and administered via an NG/PEG tube, or sprinkled on food)
Morphine m/r (MXL®) (24h)	30, 60, 90, 120, 150, 200mg caps

Diamorphine

- Diamorphine is more soluble in water than morphine, and is used as an injectable strong opioid and for use in a syringe driver for subcutaneous infusion.
- It is unusual to give diamorphine IV in a hospice setting. Subcutaneous administration is most commonly used (onset of action is 10–20 min; see Table 8.9) unless the pain is very severe and immediate relief is needed. Diamorphine is not licensed for use in some countries, including the Republic of Ireland.
- Diamorphine is approximately three times as potent as oral morphine sulfate.

Oxycodone

- Oxycodone is a strong opioid analgesic similar to morphine.
- Oxycodone is metabolized to noroxycodone, oxymorphone, and their glucuronides by CYP2D6. The analgesic activity and profile of the metabolites are not yet known, and caution is advised when using oxycodone in patients with renal impairment. There have been reports of reduced analgesic effect when used in combination with CYP2D6 inhibitors.

Table 8.9 Diamorphine preparations

Injection	5, 10, 30, 100, 500mg

Table 8.10 Oxycodone preparations

Caps: i/r	5, 10, 20mg
Tabs: m/r (12h)	5, 10, 20, 40, 80mg
Liquid	5mg/5mL, 10mg/1mL
Injection	10mg/1mL, 1mL and 2mL amps. 50mg/mL, 1 mL amp.

- Oxycodone may be given by p.o., p.r., SC, and IV routes. It is available in 4-h i/r and 12-h m/r oral preparations, and is used in a similar way to morphine (see Table 8.10). Oxycodone is also available in a fixed-ratio combined oral formulation with naloxone.
- Although a recent meta-analysis failed to find any clinically significant difference in adverse effect profile between morphine and oxycodone,[1] inter-individual variation means that some individuals who are intolerant to morphine may benefit from an opioid switch to oxycodone (➔ see section on opioid rotation/switching, pp. 280–3). Oxycodone is approximately 1.5–2 times as potent as morphine sulfate.

Hydromorphone

- Hydromorphone is a semi-synthetic derivative of morphine sulphate with similar pharmacokinetic and pharmacodynamic properties, although as a more selective mu-opioid receptor agonist it is more potent (➔ see Opioid equivalence tables, p. 284).
- Hydromorphone is metabolized in the liver to hydromorphone-3-glucoronide (H3G), which has no analgesic activity but does have neuro-excitatory properties. Hydromorphone and its metabolites are eliminated renally.
- Hydromorphone is available in p.o., SC, and IV preparations, and may also be given by the spinal route (Table 8.11).
- Hydromorphone is approximately five times as potent as morphine sulfate.

Table 8.11 Hydromorphone preparations

Hydromorphone is available in 4h i/r and 12h m/r preparations	
Caps: i/r 4h	1.3mg, 2.6mg (Palladone®)
Caps: m/r 12h	**(12h)** 2mg, 4mg, 8mg, 16mg, 24mg (Palladone® SR)
Caps may be opened and sprinkled on food	
Injection	10mg/1mL, 20mg/1mL, 50mg/1mL
Injections available in UK as a special order from Martindale (see BNF for contact details).	

Mental pain is less dramatic than physical pain, but it is more common and also more hard to bear. The frequent attempt to conceal mental pain increases the burden: it is easier to say 'My tooth is aching' than to say 'My heart is broken'.

C.S. Lewis, *The Problem of Pain*

Fentanyl

- Fentanyl is a semi-synthetic opioid with a high degree of lipid solubility.
- Fentanyl is metabolized in the liver by CYP3A4 to inactive norfentanyl, so it is of use in patients with renal failure.
- It can be given by IV, IM, SC, transdermal, and spinal routes, as well as transmucosally via the buccal, sub-lingual, or intra-nasal routes (see Table 8.12).
- Fentanyl shares the side-effect profile of morphine and other opioids, but may cause less constipation, nausea, and vomiting. Nevertheless, laxatives are generally still required.[2] In one large trial, although constipation occurred less frequently with fentanyl than with morphine, it was still the most frequent adverse effect reported with each drug (52% and 65% of adverse events reported, respectively).
- Fentanyl is approximately 100 times as potent as morphine sulfate.

Transdermal fentanyl

- Indications for the use of transdermal fentanyl include dysphagia, vomiting, and malabsorption, as well as patient choice and compliance. It has been demonstrated that there is no evidence to support the use of transdermal fentanyl as a first-line opioid. However, transdermal fentanyl is a valid choice when the oral route is not suitable.[3]
- Analgesia is delayed for at least 12 hours after application of the first patch, and steady state may not be achieved for 48h. Transdermal fentanyl has a prolonged duration of action; each patch lasts about

Table 8.12 Fentanyl preparations (examples)

Type	Doses	Starting dose
Patches	12, 25, 50, 75, 100mcg/h	25mcg/h patch every 3 days
Injection	50mcg/1mL, 100mcg/2mL, 500mcg/10mL	500mcg/24h CSCI
Lozenge with application	200, 400, 600, 800, 1200, 1600mcg	200mcg lozenge regardless of regular opioid dose
Sublingual tablet	100, 200, 300, 400, 600, 800mcg	–
Effervescent buccal tablet	100, 200, 400, 600, 800mcg	–
Nasal spray	50, 100, 200mcg/dose	–

72 hours, and plasma concentrations are halved about 17 hours after removal. As a result, transdermal fentanyl should only be used in those patients with stable opioid requirements, and should not be used for titration of analgesia where pain is uncontrolled.

- Up to 25% of patients need a patch change every 48h owing to pharmacokinetic variability.

Oral i/r morphine is commonly used as the breakthrough analgesic, though oral transmucosal fentanyl citrate may also be used (➔ see p. 271).

The patch is applied on a healthy, non-hairy part of the skin. Increased body heat (e.g. fever, humid climate) and direct heat (e.g. from an electric blanket or heat pad) may increase the rate of absorption of fentanyl. Sweating may decrease drug absorption because it prevents the patch from sticking to the skin. Local skin erythema or pruritus has been reported with use of transdermal fentanyl (<5%).

Although both fentanyl and morphine act at the mu receptor, patients switched from long-term morphine to fentanyl may experience withdrawal symptoms despite good pain relief because fentanyl is a highly selective mu agonist.[4] Symptoms may be treated using rescue doses of i/r morphine for a few days until they resolve.

Used fentanyl patches should be disposed of safely, as a substantial amount of fentanyl can remain in patches (even after 3 days in situ). In a group of patients studied, 28–84% of fentanyl remained in used patches.[5] Patches should be folded with the sticky sides together, wrapped, and disposed of either by returning to the pharmacist, or placing in the rubbish well out of reach of children and others.

Subcutaneous fentanyl

Administration of fentanyl by subcutaneous infusion will allow therapeutic blood levels to be achieved rapidly, and also allows for the use of fentanyl in patients with uncontrolled pain. Calculate dose as equivalent to transdermal patch, e.g. 25mcg/h = 600mcg/24h; for convenience (and considering the widely variable absorption from a patch), use 500mcg/24h CSCI as equivalent to a 25mcg/h patch (➔ see Opioid rotation/switching, pp. 280–3). If very large volumes in a syringe driver are required at high doses, the use of alfentanil should be considered.

Starting a fentanyl patch

- The starting dose of transdermal fentanyl is calculated on the basis of the oral morphine equivalent dose and individual patient factors. Consult tables and adjust appropriately (➔ see p. 284).
- From i/r opioid: apply patch when convenient and use oral i/r opioid only as required.
- From twice-daily m/r opioid: apply patch at the same time as the last dose of m/r oral opioid.
- From once-daily m/r opioid: apply the patch 12h after the last dose of m/r opioid.

Breakthrough/rescue doses of i/r opioids may be needed whilst transdermal absorption is established.

Dose titration for a fentanyl patch
It takes up to 72 hours for a steady state of fentanyl to be achieved. Titration, in 12mcg/hour increments if required, should take place no more frequently than every 3 days.

Switching from patch to oral m/r opioid
The dose of oral m/r opioid is calculated by consulting dose conversion tables. The dose should be adjusted appropriately for individual factors.

Remove patch and give the first dose of oral m/r opioid approximately 8h later. An i/r opioid needs to be available on a p.r.n. basis.

Use of transdermal fentanyl during the last days of life
If a patient appears well pain-controlled, the fentanyl patch should be continued as normal, and breakthrough doses given as required.

If the patient has uncontrolled pain and death appears to be imminent, it is often not appropriate to stop the fentanyl patch and switch to an alternative opioid administered via syringe driver (because of the adverse effects associated with the inaccurate estimations of equivalence dose in the terminal phase). In these circumstances, the fentanyl patch may be continued and supplementary regular analgesia may be given by a second opioid infusion via a syringe driver.

Note: Care must be taken to use the *total 24-h dose of opioid* as the basis for calculations of breakthrough doses.

Oral transmucosal fentanyl citrate (OTFC)
Fentanyl is rapidly absorbed through the buccal and nasal mucosa, leading to rapid onset of pain relief. A number of formulations of OTFC are available. These preparations were developed specifically for the management of breakthrough and incident pain.[6] However, the benefits of transmucosal fentanyl over oral morphine need to be considered because of the substantial cost difference.

The maximum effect is reached within 20–40 min, with a duration of action of 1–3h. The optimal dose of OTFC cannot be predicted from, and is not directly related to, the daily dose of regular opioid being taken for background pain. Therefore individual titration is required according to the individual product SPC. There is no conversion ratio between fentanyl lozenges and other opioid formulations (including fentanyl patches).

General guidelines for the use and titration of OTFC preparations (see specific product literature for individual preparations)
- The initial dose of the OTFC is not related to the dose of regular background opioid.
- OTFC should only be initiated when a patient is taking at least 60mg oral morphine or other strong opioid equivalent.
- No more than two doses of the OTFC preparation should be used to treat one pain episode.

- The dose of OTFC should be titrated according to the individual product instructions until an effective dose is identified.
- If multiple doses of OTFC are required in one day, an increase in background analgesia should be considered.
- OTFC preparations are considerably more expensive than oral morphine or oxycodone, and would not be considered a first-line analgesic for cancer-related breakthrough pain.
- Partially consumed OTFC preparations should be dissolved under hot running water and disposed of out of the reach of children.

Alfentanil

- Alfentanil is a selective mu-receptor opioid agonist, similar to fentanyl. However, it has a more rapid onset of action and a shorter duration of action.
- Alfentanil is mainly metabolized in the liver to inactive compounds, and the evidence supporting its use in the palliative setting relates mainly to its usefulness in renal impairment/failure.[7]
- Alfentanil is available in injectable form, and can be administered via the SC, IV, and spinal routes (Table 8.13). Availability of a highly concentrated formulation allows large doses to be administered in small volumes via CSCI.

Its short-lasting effect means it has been used for incident pain, e.g. dressing changes, but it is generally not used for other types of breakthrough pain.

Alfentanil (via the subcutaneous route) is approximately 32 times as potent as oral morphine sulfate, e.g. 30mg p.o. morphine/24h ≡ 1mg alfentanil SC 24h.

Sufentanil

Sufentanil is a synthetic opioid very similar to fentanyl, but with a more rapid onset and shorter half-life. It can be used as an alternative to alfentanil if the fentanyl dose necessitates too large a volume for the portable syringe driver in use. It has also been used sublingually. The clinically derived sufentanil to fentanyl relative potency is approximately 20:1.

Buprenorphine

Buprenorphine is a potent semi-synthetic opioid with mixed agonist/antagonist properties. It has been shown, in *in vivo* studies, to produce the same level of analgesic effect as other strong opioids, including morphine sulfate and fentanyl.[8] No ceiling dose has been shown for the analgesic effect of buprenorphine in clinical studies.[9]

Buprenorphine is metabolized in the liver, principally to an inactive metabolite, norbuprenorphine. It may be used in mild-to-moderate liver failure, and in renal failure.

Table 8.13 Alfentanil preparations

Injection	1mg/2mL, 5mg/10mL, 5mg/1mL
Starting dose	500mcg/24h CSCI (equivalent to diamorphine 5mg CSCI)

It may be given by the epidural, IM, IV, SC, and SL routes, but the transdermal route is most commonly used in palliative care practice (see Table 8.14). It is available in two forms of transdermal delivery systems. Both delivery systems contain the active drug incorporated into a polymer matrix, which is also the adhesive layer. The time to reach steady-state plasma concentrations is approximately 24–48 hours, and additional analgesia may be required during this time. Buprenorphine concentrations decrease to about one-half in the 12 hours following patch removal. It has an apparent half-life of about 26 hours.

Buprenorphine is approximately 75 times as potent as oral morphine sulfate.

Transdermal buprenorphine should be used only in those patients with stable pain. It should not be used for titration in patients with uncontrolled pain.

The use of buprenorphine in association with other opioids, as, for example, during opioid switching, or for the management of breakthrough pain, has been of concern because of a possible partial agonist effect, which might reduce analgesia or induce withdrawal symptoms. However, recent data suggest that no interference between buprenorphine and other opioid mu-agonists exists within the usual clinical dose ranges.[10,11]

Buprenorphine may have a wider safety profile with respect to respiratory depression compared to other opioids—because of its partial agonist activity, it has a demonstrated ceiling effect on respiratory depression. However, in the event of respiratory depression occurring, higher doses of naloxone may be required compared with other opioids. Respiratory stimulants are occasionally required, as respiratory depression may only be partially reversed by opioid anatagonists.

There is insufficient evidence to support the use of sublingual, intramuscular, or subcutaneous buprenorphine for the management of cancer-related pain.[12] Alternative oral opioids, such as i/r morphine, are generally used to provide breakthrough pain relief for patients using transdermal buprenorphine.

Methadone

Methadone is a synthetic opioid with mixed properties: it is a mu- and delta-opioid receptor agonist and an NMDA-receptor antagonist.

It has been shown that methadone is a valid choice as a strong opioid for the management of cancer pain.[13] However, owing to its complex pharmacodynamic profile, methadone should only be used in the palliative care setting by specialists experienced in its use. Even when used under the

Table 8.14 Buprenorphine preparations

bi-weekly patches	35mcg/h, 52.5mcg/h, and 70mcg/h patches, which release the drug over a 3–4 day period
weekly patches	5mcg/h, 10mcg/h, and 20mcg/h patches, which release the drug over a 7-day period
Tabs (sublingual)	200mcg

guidance of experienced physicians, occasional serious toxicity can occur during the administration of methadone.[14]

Methadone is extensively metabolized in the liver by the cytochrome P450 CYP3A3/4 isoenzyme to inactive metabolites. Metabolites are excreted mainly by the faecal route, and so do not accumulate in renal failure.

Methadone has the potential for numerous and complex drug interactions.[15, 16] Its metabolism is increased by a number of other drugs, and their use in combination with methadone may then precipitate pain flare-up and opioid withdrawal symptoms. Other interactions that inhibit metabolism can lead to overdose and toxicity (Table 8.15).

Methadone is absorbed well from all routes of administration, and may be given by the p.o., p.r., IV, and SC routes. It is available as an oral solution and as an injectable formulation. Oral bioavailability is 80%. It is a basic and lipophilic drug that is subject to considerable tissue distribution and sequestration, and has a characteristically long half-life in plasma of around 24 hours (range 13–100 hours).[17, 18]

Tissue accumulation of methadone with chronic administration results in the potential for toxicity. Also, there is considerable inter-individual variation in methadone pharmacokinetics, so that a high level of individual titration and monitoring is required when introducing and titrating methadone for the management of cancer pain.

All the typical opioid side effects can be expected. Methadone also has an antidiuretic effect. Its use has been associated with prolongation of the QT interval, and in certain situations—for example, patients with known structural heart disease or a history of arrhythmia—ECG monitoring should be performed prior to and during methadone treatment.

Equianalgesic ratios of morphine (and other opioids) to methadone are dose-dependent. In single-dose studies, these ratios may vary from 1:1 at low doses of an oral opioid to as high as 20:1 for patients receiving oral morphine in excess of 300mg per day. Opioid rotation to methadone is complex because of the wide variability of equianalgesic ratios, but there have been several guidelines published (➔ see Opioid rotation/switching, pp. 280–3).[19]

Pethidine

Pethidine is a synthetic opioid and has similar agonist effects to morphine. However, it has a short duration of action, and, when given regularly, active metabolites accumulate and can cause convulsions. Although accumulation of metabolites is more likely in patients with renal disease, toxicity has been

Table 8.15 Interactions which interfere with methadone metabolism

Decrease methadone levels	Increase methadone levels
Phenytoin	Fluconazole
Phenobarbital	SSRIs
Carbamazepine (not sodium valproate or gabapentin)	
Rifampicin	

observed in patients with normal renal function and, as a result, its use is contraindicated in the management of pain in the palliative care setting.

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Opioid adverse effects and toxicity

Opioid-related adverse effects

The management of opioid-related adverse effects is a fundamental aspect of opioid therapy, and clinicians should adopt a proactive approach wherever possible. The use of opioid analgesia should not be affected by unfounded fears about pharmacological tolerance, dependence, or respiratory depression. In the palliative care setting, pharmacological tolerance and psychological dependence rarely occur.

There is often significant inter-individual variation in sensitivity to opioid-related adverse effects, and this may be explained, in part, by genetic variability. Other factors influencing the development of adverse effects are as follows:

- the presence of renal and hepatic impairment
- the use of polypharmacy
- the patient's age
- the patient's cognitive function
- the extent of the patient's disease
- the dose and type of opioid
- the route of administration of opioid

Many of the side effects caused by opioids are non-specific, so it is important as a first step to determine whether the symptoms are related to opioid use or to underlying disease.

Management of opioid-related side effects

Common management strategies for various opioid-related side effects are listed in Table 8.16, and are mainly based on a dose reduction of systemic opioid ± use of a specific therapy to treat the adverse effect.

Additional strategies for the management of opioid-related side effects include the following:

- opioid switching
- use of adjuvant analgesics that act in a synergistic manner to reduce opioid requirements
- supplemental analgesia using nerve blocks
- alternative routes of administration, such as epidural

Opioid toxicity

Opioid toxicity is when the dose exceeds the clinical requirement. This may be precipitated by:

- rapid increase in opioid dose, or inappropriate use of opioids for the management of an opioid-insensitive pain
- dehydration or renal impairment
- infection
- changes in systemic function, e.g. hepatic function, weight loss
- reduction in analgesic requirements because pain is relieved by other methods, e.g. post-radiotherapy
- drug interactions, e.g. the co-administration of amitriptyline increases the bioavailability of morphine

Symptoms and signs of opioid toxicity

- drowsiness
- hallucinations (most commonly visual)
- confusion
- vomiting
- myoclonus
- pinpoint pupils
- respiratory depression (if severe)

Management of opioid toxicity

- treat the underlying cause where appropriate
- ensure adequate hydration
- reduce opioid dose
- prescribe haloperidol for management of delirium
- prescribe benzodiazepine (e.g. clonazepam, midazolam) for symptomatic management of myoclonus
- consider opioid rotation if dose reduction fails to resolve toxicity or if pain is poorly controlled

Respiratory depression

Pain acts as a physiological antagonist to the central depressant effect of opioids, and strong opioids, when used appropriately, do not cause respiratory depression in patients with pain. Clinicians should take care to distinguish between true respiratory depression attributable to opioids and the slow and irregular breathing that may accompany the terminal phase.

If mild respiratory depression does occur, reduction of the opioid dose is usually all that is required immediately. Subcutaneous infusions of opioids should be temporarily stopped to allow plasma levels to decrease, before restarting at a lower dose. Further oral doses should be omitted or reduced, and the patient should be re-assessed before restarting.

Use naloxone with caution in palliative care; larger than recommended naloxone doses can reverse analgesia, leading to intense pain/distress. They may result in hypertension, arrhythmias, pulmonary oedema, and cardiac arrest. It is advised to follow local/BNF guidance for using the drug in treating significant respiratory depression.

Indications for use of naloxone

- respiratory rate <8 breaths/min, **or**
- <10–12 breaths/min, difficult to rouse, and clinically cyanosed, **or**
- <10–12 breaths/min, difficult to rouse, and SaO_2 <90% on pulse oximeter

Management of respiratory depression

- stop opioid
- secure IV access
- dilute 0.4mg naloxone in sodium chloride 0.9% to total of 10mL
- give 0.5mL–2.5mL (=20–100mcg naloxone) every 2min IV until satisfactory respiratory status
- review renal function, pain and analgesic requirements

Table 8.16 Common management strategies for various opioid-related side effects

Opioid-related nausea and vomiting	Although these symptoms are commonly present during initiation of opioid therapy, they are frequently self-limiting and usually require only a short course of anti-emetic therapy.
	If symptoms persist, metoclopramide 10mg p.o. t.d.s. or cyclizine 50mg p.o. t.d.s. are useful first-line anti-emetics (NB: risk of cardiac events with metoclopramide). Haloperidol 1.5–3mg o.m. initially is also useful.
Opioid-related constipation	**Prescription of regular, prophylactic laxatives is recommended.**
	Studies comparing laxatives, especially in palliative care patients, are lacking. Various laxatives have been investigated, but findings remain inconclusive and choice of laxative is often dependent on local practice. A combination of a stimulant laxative and a stool softener may be used.
	Peripherally acting opioid antagonists, including methylnaltrexone and naloxagol, have been developed specifically for opioid-induced constipation.
	If the problem persists, laxatives should be titrated upwards, and enemas may be used.
	If the problem is severe, opioid rotation can be considered. Fentanyl and buprenorphine may be less constipating.
	Consider non-pharmacological approaches, such as increased fluid intake, dietary fibre, and mobilization, if appropriate.
Opioid-related drowsiness	This symptom is commonly present in the first days of opioid therapy, and is usually self-limiting. Patients should be advised to expect some sedation during the first days of treatment and during dose escalation, and not to drive or use machinery.
	If persistent, consider treatment of contributing factors: • sleep hygiene • review of other centrally acting drugs, e.g. benzodiazepines • correction of metabolic disturbances (e.g. hypercalcaemia)
	If pain is well controlled, consider a reduction of opioid dose. If pain is poorly controlled, consider opioid rotation.
Opioid-related delirium	Opioid-related delirium is often associated with the combined effect of the opioid with other contributing factors, e.g. infection, electrolyte disturbance, CNS metastases, or organ failure. Treat contributory causes where appropriate and possible.
	If pain is controlled, consider a reduction of opioid dose. If pain is present, consider opioid rotation or use of adjuvants.
	Discontinue other centrally acting agents.
	Use neuroleptics, such as haloperidol.

Opioid-related xerostomia (dry mouth)	Meticulous mouth care.
	Consider stopping anticholinergic drugs where possible.
	Pilocarpine 4% eye drops by mouth or 5mg by mouth three times daily may be of use.
Opioid-related pruritus	More common with spinal than with systemic opioids • consider opioid rotation • if unsuccessful, treat opioid-induced pruritus with 5-HT_3 antagonists such as ondansetron
Opioid-related sweating	Exclude other causes of sweating
	Consider opioid rotation
	Consider use of antimuscarinic drugs
Rarely, hyperalgesia and allodynia	These have been reported with high-dose opioids. The symptoms may be associated with signs of toxicity. Characteristically, the patient reports that an increase in the opioid dose leads to worsening pain. Substitution of an alternative opioid often resolves the symptoms. Alternatively, reduction of dose and the addition of an alternative co-analgesic may be useful.

NB: These doses are lower than referenced doses for acute opioid overdose (0.4mg-2mg).

Naloxone has a half-life of 5–20 min. As the half-life of most opioids is longer than this, it is important to continue to assess the patient and repeat naloxone therapy at further intervals if necessary.

Opioid rotation/switching

When prescribing opioids for cancer pain, a minority of patients will experience inadequate pain relief, persistent unacceptable side effects, or a combination of the two, despite dose titration and management of predictable side effects.[1] Such patients may benefit from a change in their opioids, called 'opioid switching' or 'opioid rotation'. Opioid switching involves the discontinuation of the previously used opioid and initiation of the new one at the equianalgesic dose.

The biological mechanisms for the effectiveness of opioid rotation are explained by the following:

- inter-individual variation in the pharmacokinetics, pharmacodynamics, and pharmacogenomics of strong opioids
- incomplete cross-tolerance to the new opioid, allowing a lower effective equivalent dose of the new opioid, potentially reducing side effects[2]

Opioid rotation may be required in up to 44% of patients with cancer-related pain and improvement in effective analgesia is seen in more than 50% of patients.[3] Non-specialists should seek specialist palliative care advice if opioid rotation is required.

Indications for opioid rotation

Predictable side effects such as nausea and constipation are not an immediate indication for opioid rotation. Where opioid rotation is being considered because of poorly controlled pain, the use of adjuvant agents or non-pharmacological interventions should be considered. If side effects occur on a previously stable dose of an opioid, precipitating factors should be considered, e.g. dehydration. These factors are managed prior to, or in addition to, opioid rotation.

Choice of alternative opioid

Individual opioids have characteristics that favour their preferential use by clinicians in certain clinical situations.

A number of factors influence the choice of an appropriate second-line opioid in rotation:

- individual patient factors (e.g. preference, compliance, renal and other organ function, co-morbidities, outpatient vs inpatient setting, stable vs uncontrolled pain)
- drug profile
- possible/desirable routes of administration
- comparative analgesic effects
- comparative adverse effect profile
- other potential therapeutic effects
- availability

Principles of opioid rotation

Regular review and reassessment of patients is required after opioid rotation, as conversion ratios are approximate, and considerable inter-patient variation may occur.

- If the patient's medication is switched, there may be incomplete cross-tolerance. This is where there is tolerance to a currently administered opioid that does not extend completely to other opioids. It may mean that a lower dose of the new opioid is required. It is therefore recommended that a 25–50% reduction of the calculated dose of the new opioid should occur to allow for this. The new regimen should then be re-titrated according to patient response. The patient should be monitored closely, especially at higher doses.
- Caution should be exercised, especially when rotating from high doses.
- The setting in which a patient is being managed should be taken into account, with a more conservative approach appropriate for patients who are in a less intensively monitored setting, e.g. at home.
- Caution should be exercised in the elderly and in patients with renal or significant hepatic impairment. In severe renal impairment or dialysis patients, alfentanil may be the preferred opioid.
- The breakthrough dose for the new opioid is calculated as usual: approximately 1/6 daily dose (i.e. 4-hourly dose). For a patient on oral morphine sulfate 60mg over 24 hours, breakthrough dose is 10mg orally, but a lower dose may be effective in some patients.
- Contact the specialist palliative care team for advice regarding opioid rotation if required.

Suggested regimen for opioid rotation

- Calculate the equianalgesic dose of the new drug according to opioid equivalence tables.
- Dose adjustment should be performed in order to account for incomplete cross-tolerance to the new opioid and inter-individual variability in potency.
- The calculated dose of the new opioid should be reduced by about 30–50%.
- Further adjust the dose, if necessary, according to prior pain control (e.g. smaller reductions may be indicated in patients with uncontrolled pain).
- Regularly reassess and titrate the new opioid against pain and side effects.

The relative potencies of different opioids

The equianalgesic doses of different opioid drugs are only approximations. A number of factors can affect their accuracy:

- individual patient variation (differences in absorption, metabolism, excretion, concurrent medications)
- the sequence of opioid switching
- equianalgesic doses can vary according to the dose of opioid (e.g. at higher doses, more conservative estimates of opioid conversion are recommended)
- some estimations are derived from studies of single doses rather than continued therapy, and may therefore require adjustment in clinical practice
- the multidimensional nature of pain may also contribute to observed variability

NB: Most relative potencies relate to the potency of a strong opioid in relation to morphine. When switching from a strong opioid other than morphine sulfate, it may be necessary to convert the dose of the initial opioid to the oral morphine equivalent dose, and then use this to determine the dose of the new opioid.

Although guidelines and conversion tables should be consulted, each drug must be titrated against pain and side effects for each individual patient.

Rotating to oral methadone from another strong opioid

NB: This should only be performed in settings where there is a high degree of clinical supervision, and under the guidance of a pain or palliative medicine specialist experienced in the use of methadone.

The relative potency ratio of methadone when converting from other strong opioids has been shown to depend on a number of factors, including the reason for opioid rotation, the route and method of switching, and the direction of the switch. It has been demonstrated that higher doses of initial strong opioid require a higher conversion ratio than when rotating from lower doses of initial opioid, and ratios vary from 4:1 at lower initial opioid doses, to 12:1 when rotating from higher initial opioid doses. There is increasing evidence that incomplete cross-tolerance between methadone and other strong opioids means that lower equianalgesic doses of methadone than those published in commonly used opioid dose conversion tables may be effective.

When rotating from other strong opioids to methadone, various methods of rotation have been proposed. The most commonly used methods are the 'stop-and-go ad libitum' method and the 'three-day switch' method. On the basis of the best available evidence, the ad libitum method is safe and efficacious.

Modified ad libitum method (adapted from the Palliative Care Formulary)

- Stop morphine.
- If switching from immediate-release morphine (e.g. Oramorph®):
  - give the first dose of methadone (after stopping morphine) ≥2h (if pain present) or 4h (if pain-free) after the last dose of morphine.
- If switching from modified-release morphine:
  - Give the first dose of methadone (after stopping morphine) ≥6h (if pain present) or 12h (if pain-free) after the last dose of a 12h preparation (e.g. MST®), or ≥12h (if pain present).
  - Give a single loading dose of oral methadone 1/10 of the previous total 24h oral morphine dose, up to a maximum of 30mg.
  - Give oral methadone (1/3 of the loading dose, i.e. 1/30 of the previous total 24h oral morphine dose) every 3 hours if needed, up to a maximum of 30mg per dose.

Example 1	Morphine 300mg/24h p.o. = loading dose of methadone 30mg p.o., with 10mg 3-hourly p.r.n.
Example 2	Morphine 1200mg/24h p.o. = loading dose of methadone 120mg p.o., with 40mg 3-hourly p.r.n.; **however, both are limited to the maximum of 30mg**

- On day 6, the amount of methadone taken over the previous 2 days is noted and divided by 4 to give a regular 12-hourly dose, with 1/6 to 1/10 of the original 24h dose given every 3h p.r.n.

Example	Methadone 80mg p.o. in previous 48h = methadone 20mg every 12h and 5mg p.o. every 3h p.r.n.

- If ≥2 doses/day of p.r.n. methadone continue to be needed, the dose of regular methadone should be increased once a week, guided by p.r.n. use.

- In order to convert another oral opioid (other than morphine) to oral methadone, the morphine equivalent daily dose should be calculated, and the guidelines for morphine sulfate followed as noted previously.
- For patients in severe pain and who need more analgesia in <3h:
  - Give the previously used opioid every hour p.r.n. (50–100% of the p.r.n. dose used before switching). (If neurotoxicity was apparent with the pre-switch dose, use an appropriate dose of an alternative strong opioid).
  - If there has been a rapid escalation of the pre-switch opioid dose, calculate the dose of methadone using the pre-escalation dose of the opioid. If a patient becomes over-sedated, reduce the dose generally by 33–50% (some centres monitor the level of consciousness and respirations every 4h for 24h). If a patient develops opioid withdrawal symptoms (rare), give p.r.n. doses of the previous opioid until symptoms settle.

Subcutaneous methadone

- Although SC methadone has been used, there may be problems with skin reactions, partly because methadone in solution is acidic. If it is necessary to use SC methadone, dilute it as much as possible.
- In order to convert from oral methadone to SC methadone:
  - 1/2 to 3/4 of the 24h oral dose should be prescribed subcutaneously over 24 hours.
  - Direct CSCI switching between other opioids and methadone is not recommended without adequate familiarity with using methadone.

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Opioid equivalence tables

Note: Equivalencies may differ between tables and it is recommended that the reader refer to local guidance. Please read the conversion notes before using the tables in this chapter (Tables 8.17–8.20).

Table 8.17 Opioid conversion guide

p.o. (oral) to SC (subcutaneous)	Conversion	Example
Oral morphine to SC diamorphine	Divide by 3	30mg oral morphine = 10mg SC diamorphine
Oral morphine to SC morphine	Divide by 2	30mg oral morphine = 15mg SC morphine
Oral morphine to SC alfentanil	Divide by 30	30mg oral morphine = 1mg SC alfentanil
Oral oxycodone to SC oxycodone	Divide by 2	10mg oral oxycodone = 5mg SC oxycodone
Oral hydromorphone to SC hydromorphone	Divide by 2	4mg oral hydromorphone = 2mg SC hydromorphone
p.o. (oral) to p.o. (oral)	**Conversion**	**Example**
Oral morphine to oral oxycodone	Divide by 2	30mg oral morphine = 15mg oral oxycodone
Oral morphine to oral hydromorphone	Divide by 7.5	30mg oral morphine = 4mg oral hydromorphone
Oral tapentadol to oral morphine	Divide by 2.5	50mg oral tapentadol = 20mg oral morphine
Oral tapentadol to oral oxycodone	Divide by 5	50mg oral tapentadol = 10mg oral oxycodone
Oral tramadol to oral morphine	Divide by 10	100mg oral tramadol = 10mg oral morphine
Oral tramadol to oral tapentadol	Divide by 4	200mg oral tramadol modified release = 50mg oral tapentadol modified release
SC (subcutaneous) to SC	**Conversion**	**Example**
SC diamorphine to SC alfentanil	Divide by 10	10mg SC diamorphine = 1mg SC alfentanil
SC morphine to SC diamorphine	Divide by 1.5	15mg SC morphine = 10mg SC diamorphine
SC morphine to SC oxycodone	Divide by 2	10mg SC morphine = 5mg SC oxycodone Note manufacturers advise a 1:1 ratio
SC morphine to SC alfentanil	Divide by 15	15mg SC morphine = 1mg SC alfentanil

Conversion notes

- Dose conversions are approximate only and are given as examples.
- Where there is no direct conversion between opioids, use oral morphine equivalents; i.e. convert the opioid to the equivalent oral morphine dose and then on to the required opioid.
- When changing from one opioid to another because of potential toxicity, dose reduction may be necessary. It is recommended to reduce the calculated dose of the new opioid by 25–50% to account for incomplete cross-tolerance. The new regimen should then be re-titrated to patient response.
- Review patient regularly after any changes.
- Especially at higher doses, close monitoring will be required.
- Caution should be used in the elderly and in patients with renal or significant hepatic impairment. Consider reduced doses.
- Breakthrough doses for each opioid are calculated as approximately 1/6 daily dose (i.e. 4-hourly dose) but lower doses may be used if effective.
- **For further advice, contact your local palliative care team/manager.**

Table 8.18 Opioid equivalence for transdermal patches—adult use (fentanyl) conversion guide

Fentanyl patch	**Replace patch every 3 days**
Initial dosage of transdermal patch based on oral daily morphine dosage for patients on stable and well-tolerated opioid therapy using a ratio of 100:1	
Fentanyl patch (micrograms/hr)	**24** hourly oral morphine dose (mg)
12	30–59
25	60–89
37	90–119
50	120–149
62	150–179
75	180–239
100	240–299
125	300–359
150	360–419
175	420–479
200	480–539
225	540–599
250	600–659
275	660–719
300	720–779

Table 8.19 Bi-weekly patch (buprenorphine) conversion guide

patch (buprenorphine)	Replace patch TWICE WEEKLY (every 3 or 4 days)
patch (micrograms/hr)	**24 hour oral morphine dose (mg)**
35 micrograms/hr	~ 63–97mg
52.5 micrograms/hr	~ 95–145mg
70 micrograms/hr	~ 126–193mg
140 micrograms/hr	~ 252–386mg

Transdermal patches are not suitable for patients who require rapid titration of strong opioid medication for severe pain and should be restricted to those diagnosed with stable pain.

Note: Conversion ratios between transdermal buprenorphine and oral morphine have been shown to vary widely.

Table 8.20 Weekly patch (buprenorphine) conversion guide

patch (buprenorphine)	Replace patch EVERY 7 DAYS		
patch (micrograms/hr)	Oral dose over 24h (mg)		
	Morphine	Tramadol	Codeine/dihydrocodeine
5micrograms/hr	~ 10–12	~ 100	~ 120mg/day
10micrograms/hr	~ 20–24	~ 200	~ 240mg/day
20micrograms/hr	~ 40–48	~ 400	see below
20micrograms/hr patch exceeds maximum daily dose of codeine/dihydrocodeine			

Changing the route of administration of opioids

The oral route should be used for administration of opioid analgesia, if practical and feasible. If a patient is unable to take oral opioids, a number of alternative routes of administration exist, including the subcutaneous, intravenous, transmucosal, transdermal, topical, and spinal routes.

In the palliative care setting, the intramuscular (IM) route is normally avoided because of issues of painful injections, cachexia, and reduced muscle mass.

Opioids have different analgesic potencies when administered by different routes. Doses of opioids therefore need to be adjusted when their route of administration is altered. For example, intrathecal and epidural morphine are approximately 100 and 10 times, respectively, more potent than oral morphine.

Subcutaneous route

The SC route is often used, and is appropriate for those patients who are unwilling or unable to take oral medications for reasons such as the following:

- reduced level of consciousness
- dysphagia
- nausea/vomiting
- tablet burden
- malabsorption

Transdermal route

The transdermal route is suitable for patients who have stable pain, following introduction and titration of analgesia using the oral or subcutaneous routes. Medication for breakthrough pain via the oral or transmucosal route should be prescribed while on transdermal opioids.

Topical route

There has been some interest in the efficacy of topical opioids for the management of ulcers and pressure sores. The use of topical opioids is associated with the potential advantage of a reduction or avoidance of the adverse effect profile associated with the use of systemic opioids. Most studies describing the topical effects of morphine have mixed the opioid in IntraSite® gel, although there are anecdotal reports in which morphine (or diamorphine) has been mixed with silver sulfadiazine cream or metronidazole gel.

A randomized, double-blind, placebo-controlled, crossover pilot study reported an analgesic effect when morphine was applied topically to painful ulcers.[1] However, patient numbers were small and, therefore, the data should be interpreted with caution. Treatment was generally well tolerated by patients, and although local reactions were described during the study, these were mild and possibly not related to morphine. No systemic adverse effects were reported.

At present, there is insufficient evidence to support the use of any specific opioid, dose, interval of administration, method of titration, or carrier agent for this approach.

Spinal route

Spinal opioid therapy may be effective for treating cancer pain where systemic treatment has failed, owing to either intolerable side effects or inadequate analgesia.

Intravenous route

The intravenous route may be preferred to the subcutaneous route in specific circumstances (e.g. IV line in situ, generalized oedema, coagulation disorders), or where rapid titration of analgesia for severe uncontrolled pain is required.[2]

The average relative potency ratio of oral morphine to subcutaneous or intravenous morphine is between 1:2 and 1:3 (i.e. 20–30mg of morphine by mouth is equianalgesic to 10mg by SC or IV injection).[3]

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Choice of analgesic—adjuvant analgesics

Overview of the management of neuropathic pain

The medical treatment of neuropathic pain is unsatisfactory, and pain can prove difficult to control in a significant number of patients with this condition. Current recommendations are outlined in Box 8.1.

The early trials of analgesics for neuropathic pain considered neuropathic pain as a uniform entity, but more recent trials have assessed various pain syndromes. It has emerged from these studies that analgesics may vary in efficacy according to the type of pain syndrome. Most of the trials on neuropathic pain have studied patients who have post-herpetic neuralgia and painful polyneuropathy. Fewer trials have looked at neuropathic pain due to cancer infiltration, and, as a result, much of the data on the efficacy of different drugs is extrapolated from data collected from patients with non-malignant pain.

The NNT (*number* of patients *needed to treat* to obtain one responder to the active drug) is commonly used as an indication of the overall efficacy of individual drugs. It is a relatively crude measure, however, as it can be hampered by methodological variability across RCTs and a lack of consideration for other important outcomes (e.g. quality of life).

Table 8.21 lists the NNT of analgesics on the basis of data from a large meta-analysis performed by the Special Interest Group on Neuropathic Pain of the International Association for the Study of Pain (NeuPSIG). The data was taken from class I/II studies on painful polyneuropathy with 95% confidence intervals (CIs). Unless otherwise specified, the NNT used was for 50% pain relief.

Table 8.21 NNT for drugs for neuropathic pain in adults (any aetiology)

Drug	NNT (95% CI)
Tricyclic antidepressants (amitriptyline, clomipramine, imipramine)	**3.6**(3.0–4.4)
Serotonin-noradrenaline reuptake inhibitors	**6.4**(5.2–8.4)
Pregabalin	**7.7**(6.5–9.4)
Gabapentin	**7.2**(5.9–9.1)
Strong opioids	**4.3**(3.4–5.8)
Tramadol	**4.7**(3.6–6.7)

Abbreviations: NNT, number needed to treat; CI, confidence interval

Data sourced from Finnerup NB, Attal N, Haroutounian S, McNicol E, Baron R, Dworkin RH, et al. (2015) Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. Lancet Neurol, 14(2):162–73.

Box 8.1 Recommendations for neuropathic pain management

First-line

- Tricyclic antidepressants
  - amitriptyline, imipramine, clomipramine
  - 75–150mg/day
- Serotonin-noradrenaline reuptake inhibitors
  - duloxetine 60–120mg/day
  - venlafaxine ER 150–225mg/day
- Pregabalin
  - 300–600mg/day
- Gabapentin
  - 1200–3600mg/day

Second-line

- Lidocaine patches (peripheral neuropathic pain)
  - 1–3 patches to the region of pain once a day for up to 12 hours
- Capsaicin high-concentration patches (peripheral neuropathic pain only)
  - 1–4 patches to the painful area every 3 months
- Tramadol
  - 200–400mg/day

Third-line

- Strong opioids
  - per individual titration

Pharmacological management of neuropathic pain

Opioid analgesics

Opioid agonists may relieve neuropathic pain by binding to the mu-opioid receptors in the CNS, dampening neuronal excitability. In addition, opioids may be helpful because many patients with cancer who are experiencing neuropathic pain have a nociceptive component to their pain.

Maximum effectiveness for neuropathic pain appears to be associated with doses less than or equal to 180mg morphine/day, with no additional benefit gained for higher doses.[1]

Methadone may be considered to be different from the other opioids with respect to impact on neuropathic pain. It can either be tried as an alternative to a first-line opioid, or introduced later, when other options have failed (see Methadone, pp. 94–5).

Antidepressant drugs

The mechanism of action of antidepressant drugs in the management of neuropathic pain is unclear.[2, 3] Analgesia is often achieved at a lower dosage and faster (usually within a few days) than the onset of any antidepressant effect (which can take up to 6 weeks). The pain-relieving properties of antidepressants are independent of any effect on mood.

Two main groups of antidepressants are commonly used:

- the older tricyclic antidepressants (TCAs)
- the newer selective serotonin reuptake inhibitors (SSRIs) and serotonin-noradrenaline reuptake inhibitors (SNRIs)

TCAs

TCAs are recommended as first-line drugs for the treatment of neuropathic pain; however, potential toxicity needs to be considered in first-line use and in terms of dose (see Table 8.22). It is recommended that doses of 75mg/day or less be used for patients over the age of 65 owing to risks of anticholinergic and sedative side effects.[2] An increased risk of sudden cardiac death has been reported at doses higher than 100mg/day.[3]

In terms of NNT, they appear to have a similar efficacy regardless of the underlying condition: diabetes mellitus, post-herpetic neuralgia, traumatic nerve injury, or stroke.

TCAs may be subdivided into two categories based on their chemical structure: tertiary and secondary amines:

- The **secondary amines** (e.g. **desipramine** and **nortriptyline**) appear to be as effective as the **tertiary agents** (e.g. **imipramine** and **amitriptyline**) as analgesics in the treatment of neuropathic pain, but they produce markedly fewer adverse effects (Table 8.23).
- Adverse effects from TCAs can be significant, and may lead to up to 20% of patients withdrawing from treatment. TCAs are contraindicated in those patients with recent MI, arrhythmia, mania, and those taking MAOIs. It should be used with caution in glaucoma.

Table 8.22 Amitriptyline preparations

Tabs	10mg, 25mg, 50mg
Syrup	25mg/5mL, 50mg/5mL

Suggested treatment schedule:

Start with amitriptyline 10–25mg nocte.

Slowly titrate, as tolerated.

Some patients do not see a benefit until after 4–6 weeks of treatment, and effective dosages are highly variable, but the average dosage is 75mg/day.

1. Severity of pain and the patient's prognosis will dictate how long to persevere with antidepressants.
2. Many patients do not tolerate amitriptyline, especially in higher doses, therefore consider changing to a secondary amine.

Table 8.23 Amitriptyline—adverse effects

Anticholinergic effects	Dry mouth, constipation, blurred vision, urinary retention, dizziness, tachycardia, memory impairment, delirium
Alpha-1-adrenergic effects	Orthostatic hypotension/syncope
Cardiac conduction delays/heart block	Arrhythmias, Q–T prolongation
Other side effects	Sedation, weight gain, excessive perspiration, sexual dysfunction

SSRIs and SNRIs

SSRIs and SNRIs are classes of antidepressants that act by selectively inhibiting the presynaptic reuptake of serotonin and noradrenaline.

SNRIs (e.g. duloxetine and venlafaxine) have the advantage that they are generally safer to use than TCAs.

The most common adverse effects associated with SNRIs are nausea, dizziness, drowsiness, constipation, increased sweating, and dry mouth. Duloxetine is contraindicated in those taking MAOIs and should be used with caution in glaucoma.

SSRIs (e.g. citalopram and fluoxetine) are observed to be less efficacious than other antidepressants in the treatment of neuropathic pain. At present, there is insufficient evidence to support their use for neuropathic pain.[2]

Anti-convulsant drugs

As with epilepsy, neuronal hyperexcitability is thought to be of importance in the pathogenesis of neuropathic pain. Anticonvulsants act through a variety of mechanisms to depress synaptic transmission, elevate the threshold for the repetitive firing of nociceptive neurones, and reduce discharges from the dorsal root ganglion cells.

Gabapentin/pregabalin

The combination of morphine and gabapentin has been shown to be of use in the management of post-herpetic neuralgia. Research has demonstrated

synergistic effects, with better analgesia at lower doses of each drug than either given alone.[3]

- For preparations, see Table 8.24.
- Gabapentin and pregabalin bind to voltage-gated calcium channels in the dorsal horn, resulting in a decrease in the release of excitatory neurotransmitters such as glutamate and substance P.
- Pregabalin is an analogue of gabapentin; it has the same mechanism of action but with a higher affinity for the presynaptic calcium channel.
- Both drugs have a similar adverse-effects profile, which includes dizziness, drowsiness, peripheral oedema, and dry mouth.
- Gabapentin should be titrated slowly according to individual tolerance, and is administered t.d.s.
- Pregabalin has a short onset of action, and is administered b.d.
- Doses of both drugs should be adjusted in patients with renal impairment.
- At the time of writing this edition, the UK government announced plans to reclassify the prescription drugs pregabalin and gabapentin as class C controlled substances, after experts issued safety warnings following an increase in deaths linked to their use.

Carbamazepine is associated with frequent and severe adverse reactions, including sedation, dizziness, gait abnormalities, hyponatraemia, hepatitis, and aplastic anaemia. Slow dose titration is recommended. Lamotrigine is generally well tolerated and has shown efficacy in the treatment of diabetic peripheral polyneuropathy. Adverse effects include dizziness, nausea, headache, and fatigue. It may induce potentially severe allergic skin reactions.

Table 8.24 Anti-convulsant drug preparations

Gabapentin	
Caps	100mg, 300mg, 400mg
Tabs	600mg, 800mg
Starting dose	Day 1: 300mg nocte Day 2: 300mg b.d. Day 3: 300mg t.d.s. p.o.
Usual maintenance dose	0.9–1.2g/24h
Maximum recommended dose	1.8g/24h Doses up to 2.4g/24h (and even higher) have been used
Pregabalin	
Caps	25mg, 50mg, 75mg, 100mg, 150mg, 200mg, 300mg
Oral solution	20mg/mL
Starting dose	50–75mg b.d. Starting at 25mg b.d. in the frail or elderly may be effective and avoid side effects. If necessary, increase dose every 3–7 days up to a maximum of 300mg b.d.

Sodium valproate has been used for many years as an anticonvulsant. RCTs have only recently been carried out with this drug in the study of peripheral neuropathic pain. At present, there is insufficient evidence to recommend the use of carbamazepine or lamotrigine for neuropathic pain, and sufficient evidence to recommend against the use of sodium valproate.[4]

Topical analgesics

Lidocaine

Topical agents work locally, directly at the site of application, with minimal systemic effects. Lidocaine, like other local anaesthetics, acts through the inhibition of voltage-gated sodium channels. Lidocaine patches appear to be safe with very low systemic absorption and only local adverse effects (mild skin reactions). Up to three patches a day for a maximum of 12 hours may be used to cover the painful area. The limited evidence for the effectiveness of lidocaine patches has been derived almost entirely from the non-cancer pain setting. Clinical practice indicates that lidocaine plasters can be helpful to carefully chosen patients with neuropathic pain limited to a defined area of superficial allodynia or hyperalgesia.

Capsaicin

Capsaicin is thought to elevate the pain threshold by reducing the amount of substance P available to act as a neurotransmitter. Capsaicin is available in a 0.075% or 0.025% cream, or a high-dose 8% patch (Table 8.25). Capsaicin is a derivative of chilli pepper and must be applied with gloves and according to instructions. Although the pain may increase to start with, perseverance may provide relief.

N-methyl-D-aspartate (NMDA) receptors

The NMDA receptor is thought to be involved in the development of the 'wind-up' phenomenon of neuropathic pain.

NMDA receptors are widely spread throughout the CNS, particularly in the spinal cord. Stimulation of pain fibres in the periphery causes the release of excitatory amino acids such as glutamate and aspartate, which in turn activate the NMDA receptor complex. A phenomenon known as 'wind-up' then occurs, producing a magnified pain response which, clinically, is associated with the features of neuropathic pain such as allodynia (pain produced by a stimulus that is not normally painful, e.g. light touch) and hyperalgesia (an exaggerated and prolonged pain response to a mildly painful stimulus).

Ketamine and methadone are NMDA antagonists, and this may explain their efficacy in the management of neuropathic pain.

Table 8.25 Capsaicin preparations

Patch	8%
Cream	0.075% 45g, 0.025% 45g
Starting dose	Apply topically 3–4 times daily

Ketamine

Ketamine is a dissociative anaesthetic which has strong analgesic properties. Its analgesic effect may be partly due to NMDA receptor blockade, i.e. receptor antagonism. Clinical reports indicate that, when added to opioids, low subanaesthetic ketamine doses may give improved analgesia with tolerable adverse effects. See Box 8.2.

Ketamine undergoes first-pass hepatic metabolism to an active metabolite. Drugs that interact with CYP34A have the potential to affect ketamine metabolism (e.g. azole antifungals, macrolide antibacterials, HIV protease inhibitors, and ciclosporin).

Ketamine may be used by p.o., SC, IV, epidural, and intrathecal routes, and has been reported to have been used over a very wide range of doses. It has been suggested that it may be more potent given orally than parenterally.

The dose-dependent psychomimetic side effects of ketamine, including sedation, nausea, disagreeable psychological disturbances and hallucinations, may be minimized by the use of a benzodiazepine or antipsychotic.[5]

Ketamine can have a direct irritant effect on the urinary tract. Consider stopping and consulting a urologist if the patient experiences urinary symptoms without evidence of infection. Hepatobiliary toxicity has also been reported. Consider monitoring LFTs during long-term therapy.

Ketamine is commonly used via the oral route or via the subcutaneous route using a 'burst' protocol.

Box 8.2 Ketamine prescribing guide

Oral route

- start ketamine 10mg t.d.s–q.d.s. p.o. and p.r.n.
- increase by 10mg increments once or twice daily
- maximum reported dose 200mg q.d.s.[6, 7]

Parenteral route

- consider reducing the opioid dose when initiating parenteral ketamine
- ketamine 10mg SC stat may be given if indicated for severe pain
- start infusion of ketamine 50–100mg/24h CSCI (1–2.5mg/kg per 24h)
- increase ketamine dose by 50–100mg increments as indicated to maximum 500mg/24h CSCI

The use of short-term 'burst therapy' has also been reported: the results of a recent RCT suggest a higher rate of toxicity with insignificant increase in therapeutic effect with rapid CSCI titration.[5]

- starting dose 100mg/24h
- increase after 24h to 300mg/24h if 100mg/24h ineffective
- increase after further 24h to 500mg/24h if 300mg/24h ineffective; stop 3 days after last dose escalation

Haloperidol or a benzodiazepine may be concurrently prescribed (either orally or parenterally) if the patient experiences dysphoria or hallucinations. Some palliative care practitioners recommend that patients at high risk of experiencing these adverse effects be given these medications prophylactically.

Evidence for the effectiveness of ketamine in the management of cancer-related pain is limited and conflicting. There is insufficient data available to suggest that ketamine improves the effectiveness of opioid treatment in cancer pain.[8] There are no studies comparing various titrations, dosing schedules, or routes of administration of ketamine in managing cancer pain. Patient selection, dosing, and use in palliative care remain controversial until further evidence becomes available.

Clinicians with limited experience in using ketamine should seek expert guidance to determine management of pain with this drug.

Corticosteroids

Although corticosteroids are commonly used to treat neuropathic pain, RCTs have not been used to evaluate their effectiveness. They may act by reducing inflammatory sensitization of nerves, or by reducing the pressure effects of oedema.

Dexamethasone has the least mineralocorticoid effect, and can be used once a day, in the morning, because of its long duration of effect. A high initial dose may be used to achieve rapid results (dexamethasone 8mg/day will work in 1–3 days); the dose should then be rapidly reduced to the minimum that maintains benefit.

Long-term corticosteroids are best avoided owing to side effects, although they can sometimes buy useful time whilst allowing other methods (e.g. radiotherapy or antidepressants) time to work (Table 8.26). If no benefit is observed within 5 days, they should be stopped.

- Hydrocortisone has a high mineralocorticoid effect.
- Dexamethasone has a relatively high equivalent corticosteroid dose per tablet and less mineralocorticoid effects than either prednisolone or methylprednisolone, with consequently fewer problems with fluid retention.
- Prednisolone causes less proximal myopathy than dexamethasone.

Bisphosphonates

Bisphosphonates form part of the standard therapy for hypercalcaemia and for the prevention of skeletal events in some cancers. There is also evidence to support the effectiveness of bisphosphonates as an intervention for the management of cancer-related bone pain[9, 10] (see Table 8.27).

Table 8.26 Relative anti-inflammatory steroid doses (approximate)

Steroid	Administration	Equivalent dose (mg)
Dexamethasone	oral/SC	2
Prednisolone	oral/rectal	15
Hydrocortisone	oral/IM/IV	60
Methylprednisolone	oral/IM/IV	12

Table 8.27 Bisphosphonate preparations and bone pain

Disodium pamidronate	
Injection	15mg, 30mg, 90mg (dry powder for reconstitution)
Dose	60–90mg IV in 500mL sodium chloride 0.9% over 4h
Zoledronic acid	
Injection	4mg
Dose	4mg IV in 100mL sodium chloride 0.9% over 30min
Ibandronic acid	
Injection	6mg
Dose	6mg IV in 500mL sodium chloride 0.9% over 1–2h p.o. 50mg daily

Available bisphosphonates include disodium pamidronate, ibandronic acid, and zoledronic acid.

Adverse effects include renal toxicity, hypocalcaemia, and osteonecrosis of the jaw (ONJ). The risk of ONJ can be reduced by a dental assessment prior to treatment and avoiding invasive dental treatment when on IV bisphosphonates. Doses may need to be altered in renal impairment. Patients may also experience a flu-like reaction post-treatment.

Analgesic effect should be expected within 14 days. It is unclear for how long bisphosphonates should be continued.

Bisphosphonates should be considered for the treatment of cancer pain associated with bone metastases, in particular, where analgesics and/or radiotherapy are inadequate for the management of pain. However, there is insufficient evidence to recommend bisphosphonates for immediate effect as first-line therapy, or to define the most effective bisphosphonates, or their relative effectiveness for different primary neoplasms.

Biological treatment

Denosumab is a human monoclonal antibody that binds with high affinity to the RANKL ligand. It has been shown to be safe and effective in improving pain, quality of life, and overall survival.

❗Denosumab is not licensed for the treatment of bone pain but is used for osteoporosis and to reduce the risk of fractures in men who have undergone hormone ablation therapy in prostate cancer. It should only be prescribed under specialist supervision.

Other pharmacological interventions depending on the site of pain

See Table 8.28.

Table 8.28 Other pharmacological interventions

Pain	Possible co-analgesics
Headache due to cerebral oedema	Dexamethasone
Painful wounds	Metronidazole
Intestinal colic	Hyoscine butylbromide or hydrobromide
Gastric mucosa	Lansoprazole
Gastric distension	Domperidone
Skeletal muscle spasm	Baclofen/diazepam
Cardiac pain	Nitrates/nifedipine
Oesophageal spasm	Nitrates/nifedipine

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Interventional and non-pharmacological techniques

Radiotherapy

Cancer commonly metastasizes to bone. Although some bone metastases are painless, many frequently cause significant and debilitating pain. The management of patients with metastatic bone pain involves a multidisciplinary approach, including analgesia, radiotherapy, surgery, chemotherapy, hormone treatment, radioisotopes, and bisphosphonates. Analgesia is generally the first option in most patients. Radiotherapy or surgery can be used for localized bony metastatic disease.

Radiotherapy has been shown to be effective in decreasing metastatic bone pain and in causing tumour shrinkage. The efficacy of radiotherapy for pain related to bone metastases has been demonstrated in several high quality RCTs and systematic reviews.[1]

Up to 60% of patients will have some pain relief and about one-third of them will have complete pain relief following radiotherapy.[2]

A 'pain flare' may occur, when the pain initially becomes worse in the first few days after treatment before eventually subsiding. Half of patients who have complete pain relief achieve this within 4 weeks of treatment, and the median duration of complete relief is 12 weeks.

Single-fraction and multiple-fraction radiotherapy are equally effective at achieving pain control; however, the re-treatment rates and pathological fracture rates are higher after single-dose radiotherapy. Likely prognosis should be taken into account when deciding upon a treatment plan, and a short prognosis may favour single-fraction radiotherapy.

Radiotherapy is also an effective management option for pain relating to sites of metastatic disease other than bone, e.g. chest wall infiltration. Although there is a paucity of randomized controlled trial data, the use of radiotherapy for such indications is widespread and recommended in many consensus clinical guidelines.

Radioisotopes

Radioisotope treatment involves the administration of radioisotopes which are attracted physiologically to sites of bone mineralization. Strontium-89 and samarium-153 are approved in the USA and Europe for the palliation of pain from metastatic bone cancer.[3]

Radioisotopes have been shown to be effective in providing pain relief with response rates of between 40% and 95%. Pain relief starts 1–4 weeks after the initiation of treatment, continues for up to 18 months, and is also associated with a reduction in analgesic use in many patients. Treatment may be repeated if required.

Thrombocytopenia and neutropenia are the most common toxic effects, but they are generally mild and reversible.

The development and clinical assessment of radioisotopes has focused mainly on their use in prostate cancer. Data also exists for their use in lung and breast cancer. Tumours with little or no osteoblastic reaction—e.g. renal carcinoma and myeloma—tend to show poor response to radioisotopes, as

sites of mineralization are fewer or do not exist. External beam hemi-body irradiation is an alternative for multiple-site bone pain.

Surgical techniques

The pain of bone metastases may respond to local infiltration or intralesional injection with depot corticosteroid ± local anaesthetic. Prophylactic pinning may be considered for osteolytic metastases in long bones. Vertebroplasty, in which injection of acrylic cement is administered percutaneously into unstable fractures of the vertebrae, may be worth considering if the patient is relatively well. Spinal or epidural anaesthetic blocks may also be used to manage intractable pain.

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Anaesthetic procedures in palliative care

The majority of patients with cancer can have their pain needs met by following the WHO analgesic ladder. For a minority of those patients who do not obtain satisfactory pain relief using the WHO ladder, or who experience unacceptable side effects with systemic analgesia, interventional techniques can be useful in helping to control pain, maintain function, and improve quality of life. However, there is less empirical evidence for these procedures in comparison to the use of systemic analgesia for the management of cancer pain.[1, 2]

Anaesthetic interventions may be grouped into:

- intrathecal and epidural (neuraxial) techniques
- chemical neurolysis/nerve blocks

Indications for anaesthetic intervention

Patients may be considered for anaesthetic intervention in the following circumstances:

- when conventional oral or parenteral therapies prove unsuccessful, or where the side effects of systemic therapy are intolerable
- when the aetiology of pain is reasonably clear and a specific nerve block is likely to provide good analgesia, with minimal or acceptable side effects
- when there is identification of sympathetically maintained pain that is amenable to sympathetic blockade
- when there is incident pain which may benefit from numbness (local anaesthetic)
- when special expertise and support are available

As with all interventions, patient selection is vital for success. Selection criteria include the following:

- patient competent to consent to procedure
- patient compliant
- absence of local or systemic infection
- absence of specific allergy
- absence of significant coagulopathy
- adequate facilities for the procedure and support for post-procedural care and maintenance

Unlike the general population receiving anaesthetic input, patients with advanced cancer are often debilitated, have limited mobility, and may have a short prognosis. Therefore, it is imperative that all that can be done to alleviate their pain is performed with the least inconvenience and with minimal compromise. Although many spinal procedures can easily be carried out at the bedside, the more involved interventions, such as chemical neurolysis, necessitate the use of radiological guidance, usually in a hospital setting. With this in mind, patients should be selected for these procedures according to what is considered appropriate and acceptable to them.

The role of the clinician looking after patients in the palliative care setting is to recognize when patients may benefit from an anaesthetic intervention, and to seek specialist opinion at an early stage. Specialist anaesthetic input should be sought at all times to guide the choice of appropriate intervention, the management of adverse effects, and the titration of medications via the neuraxial route.

General principles of practice

Aseptic precautions and adequate monitoring are of utmost importance during these procedures.

Drugs and drug mixtures for intrathecal use should be preservative-free and prepared under sterile conditions. If combinations of drugs are used, care should be taken to ensure their stability and compatibility.[3] Infrequently, systemic toxicity can occur from the administration of local anaesthetic or neurolytic agents. If significant hypotension occurs due to spinal sympathetic blockade, boluses of ephedrine 3mg (i.e. 30mg/mL ampoule diluted to 10mL with sterile water, giving 3mg/mL) should be available. This is administered IV when required at 3–4 minute intervals according to response.

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Intrathecal and epidural (neuraxial) techniques

Direct delivery of opioids to the spinal cord via epidural and intrathecal techniques has proven an effective and reversible way to provide analgesia with reduced systemic side effects.[1-3] Intrathecal opioids bind to the mu- and kappa-opioid receptors in the substantia gelatinosa of the spinal cord. This is achieved to a lesser extent with epidural opioids, which exert a simultaneous systemic and intrathecal effect (10% and 90%, respectively). See Fig 8.7.

Contraindications to neuraxial techniques (relative and absolute)

- platelet count $<20\times10^9$/L with clinical symptoms of poor clotting
- full anticoagulation or INR >1.5
- active infection with concurrent septicaemia
- concurrent chemotherapy with neutropenia
- occlusion of epidural space by tumour at the site of catheter tip placement (epidural catheters only)

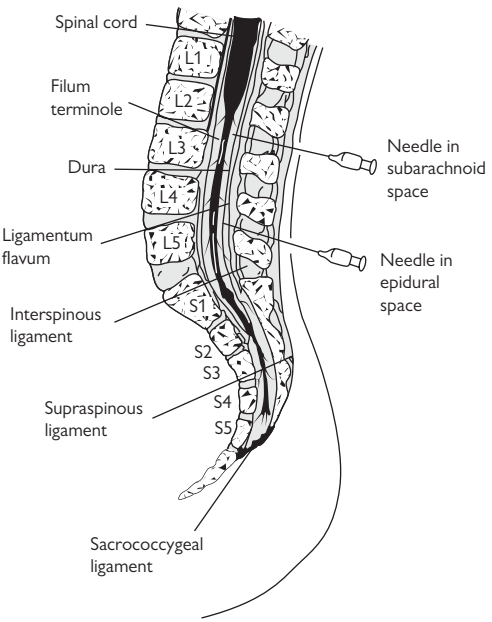


Fig 8.7 Schematic diagram of lumbosacral anatomy.

Table 8.29 Comparison of intrathecal and epidural opioid administration

Factors	Intrathecal	Epidural
Infection rates	Lower infection rates than with epidural catheters. Lower rates in totally implanted systems.	Higher rates than with intrathecal administration. Rates increase with duration of catheter placement.
Pain relief	Better for long-term	Good only for short-term
Dose	Lower (10–20% of epidural dose)	Higher
Pump refills	Less frequent, low volumes required	More frequent (higher volumes)
Side effects	Fewer	More
Technical difficulty	Easier to place, less likely to become displaced	More difficult, and catheter may migrate
Long-term complications	Less (approx 5%)	More (approx 55%)
Catheter occlusion and fibrosis	Minimal	Higher frequency (leading to loss of analgesia/pain on injection)
Epidural metastases	Less affected	More affected (may compromise drug delivery)
Overall advantage	Effective analgesia with fewer complications	

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- allergy or anticipation of unmanageable side effects
- psychosocial issues that make technique untenable
- inadequate professional support in resolving problems
- inadequately investigated symptoms

Table 8.29 compares the intrathecal and epidural routes of administration.[4]

Catheters may be externalized through the skin at the puncture site or may be tunnelled subcutaneously away from the spine. Alternatively, a totally implantable pump system may be employed if the patient has a life expectancy of several months.[5]

Follow-up care following intrathecal or epidural catheter placement

NB: Specialist advice from an anaesthetic pain specialist should be sought when required.

- All staff involved in aftercare of the patient should be familiar with the possible side effects and complications listed, and should be vigilant for them as well as for signs of infection.

- The catheter insertion site should be inspected on a daily basis.
- A pain chart should be maintained until the analgesia is considered sufficient.
- If the patient is being discharged to the community, there should be liaison with the key members of the primary care team (GP, district nurse, and community specialist palliative care nurse) prior to discharge, and written guidelines should accompany the patient home.
- Patients should not be discharged home until the dose has been stabilized to pain relief.

Comparison of continuous vs bolus techniques

See Table 8.30.

Ideally, the continuous infusion technique should be used, with a familiar delivery system, e.g. syringe pump delivering the infusion solution over 24 hours. The use of intrathecal bolus administration during pain crises has been described, but this is not considered routine practice.[6]

Adverse effects

See Boxes 8.3 and 8.4.

Management of adverse effects

NB: Specialist advice from an anaesthetic pain specialist should be sought if required.

- sedation: reduce dose of opioid
- urinary retention: usually requires once-only catheterization
- nausea: regular anti-emetic
- pruritus: consider adding spinal bupivacaine; IV ondansetron 8mg has been shown to be effective;[7,8] IV nalbuphine may be effective[9]
- respiratory depression (RR less than 8/min or excessive drowsiness): stop or reduce infusion rate; consider parenteral naloxone 100–400mcg
- hyperalgesia: reduce opioid dose and consider addition of adjuvant agent
- myoclonus: reduce opioid dose, rehydrate, and consider low-dose benzodiazepine therapy (myoclonus may not be opioid dose-dependent)
- constipation: regular laxatives from the outset of therapy

Table 8.30 Continuous vs bolus techniques

Factor	Continuous	Intermittent bolus
Dose escalation	Higher	Lower
Analgesic quality	Better	Fair
Local anaesthetic combinations	Minimal motor or haemodynamic complications	Higher risk of motor or haemodynamic complications (**caution** recommended for intraspinal administration)

Box 8.3 Technical complications of neuraxial catheters

- mechanical problems: catheter kinking, disconnection, dislodgement, pump failure
- skin breakdown at insertion site
- infection: local, catheter, epidural abscess, meningitis, systemic
- CSF leak, causing headache or loss of analgesia
- CSF seroma
- haematoma
- catheter displacement, occlusion, or migration
- nerve damage (rare but possible): procedure-related, from an inflammatory mass at catheter tip, drug-induced neurotoxicity

Box 8.4 Adverse effects attributable to spinal opioids

- minor sedation: excessive opioid dosage
- urinary retention: commonest in males during first 24 hours
- persistent nausea
- pruritus
- respiratory depression: may be significant and insidious if the patient is opioid-naive
- hyperalgesia: at higher doses
- myoclonus: at higher doses, indicating toxicity
- constipation: common within therapeutic range

Choice of drug: opioids, local anaesthetics, clonidine, ziconotide

Opioids

- Morphine is one of the least lipid-soluble opioids available, and when given in the spinal space, it has the slowest rate of uptake into the surrounding vasculature, which gives it a longer and primarily spinal site of action. Intrathecal morphine is 100 times more potent than a systemically given dose. Data from post-operative pain studies suggest that morphine is twice as potent as diamorphine by the intrathecal route.
- Diamorphine can be administered intrathecally, with a potency ratio of 1:100 (intrathecal: systemic). Diamorphine should be reconstituted in sodium chloride 0.9%. Alternatives to morphine and diamorphine are used less frequently.
- Hydromorphone is an effective and affordable option for the morphine-intolerant patient. The potency of intrathecal hydromorphone is five times that of morphine.
- Of the lipophilic drugs, both fentanyl and sufentanil are used. Greater lipid solubility may be an advantage to achieve a rapid onset of action. But this may also lead to rapid systemic absorption, a shorter duration of action, and a less dose-sparing effect when compared to systemic administration. There is no published data on dose equivalences.

NB: The dosing of opioids via the neuraxial route should be according to specialist anaesthetic advice.

Typical opioid-dosing schedules

- If patient is opioid-naive, start with intrathecal diamorphine 0.5–1mg/24h or epidural diamorphine 2.5–5mg/24h.
- If the patient is established on a systemic opioid, the dose of neuraxial opioid should be calculated based on the systemic requirements in order to minimize the potential for withdrawal phenomenon during route conversion.

Local anaesthetics

Local anaesthetic agents are sodium channel blockers and are unique in their ability to block nerve impulses conducted proximally (pain relief) and impulses conducted distally (motor blockade). The conduction blockade produced is both painless and reversible. Table 8.31 shows the most frequently used agents.

The potential side effects of local anaesthetics include:

- postural or overt hypotension due to sympathetic block
- numbness due to sensory block
- leg weakness due to motor block
- altered proprioception in low doses, even when motor weakness is not apparent
- urinary retention due to sympathetic block
- 'Total spinal'—this potentially catastrophic event can occur if a large dose of local anaesthetic is delivered erroneously to the subarachnoid space. A profound drop in blood pressure is accompanied by motor paralysis of the lower limbs, spreading to the upper limbs and respiratory muscles, and ultimately involving the brain. Both cardiovascular and ventilatory support is required until the local anaesthetic effects wear off.

Clonidine

Clonidine is an α_2-adrenergic agonist and appears to act at the level of the spinal cord. It acts synergistically with opioids, but is also a powerful analgesic when used alone in the management of neuropathic pain. It is a lipophilic compound and its spinal effect may be more pronounced with

Table 8.31 Comparison of the most frequently used local anaesthetics for spinal use

	Lidocaine	Bupivacaine	Ropivacaine
Onset	Rapid	Slower	Similar to bupivacaine
Duration	Short (hours)	2–3 times longer than lidocaine	Slightly longer than bupivacaine
Typical dosage	2mL 2% over 24h	2mL 0.5% over 24h	2mL 0.75% over 24h
Advantages	Rapid onset and offset	Synergism with opioids	May preferentially block sensory nerves
	Synergism with opioids		Two-thirds as potent as bupivacaine
			Synergism with opioids

intrathecal rather than epidural administration. The dose of clonidine is often limited by its side effects such as sedation, hypotension, and bradycardia. Nausea, pruritus, and urinary retention have also been reported. Starting doses range from 10 to 20mcg/24h and should be titrated for adequate analgesic effect and minimal side effects. Doses above 150mcg/24h should not be necessary.

Ziconotide

Ziconotide is thought to produce its analgesic effects through the blockade of specific N-type calcium channels found at the presynaptic terminals in the dorsal horn.[10] Recognized side effects of ziconotide include dizziness, gait imbalance, nausea, nystagmus, confusion, and urinary retention. These side effects usually occur after prolonged use, and may be severe. The administration of intrathecal ziconotide has been reported to be useful in the treatment of refractory pain in patients with cancer and AIDS.[11] However, clinical experience is limited, and longer-term data is awaited. Ziconotide is incompatible with morphine.

Other

Other analgesics have been tried as intrathecal agents, including midazolam, ketamine, octreotide, calcium channel blockers, and neostigmine. As yet, there is no convincing body of evidence to support their use.

Chemical neurolysis for cancer pain

The use of neurolytic techniques has diminished in recent years owing to advancements in spinal analgesia and increased life expectancy for cancer patients.[12]

However, neurolysis should be considered under the following circumstances:

- Pain is severe, intractable, and has failed to respond to other measures, or side effects of systemic analgesia are intolerable.
- The nociceptive pathway is readily identified and related to a peripheral nerve pathway or sympathetic chain.
- A trial block of local anaesthetic has been successful.
- The effects demonstrated through the local anaesthetic block are acceptable long term to the patient.

The goals of neurolysis include reduction in pain and reduction in the need for other pharmacotherapy. Neurolysis is rarely permanent, and pain returns as a consequence of regrowth of neural structures or disease progression in the treated area. When used centrally, there is a risk of motor paralysis and sphincter weakness, which are generally unacceptable to most patients. For these reasons, detailed informed consent by the patient is to be ensured by the practitioner prior to the procedure.

Neurolytic agents used

Alcohol and phenol are the two most commonly used agents.

Alcohol

Alcohol makes the solution hypobaric, hence the patient should be able to tolerate a position that allows the alcohol solution to float upwards to the affected nerve root.

Alcohol is usually associated with the following:

- a burning sensation upon injection along the distribution of the nerve, followed by warm numbness
- an increase in pain relief over a few days, maximal by 1 week

Phenol

Phenol makes the solution hyperbaric, so the patient should be able to tolerate a position that allows the phenol to sink down to the nerve roots.

Phenol is characterized as follows:

- Following injection, an initial local anaesthetic effect allows relief of pain which is then maintained by the neurolysis, which may take 3–7 days to take full effect.
- The density and duration of block are felt to be less than those of alcohol.

Visceral cancer pain is often produced through a combination of visceral afferent stimulation as well as somatic and neuropathic elements. The sympathetic chain carries much nociceptive information, and blockade of the sympathetic chain may improve both viscerally and sympathetically mediated pain.

NB: Neurolytic techniques have a narrow risk:benefit ratio, and therefore they should only be performed by experienced pain clinicians in appropriate surroundings.[13]

Most commonly used techniques

Coeliac plexus block

The coeliac plexus is responsible for transmission of nociceptive information from the entire abdominal contents, excluding the descending colon and pelvic structures. It has been successfully used to combat pain from pancreatic cancer and other upper abdominal viscera. It is a relatively safe and simple technique, performed under computed tomography (CT) guidance. Patients referred for this procedure should be able to tolerate lying on an X-ray table, and should have no coagulopathy or local infection (see Fig 8.8).

Possible complications include the following:

- orthostatic hypotension, which may persist for days
- backache at the site of needle insertion: if backache and hypotension persist, retroperitoneal haematoma should be excluded
- diarrhoea
- abdominal aortic dissection
- paraplegia and motor paralysis: rare

Superior hypogastric block

The superior hypogastric sympathetic ganglion transmits nociceptive information from the pelvis, excluding the distal fallopian tubes and ovaries. Superior hypogastric blocks have been successfully used to manage pain of pelvic origin, other than ovarian pain.

Ganglion impar block

This ganglion marks the end of the sympathetic chains and is situated at the sacrococcygeal junction. Visceral pain in the perineal area has been successfully treated with neurolytic blockade of this ganglion. These patients often present with a vague, poorly localized perineal pain, accompanied by

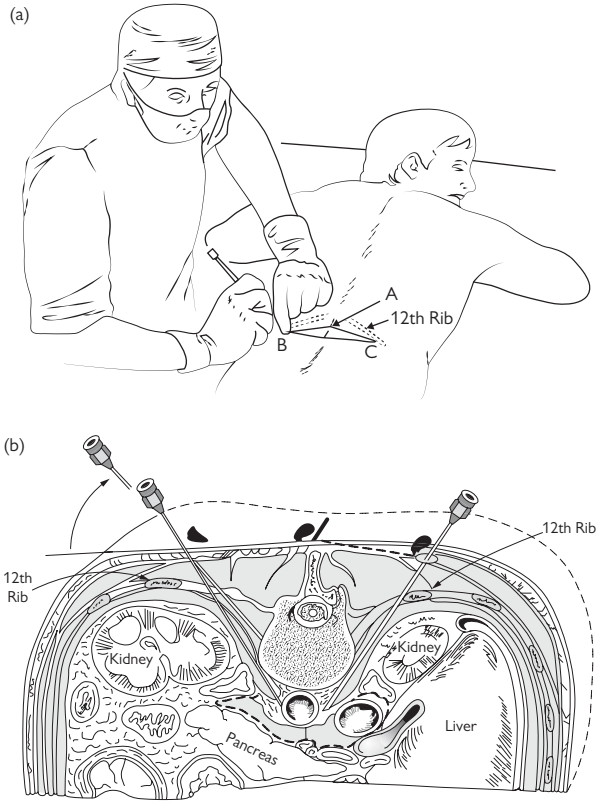


Fig 8.8 (a) Positioning for coeliac plexus block; (b) Deep anatomy showing placement of needles for coeliac placement block.

a burning sensation or urgency, and are often difficult to treat using oral pharmacology alone.

Interpleural block

Insertion of an epidural catheter into the pleural space and infusion of local anaesthetic or phenol have been described in the management of visceral pain associated with oesophageal cancer[14] and rib invasion by bone metastases (Fig 8.9). Potential complications include the following:

- pneumothorax (avoid bilateral blocks)
- phrenic nerve palsy
- trauma to local structures caused by the needle or catheter, or as a consequence of the phenol injection

Fig 8.9 Technique of intra-pleural block.

Saddle block

This is a modified low spinal technique where phenol is injected into the CSF in the lumbar area, with the intention of causing chemical neurolysis of the low sacral nerve roots that serve the perineum and perianal area. It is useful for patients complaining of pain or excoriation in the 'saddle' area, but carries the potential risk of sphincter compromise (<10%).

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Complementary therapies and other non-pharmacological pain interventions

A range of techniques and expertise exists which complement the pharmacological and interventional approaches that have dominated this chapter thus far (Table 8.32).

These techniques are not just an adjunct to medication but point to the centrality of holistic patient-centred care. Not all approaches will be appropriate for every patient, but for some, traditional medicine has little to offer either.

Table 8.32 Complementary therapies and other non-pharmacological interventions

Complementary therapies	Other non-pharmacological interventions
Acupuncture	Positioning
Reflexology	Catheterization
Aromatherapy	Reassurance
Art therapy	Good communication
Music therapy	Diversional therapy
Touch therapy	TENS
	Splinting of a fractured limb
	Psychological support

Special populations

Patients with impairment of communication

High prevalence of pain in the elderly population is a recognized reality. Almost half of those who die from cancer are over 75 years old. One study showed that 40–80% of elderly people in institutions are in pain. There is evidence that many patients suffering from some form of dementia receive no pain relief at all, despite the presence of a concomitant, potentially painful illness. The reason for this lies in the difficulty in assessing those with communication difficulties. In addition, the elderly often minimize their pain, making it even more difficult to evaluate. The only indication of pain may be a patient's unusual behaviour, which returns to normal with adequate analgesia.

Various attempts have been made to evaluate pain in such circumstances. The DOLOPLUS scale,[1] developed in 1993, is based on observations of a patient's behaviour in ten different situations that could be associated with pain. Pain is classified into somatic, psychomotor, and psychosocial aspects, and scores are allocated. A collective score level confirms the presence of pain.

Examples of unusual behaviours indicating pain

see Galloway and Turner (1999).[2]

Verbal expression

- crying when touched
- shouting
- becoming very quiet
- swearing
- grunting
- talking without making sense

Facial expression

- grimacing/wincing
- closing eyes
- worried expression

Behavioural expression

- jumping on touch
- hand pointing to body area
- increasing confusion
- rocking/shaking
- not eating
- staying in bed/chair
- withdrawn/no expression
- grumpy mood

Physical expression

- cold
- pale
- clammy
- change in colour
- change in vital signs if acute pain (e.g. BP, pulse)

Patients with a history of substance misuse

A history of addiction to opioid may compromise the effective control of cancer pain. Patients with a history of substance abuse should not be denied effective analgesia for pain.

Pain management is more complex in these patients, and assessment and management should take into account the following:

- that previous opioid use induces neuroplastic changes which can induce opioid tolerance and hyperalgesia, leading to higher opioid requirements for pain relief
- concurrent use of alcohol and other CNS depressants can have additive effects and place the patient at risk
- concurrent treatments such as methadone maintenance therapy
- co-morbid psychiatric conditions such as anxiety and depression

The risk of drug diversion or precipitation of further dependence can be reduced by avoiding very short-acting preparations such as OTFC and pethidine, using instead sustained-release preparations.[3, 4]

A multidisciplinary team approach should be employed, including the involvement of pain management and drug and alcohol specialists when possible.

The 'four As' should guide the review and fine-tuning of medications: analgesia, activity, adverse effects, and aberrant behaviour.

'Opioid-resistant' cancer pain

Pseudo-resistant?

- underdosing
- poor alimentary absorption of opioid (rare, except where there is an ileostomy)
- poor alimentary intake because of vomiting
- ignoring psychological aspects of patient care

Semi-resistant?

- bone pain
- raised intracranial pressure
- neuropathic pain

Resistant?

- muscle spasm
- abdominal cramps
- spiritual pain/total pain (➔ see Chapter 23)

Patients who have chronic unremitting pain from a deteriorating condition are particularly at risk of spiritual pain. Referral for psychological/spiritual support is important, or that of a complementary therapist.

Using Hay's[5] seven-model assessment, spiritual pain may be broken down into the following aspects:

- spiritual suffering—interpersonal or intra-psychic anguish
- inner resource deficiency—diminished spiritual capacity
- belief system problem—lack or loss of personal meaning system
- religious request—a specifically expressed religious need

At all times, the multidimensional character of pain must be considered and a multidisciplinary approach adopted.

Pain in settings with limited opioid availability

Although morphine has been on the WHO's essential medicines list since 1977, even today, 80% of the world's population lack access to it. Although local barriers to opioid availability have reduced, in many cases this has not led to an increase in the use of these medications. This inequity in access to effective analgesia is in marked contrast to other countries, such as the United States, where opioid consumption has increased; however, an increase in opioid-associated morbidity and mortality has occurred.

Positive steps are being taken by international bodies, including the WHO, in order to improve the global balance between ensuring access to those who need opioids for medicinal purposes while reducing the risks of diversion and misuse.[6]

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Chapter 9

Gastrointestinal symptoms

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Introduction

> Let your food be your medicine, and your medicine be your food.
>
> Hippocrates

A sizeable proportion of palliative care is concerned with the management of gastrointestinal symptoms. Traditionally, such symptoms have received less attention than pain management, yet the same principles apply.

Patients with pain usually show a response, or a lack of response, to treatment within hours. Patients with gastrointestinal symptoms may take several days to respond to interventions, and the temptation is thus to have a more lax attitude to monitoring gastrointestinal problems. In reality, the doctor and nurse need to be much more attentive to these problems, which deceptively cause significant patient morbidity, yet may not become obvious until major management difficulties arise.

Example

Every time a patient is prescribed a strong opioid for the first time, waiting to see whether the patient becomes nauseated or constipated will lead to major problems. The patient may become so sick that they refuse all morphine again. The patient may become severely constipated with serious and unpleasant consequences. The patient and family may lose trust in the healthcare professional. Such trust is one of the strongest tools in helping patients, and it may be difficult to repair if it is shaken so fundamentally.

Therefore

- Every time a strong opioid is prescribed for the first time, or the dose of a strong opioid is markedly increased, always prescribe or increase the dose of a laxative.
- Anti-emetics should be prescribed for the first 5–10 days of a strong opioid being started or a higher dose being initiated, but after 5 days they can and should be stopped as nausea due to the opioid side effects may wear off. In practice, if patients have tolerated analgesics on step 2 of the analgesic ladder, they will probably not need anti-emetics when changing to strong opioids.

Anticipation of problems before they occur

- Ongoing assessment of treatments and their effectiveness.
- Appropriate prescribing of background medication as well as medication for breakthrough symptoms.

Oral problems

Oral problems may affect up to 60% of patients with cancer and can impact greatly on quality of life, both physically and psychologically. They can cause eating, drinking, and communication problems, oral discomfort, and pain.[1] Common oral problems in palliative care include dry mouth, painful mouth, halitosis, alteration of taste, and excessive salivation.

Pathology and physiology

A healthy mouth is moist, clean, and pain-free with an intact mucosa. Saliva is a major protector of the tissues of the mouth. About 1500mL of saliva are produced daily by the parotid, submaxillary, sublingual, and several minor salivary glands.

Saliva is composed of a serous part (alpha-amylase), which initiates starch digestion, and a mucus component, which acts as a lubricant. It also contains calcium phosphate and bicarbonate, which help maintain healthy teeth, and other components such as mucin, which protects oral tissue from chemical and mechanical trauma and infections.

During cytotoxic therapy, the cells of the oral mucosa are vulnerable owing to their high proliferation rate. Other treatment complications may arise because of direct stomatotoxicity or indirectly because of myelosuppressive effects.

Risk factors for oral problems in patients with advanced cancer include the following:

- reduced oral intake
- debility (reduced ability to perform own oral hygiene)
- dry mouth
- dehydration
- radiotherapy—mucositis occurs about 2 weeks after initiation of therapy
- chemotherapy—mucositis occurs about 5–7 days after drug administration
- oral tumours

General mouth care

The aim of good mouth care is to prevent problems before they arise and to control unpleasant symptoms.

Assessment

Assess daily for symptoms or signs of problems such as altered taste, oral pain, dry mouth, halitosis, ulcers, oral or pharyngeal candidiasis, or dental problems.

- Regularly examine lips, tongue, teeth, and oral mucosa.
- Involve the local dental team if necessary.
- Assess the patient's ability to carry out mouth care effectively.
- Encourage good oral hygiene for general well-being.

An oral assessment tool may be useful. Eilers et al.'s oral assessment guide has been found to be appropriate for use in patients with advanced cancer.[2]

Management

Basic oral care

- By staff or patient if able.
- Keep mouth moist—encourage regular sips of fluids/oral rinsing.
- Brush teeth twice daily with soft toothbrush and fluoride-containing toothpaste.
- Rinse mouth thoroughly and frequently with warm water or sodium chloride 0.9% (helps removal of oral debris and is soothing and non-traumatic).
- Gently clean a coated tongue with a soft toothbrush or sponge.
- Apply moisturizing cream or white soft paraffin (petroleum jelly) to lips.
- Dentures should be removed at night and cleaned with a soft toothbrush and unperfumed soap or denture toothpaste.
- Soak dentures overnight in cleansing solution.

If the patient is unconscious or too unwell to carry out oral hygiene, instruct and involve family in this important area of care.

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Management of oral problems

Coated tongue/dirty mouth

In addition to basic oral care, if there is no candidiasis:[1-3]

- Use mouthwashes to remove debris, e.g. warm water or 0.9% sodium chloride.
- Gently brush with a soft toothbrush or sponge.
- Pineapple or effervescent vitamin C tablets have been used in the past to debride a furred tongue; however, as they are acidic, they may exacerbate a sore tongue and contribute to dental damage through cavitation.

Dry mouth (xerostomia)

Xerostomia is the subjective feeling of a dry mouth and is often associated with difficulties with speech, chewing, or swallowing, the need to keep drinking, and loss of taste. This is a common problem in advanced cancer, and appropriate management may involve the use of both saliva stimulants and substitutes.

Causes

- drugs, e.g. antimuscarinics, antidepressants, opioids, diuretics
- dehydration
- anxiety
- mouth breathing
- radiotherapy—damage to salivary glands
- oxygen therapy (non-humidified)
- obstruction, infection, or malignant destruction of salivary glands

Management

- treat underlying cause if possible, e.g. infection, dehydration
- review medication
- provide basic oral care regimen (see earlier)
- general measures (little scientific rationale)
  - sipping semi-frozen drinks
  - sucking ice-chips in gauze (to prevent mucosal freezing)
  - chewing pineapple pieces
  - sugar-free chewing gum
  - white soft paraffin applied to lips
  - oral sprays may be beneficial[3]
- Consider saliva substitutes. Short duration of action; may need to use every 30 min, but especially pre-meals. Proprietary examples include:
  - Biotène® Oralbalance® or BioXtra® gel
  - Salivix® sugar-free pastilles (encourages production)
  - methylcellulose solution, e.g. Glandosane® spray
  - Saliva Orthana (NB: pork mucin-based spray—may be no more beneficial than placebo)
- Saliva stimulation
  - pilocarpine: a parasympathomimetic agent which stimulates salivary gland secretion. Dose: pilocarpine 5mg tablets p.o. t.d.s during or directly after meals. Very common side effects include headache,

flu-like sundrome, nausea, urinary frequency, and sweating. (It should be avoided in bowel obstruction, glaucoma, asthma, COPD, and cardiac disease.)
- pilocarpine 4% eye-drop solution has been used in raspberry syrup or peppermint water (3 drops of 4% = 6mg taken orally t.d.s.—unlicensed use[4]).
- bethanechol—25mg t.d.s. with meals. Reduce to 10mg t.d.s. if patients experience excessive salivation (unlicensed use).

Painful mouth and stomatitis

Stomatitis refers to painful, inflammatory, and ulcerative conditions affecting the mucous membranes lining the mouth and may be caused by:
- ulceration—viral, aphthous, and neutropenic ulcers
- inflammation due to oral candidiasis or dental abscess
- mucositis post radiotherapy or chemotherapy
- iron deficiency (angular stomatitis and glossitis)
- vitamin C deficiency (gingivitis and bleeding)
- dry mouth
- tumour infiltration
- dental and denture problems

Management

General measures
- treat underlying cause if possible, e.g. infection
- maintain good oral hygiene—tepid water or normal saline mouth washes
- avoid foods that trigger pain, e.g. acidic foods
- avoid tobacco and alcohol
- ensure ENT/oncology review

Drug treatment

Generalized oral pain
- Topical analgesia
  - local anaesthetics, e.g. lidocaine spray 10% or ointment 5% before food and p.r.n. (beware pharyngeal anaesthesia and risk of aspiration)
  - NSAID: e.g. benzydamine hydrochloride oral rinse 15mL every 1.5–3hr, gargle for 20–30sec before spitting out (dilute 1:1 if it stings) or benzydamine spray—relatively short duration of action
  - diclofenac dispersible tablets or flurbiprofen lozenges
  - choline salicylate oral gel (Teejel) apply not more than 3 hourly; avoid excessive use as it can lead to ulceration
  - antihistamines: diphenhydramine—not available in UK and doxepin (TCA and histamine antagonist); taken as an oral rinse containing doxepin 25mg/5mL up to six times a day; must not be swallowed
  - opioids: locally prepared morphine sulfate 0.2% (2mg/mL) solution; take 10mg/5mL every 3–4 hours; hold in mouth for 2min and then spit out or swallow
  - cocaine mouthwash 2% q.d.s. is used for mucositis in some centres; use only in severe cases; risk of systemic absorption; hold in mouth for 2–3min and do not swallow

- systemic analgesics
  - non-opioids and opioids; a parenteral opioid should be administered when topical measures are inadequate; consider ketamine for persistent oral neuropathic pain
- protection for ulcerated area[5]
  - see discussion of ulceration in following
  - carmellose sodium: paste—apply paste to sore area after food
  - polyvinylpyrrolidine and sodium hyaluronate oral gel (Gelclair®) t.d.s., 30–60min before food; mix contents of sachet with 40mL water, rinse around mouth for 1min, gargle, and then spit out
  - sucralfate susp. 1g/5 mL q.d.s.; no benefit in radiation-induced oral mucositis but may help other causes of stomatitis

Ulceration of oral mucosa

Causes include trauma (chemical or physical), recurrent aphthae, infections, cancer, nutritional deficiencies, haematinic deficiency (iron, folate, vitamin B_{12}), and drug therapy.

Management

- identify and treat cause where possible.
- consider referral for further investigation if mouth ulcer persists
- pain relief—as for stomatitis

Aphthous ulcers

- Topical corticosteroids for 5 days, e.g. triamcinolone 0.1% paste applied nocte, or if severe can be used 2–3 times a day after food. Hydrocortisone muco-adhesive pellets 2.5mg q.d.s.—tablets placed at the site of ulcer and allowed to dissolve. Alternatively, betamethasone sol. tablets 500micrograms, dissolved in 20mL water rinsed around mouth q.d.s.[5]
- Doxycycline mouthwash (for resistant ulcers). Dissolve doxycycline 100mg capsule into 10mL of water and rinse around mouth for 2–3min, four times a day, and then spit out.[6]
- Chlorhexidine gluconate 0.2% mouthwash can be used to prevent secondary infection.
- Mucosal protectors—carmellose sodium, Gelclair® (rinse around mouth for 1 min; do not eat or drink for 1 hour after to allow time to work), or MuGard®.
- Persistent and severe ulcers may respond to thalidomide (seek specialist advice).

Infection

- fungal—candidiasis is most common in patients with cancer
- viral—e.g. herpes simplex
- bacterial—e.g. coliforms or staphylococci

Predisposing factors

- reduced salivary flow
- immunosuppressants
- chemotherapy

- antibiotics
- poor nutritional state
- diabetes
- wearing dentures
- poor oral hygiene

Candidiasis

NICE reports that up to 30% of patients with cancer have candidiasis. Presenting features may include the following:

- dry mouth
- loss of taste
- smooth red tongue
- adherent white plaques on tongue or mucous membranes
- soreness
- dysphagia (remember oropharyngeal/oesophageal candidiasis)
- angular cheilitis

Investigation

Swabs are not routinely taken in palliative care, although they may be useful since fungal infections may become resistant to standard treatment.

Treatment

- specific treatments should be accompanied by good oral hygiene
- no clear evidence to suggest the superiority of the various antifungal agents in this patient population
- remember to treat dentures—clean with chlorhexidine or dilute sodium hypochlorite; avoid food for 30min after mouthwash or gel
- topical nystatin susp. 100,000U/mL; dose: 2–5mL q.d.s. p.o. for 7 days (reduced activity if nystatin combined with chlorhexidine mouthwash, therefore leave 30min gap) or
- miconazole oral gel 24mg/mL, apply 5–10mL q.d.s. for 5–7 days
- for moderate-to-severe candidiasis:
  - fluconazole tabs/susp.; dose: 50–100mg o.d. for 7–14 days
  - itraconazole is an alternative, but less suitable for patients at high risk of heart failure; not generally used first-line; dose 100mg once daily for 7–14 days

Resistance to nystatin is uncommon although resistance to miconazole is becoming increasingly common, especially in people who are immunocompromised.

Note: Systemic antifungal drugs and topical miconazole may interact with several drugs metabolized by the cytochrome P450 enzymes, including phenytoin, warfarin, sulfonylureas, and midazolam. It is always best to check for possible interactions when co-prescribing.

Viral infection

Herpes simplex infection—uncomplicated infection on lip, apply aciclovir 5% cream five times a day for 5 days. For intraoral infection, commence oral aciclovir 200mg five times daily for 5 days.

Bacterial infection

Malignant ulcers or local tumour may be associated with halitosis due to anaerobic bacteria.

Treatment

- metronidazole has been shown in cutaneous malignant ulcers to give a marked reduction in odour; treatment may however be required long-term as odour usually returns after treatment stops
- dose 200mg—400mg t.d.s. p.o. for 2 weeks; if malodour recurs, re-treat for 2 weeks, then continue indefinitely with 200mg b.d.
- other alternatives are per rectum (PR) metronidazole and metronidazole gel 0.75% as topical application
- may be used as mouthwash if adverse effects—metronidazole susp. 400mg (10mL) t.d.s. and spit out

Drooling

May be due to the overproduction of saliva (sialorrhoea) or inability to swallow normal amounts of saliva. Drooling is common in MND (40%) but uncommon in advanced cancer (except head and neck).

Causes

- neuromuscular
  - MND
  - carcinoma of the pharynx
  - CVA
  - Parkinson's disease
  - cerebral palsy
  - brain tumours
- oral factors
  - ill-fitting dentures
  - deformity post-surgery, e.g. oral surgery, dysphagia
- drugs
  - cholinesterase inhibitors
  - antipsychotics
- others
  - clonazepam and ketamine

Management

Non-drug treatment

- head positioning
- suctioning

Drug treatment

Choice will depend on local availability and the patient's circumstances. There is limited data to guide drug and dosage recommendation.

- antimuscarinic drugs (if patient is able to swallow) will reduce saliva production
- most patients will not be able to swallow tablets or capsules, or large volumes, and a number will have PEG tube feeding
- drugs that do not cross the blood-brain barrier minimize risk of sedation and other central side effects; however, they may be poorly and unpredictably absorbed when given orally

- first-line
  - hyoscine hydrobromide 1mg/3days transdermal patch; central side effects can occur, especially in the elderly
  - amitriptyline 10–25mg p.o. nocte
  - atropine eye drops 1% 1–4 drops p.o./sublingual q.d.s.
- second-line
  - glycopyrronium p.o./sublingual 0.2–1mg t.d.s.; most reliable way of establishing effective symptom control rapidly may be with CSCI; locally prepared oral solutions can be used with enteral feeding tube
- further options
  - propantheline 15mg t.d.s. (on empty stomach), but use is often limited by side effects
  - injection of botulinum, radiotherapy, or surgery, though patients need relatively long prognosis

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Nausea and vomiting

Sickness is felt but health not at all.

Traditional proverb

Nausea is an unpleasant feeling of the need to vomit often accompanied by autonomic symptoms.

Vomiting is the forceful expulsion of gastric contents through the mouth.[1]

Nausea and vomiting are symptoms which can cause patients and their relatives deep distress. They occur in 50–70% of people with advanced cancer.[2] Of the two, nausea causes most misery; many patients can tolerate one or two episodes of vomiting a day, while prolonged nausea is profoundly debilitating. There are many causes of nausea, and it is important to analyse the likely cause so that appropriate therapy can be initiated.

Evaluation

- distinguish between vomiting, expectoration, and regurgitation
- separately assess nausea and vomiting
- enquire whether nausea is absent for prolonged periods after vomiting or whether it is persistent
- review drug regimen
- if there is a likelihood of cerebral secondaries, check the fundi for papilloedema (although its absence does not exclude raised intracranial pressure)
- examine the abdomen
- do a rectal examination if faecal impaction is a possibility
- consider checking plasma concentrations of creatinine, calcium, albumin, and digoxin
- consider radiological investigations if major doubt remains about the cause
- note the content of the vomitus, e.g. undigested food, bile, faeculent
- timing of onset of nausea or vomiting
- associated symptoms (e.g. the headaches of raised intracranial pressure are coincidental with vomiting)

Causes

Common causes of nausea and vomiting in advanced cancer include the following:

- gastrointestinal, e.g. gastric stasis, intestinal obstruction
- drugs, e.g. opioids, antibiotics, NSAIDs, iron, digoxin
- metabolic, e.g. hypercalcaemia, renal failure
- toxic, e.g. radiotherapy, chemotherapy, infection, paraneoplastic
- increased intracranial pressure—tumour or bleeding
- cerebral oedema or skull metastases
- psychosomatic factors, e.g. anxiety, fear
- pain

Treat reversible causes

- severe pain
- infection
- cough
- hypercalcaemia
- tense ascites
- raised intracranial pressure (using corticosteroids)
- emetogenic drugs—stop or reduce dose
- anxiety—pharmacological and psychological management

Opioid-induced nausea and vomiting

Opioids can cause nausea and vomiting through a number of different possible mechanisms. These include stimulation of the chemoreceptor trigger zone, increased vestibular sensitivity, gastric stasis or impaired intestinal motility, and constipation.

Haloperidol is usually recommended as first-line treatment for opioid-induced nausea and vomiting; however, metoclopramide (for gastric stasis), cyclizine, or hyoscine hydrobromide may all be effective in certain patients. $5HT_3$ antagonists have also been shown to be useful but are expensive for long-term use.

Management

Non-pharmacological management of nausea and vomiting

- Provide a calm, reassuring environment away from the sight and smell of food.
- Avoid exposure to foods that precipitate nausea, which may mean transferring the patient to a single room.
- Give small snacks, e.g. a few mouthfuls, and not large meals.
- Suggest that if the patient is the household cook, someone else may need to take on this role.
- Control malodour from colostomy, fungating tumour, or decubitus ulcer.
- Relaxation techniques and acupressure wrist bands—these devices are helpful to some patients, particularly those who prefer non-pharmacological treatments.

Drug management of nausea and vomiting

See Table 9.1. There are many neurotransmitter receptors involved in nausea and vomiting. These include those for histamine, acetylcholine, 5-hydroxytryptamine, and dopamine located in varying concentrations, largely in the vomiting centre and the chemoreceptor trigger zone in the midbrain.

In simple terms, neural impulses from a variety of emetic stimuli are relayed to these sites in the brainstem, triggering the vomiting reflex. A single anti-emetic may be adequate to suppress symptoms, but if there are different causes for the vomiting, it may be necessary to combine drugs. For instance, if the cause of vomiting is thought to be raised intracranial pressure and uraemia, it may be necessary to combine, for example, cyclizine and haloperidol.

Levomepromazine antagonizes several receptors and may thus be a useful single alternative at a dose of 6mg o.d. or b.d. orally; doses higher than this often cause sedation.

Table 9.1 Anti-emetic drug choice

Cause of vomiting	Choice of anti-emetic drug
Drug- or toxin-induced	Haloperidol 1.5mg nocte/b.d. Levomepromazine 6mg nocte or b.d.
Radiotherapy	Ondansetron 8mg stat then 8mg b.d. up to 5 days Haloperidol 1.5–3mg nocte/b.d.
Chemotherapy	Ondansetron 8mg stat then 8mg b.d. up to 5 days Dexamethasone 4–8mg o.d. (often as part of a chemotherapy regimen) Metoclopramide—up to 20mg q.d.s. Aprepitant 125mg stat, then 80mg o.d. for 2 days; consider adding for resistant nausea and vomiting
Metabolic, e.g. hypercalcaemia	Haloperidol 1.5mg nocte/b.d. Levomepromazine 6mg nocte
Raised intracranial pressure	Cyclizine 50mg t.d.s. or 150mg/24h SC Dexamethasone 4–16mg daily
Bowel obstruction	Cyclizine 150mg/24h via CSCI Hyoscine butylbromide 40–120mg/24h SC Octreotide 300–1000mcg/24h SC Ondansetron 8–24mg/24h p.o., IV, or SC
Delayed gastric emptying	Metoclopramide 10mg t.d.s. or 40–100mg/24h via CSCI Domperidone 10mg t.d.s.
Gastric irritation	Treat gastritis, e.g. proton pump inhibitor. Stop gastric irritants, e.g. NSAIDs Cyclizine 50mg t.d.s. Ondansetron 8mg b.d.

It may be possible to control nausea with oral medication, but persistent vomiting requires drug delivery by an alternative route such as per rectum or, more reliably, subcutaneously by means of stat doses or continuously via a syringe driver.

Side effects

All anti-emetics have side effects with which it is necessary to be familiar.

- Monitor for minor extrapyramidal effects of the dopamine antagonists; haloperidol and metoclopramide may cause restlessness and inability to keep still (akathisia). Avoid in patients with Parkinson's disease.
  - More marked signs include Parkinsonian effects such as stiffness and tremor. The effect can be reversed by stopping the drug. If necessary, a small dose of an antimuscarinic drug, such as procyclidine, can be given. Domperidone is an alternative to metoclopramide since extrapyramidal problems are fewer.
- Cyclizine and the phenothiazines (e.g. levomepromazine) are associated with anticholinergic side effects such as dry mouth, blurring of vision, and urinary retention.
- $5HT_3$ antagonists cause constipation.

Management of nausea and vomiting: practical guide

Identify any causes of nausea and vomiting that can best be treated specifically:

- constipation—remember to do a rectal examination
- gastritis—epigastric discomfort and tenderness
- raised intracranial pressure—neurological signs
- oropharyngeal candida
- hypercalcaemia—dehydration, confusion
- drug-induced—recent introduction of morphine
- intestinal obstruction

Choose an anti-emetic based on the most likely cause of nausea and vomiting (Fig 9.1):

- drug or metabolic—haloperidol
- gastric stasis—metoclopramide
- GI tract involvement or cerebral tumour—cyclizine
- anxiety-related—consider a benzodiazepine
- nausea and vomiting in cancer is often multifactorial
- If first-choice drug is unsuccessful or only partially successful after 24h, the cause should be reassessed, the dose of anti-emetic optimized, or an alternative anti-emetic used.
- If confident that there is a single cause for the nausea and vomiting, consider increasing the anti-emetic dose (especially metoclopramide), or changing to a second-line specific anti-emetic (e.g. ondansetron for drug-induced nausea).
- If cause is uncertain or further investigation is not appropriate, haloperidol should be tried first. Cyclizine may be added if haloperidol is ineffective. If symptoms persist, levomepromazine or dexamethasone can be considered after seeking specialist advice.
- Combinations of anti-emetics with different actions (e.g. at different receptor sites) are often needed and can act additively.
- If using more than one anti-emetic, one from each class of anti-emetics should be considered; see Table 9.1.
- Cyclizine and haloperidol are a logical combination.
- Levomepromazine acts at several receptor sites, and alone may replace a previously unsuccessful combination.
- Levomepromazine may be useful as a non-specific, second-line anti-emetic for nausea and vomiting of any or unknown aetiology.
- Cyclizine may antagonize the prokinetic effects of metoclopramide; they should not usually be mixed.

General points

- Always prescribe anti-emetics *regularly*—not p.r.n.
- If vomiting is preventing drug absorption, use an alternative route, e.g. CSCI.
- Dexamethasone 4mg daily often contributes an anti-emetic effect for nausea and vomiting of unknown mechanism.

- Check blood U&E, LFTs, and calcium
  - renal failure—consider lowering the dose of opioid or alternative opioid
  - hypercalcaemia—treat with intravenous bisphosphonates.
- Monitor carefully if giving prokinetic drugs (e.g. metoclopramide) in intestinal obstruction in case intestinal colic and vomiting increase.
- Always reassess the patient regularly as the cause of nausea and vomiting can change with time.
- Levomepromazine tends to cause sedation at doses above 25mg.
- Octreotide dries up gastrointestinal secretions tending towards constipation.
- Granisetron and ondansetron are also associated with constipation.

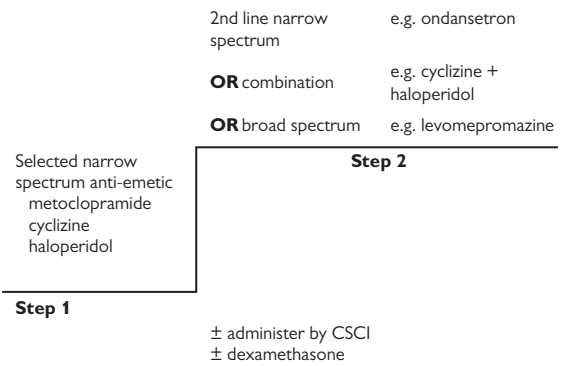


Fig 9.1 Anti-emetic ladder.

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Anti-emetic drugs

See Table 9.2.

Antihistamines

The vomiting centre is rich in histamine and acetylcholine receptors. Most antihistamine drugs are also antimuscarinic.

Cyclizine is a commonly used antihistamine anti-emetic. Acting at the vomiting centre, it is useful for vomiting of many causes.

- dose: 25–50mg t.d.s. orally or 100–150mg/24h CSCI
- side effects: antimuscarinic effects, including dry mouth, drowsiness, headache, fatigue

Antimuscarinics

Hyoscine hydrobromide is a potent antimuscarinic. It is especially useful if there is intestinal obstruction or colic as it reduces peristalsis. However, the availability of alternatives that do not cause cerebral side effects has led to it being less widely prescribed than in the past.

- dose: available as buccal tablets and transdermal patches and can be used by CSCI: 200–1200mcg/24h CSCI
- side effects: dry mouth, drowsiness, or confusion may be more severe than with cyclizine

Antipsychotics

Drugs and metabolic disturbances cause vomiting by stimulating the CTZ. Antipsychotics (as potent dopamine antagonists) block this pathway and are very effective against drug- or metabolic-induced nausea and vomiting (e.g. opioids and renal failure).

Table 9.2 Receptor affinity of anti-emetic drugs

Agonist/Antagonist	ACh_M	H_1	$5HT_2$	D_2	$5HT_3$	$5HT_4$	NK1
	Ant	Ant	Ant	Ant	Ant	Ag	Ant
Hyoscine hydrobromide	+++						
Cyclizine	++	+++					
Haloperidol				+++(*)			
Ondansetron/granisetron					+++		
Metoclopramide				++	(+)	++	
Domperidone				++			
Levomepromazine	+	+	++	+(*)			
Aprepitant							++
Olanzapine	++	+	++	++	+		

* Prokinetic effect of metoclopramide and domperidone is partly attributed to D_2 antagonism—however, there is no evidence that haloperidol or other neuroleptics have prokinetic activity

- **Haloperidol**. Dose: 1.5mg nocte orally (0.5–1.5mg b.d.) or 2.5–5mg/24h CSCI. Side effects: sedation and extrapyramidal effects are rare at these low doses.
- **Prochlorperazine** is relatively more sedative but is available in buccal and suppository form. Prochlorperazine cannot be given subcutaneously as it is irritant.
- **Levomepromazine** is a sedative, broad-spectrum anti-emetic which is effective in low doses. Some patients show a narrow therapeutic window. Dose: 6mg nocte or b.d. orally or 5–25mg/24h CSCI. Oral bioavailability of levomepromazine is approx. 40%. Side effects: antimuscarinic side effects, postural hypotension, and drowsiness, especially with doses >25mg.

Note: Phenothiazines and haloperidol should be avoided with amiodarone since there is an increased risk of ventricular arrhythmias. The low, anti-emetic doses of haloperidol used in palliative care probably carry a low risk.

Prokinetic drugs/drugs altering gastric motility

- **Metoclopramide** acts peripherally on the gut, restoring normal gastric emptying. It also acts at the CTZ and thus helps drug-induced nausea. Dose: 10mg t.d.s. p.o. or 30–80mg/24h CSCI. Side effects: extrapyramidal effects are rare, but most common in young female patients. Owing to risk of tardive dyskinesia, the European Medicines Agency (EMA) issued guidance advising maximum dose of 30mg/day with max duration of 5 days. However, they recognize that the risk:benefit ratio may be different in certain populations.
- **Domperidone** is very similar to metoclopramide. Can be given orally or rectally. It is not as effective as metoclopramide but is less likely to cause central adverse effects because it does not cross the blood-brain barrier. Recent epidemiological studies show domperidone may be associated with increased risk of ventricular arrhythmias and sudden cardiac death, especially in people over 60 years and in people who receive daily oral dose of over 30mg.[2] Avoid in those with underlying cardiac disease or liver impairment, and in those concurrently receiving either a drug that can prolong the QT interval or is a known CYP3AF inhibitor.

$5HT_3$ antagonists

$5HT_3$ receptors are found in the chemoreceptor trigger zone. Antagonists are very effective against acute-phase chemotherapy and radiotherapy-induced nausea, with little to choose between ondansetron and granisetron, but their place in other situations (e.g. intestinal obstruction) is as yet uncertain.

Ondansetron has been shown to be ineffective in the treatment of motion sickness, but effective at treating morphine-induced nausea and vomiting. $5HT_3$ antagonists may work synergistically with haloperidol in some cases.

In the UK, $5HT_3$ antagonists are only licensed for chemotherapy-induced and post-operative emesis.

Other drugs

Corticosteroids often have a non-specific benefit in reducing nausea and vomiting.

Additional drugs

Newer atypical antipsychotics may be expected to show anti-emetic effects. Olanzapine has a similar pharmacological profile to levomepromazine, with high affinity for multiple dopamine, serotonin, alpha1-adrenergic, H1, and cholinergic receptors. The usual anti-emetic dose is 5–10mg/day by mouth. A lower starting dose of 2.5–5mg/day is recommended for elderly or debilitated. It causes fewer extrapyramidal side effects than other antipsychotics. Main side effects are somnolence and weight gain.

Risperidone has potent $5HT_2$ antagonist effects as well as being antidopaminergic, but there is no published evidence to date of any anti-emetic effect. It should be avoided in patients with cerebrovascular disease.

Aprepitant is the first member of the neurokinin receptor-antagonist class of anti-emetics now marketed. To date, its use is specifically for acute and delayed nausea and vomiting associated with platinum-based chemotherapy, in combination with dexamethasone and a $5HT_3$ antagonist.

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Constipation

Constipation is defaecation that is unsatisfactory because of infrequent stools, difficult stool passage, or seemingly incomplete defaecation. Stools are often dry and hard, and may be abnormally large or abnormally small.

The definition of constipation is subjective because different people have different views about what is infrequent, difficult, dry, hard, and abnormally large or small.

It is possible to be constipated and have normal or even soft stools, e.g. when there is failure of bowel propulsion.

Stool frequency varies considerably in the normal population. About 50% of those people admitted to British hospices with cancer report constipation, but this is an underestimate of the prevalence, as some people will be using laxatives. About 80% of people with cancer will require treatment with laxatives at some time.

Causes

Constipation is generally caused by multiple factors:

- direct effects of cancer
  - bowel obstruction due to either tumour in the bowel wall or external compression by abdominal or pelvic tumour
  - compression or infiltration of the lumbosacral spinal cord, cauda equine, or pelvic plexus
  - hypercalcaemia
  - painful defaecation
  - autonomic neuropathy, a non-metastatic manifestation of malignancy, particularly associated with small-cell carcinoma of the lung and carcinoid tumours
- secondary effects of disease
  - inadequate diet (poor intake, limited fibre)
  - dehydration, e.g. vomiting, polyuria, fever
  - weakness or dyspnoea—prevents effective straining
  - confusion
  - depression
  - inactivity
  - unfamiliar toilet arrangements or lack of privacy
  - increased fluid loss, e.g. vomiting, polyuria, fever
- medication
  - opioids (90% of patients taking opioids require laxatives)
  - drugs with antimuscarinic effects, e.g. cyclizine, hyoscine, phenothiazines, tricyclic antidepressants, some anti-epileptic drugs, anti-Parkinsonian agents
  - diuretics
  - antacids (calcium and aluminium compounds)
  - serotonin antagonists, e.g. ondansetron/granisetron
  - iron
  - anti-hypertensive agents
  - cytotoxics, e.g. vinca alkaloids
  - platinum-based chemotherapy agents
  - somatostatin analogues, e.g. octreotide/lanreotide

- other concurrent disease, e.g. diverticular disease, inflammatory bowel disease, irritable bowel syndrome, endocrine and metabolic conditions (e.g. Type 1 & Type 2 diabetes, hypercalcaemia, hypothyroidism, hypokalaemia), hernia, colonic strictures (following diverticulitis, ischaemia, surgery), rectocoele, rectal prolapse/ulcer, anal fissure or stenosis, haemorrhoids, dyssynergic defaecation, weak levator muscles, spinal cord damage, severe neurological diseases, severe intellectual disability

Complications of constipation

- pain and abdominal distension—colic or constant abdominal discomfort
- intestinal obstruction
- urinary retention, frequency, and urinary tract infection
- faecal incontinence (overflow diarrhoea)
- faecal retention, rectal distension, and loss of sensory and motor function
- faecal impaction, particularly in the immobile
- rectal bleeding and prolapse
- increased agitation
- an autonomic dysreflexia (severe hypertension and risk of seizures, haemorrhage and cardiac arrest) if left untreated in paraplegic people with lesions above T6

These complications can cause great distress to patients, therefore every effort must be made to avoid them.

Management of constipation

Prevention

- Enquire about bowel function regularly.
- Encourage fluid intake and fibre/fruit intake.
- Encourage mobility.
- Provide privacy and avoid use of a bedpan if possible.
- Alleviate contributory factors, e.g. anal fissure, painful haemorrhoids, or local tumour.
- Prescribe a stimulant laxative when commencing opioids.

Treatment

- Treat any faecal loading or impaction.
- Start treatment with a stimulant laxative, e.g. sodium picosulfate, senna.
- Titrate the dose to achieve comfortable defaecation without colic.
- Increase dose in line with any increase in dose of opioid.
- Add an osmotic laxative/stool softener if colic is a problem.
- Titrate to achieve optimal stool frequency, consistency and, most importantly, comfort.
- If response remains insufficient and there is hard, impacted stool in the rectum, consider use of a suppository/enema.
- If response is inadequate and there are no faeces in the rectum, consider adding a pro-kinetic agent such as metoclopramide, domperidone, or erythromycin. (Do not use a pro-kinetic agent if the patient has symptoms of colic.)

Laxatives

Choice of laxative

- A number of laxative combinations may be equally effective.

- Patient preference may dictate choice.
- Patient comfort is the priority.
- Start treatment with a stimulant laxative.
- Add an osmotic laxative or a stool softener if colic is a problem.
- Remember, in a palliative care situation, higher and more frequent doses than specified by the product licence may be needed.
- Methylnaltrexone, a peripherally acting opioid antagonist, represents an additional approach to the management of opioid-induced constipation. A recent Cochrane review concluded that there is some evidence that, compared with placebo, methylnaltrexone is effective in patients taking opioids who have not had a good response with conventional laxatives.

Traditionally, laxatives are divided into
- stimulants
- osmotic agents
- faecal softeners
- bulking agents

In reality, these categories are arbitrary as there is much overlap between the agents. For example, an osmotic agent will act as a stimulant by decreasing the GIT transit time by increasing pressure within the bowel. see Tables 9.3 and 9.4.

Stimulants, e.g. sodium picosulfate, senna, dantron, bisacodyl

Avoid stimulants if there is the possibility of intestinal obstruction. Dantron is useful with a softener such as docusate (co-danthrusate) or poloxamer (co-danthramer) for opioid-induced constipation, but may colour urine red and cause excoriation around the perineum if in contact with skin. (Dantron is only licensed for use in patients with a terminal illness.) Titrating up low doses of sodium picosulfate may be a better alternative.

Osmotic agents, e.g. lactulose, magnesium salts, macrogols

In palliative care, the use of osmotic agents is often inappropriate because of the need to drink 2–3 litres per day for the agents to function well. In addition, lactulose may be unpalatable and cause uncomfortable abdominal bloating and flatus.

Macrogol (polyethylene glycol) in the palliative setting, particularly in intractable constipation and faecal impaction, may have a particular role to play.[1]

Lactulose is usually to be avoided in the palliative care setting because of the following:
- can increase abdominal cramps
- sweet taste can be hard for the palliative care patient to tolerate
- causes flatulence
- should be consumed with large volumes of liquid, which palliative care patients are often unable to take

Faecal softeners, e.g. docusate

Faecal softeners are useful in conjunction with a stimulant (e.g. docusate + dantron in co-danthrusate and docusate + poloxamer in co-danthramer). It may be safer to use docusate alone in resolving intestinal obstruction.

Table 9.3 Classification of commonly used laxatives

Category	Example	Description	Comment
Osmotic laxatives	**Lactulose** **Polyethylene glycol**	Osmotic laxatives are not absorbed from the gut and so retain water in the lumen by osmotic action (this action may be partial). This increase in volume will encourage peristalsis and consequent expulsion of faeces.	Can cause abdominal distension and abdominal cramps. Patients need to drink over a litre a day, which may not be practical.
Surfactant laxatives	**Docusate/ poloxamer**	Act to reduce surface tension and improve water penetration of the stools.	Generally start with 100mg b.d. If necessary, increase to 200mg b.d.-t.d.s.
Stimulant laxatives	**Sodium picosulfate** **Senna** **Bisacodyl**	Senna and bisacodyl both rely on bacterial transformation in the large bowel to produce active derivatives and so have little small intestinal effect.	Can cause abdominal cramps. Should be avoided in patients with intestinal obstruction. Suggested starting doses: sodium picosulfate 5–10mg nocte. Senna 15mg nocte if not constipated, 15mg b.d. if constipated. Bisacodyl 10–20mg nocte.
	Dantron	Absorbed from the small bowel and undergoes first-pass hepatic metabolism to glucuronide forms. These may be secreted in the bile and converted to the active drug, prolonging its action.	Dantron is available only combined with a surfactant softener, e.g. co-danthramer with poloxamer, or co-danthrusate with docusate. Dantron-containing preps are subject to licence evidence from animal studies that in high doses it can cause tumours. It is licensed for use in analgesic-induced constipation in terminally ill patients. Dantron may colour urine red. It should be avoided in patients who may be incontinent of urine or faeces, as it can cause severe rashes if it comes in contact with the skin.
Peripheral opioid antagonists	**Methylnal-trexone**	Displaces opioids from the GI tract. Does not cross the blood–brain barrier. Indication for laxative refractory opioid-induced constipation.	Given by SC injection 8–12mg, depending on weight. Average time to response 30–60 min after dose. Further preparations on clinical trial.

Table 9.4 Onset of action by time

Bisacodyl tablet	10–12h	Macrogols	24–48h
Bisacodyl supps	20–60min	Methylnaltrexone	30–60min
Dantron	6–12h	Microlax® enema	20min
Docusate	24–48h	Phosphate enema	20min
Glycerin supps	1–6h	Senna	8–12h
Lactulose	48h	Sodium picosulfate	6–24h

Bulk-forming agents, e.g. methylcellulose, ispaghula husk, sterculia

Patients are rarely started on bulk-forming preparations in the palliative care setting because they have been implicated in worsening constipation when used with reduced fluid intake. They are also unpalatable and may aggravate anorexia.

Rectal agents (bisacodyl/glycerol suppositories, Micralax enemas)

About one-third of patients need rectal measures. This includes suppositories and enemas. As far as possible, rectal interventions should be avoided in patients who are neutropenic or thrombocytopenic because of the risk of infection or bleeding, respectively.

Bisacodyl is a rectal stimulant and should be placed in direct contact with the rectal mucosa. If appropriately placed, it should stimulate an evacuation within 1 hour. Glycerol is a faecal lubricant which facilitates defaecation by softening the stool.

For more severe constipation

Use arachis oil enema (130mL) overnight to penetrate hard stool, soften, and lubricate. Follow with high phosphate enema in the morning to stimulate bowel clearance.

Do **not** attempt manual evacuation of impacted stool without some form of sedation or analgesia. In circumstances of intractable constipation, close consultation with nursing colleagues is vital if a clear strategy for managing the problem is to be achieved.

Faecal impaction

If the patient has faecal impaction despite the use of a combination of stimulant and softening laxative, try one of the following:

- bowel washout with an oral macrogol, e.g. Movicol®
- bisacodyl +/– glycerol suppositories
- sodium phosphate enema or an arachis oil retention enema
- manual removal (with midazolam, morphine, or caudal anaesthesia)
- once successful, it is imperative to start regular oral measures to prevent recurrence of the problem

Reference

1. Muldrew DHL, Hasson F, Carduff E, Clarke M, Coast J, Finucane A, et al. (2018) Assessment and management of constipation for patients receiving palliative care in specialist palliative care settings: a systematic review of the literature. *Palliative Medicine*, **32**(5):930–8.

Diarrhoea

Diarrhoea is a less common symptom than constipation amongst patients requiring palliative care and has been defined as the passage of more than three unformed stools within a 24h period.

As with constipation, patients can understand 'diarrhoea' in different ways, and clarification of the term is always required.

Up to 10% of patients admitted to a hospice complain of diarrhoea.

Aetiology

A **cause** for the diarrhoea should be looked for prior to giving anti-diarrhoeal agents. The most common causes of diarrheoa in the palliative care setting are as follows:

- **Imbalance of laxative therapy** (especially when laxatives have been increased to clear severe constipation). Diarrhoea should settle within 24h if laxatives are stopped. Laxatives should be reintroduced at a lower dose.
- **Drugs** such as antibiotics and antacids, NSAIDs, or iron preparations.
- **Faecal impaction** is associated with fluid stool which leaks past a faecal plug or a tumour mass.
- **Radiotherapy** involving the abdomen or pelvis is likely to cause diarrhoea, especially in the second or third week of therapy.
- **Malabsorption** associated with:
  - *Carcinoma* of the head of the pancreas with insufficient pancreatic secretions, and therefore less fat absorption and resultant steatorrhoea.
  - *Gastrectomy*, resulting in poor mixing of food with pancreatic secretions causing steatorrhoea. Vagotomy can cause increased water secretion into the colon.
  - *Ileal resection* reduces the ability of the small intestine to reabsorb bile acids. These acids increase fluid in the colon and contribute to explosive diarrhoea. A resection of over 100cm of terminal ileum will outstretch the liver's capacity to compensate for the bile salt loss, and fat malabsorption will compound the diarrhoea.
  - *Colectomy*: immediately following surgery for a total or a near-total colectomy, the water in the gut cannot be adequately absorbed. Although this tends to settle over a week, the bowel seldom returns to its pre-surgical function. The small intestine is unable to adequately compensate for the loss of this colonic water-absorbing capacity. This can lead to an ongoing daily loss of an extra 400–1000mL of gut fluid rectally. Such patients often require an ileostomy and need an extra litre of fluid and 7g of extra salt a day with vitamin and iron supplements.
- **Colonic or rectal tumours** can cause diarrhoea through causing partial bowel obstruction or through increased mucus secretion.
- **Rare endocrine tumours** which secrete hormones cause diarrhoea, e.g. carcinoid tumour.
- Concurrent disease such as gastrointestinal infection, e.g. *Clostridium difficile*.
- Unusual dietary habits.

Investigation

Faecal impaction needs to be excluded by a rectal and abdominal examination. Persistent watery diarrhoea with systemic upset, which might indicate an infective cause, may require investigation.

Diagnostic diarrhoea patterns

Defaecation described as 'diarrhoea' happening only two or three times a day without warning suggests anal incontinence.

Profuse watery stools are characteristic of colonic diarrhoea.

Sudden onset of diarrhoea after a period of constipation raises suspicion of faecal impaction.

Alternating diarrhoea and constipation suggests poorly regulated laxative therapy or impending bowel obstruction.

Pale, fatty, offensive stools (steatorrhoea) indicate malabsorption due to either pancreatic or ileal disease.

Treatment

General measures

- ensure adequate fluid and electrolyte replacement is given, e.g. by encouraging constant sipping, by using oral rehydration salts or, if necessary, IV fluids
- reassurance that most diarrhoea is self-limiting

Non-specific drug treatment

- Opioids such as codeine and loperamide act via gut opioid receptors to reduce peristalsis and increase anal sphincter tone. Loperamide alone does not cross the blood-brain barrier and is the anti-diarrhoeal opioid of choice. Start with 4mg p.o. stat and continue with 2mg after each loose bowel action up to 5 days (maximum recommended dose 16mg/24h).
- Mucosal prostaglandin inhibitors, such as aspirin, reduce intestinal electrolyte and water secretion caused by prostaglandins. Aspirin may help with radiation-induced diarrhoea.

Specific measures

- See Table 9.5.

Table 9.5 Causes and management of bowel difficulties

Cause	Management
Subacute small bowel obstruction	see text, Intestinal obstruction
Laxatives (including self-administered magnesium-containing antacids)	Discontinue and review
Faecal impaction (with anal leakage or incontinence)	see text, Constipation
Antibiotic-associated diarrhoea/ pseudomembranous colitis (recent or broad-spectrum antibiotics)	Check stool for *Clostridium difficile*: if present, treat as per local antibiotic guidelines
Radiotherapy-induced	Ondansetron, aspirin, colestyramine
NSAID	Try stopping or changing NSAID
Misoprostol	Use a PPI or other alternative
Pre-existing disease, e.g. Crohn's or ulcerative colitis	Corticosteroids or sulfasalazine
Ileal resection (causing bile salt diarrhoea)	Colestyramine
Steatorrhoea/fat malabsorption	Pancreatic enzymes ±PPI (reduces gastric acid destruction of enzymes)
Carcinoid syndrome	$5HT_3$ antagonists, octreotide
Zollinger-Ellison syndrome	H_2 antagonist, e.g. ranitidine
Non-specific profuse secretory diarrhoea	Opioids such as loperamide, codeine, and morphine may be necessary

The somatostatin analogue octreotide has a place in the management of severe, profuse secretory diarrhoea, such as that associated with HIV infection when other agents have failed to work. It is best given by CSCI.

Intestinal obstruction

Intestinal obstruction most commonly occurs with carcinoma of the ovary or bowel. The obstruction may be intramural, intraluminal, or extraluminal due to surrounding peritoneal disease, and is often at multiple sites. In addition, there may be a functional obstruction due to peristaltic failure. There may be a combination of all these. In many patients, particularly in functional obstruction, symptoms spontaneously resolve and worsen again over time.

A plain abdominal X-ray may be helpful in excluding constipation.

If surgical intervention is inappropriate, symptomatic measures using medication are the mainstay of treatment, avoiding the standard 'drip and suck' approach, which may be distressing and is ineffective in 80% of patients.

- In the presence of advanced peritoneal disease, the most likely cause of obstruction is malignant tumour. If the obstruction is localized, if there is no diffuse intra-abdominal disease, and if the patient is fit enough, a surgical opinion should be sought.
- The potential mortality and morbidity associated with surgery should be weighed against quality of life in a patient with a likely short prognosis.
- Symptomatic treatment of nausea, vomiting, colic, pain, diarrhoea, and constipation should be started alongside targeted specific treatments.
- Do not forget measures such as frequent mouth care and advice about small amounts of food and drink as tolerated. Consider IV/SC fluids on a case-by-case basis. Oral medications will not always be absorbed; parenteral drugs should be used.

Reducing bowel wall oedema

Bowel wall oedema can be reduced using dexamethasone 8–16mg SC before midday.

The evidence for such an approach is equivocal, but if a 3-day trial proves beneficial and vomiting subsides, it may be useful to consider continuing with reducing doses of oral steroids. Whether improvement is due to steroids or to the passage of time remains the subject of debate.

If dexamethasone is not helpful after 3 days, it should be stopped (unless the patient has been on steroids more than a week, in which case it should be tapered slowly).

Stimulating gut motility

Gut motility can be stimulated by using metoclopramide 30–120mg/24h via subcutaneous infusion. Beware of any increase in gut colic, and stop if obstruction is not resolving.

For complete obstruction or obstruction not resolving with the foregoing measures in 24–48h, focus on treating the symptoms rather than the underlying cause:

- Nausea and vomiting
  - cyclizine 100–150mg/24h CSCI
  - ± haloperidol 3–5mg/24h CSCI
  - or levomepromazine 5–25mg/24h CSCI
  - consider ondansetron 8–24mg/24h p.o., IV, or SC

- Colic
  - hyoscine butylbromide 60–120mg/24h CSCI (morphine may also be needed for background pain)
- Diarrhoea
  - codeine 30–60mg p.o. 4 h, or
  - loperamide 2–4mg p.o. 4 h; ❗ use with caution if possibility of reversible obstruction
- Constipation
  - Ensure that reversible constipation is not contributing to the obstruction. Gentle rectal measures or a small dose of a faecal softener such as docusate (200mg b.d.) may be used, particularly if there is no colic and obstruction is thought to be colonic and subacute. More vigorous measures should be avoided for fear of aggravating symptoms.

If intestinal obstruction is still not resolving

Reduce or encourage reabsorption of gut secretions and reduce intestinal motility using:

- hyoscine butylbromide 40–120mg/24h CSCI
- octreotide 250–750mcg/24h CSCI (higher doses have been used)
- ranitidine 200mg/24h CSCI
- pantoprazole 40mg IV o.d.
- nasogastric tube: if vomiting is not subsiding, or if very distressing and/or faecal, it may be necessary to use a nasogastric tube after full discussion with patient and carers. Although this is an infrequent practice in a hospice setting, and can be seen as a very undignified approach to patient care, it can bring comfort in exceptional circumstances.
- venting gastrostomy: with occasional, clinically stable patients who are distressed by vomiting but who have a prognosis of at least weeks, and who are keen to resume oral intake, it may be an option to discuss venting gastrostomy and subcutaneous fluids. In practice, venting gastrostomies are rarely performed.

Hiccup

Hiccup or hiccough?

Hiccup is a word imitative of the sound, first documented by the OED in 1580 as replacing an earlier *hiccock*, which had cognates in Dutch, Old Norse, etc. *Hiccough* is a re-spelling by the ignorant anxious to suggest an incorrect etymology, and is first found around the mid-seventeenth century. It may be more frequent in British than in North American English, but that does not make it in any way 'correct'.

Definition

Hiccups involve a sudden, involuntary (reflex)—usually a diaphragmatic contraction causing sudden inspiration. The incoming air is stopped by closure of the glottis, which produces the characteristic sound.[1]

Hiccups are usually transient, lasting <48 hours. Persistent or protracted hiccups last between 48 hours and 1 month. Intractable hiccups last >1 month.

Causes

- peripheral
  - via vagus nerve: gastric distension, gastritis/gastro-oesophageal reflux, hepatic tumours, ascites/abdominal distension/intestinal obstruction
  - via phrenic nerve: diaphragmatic tumour involvement, mediastinal tumour/ intrathoracic nodes
- central (medullary stimulation)
  - raised intracranial pressure
  - brain stem CVA/tumour
  - uraemia (also causes gastric stasis)
- systemic: renal failure, hypercalcaemia, corticosteroids, Addison's disease, hyponatraemia

Management of hiccup

Physical manoeuvres are often effective, at least temporarily. These include:

- stimulation of the nasopharynx
  - sipping iced water, swallowing granulated sugar, tasting vinegar, biting on a lemon
- interrupting normal respiratory function
  - Valsalva manoeuvre, breath holding, hyperventilating, or rebreathing into a bag, etc.
- counter-irritation of the diaphragm
  - pulling knees up to the chest, leaning forward to compress the chest.

Medication

For simplicity, use metoclopramide if the cause is thought to be peripheral, or Bactofen if central, as first-line drugs.

- reduce gastric distension +/– gastro-oesophageal reflux
  - prokinetic drugs, e.g. metoclopramide 10mg t.d.s.
  - anti-flatulent (carminative): peppermint water 10–20mL b.d. (don't use with metoclopramide as they have opposing actions on the gastro-oesophageal sphincter)

- anti-flatulent (defoaming agent): simeticone, e.g. in Altacite Plus® 10mL q.d.s.
- PPI: lansoprazole 30mg p.o. mane

- use muscle relaxant
  - calcium channel blocker, e.g. nifedipine 10–20mg t.d.s.
  - GABA agonist: baclofen 5–20mg t.d.s.
  - benzodiazepine: midazolam 10–60mg/24h at end of life
- suppress central hiccup reflex
  - dopamine antagonist: metoclopramide as previously, haloperidol 1.5–3mg nocte, levomepromazine 3–6mg nocte, methylphenidate 5–10mg b.d.
  - GABA agonist: baclofen 5–20mg t.d.s.
  - anti-epileptic: sodium valproate 15mg/kg/24h in divided doses, gabapentin 100–400mg t.d.s.
- use alternative
  - dexamethasone oral 4–8mg mane may reduce compression/irritation from hepatic, mediastinal, or cerebral disease/tumour; stop if no benefit after 1 week[2]

References

1. NICE (2017, September). Clinical Knowledge Summaries—Hiccups—Revised.
2. Scottish Palliative Care Guidelines (2017).

Further reading

Leon YS, Kearny AM, Baker PG. (2018) Management of hiccups in palliative care patients. *BMJ Supportive and Palliative Care*, **8**:1–6.

Anorexia/cachexia/asthenia

Primary anorexia is the absence or loss of appetite for food.

Cachexia is a condition of profound weight loss and catabolic loss of muscle and adipose tissue. It is often associated with primary anorexia and fatigue.

Asthenia

Characterized by:

- fatigue or easy tiring and reduced sustainability of performance
- generalized weakness resulting in a reduced ability to initiate movement
- mental fatigue characterized by poor concentration, impaired memory, and emotional lability

Secondary anorexia

Secondary anorexia is often due to several conditions that may be reversible and should be actively sought, including the following:

- dyspepsia
- altered taste
- malodour
- nausea and vomiting
- sore mouth
- pain
- biochemical: hypercalcaemia, uraemia, hyponatremia, gastric stasis
- constipation
- secondary to treatment: drugs, radiotherapy, chemotherapy
- anxiety
- depression

Early satiety (patient hungry but then feels full) occurs with a small stomach, hepatomegaly, and gross ascites. Anxiety and depression will contribute to loss of appetite. Patients are 'put off' by too much food and food which is unappetizing. These symptoms, which are closely interrelated, occur in about 70% of patients with advanced cancer, particularly gastric and pancreatic cancer.

Management

- assess and treat any reversible causes as outlined previously
- involve the dietician and multidisciplinary team to maximize treatment goals
- non-drug treatments
  - explore the patients' and carers' fears of anorexia
  - reassure patients that it is normal to feel satisfied with less food
  - consider whether advice on food fortification/supplementation would be appropriate for this patient at this point of their illness
  - suggest smaller helpings to allow patients to eat small amounts of what they enjoy frequently

Evidence-based drug treatments

- **corticosteroids,** e.g. dexamethasone 2–4mg o.d.
  - appetite stimulant, and may help nausea
  - may improve subjective feeling of anorexia and weakness

- non-specific central euphoric effects
- effects generally short-lasting (weeks)
- onset of side effects rapid
- prescribe for 1 week and if helpful reduce gradually to lowest effective dose; if no effect, stop

- **progestogens,** e.g. megestrol acetate 160–800mg o.d.
  - improve appetite, nutritional status, and calorie intake
  - take for 2–3 weeks to produce effect
  - associated with modest weight gain (though not gain in lean body mass)
  - effects may last for months
  - increased incidence of thrombotic episodes
  - expensive
- **prokinetic drugs,** e.g. metoclopramide 10mg t.d.s.
  - try if early satiety, gastric stasis (many patients with malignancy have associated autonomic dysfunction)

Total parenteral nutrition

➔ see Chapter 24.

Universal benefit and efficacy have not been clearly proven with TPN. In view of this—together with its practical disadvantages and the risk of side effects and complications—its routine use is not recommended. Agreement exists that it is not advisable to introduce artificial nutrition if the life expectancy is shorter than 2 months. However, it is still unclear what should be done if life expectancy is greater than 2 months.

Aggressive nutritional therapy could perhaps be justified in particular situations such as when patients are recovering from surgery or awaiting chemotherapy.

Hydration

➔ see Chapter 1, Ethical issues and the person in the patient.

There is often an overwhelming need for relatives and staff to give dying patients food and water, but this must not be allowed to override the patients' need for comfort.

Avoiding overhydration in a dying patient may improve comfort, by minimizing urinary output (and therefore the need for catheterization) and the volume of distressing bronchial secretions. In bowel obstruction, gastric secretions will be minimized, thereby reducing the frequency of vomiting and the need for a nasogastric tube. A dry mouth can be treated with local measures.

In contrast, those patients who may survive for many months but who are unable to swallow adequately may find life easier with, for instance, a percutaneous gastrostomy tube. However, when these patients are dying it is necessary to explain to the relatives why it may be helpful to reduce fluid input.

Ascites

Ascites is the term used to describe the development of excessive fluid within the peritoneal cavity. The healthy adult has about 50mL transudate in the peritoneal cavity. This has a protein level of about 25% of that found in plasma. Peritoneal fluid turnover is 4–5mL/h in health.

Malignant ascites

- Malignant ascites accounts for about 10% of all cases of ascites and occurs in up to 50% of all patients with cancer.
- Classified according to the serum ascites-ascitic albumin gradient (SA-AG).
- SA-AG >11g/L indicates portal hypertension; causes include cirrhosis, cardiac failure, and nephrotic syndrome.
- Ascites due to peritoneal disease usually has a SA-AG level <11g/L. Differential diagnosis would include pancreatitis and tuberculosis.
- Ascites may be the presenting feature of the malignancy or it may be indicative of a recurrence or metastatic spread. It is often indicative of end-stage disease.
- Malignant ascites is due to peritoneal deposits, massive liver metastases causing portal hypertension, or blockage of subdiaphragmatic lymphatics.

Causes

Malignant ascites

- ovarian primary (50% of cases)
- unknown primary (20% of cases)
- stomach, colon, pancreatic primary (most of the remainder)

Non-malignant ascites

- Cardiac failure, liver failure, and renal failure are common causes of non-malignant ascites, accounting for 90% of ascites.

It is important that in patients with cancer, the ascites should not automatically be attributed to underlying malignancy, as management options for malignant and non-malignant disease are very different.

Management

Treatment of the primary cancer, usually with chemotherapy, may be the most effective measure to reduce ascites. However, analgesics and good symptom control may be all that is necessary, particularly for a patient who is bed-bound and has a short prognosis. Diuretics have a limited role in the management of malignant ascites.

Patients with portal hypertension are more likely to respond to diuretics. Doses must be adequate and include a combination of spironolactone and a loop diuretic, e.g. furosemide, though paracentesis will provide more immediate relief.

Paracentesis is the mainstay in treatment and is described in the following. An alternative to repeated paracentesis is insertion of a PleurX drain.

A **PleurX drain** is a tunnelled indwelling peritoneal catheter that is inserted into the abdominal cavity. It should be considered in patients with treatment-resistant, recurrent malignant ascites.[1] It has been shown to be a safe, effective, and relatively easy procedure for patients with refractory ascites. It can be managed by patients at home to remove small aliquots of ascites on a regular basis or when it becomes symptomatic.[2]

Paracentesis

Note: There is little evidence about malignant paracentesis and hence it is hard to be doctrinaire about it.

General

- Paracentesis is a simple procedure, which can be performed as a day-case or as an inpatient.
- In tense, symptomatic ascites there may be up to 12 litres of ascites present.
- Removal of 4–6 litres is usually enough to give symptomatic relief and can be removed quickly and safely without the need for intravenous fluids, provided there is no evidence of portal hypertension.[3]
- A significant improvement in symptoms of abdominal pressure occurs through removal of the first few litres of fluid.
- Intravenous albumin: no proven role in paracentesis related to peritoneal malignancy. However, it should be considered if there is portal hypertension +/- cirrhosis or SA-AG >11g/L, especially in the setting of large volume paracentesis.
- Intravenous fluids: not routinely required, but consider if the patient is hypotensive, dehydrated, or known to have severe renal impairment, and paracentesis is still indicated.[4]

Indications

- Pain, discomfort, or tightness due to stretching of the abdominal wall.
- Dyspnoea, usually exacerbated by exertion, due to upward pressure on the diaphragm.
- Nausea, vomiting, and dyspepsia due to the 'squashed stomach' syndrome.
- Patients are usually symptomatic only when the abdominal wall is tensely distended.

Complications

- Serious complications are uncommon.
- The most common complications include an ascitic fluid leak, which can occur in up to 5% of procedures, and unsteadiness/fainting post-procedure.[5]
- Other potential complications include perforation of an abdominal viscus (0.6%), haemorrhage (0.2% require transfusion), and wound infection.
- The removal of large volumes of fluid, particularly in patients with renal or hepatic impairment, can cause a fluid shift with hypotension, leading to symptoms of dizziness, fatigue, and malaise.

Investigations prior to paracentesis

- An ultrasound scan will confirm the presence of ascites, and may determine whether it is 'pocketed' by tumour adhesions. (Even in the presence of loculations, a drain can improve symptoms, as presumably the loculated pockets interconnect.)
- A scan should be performed if ascites is not easily clinically identified or there is a chance of bowel obstruction, and to confirm route of access for a drain.
- Blood tests are only necessary in patients at risk—i.e. patients with known liver disease or extensive bruising, especially around the venepuncture site.

Contraindications

The benefits of paracentesis in patients with appropriate indications almost always outweigh the risks. Some relative contraindications include clinically apparent disseminated intravascular coagulation or primary fibrinolysis.

Follow-up care

- Ascites will usually re-form after a paracentesis; however, this can vary between one and many weeks.
- PleurX drains should be considered for patients who require repeated paracentesis.

The paracentesis procedure

- Ideally carried out with ultrasound guidance.
- The patient should be asked to pass urine before the procedure.
- Pulse and blood pressure should be measured and recorded.
- The patient should lie in a semi-recumbent position.
- It may be helpful if the patient tilts 30 degrees towards the side of the paracentesis.

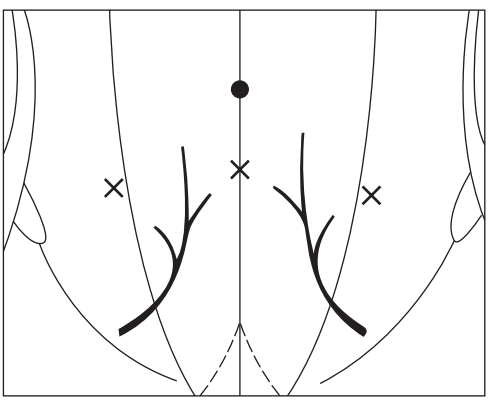


Fig 9.2 Usual sites for paracentesis, avoiding the inferior epigastric arteries.

- use the left iliac fossa unless local disease is present, avoiding scars and the inferior epigastric arteries (see Fig 9.2)
- confirm that the site is dull to percussion
- using an aseptic technique, anaesthetize the skin locally
- if ascitic fluid cannot be easily located using the anaesthetic infiltrating needle, stop and reconsider
- a large-bore intravenous cannula or 'Bonanno' catheter can be used
- remove the catheter once the specified volume has drained, or the drainage has slowed to a minimum
- aim to remove the drain within 6 hours; max 24 hours
- apply a sterile gauze and an adhesive dressing to the area
- if leakage is heavy, a stoma bag may be required; sutures rarely required
- recheck pulse and blood pressure

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Tenesmus and tenesmoid pain

Tenesmus is the painful sensation of rectal fullness, usually caused by local rectal tumour. There may be an associated spasm of smooth muscle, or neuropathic pain from lumbosacral plexus infiltration causing stabbing or more continuous pain. It may be difficult to distinguish from pudendal neuralgia.

Management

- prevent and treat constipation
- opioid analgesia may be helpful, but not reliably so
- NSAID, e.g. diclofenac 50mg t.d.s.
- radiotherapy
- nifedipine m/r 10–20mg b.d.
- co-analgesics as for neuropathic pain
- amitriptyline
- anticonvulsants
- corticosteroids
- lumbar sympathectomy: >80% success rate
- spinal infusion of local anaesthetic ± opioids

Dyspepsia

Dyspepsia can be caused by acid-induced damage, abnormal motility, or oesophageal reflux.

Gastro-oesophageal reflux disease (GORD)/oesophagitis

Assessment

- exclude or treat oesophageal Candida infection
- consider oesophageal spasm
- avoid drugs which cause oesophagitis—potassium, NSAIDs
- consider pain of cardiac origin

Treatment

- raise head of bed to reduce acid reflux
- PPI, e.g. lansoprazole 30mg daily for moderate or severe symptoms; start with treatment dose then step-down after a few weeks; or omeprazole 20mg p.o. or 20–40mg in 100mL 0.9% saline as a sub-cut infusion over 3 hours
- metoclopramide 10mg t.d.s. if signs of gastric stasis or distension
- antacid, for mild symptoms
- consider paracentesis for tense ascites
- consider erythromycin
- mirtazapine may help resistant gastric stasis

NSAID- and steroid-related dyspepsia

Treatment of drug-related dyspepsia

- Consider stopping or reducing dose of NSAID/steroids.
- PPI, e.g. lansoprazole 30mg o.d. for severe symptoms or proven pathology. Start with treatment dose and reduce after 4 weeks. For milder symptoms, start with maintenance dose (15mg) and increase later if needed.
- If symptoms persist on treatment dose of PPI, and NAID is needed by the patient to control pain, consider changing to a selective COX-2 inhibitor, though be mindful of the concerns raised in relation to associations between COX-2 inhibition and cardiovascular events.

Indications for prophylaxis

- prescribing NSAID with recent history of dyspepsia
- prescribing steroids with recent history of dyspepsia
- co-prescribing NSAID with steroids, anticoagulants, or aspirin
- prescribing NSAID in elderly patient >70 years (less clear evidence—use judgement)

Drugs for dyspepsia

Proton pump inhibitors (PPIs)

- little difference in efficacy between the current PPIs available
- a single daily dose is appropriate for PPIs rather than divided doses
- lansoprazole and omeprazole can be taken before or after food with equal efficacy

Antacids

Aluminium-containing antacids cause constipation, whereas magnesium-containing antacids are laxative.

Prostaglandin analogues

Misoprostol is effective at preventing NSAID-induced ulcers, but is less well tolerated than PPIs; diarrhoea is a common side effect. Misoprostol is available in combination with diclofenac, which avoids the problem of non-compliance that can arise when the gastroprotective drug is given separately from the NSAID.

H_2 antagonists

H_2 antagonists are less effective at acid suppression than PPIs, and are less effective clinically at healing ulcers. Ranitidine has significantly fewer drug interactions and adverse effects than cimetidine.

Adding an H_2 antagonist to high-dose PPI can be considered, however, if there is an inadequate response to PPI. In addition, ranitidine has a place in encouraging gastric emptying and is increasingly used in situations where there is concern about bowel obstruction developing.

Gastrointestinal bleeding

Gastric bleeding and melaena

Assessment

Consider the commonest causes:

- tumour bleeding
- clotting disorders
- peptic ulcer ±NSAIDs

Management considerations for gastrointestinal bleeding

- review or stop NSAIDs, antiplatelets, corticosteroids, anticoagulants
- blood tests for clotting screen and platelets and treat if appropriate
- consider radiotherapy referral if bleeding due to tumour
- small bleeds can herald a larger haemorrhage: consider siting an intravenous cannula to administer emergency drugs

Upper gastrointestinal tract bleeding

Treatment in most care settings:

- proton pump inhibitor (oral or IV)
- oral tranexamic acid (1g q.d.s initially)
- oral sucralfate (2g b.d. p.o.)—limited evidence to support its use
- consider IV/IM octreotide/somatostatin: weak evidence to support use in upper gastrointestinal haemorrhage; octreotide reduces splanchnic arterial flow and gastric acid and pepsin secretion
- consider oral thalidomide (100–300mg p.o. nocte)
- etamsylate—no evidence
- omeprazole—few case reports of intravenous use

Options in hospital:

- definitive treatment of tumour if possible
- refer for radiotherapy if patient well enough
- consider arterial embolization or cryotherapy
- consider IV pressins: terlipressin has been shown to significantly reduce all-cause mortality in acute oesophageal variceal haemorrhage; however, its use is limited in palliative settings by the need for IV administration and potentially serious side effects.

Rectal bleeding

Assessment

Consider the commonest causes:

- tumour bleeding
- post-radiotherapy
- clotting disorders
- pelvic infection
- haemorrhoids

NSAIDs can cause lower gastrointestinal bleeding as well as the better-documented upper GI bleeding.

Treatment
- review or stop NSAIDs
- treat any evidence or signs suggestive of pelvic infection
- consider radiotherapy referral
- blood tests for clotting screen and platelets and treat as appropriate

Treatment in most care settings
- tranexamic acid 1g t.d.s. p.o.
- rectal sucralfate (2g suspension or 2g tablets mixed with aqueous jelly b.d.)
- rectal tranexamic acid (instil 50mL of 500mg/5mL injection as enema b.d.)
- consider oral thalidomide (50–100mg daily initial dose)

Treatment in hospital
- consider radiotherapy to tumour site
- consider referral for endoscopy: laser treatment, cryotherapy, argon plasma coagulation, or application of formalin, alum packs, or fibrin glue)
- discuss with interventional radiologist

Major gastrointestinal or rectal bleeding

If patient's condition is not stable, with history of major haemorrhage or ongoing bleeding:
- consider whether the patient should be transferred to an acute medical/endoscopy unit
- site an IV cannula to anticipate the need for emergency drugs
- anticipate possible dying phase; full supportive care of active treatment is inappropriate

Treat anxiety or distress as needed
- midazolam 2–5mg initially by slow IV titration (diluted 10mg in 10mL with saline)
- if no IV access, midazolam 5–10mg SC (or IM if shocked/vasoconstricted)

The case for PPIs in gastrointestinal bleeding

- Acid suppression in early studies did not help in the management of acute bleeding.
- Some evidence that PPIs and H_2 antagonists reduce rebleeding and the need for surgery, though they do not appear to have any effect on mortality.
- It has more recently been shown that intensive therapy aimed at achieving complete acid suppression does substantially reduce the risk of recurrent bleeding after initial endoscopic treatment.
- Pharmacokinetic studies have shown that a bolus of 80mg pantoprazole or omeprazole followed by immediate continuous infusion of 8mg/h will result in an intragastric pH of 7 within 20 minutes. This has been continued for 72h in studies.[1]

Support for patient and family

Bleeding is very frightening. Ensure that the patient and family are well supported. Ensure that drugs are readily available for sedation if necessary and that dark bed linen (to disguise the amount of blood loss) is accessible.

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Bowel stoma care

A bowel stoma is an artificial opening, created surgically, to allow faeces to leave the patient's body by a new route through a spout or outlet on their abdomen.

The majority of stomas encountered in patients with palliative care needs have been fashioned following surgical resection for cancer, or as a by-pass for inoperable or recurrent cancers of the bowel or ovary causing obstruction.

Any patient with a stoma (whether newly created or created many years ago, e.g. in Crohn's disease) and malignant intra-abdominal disease is at risk of a number of different symptoms which need appropriate management. These include abdominal pain (constant or intermittent colic), nausea, vomiting, abdominal distension, constipation, diarrhoea, and depression, all of which may impact on the holistic management of the patient.

Bowel stomas are generally created from the colon (colostomy) or ileum (ileostomy). The bowel proximal to the stoma continues to function in the normal way whereas function distal to this is normally lost.

Temporary (de-functioning) stomas

These include loop ileostomies or colostomies, which are usually created to protect an anastomosis or to facilitate decompression or healing in the distal bowel. The bowel loop is usually brought out onto the abdominal wall (right and left iliac fossa, respectively, for ileostomy and colostomy) and may be supported by a temporary rod or bridge so that it does not retract. The proximal opening allows the passage of stool, which is collected in a stoma bag, and the distal opening leads to the redundant section of bowel. Mucus and old faeces may be expelled through the rectum. A temporary transverse colostomy may be created at an emergency operation for bowel obstruction since it is a relatively easy procedure in a sick patient.

Permanent stomas

These are end sections of bowel which are brought to the skin surface. The potential stoma site along the path of the bowel is planned preoperatively, if possible, to allow optimal positioning of a stoma bag for the individual.

- Panproctocolectomy—a permanent ileostomy is created from the terminal ileum. The rectum and anus are removed.
- Total colectomy—an ileostomy is formed and the rectal stump is retained, which may be brought out onto the abdominal wall as a mucus fistula.
- Abdominoperineal (A-P) excision—the rectum and anus are removed, leaving a colostomy in the left iliac fossa.
- Hartmann's procedure—excision of sigmoid colon or upper rectum. An end colostomy is formed and the rectal stump is closed and left in the pelvis.
- Pelvic exenteration—a radical operation to remove pelvic organs. A colostomy and urostomy are formed. Men are likely to become impotent. An artificial vagina can be created for women.

Issues in stoma management

The stool consistency of a sigmoid colostomy is no different from that passed naturally in health through the anus. The less formed the stool, the further proximal in the colon (is) the colostomy. The formation of an ileostomy or colostomy should not in itself interfere with sexual function unless the definitive surgery interfered with the pelvic nerve supply.

Stoma appliances and problems

Stoma appliances are disposable, self-adhesive, and skin-friendly. The type of appliance used is determined by several factors which include the shape and position of the stoma itself, including body contours, the type of effluent, skin type, and the needs of the individual, such as lifestyle and ability to self-care. Adequate adherence, comfort, and skin protection are paramount.

Ileostomy appliances are drainable for ease of emptying semi-formed/liquid stool. Modern appliances have integral Velcro-type closures. The bags are emptied several times a day and changed every 1–3 days.

- Colostomy appliances may be in one piece, such that the whole appliance needs removing every time the bag needs changing. Alternatively, a two-piece appliance is used, which allows the flange to remain in position for several days, allowing the non-drainable bag to be changed as necessary, thus protecting the skin from the trauma of frequent changes.
- The flange size should be cut to fit accurately around the base of the stoma. The peristomal skin must be kept healthy and intact.
- A stoma usually shrinks in size during the first few months but should always retain the bright-red colour, indicating a good blood supply.
- Checks for colour, odour, consistency, and volume should be made routinely.

Psychological care

Enjoyment, comfort, and satisfaction with life for the patient and their family need support from healthcare professionals, giving adequate time for answering questions and responding to needs. Frequently, patients have a short prognosis, and the stoma is a visible daily reminder of this. In addition, they may be distressed by a feeling of no longer being in control. They have to learn new skills at a time when it is important to be concentrating on other more important issues, and they may be having to adapt reluctantly to relying on others for care. Relationships with family, friends, and particularly spouses may be affected.

Overactive stoma

A cause may need to be identified and treated. Diet may need to be altered until overactivity settles. Foods such as cooked white rice and stewed apple may help. Marshmallows and 'jelly babies' may help in thickening the output from an ileostomy. Extra fluids orally should be encouraged to maintain hydration, especially in hot weather. A drainable bag may be necessary temporarily for a colostomy if the output is liquid. Some medication, particularly longer-acting modified-release preparations—e.g. morphine sulfate m/r enteric-coated drugs and capsules—may not be absorbed adequately, and are not recommended with ileostomies.

Loperamide (taken 30min before meals) in the form of 'melts' or tablets, but not capsules, may be helpful in patients with an ileostomy. It may be started at a dose of 2mg four times a day and slowly titrated up to a maximum dose of 64mg daily.[1] The dose required will depend on the volume of stomal loss and should be increased by 2mg until the desired consistency of the stomal loss is reached.

If all else fails, systemic opioids and antisecretory agents may be needed.

Constipation

A cause should be sought where possible, and may include medication, particularly opioids, partial/complete bowel obstruction, and dehydration. It may be necessary to instil warm arachis oil (only 5mL for a short time) through a Foley catheter with the balloon inflated to aid enema retention. The patient will usually be turned on the right side if the stoma is in the left iliac fossa, to allow oil to flow across the transverse colon. The oil may cause difficulties with flange adhesion and the possibility of nut allergy should always be considered. Suppositories and phosphate/Microlax® micro-enemas may also be useful. As a general rule, bulking aperients such as ispaghula husk are not used in palliative care.

Odour

This is rarely a problem with modern appliances which contain charcoal filters. Proprietary stoma deodorizing agents are available. A few drops of vanilla essence placed in a bowel stoma bag may help, while topical metronidazole may be helpful for offensive fungating tumours in the region of the stoma.

Bleeding

Stomas may bleed owing to clotting deficiencies and fungating tumours. Wafers of alginate dressing soaked in tranexamic acid or adrenaline may help with local pressure. Silver nitrate may be used for oozing granulation tissue. Bleeding from local cancer growth may abate with radiotherapy or cryotherapy.

Skin excoriation

Skin excoriation is a rare occurrence with modern appliances and good skin care. Various preparations are available to aid skin protection, including pastes to make a level surface onto which an appliance can be fitted. This is particularly important in the case of an ileostomy, when damage to the skin from digestive enzymes must be avoided.

Flatulence

Flatulence can usually be minimized by avoiding various foods and medication such as lactulose.

A diet containing fibre such as porridge, root vegetables, and brown bread is advised, although the terminally ill may not find these foods palatable. In relatively good health, most people with stomas can eat most foods, although certain food such as vegetables and fruit may cause an increase in stoma activity with embarrassing flatulence and odour. Camomile tea and peppermint tea or capsules may be helpful.

Enterocutaneous fistulae

Enterocutaneous fistulae may occur in 3% of patients with advanced malignant disease. Patients with gastrointestinal tumours and those who have had

abdominal radiotherapy are most at risk. A dehisced wound may also need management with a stoma appliance, and may need a stoma appliance if the effluent is greater than 100mL per 24h.

Meticulous preparation of the skin will be needed prior to applying an appliance. Suction may be needed while cleansing and preparing the fistula if there is excessive exudate, or it may need to be spigotted with a balloon catheter for a while. Various pastes, fillers, and skin barriers may be needed to protect the skin and ensure a good fit to the edges of the wound. The stoma appliance may need to be adapted over time to take account of the change in size of the tumour and the weight loss of the patient.

Gastrostomy

Indications

- Feeding: when the patient is unable to swallow adequately or safely, such as those patients with motor neurone disease or with head and neck cancers.
- Gut decompression: a venting gastrostomy is occasionally used in a relatively fit patient with intestinal obstruction who wants to be able to eat. In this situation, the patient is able to take nutrients by mouth but food contents are expelled through the gastrostomy.

However, in patients with advanced disease, the decision to insert a gastrostomy has to be judged carefully. It is important to distinguish starvation, which responds to feeding, from cachexia, which does not respond to feeding alone. The latter is more likely in the presence of large tumour masses, certain tumour types, or ongoing sepsis.

Types of gastrostomy

Percutaneous endoscopic gastrostomy (PEG)

A PEG tube is inserted under sedation and local anaesthetic using a 'pull' technique. Throughout its lifetime, the PEG tube should be rotated through 360° at least twice a week to prevent adhesion formation.

Radiologically inserted gastrostomy (RIG)

The RIG tube is inserted in the radiology department without sedation by a 'push' technique under fluoroscopic control. The tube is thinner than a PEG tube, held in place by its pigtail shape. It should *not* therefore be rotated, or it will dislodge.

Surgical gastrostomy

Surgical gastrostomy is carried out under general anaesthetic, usually when it is impossible to insert a PEG or RIG.

Care of the gastrostomy tube

The fixation plate should be maintained at 1.0–1.5cm from the abdominal exit stoma. A 50mL flush of sterile water should be used before and after every feed or administration of medication, and regularly three times a day. Soda water—but not other fizzy drinks (which are too acidic)—can be used to unblock stubborn blockages.

Feeding

Patients should be maintained at an angle of 30–45° during feeding and for 2h after to reduce the risk of aspiration. Many centres are less keen for feeding to occur during sleep because of the aspiration risk.

Problems with gastrostomies

- dislodgement
- blockage
- leakage: chemical digestion of surrounding skin
- overgranulation
- infection

A major concern with the use of PEG and RIG tubes in the UK involves ensuring that the best possible decision about when to insert a tube is taken.

Often the clinical team that asks for a tube to be inserted is different from the team which carries out the procedure, which in turn is different from the team that manages the tube once it has been inserted.

While tube insertion can play a crucial role for certain patients, especially where clear objectives for the intervention have been discussed and documented with the patient and family, figures show that a large percentage of patients die within weeks of tube insertion, perhaps before they have had time to gain benefit from the procedure and its management.

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Chapter 10

Respiratory symptoms

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Breathlessness

- Normal breathing is maintained by regular rhythmical activity in the respiratory centre in the brainstem. This is stimulated by *mechanical receptors* (stretch receptors in the airways, lung parenchyma, intercostal muscles, and diaphragm) and by hypoxia and high levels of CO_2 (detected by *chemoreceptors* in the aortic and carotid bodies and in the medulla).
- Breathlessness is 'an uncomfortable awareness of breathing'.[1]
- Breathlessness is a complex symptom involving physical, pathological, psychological, social, and functional aspects (see Fig 10.1).
- The primary mechanism is a mismatch between the drive to breathe and the ability to breathe.
- In malignant lung disease, breathlessness is usually a combination of underlying lung disease and stimulation of the mechanical receptors in the airways due to physical distortion. Blood gases may be normal.
- It is a common symptom in palliative care and increases in frequency and intensity as death approaches despite symptomatic treatment.
- Chronic breathlessness is considered refractory in palliative care when all reversible causes have been optimally treated and the person still has breathlessness at rest or on minimal exertion.
- Fatigue and respiratory muscle weakness may be factors contributing to breathlessness in patients with advanced cancer and end-stage organ failure.

Assessment and investigation

Aim to identify the reversible/treatable underlying causes of breathlessness

- A good history and examination are vital.
  - Assess the speed of onset of breathlessness (hours, days, weeks, months).
  - Assess the pattern of breathlessness (is it present at rest, on minimal exertion predictably, only in response to particular stimuli; exacerbations that occur unpredictably or a combination of these).

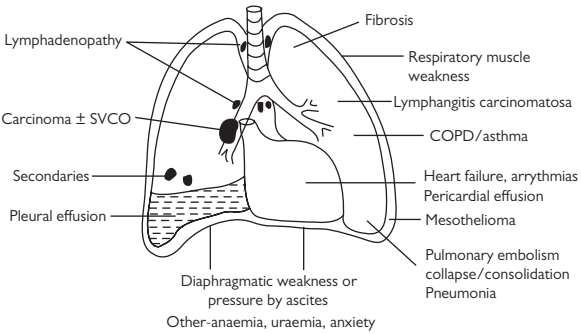


Fig 10.1 Causes of breathlessness.

- Ask about pre-existing cardio-respiratory disease.
- Ask about fevers, pleuritic chest pain.
- Consider exacerbating and relieving factors.
- Look for evidence of severity (use of accessory muscle, signs of pulmonary hypertension, right heart failure, adequacy of tissue oxygenation).
- Look for contributory factors (anaemia, bronchospasm, effusions).

- Targeted investigations that would help the management plan for the individual patient:
  - pulse oximetry to check for hypoxaemia
  - full blood count to identify anaemia, polycythaemia
  - chest X-ray to reveal pneumonia, pleural effusion, heart failure
  - CT pulmonary angiogram (CTPA) if pulmonary emboli suspected
- The aim of treating breathlessness symptomatically is to reduce breathlessness at rest and on exertion.
  - Rarely can all breathlessness be relieved.
  - For most people, breathlessness can be reduced appreciably by dealing with reversible causes, with non-pharmacological interventions, and with pharmacological therapies.

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Breathlessness management

Principles of management

Consider:

- treatment of reversible underlying causes including disease-specific treatments
- symptomatic management—non-pharmacological measures
- symptomatic management—pharmacological measures

General management

Explain to patients and their caregivers all the factors that are contributing to breathlessness. For each of the contributing factors, outline the likely causes, the disease-specific treatments for each, and the symptom-related interventions.

Being breathless is very frightening. It is important to provide a supportive environment and reassure the person that everything will be done to reduce their sensation of breathlessness. Having a sense of mastery over the symptom is a key aim of therapy.

Patients may find it helpful to discuss fears openly, and to acknowledge the impact of breathlessness on their lives by reflecting on the things that they can no longer do because of breathlessness. A clear explanation of how episodes of breathlessness will be managed can do a great deal to reduce anxiety. Providing information on when and where to reach out for additional help (general practitioner, community nurse, emergency department) is an important part of the plan for relieving breathlessness. This level of involvement also reinforces the confidence of the patient and family on the healthcare team and reduces distress.

Watching breathlessness in the person for whom they are providing care is an ongoing cause of distress for the caregivers. Caregivers can be a significant part of the management plan for breathlessness by ensuring that their doubts and concerns are addressed and they are empowered by educating them on care.

Treatment of reversible causes and disease-specific measures

Reversible or treatable causes of breathlessness should be identified and managed appropriately (see Table 10.1).

- Interventions need to be considered in terms of the potential benefits vs risks posed to each individual patient, taking into account the status of the life-limiting illness and any recent deterioration in performance status, as well as the patient's expressed wishes.
- It is important to ensure that interventions directed at treating underlying causes will make a substantial-enough difference to the person's breathlessness to warrant them. For example, small pleural effusions rarely account for a person's breathlessness, and draining very small effusions will make no difference to their breathlessness, but would instead worsen the distress and add cost.

Table 10.1 Management of potentially reversible causes of breathlessness

Cause	Management options
Bronchospasm	Bronchodilators Corticosteroids
Infection	Antibiotics (consider atypical pneunomias) Add corticosteroids if infective exacerbation of COPD
Pleural effusion	Therapeutic pleural aspiration, drainage, and pleurodesis
Pulmonary embolism	Anticoagulation (low molecular weight heparin is the preferred choice)
Heart failure	Diuretics Nitrates Anti-arrhythmics if indicated
Anaemia	Blood transfusion, iron
Lymphangitis carcinomatosa	Corticosteroids
Large airway obstruction	Radiotherapy Stenting if extrinsic compression Laser treatment for intraluminal cancer Brachytherapy Corticosteroids

Symptomatic treatment

The approach to care should include management of the distress of breathlessness while managing any reversible causes. For many people, no reversible cause(s) will be found, and the clinical approach is to focus on improving the person's experience of breathlessness and its impact on their life, including activities of daily living. Symptomatic management requires a multidisciplinary team approach and includes non-pharmacological and pharmacological strategies.

Optimizing reversible components of breathlessness

Bronchodilators

Even in the absence of an obvious 'wheeze', there may be an element of reversible bronchoconstriction. Hence, consider a trial of bronchodilators.

- beta-adrenoceptor agonists
  - salbutamol 2.5–5mg p.r.n./6h via nebulizer or two puffs p.r.n. via spacer
  - beware of increased anxiety, tremor, and tachycardia if used regularly
- anticholinergic bronchodilators
  - ipratropium bromide 250–500mcg/6h via nebulizer, or two puffs q.d.s. via spacer device—can be given in combination with salbutamol
- sodium chloride 0.9% 5mL via a nebulizer p.r.n. may help to make tenacious secretions less viscous

Corticosteroids

If patients have underlying chronic obstructive pulmonary disease (COPD), consider inhaled or systemic steroids for managing any worsening of breathlessness.

In cancer, steroids are thought to reduce tumour-associated oedema and may improve breathlessness due to multiple lung metastases, tracheal obstruction, or lymphangitis carcinomatosis. Benefit should be apparent within 4–7 days.

- dexamethasone 4–8mg p.o. o.d. or prednisolone 25–50mg p.o. o.d.
- stop if no improvement within 7 days

Non-pharmacological management of breathlessness

A non-pharmacological approach to breathlessness is the crucial next step after the reversible components of breathlessness have been optimized. This approach is equally applicable for those with advanced cancer and end-stage respiratory or cardiac disease. In less severe breathlessness, non-pharmacological management strategies form the major part of interventions employed.

- A draught of air from a fan or from an open window is frequently very helpful at reducing breathlessness from exercise or at rest.
- Appropriate positioning of the patient in bed is an important intervention:
  - upright position uses gravity to assist in lung expansion and to reduce pressure from the abdomen on the diaphragm
  - lying high on one side can be helpful in a patient with copious secretions; it also prevents aspiration
  - sitting with body bent forward, arms resting on thighs with the wrists relaxed, assists relaxation of the upper chest muscles and allows free movement of the diaphragm
  - sitting on a chair taking support of a table is effective in treating acute onset shortness of breath in those with cardiac failure
- physiotherapy input: breathing exercises, techniques to optimize breathing, chest wall vibration, and walking aids
- occupational therapy input: to help minimize breathlessness while undertaking essential activities of daily living (bathing, preparing meals, dressing)
- energy conservation techniques, pacing of activities, and help with prioritizing and planning essential activities
- relaxation techniques—massaging the patient's back during an episode of respiratory panic can encourage muscular relaxation and is reported to be comforting
- use of cognitive behavioural therapy to help manage fears and negative thoughts associated with breathlessness is a potential therapy in cognitively intact patients who have the energy to engage with the therapist
- complementary therapies, including acupuncture, may be helpful
- multidisciplinary breathlessness clinics that provide breathlessness support services are available in few specialty centres

Pharmacological management of breathlessness

Opioids

Morphine substantially reduces inappropriate and excessive respiratory drive through its effect on the ventilatory response to hypoxia and hypercapnia. By slowing the respiratory rate, breathing may be made more efficient. This reduces both the sensation of breathlessness and associated anxiety. Morphine is safe for palliative management of breathlessness.

Morphine, when used in low doses and carefully titrated, does not cause CO_2 retention or clinically significant respiratory depression. There is evidence to support its use among patients with cancer, heart failure, COPD, and pulmonary fibrosis.

- Regular, low-dose extended release morphine 10–20mg p.o. o.d. is useful in constant breathlessness.
- If unavailable, use i/r morphine 2.5mg p.o. regularly every 4h.
- Use the SC route for morphine if the patient is unable to swallow.

If a person is already on morphine for pain, increase the dose by 25% if there is new breathlessness that needs to be treated symptomatically.

Currently there is limited evidence to support the use of nebulized opioids for breathlessness, although some patients derive good symptomatic relief from its use.

Benzodiazepines

Anxiety from breathlessness can worsen the sensation of breathlessness, which in turn worsens the anxiety. To have a sense of mastery over breathlessness, this cycle needs to be broken. Benzodiazepines are particularly helpful in this situation. They are not first-line drugs for breathlessness.

- Longer-acting benzodiazepines are useful when there is severe anxiety or at night, when breathlessness and associated anxiety interrupt sleep.
  - Diazepam 2–5mg nocte p.o. or clonazepam 0.5–1mg nocte p.o. or sublingually.
- Benzodiazepines with shorter half-lives can be useful in crisis situations, but agitation/anxiety may manifest as the medication's effect wears off.
  - Lorazepam 0.5–2mg p.r.n. has fast onset and a short half-life, and is well absorbed sublingually—it can be used for self-administration by patients.
  - Midazolam 2.5–5mg SC.

Furosemide

A number of studies have shown benefit from nebulized furosemide for reducing breathlessness by a mechanism of action unrelated to its diuretic effect. Nebulized furosemide appears to protect from bronchoconstriction and may have a positive effect on airway stability.

Cannabinoids

Despite interest in their respiratory effects, benefit in breathlessness has not been confirmed by RCTs.

Oxygen

Hypoxic respiratory drive usually starts with PaO_2 <8kPa (roughly equivalent to an oxygen saturation (SaO_2) of 90%) and this drive gets stronger as oxygen saturation decreases. Oxygen may help breathlessness in patients who are hypoxaemic either at rest or on exertion.

Oxygen may help breathless patients with a normal PaO_2, especially if they have COPD. Most people with breathlessness with cancer are not hypoxic and may derive little symptomatic benefit from oxygen. Oxygen therapy is not very useful in patients with severe airflow limitation whose main complaint is dyspnoea but who maintain a PaO_2 >60 mmHg (8 kPa) and who show no secondary effects of chronic hypoxia.

It is difficult to predict which patients will derive benefit from supplemental oxygen therapy purely from their oxygen saturation. The effect of flow of oxygen or air over the mouth or nose can also improve the sense of breathlessness in those with normal oxygen saturation. For many people, a trial of oxygen is the best way to determine the benefit that they may derive from the therapy.

The use of supplemental oxygen therapy needs to be considered on an individual basis, after ensuring that reversible factors have been identified and managed. Polycythaemia, clinical or electrocardiographic evidence of pulmonary hypertension, and/or episodes of right heart failure reflect the systemic effects of chronic hypoxaemia and strengthen the case for therapeutic oxygen use.

Possible adverse effects that need to be considered are the following:

- psychological dependence
- the equipment may restrict mobility and daily activities
- oxygen masks or nasal prongs may make communication difficult
- fire hazard and risk of burns, especially if the patient prefers to continue smoking
- the high cost of oxygen therapy
- discomfort due to local irritation, drying effect on the upper airways

Domiciliary oxygen

Intermittent or continuous domiciliary oxygen is prescribed for palliation in people with breathlessness when clinical evaluation and oxygen trials indicate it. When the requirement for supplemental oxygen is more than 8h/day, an oxygen concentrator is generally more cost-effective. It is useful to note that when adjusted to a flow of 2L/min of oxygen a 1360L cylinder gives about 11 hours of use.

Delivery rates are shown in Table 10.2.

Table 10.2 Oxygen delivery

Method	Flow rate (L/min)	O_2 delivered (%)
Nasal cannulae	1	24
	2	28
Ventimask	2	24
	6	35

Pharmacological approaches in the terminal phase

- Breathlessness usually worsens in the last weeks or days of life. This worsening occurs despite the symptomatic measures outlined. Given its prevalence and severity, particular attention would be required in the last days or hours.
- If a person is hypoxaemic, treat with oxygen.
- In the last hours or days of life, management is based around pharmacological interventions and careful positioning of the patient.
- For refractory breathlessness, sedation may be necessary to alleviate the distress of the patient. This requires empathetic communications, clarifications, and consent of the close family.
- Medications to manage breathlessness include an opioid (morphine) and a benzodiazepine (clonazepam or midazolam), which can be delivered as a continuous infusion using a syringe driver.

Exploring the patient's experience of breathlessness

An essential prerequisite to managing breathlessness involves understanding what breathlessness means to this person in their particular situation.

- Ask the patient to describe what it is like to live with their breathlessness.
- Ascertain the patient's exercise tolerance and ask them to identify factors that either trigger or alleviate breathlessness.
- Explore the impact of breathlessness on the patient's daily life. Ask what they are giving up in order to minimize or avoid breathlessness. Assist them in coping with and adjusting to the loss of roles and activities.
- It is important to be aware of the extent to which depression may be generated or worsened by refractory breathlessness.
- Take time to talk sensitively and at the patient's pace about their disease experience and the feelings that this generates.
- Encourage venting, and address the feelings of helplessness, anxiety, and fears associated with breathlessness.
- Gently help the patient to confront their fears of suffocation, choking, of not being able to get another breath, or of dying during an episode of acute breathlessness. Offer reassurance that these are unlikely eventualities.

The term *total breathlessness* translates the well-recognized 'total pain' model to the realm of dyspnoea and addresses the patient's experiences of this symptom in the physical, psychological, social, and spiritual domains.

Further reading

Bove DG, et al. (2018) First year experiences with a palliative out-patients structure for patients with COPD: a qualitative study of health professionals' expectations and experiences. *BMC Palliative Care*, **17**(1):113.

Teaching skills to assist breathless patients

The patient is offered an educational programme, consisting of a number of skills and strategies, to help reduce the distress of breathlessness experience. The programme is dependent on a partnership creating a therapeutic working relationship between the patient and professional, and has three main aims:

1. To enable efficient and effective breathing, where possible

- Breathing re-training is a core part of this approach. This involves teaching the patient to use diaphragmatic breathing exercises as a controlled breathing technique when they feel breathless (as opposed to the tendency to breathe rapidly using the upper respiratory accessory muscles, which tire easily, leading to inefficient lung aeration).
- Diaphragmatic breathing exercises involve a combination of the following:
  - pursed lip breathing, which promotes control, slows the respiratory rate, increases tidal volume, and decreases the possibility of airway collapse in people with COPD
  - controlled breathing with the diaphragm or lower chest helps to improve function and breaks the inefficient pattern of upper chest breathing

2. To enable the patient to feel in control, by reducing anxiety and panic

- Reducing tension and anxiety by using relaxation helps to manage breathlessness. The concept of the mind-body link is discussed in detail with the patient. Relaxation and distraction techniques are taught with the purpose of reducing the underlying tension and as a tool for use when anxiety and panic exacerbate breathlessness.

3. To enable the patient to adapt and conserve energy for those activities that are most important to him/her

- Pacing, prioritizing, and problem-solving in relation to activity are all explored with the patient.
- Advice is offered on managing activities of daily living such as:
  - talking, including conversations on the telephone
  - washing/showering/bathing
  - preparing meals
  - eating
  - engaging with children/grandchildren
  - climbing stairs
  - carrying shopping/heavy objects
  - bending
  - gardening
  - dressing and undressing
  - sexual activity

Goal-setting in relation to activity is encouraged. It is important that this is realistic and achievable. The patient is given both verbal and written information on breathing skills, with ways of adopting these on a daily basis.

The breathlessness support service—a multiprofessional integrated service that combines respiratory, physiotherapy, occupational therapy, and palliative care assessment and management—has been proven to be an early effective integrative service in the management of chronic breathlessness.[1] It consisted of consultation to assess the patient in detail; a 'breathlessness package', including information, management, and pacing guidance; a handheld fan or water spray; and a poem (a short mantra to help breathing and relaxation) as a crisis plan. Multidisciplinary team members made follow-up visits to assess the need for additional home aids and adaptations, to reinforce self-management, and to provide confidence and further guidance on pacing and exercises. Review consultations were undertaken at regular intervals to replan as required. The impact was significantly positive.

Reference

1. Higginson IJ et al. (2014). An integrated palliative and respiratory care service for patients with advanced disease and refractory breathlessness: a randomised controlled trial. Lancet Respir Med 2(12):979–87.

Pleural aspiration (thoracocentesis)

General

Aspiration of a pleural effusion can give symptomatic relief from breathlessness. A pleural effusion large enough to cause dyspnoea will be detectable clinically. Aspiration of 300–500mL fluid will usually give some symptomatic improvement, but up to 1.5L may be aspirated in some cases. Aspiration of less than 300mL is unlikely to be causing the breathlessness, and therefore also unlikely to relieve the person's distress.

Complications

- pneumothorax—a significant pneumothorax is less likely if simple precautions are taken
- bleeding or haemothorax—could occur either from damage to the pleura or lung, or a vascular tumour
- infection is rare, provided an aseptic technique is used

If a small IV cannula is used for aspiration rather than a large-bore chest drain, very little air can enter through the cannula if reasonable care is taken. A routine check X-ray after aspiration is not essential in a palliative care setting. Aspiration of a very large effusion that is causing the heart and mediastinum to be displaced may cause cardiorespiratory compromise. Such an aspiration should only be carried out with appropriate monitoring and standby supports.

Investigations

A chest X-ray will show a pleural effusion, but if there is also underlying collapse/consolidation, it can be difficult to confirm. An ultrasound scan will confirm the presence of a pleural effusion, and for greater accuracy, radiologists can be requested to mark the site for aspiration.

Chest X-ray or ultrasound scan should be performed:

- to confirm a clinically diagnosed pleural effusion
- if the clinical signs are not straightforward

Platelet count and a clotting screen should be checked if the patient has any symptoms of bleeding, or unexplained bruising, or has had recent chemotherapy, known bony infiltration, or a haematological malignancy.

Contraindications

- local skin infection
- coagulopathy—platelets <40 or INR >1.4
- presence of local pleural tumour is a relative contraindication, as physical access to the pleural space may be more difficult and tumour cells may be seeded in the chest wall

The procedure

- The patient should sit leaning forward, resting their head on folded arms, which are leaning on a pillow on a bedside table.
- Ensure the patient is in a comfortable position which can be maintained without distress during the procedure.

- Use the site marked by ultrasound scan, or choose a point in the posterior chest wall, medial to the angle of the scapula, one intercostal space below the upper limit of dullness to percussion (the mid-axillary line can also be used).
- Confirm that the site is dull to percussion.
- Avoid the inferior border of the rib above since the neurovascular bundle runs in a groove inferior to the rib.
- Clean the skin and use an aseptic technique throughout.
- Infiltrate the area with local anaesthetic from skin to the pleura.
- It is helpful to advance the same needle until pleural fluid is obtained to confirm that the site is suitable for aspiration and to gauge the depth of pleural fluid beneath the skin surface.
- Introduce a large-bore IV cannula with syringe attached until fluid is just obtained, then advance a further 0.5–1cm to ensure that the cannula is in the pleural space.
- Asking the patient to exhale against pursed lips (to increase intrathoracic pressure), remove the metal trochar or needle and immediately attach a 50mL syringe via a three-way tap.
- Tip: a piece of tubing (e.g. cut from a fluid giving set) can be attached to the other port of the three-way tap for ease of disposal of fluid into a suitable container.
- Aspirate fluid 50mL at a time slowly, until:
  - 1L has drained (1500mL maximum), or
  - the patient starts to cough excessively, or
  - giddiness, light-headedness, or chest discomfort occur
- Remove the cannula, having asked the patient to take a breath, and immediately seal with flexible collodion BP, and cover with a dressing.

Non-invasive positive pressure ventilation (NIPPV)

Non-invasive positive pressure ventilation is used to support people with deteriorating respiratory function. It is most commonly used in palliative care for patients with motor neurone disease (MND).[1, 2]

Indications of deteriorating respiratory function

- disturbed sleep
- morning headaches
- daytime fatigue or sleepiness
- breathlessness at rest with excess use of accessory muscles of respiration
- increased respiratory rate
- weak cough

NIPPV requires specialized assessment and care. Ventilation can be delivered either as intermittent positive pressure or bi-level positive pressure (bi-pap), where different pressures are delivered in the inspiratory and expiratory phases.

There are several different systems, but all include a ventilator in a portable case and tubing attached to either a nasal or facial mask. It is advisable to have one with a battery back-up. Some are adapted to plug into the cigarette lighter in a car.

Following the assessment, a period of adjustment may be necessary when NIPPV is used for brief periods of 10–15 minutes. The patient often requires additional ventilatory support at night and this requirement may increase to longer periods as respiratory function deteriorates.

Some common problems associated with NIPPV

- mask leak—choosing the right size, repositioning the mask, and adjusting the straps for better fit can help
- skin irritation—care for the skin under the pressure area is essential; it may be necessary to rotate nasal and facial masks or use dressing pads to alleviate pressure
- difficulty in eating and drinking—the mask should be removed to allow oral intake and to reduce the risk of aspiration
- impact on body image—this can affect the patient and the carers; empathetic communication would help
- psychological impact of the use of NIPPV—careful assessment, explanations, clarifications, and psychological support
- ethical issues over stopping ventilation—timely discussion on choices at the end of life is of utmost importance and should be initiated, clarified, and documented sensitively much before NIPPV is commenced

References

1. Oliver, D., Borasio, G.D., Walsh, D. (2014) *Palliative Care in Amyotrophic Lateral Sclerosis* (3rd edn). Oxford: Oxford University Press.
2. MND Association. Information Sheets No.14A, 14B and 14D, http://www.mndassociation.org

Cough

Cough is a complex physiological mechanism to protect the lungs and airways. There are numerous causes of pathological cough, which may be malignant or non-malignant. Cough may be present in up to 50% of patients with terminal cancer and in up to 80% of patients with lung cancer. It occurs as a result of stimulation of the mechanical or chemical receptors in the respiratory tract.

Prolonged bouts of coughing can be exhausting and frightening, especially if associated with breathlessness or haemoptysis, and can lead to vomiting, pain, disturbed sleep, or syncope.

Management

- where possible, treat any reversible underlying causes
- consider disease-specific treatments—palliative radiotherapy or chemotherapy relieves cough in a significant number of patients in whom the mass effect of cancer is the main cause of their cough
- symptomatic treatments—as outlined in the following

Symptomatic management of cough

It is important to distinguish between a *productive* and *non-productive* cough when considering a treatment plan for the symptom.

Productive/wet cough

Promotion of an easy, effective cough to clear the mucus should be the aim of therapy, unless the patient is dying and is too weak to expectorate. Antibiotics may be appropriate and should be considered for improving cough, even in very ill patients.

Occasionally, bronchorrhoea (voluminous amounts of clear frothy sputum, occurring in 6% of cases of alveolar-cell cancer of lung and 9% of other lung cancers) may be very debilitating. Radiotherapy has been found helpful. Other suggested symptomatic treatments are largely anecdotal.

Approach for patients who are still able to cough effectively

- Steam inhalation or nebulized sodium chloride 0.9% 2.5mL q.d.s. and p.r.n. may help to loosen tenacious mucus and aid expectoration.
- Carbocisteine (500–750mg t.d.s. p.o.) may reduce sputum viscosity.
- Percussion, postural drainage, and advice on breathing techniques can help mobilize the secretions.
- Nebulized salbutamol would help by treating the component of bronchospasm.

Antitussives should ideally be avoided in this group of patients, but may be helpful at night to aid sleep (Table 10.3).

For patients who are dying and too weak to cough

- antimuscarinic drugs, e.g. ipratropium [nebulized]), glycopyrronium (SC), hyoscine butylbromide (SC), or hyoscine hydrobromide
- cough suppressants (see the following—usually diamorphine CSCI if the patient is dying)
- corticosteroids

Table 10.3 Opioid and antitussive dose

Opioid	Comparable antitussive dose
Pholcodine	10mg
Dextromethorphan	10–15mg
Codeine	15mg
Dihydrocodeine	15mg
Morphine	2.5–5mg

Dry cough

A dry cough should be suppressed once reversible causes are treated. Nebulized sodium chloride 0.9% 2.5mL q.d.s. can be helpful in reducing the irritation due to dry airways caused by mouth-breathing or breathing dry oxygen. It can help to loosen the thick and tenacious bronchial secretions, making it easier to expectorate.

Cough suppressants

When disease-directed therapies fail to reduce cough, the aim of therapy is to suppress the cough, especially in the terminal phase of the illness. Also see Table 10.4.

- peripheral suppressants
  - bupivacaine (5mL of 0.25% t.d.s.)
  - lidocaine (5mL of 0.2% t.d.s.)

Both have been used via *ultrasonic nebulizers* with effect—these agents act by anaesthetizing the sensory nerve endings involved in the cough reflex.

Note: Pharyngeal anaesthesia occurs, so food and drink should be avoided for an hour or so after treatment to avoid aspiration. The first dose should be given as an inpatient in case of reflex bronchospasm.

- non-opioid cough suppressants
  - simple linctus 5mL up to q.d.s.
  - inhaled sodium cromoglicate 10mg q.d.s. has been used for cough in lung cancer; it usually acts within 48h
- opioid cough suppressants
  - codeine 30mg q.d.s.; increased if needed to 60mg q.d.s.
  - codeine linctus (15mg/5mL) 5–10mL q.d.s.
  - pholcodine 5–10mL q.d.s. is non-analgesic; causes less sedation and constipation than codeine
  - morphine, initially 5mg/4h p.o.

Table 10.4 Cough suppressants

Cause	Treatment
Pharyngeal irritation	Simple linctus
Bronchial irritation	Nebulized bupivacaine

(If a patient is already taking opioids, a dose increment can be tried, but there is little evidence supporting the use of high doses of opioids for cough.)

- gabapentin
  - Doses of up to 1800mg daily orally have been shown to reduce chronic refractory cough in non-palliative care settings. The therapy is relatively well tolerated and complements other approaches that are available.

Diazepam may also be needed to relieve anxiety and distress and as a central cough depressant.

Haloperidol and antitussives

Studies on experimental models have shown that pre-treatment with haloperidol markedly reduces the antitussive effect of pentazocine and dextromethorphan. Haloperidol is a potent sigma-ligand and it is suggested that the antitussive effect is mediated by sigma-sites. Clinical relevance is unknown, but a trial of an anti-emetic other than haloperidol may be worth trying if a patient has intractable cough which is resistant to antitussives.

Antibiotics

Even in the last days of life, infected chest secretions may be copious and more effectively treated with antimicrobials than with symptomatic measures alone. However, their outcome may be poor in the presence of drug-resistant pathogens and frailty of patients, especially near the end of life.

Frequently, patients have had several prior courses of antibiotics, in which case a short course of a broad-spectrum antibiotic may be justified.

Offensive sputum, which is suggestive of anaerobic infection, may respond to metronidazole.

Nebulized gentamicin is used quite frequently in patients with cystic fibrosis. Purulent secretions colonized with Gram-negative organisms can be treated with nebulized gentamicin 80mg t.d.s. with a significant reduction in the volume of secretions. Negligible systemic absorption has been shown.

Further reading

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Chapter 11

Genitourinary problems

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Anatomy and physiology of the bladder and micturition

Patients with palliative care needs may suffer a variety of symptoms attributable to dysfunction of the urinary system. Disturbance of the genitourinary system can result not only in debilitating symptoms but also loss of confidence, embarrassment, and psychological distress. It is important to understand the basic anatomy and physiology to aid in the management of what can be a distressing range of symptoms.

Bladder wall

- The bladder wall is made up of detrusor muscle, which is a smooth muscle with an adventitial outer covering together with a supporting inner submucosa for a specialized transitional-cell epithelium.
- Detrusor muscle forms a functional syncitium with relatively indistinct muscle layers. The outer and inner layers of muscle bundles tend to be longitudinal in orientation with a middle layer circularly orientated.
- Bladder emptying is accompanied by detrusor contraction.
- The trigone is a smooth, sensitive triangular area at the base of the bladder with apices formed by the ureteric orifices and the internal urinary meatus or bladder neck.

Sphincter-active urethra

- The distal sphincter mechanism is situated just beneath the prostate in males and in the distal half of the urethra in females. There is a smooth muscle component and a striated muscle component within the wall of the urethra.
- The striated muscle component, the intrinsic rhabdosphincter, is the most important component for maintaining continence.
- The striated sphincter contains fatigue-resistant, slow-twitch fibres that are responsible for passive urinary control. Voluntary contraction of the levator ani musculature is responsible for active continence.

Nerve supply of the bladder and urethra

- Normal micturition is partly a reflex and partly a voluntary act.
- Parasympathetic nerve fibres in the anterior sacral roots of S2 to S4 are the principal motor supply to the detrusor muscle. Parasympathetic (cholinergic) nerve stimulation results in bladder contraction and bladder neck sphincter relaxation, allowing micturition.
- Smooth muscle in the region of the bladder neck and prostate is regulated by sympathetic fibres from the hypogastric plexus arising from T11 to L2. Sympathetic stimulation relaxes the detrusor muscle (beta-adrenoceptors) and contracts the bladder neck sphincter, thus preventing micturition. The role of the sympathetic nervous system in the female is less exact.
- The functional innervation of urethral smooth muscle is adrenergic.

- Somatic innervation comes from S2 to S4 as the pudendal nerve to the striated muscle of the sphincter.
- The neurovascular bundles running alongside the prostate carry the autonomic innervation of the sphincter-active urethra as well as the cavernous nerves responsible for erections. It is these nerves which may be damaged during radical prostatectomy with resulting erectile dysfunction.

Clinical relevance of the nerve supply

Commonly used drugs in the field of palliative medicine, such as hyoscine and tricyclic antidepressants, cause urinary retention by effecting relaxation of the detrusor muscle and contraction of the bladder neck mechanism. Alpha-blockers (including doxazosin and tamsulosin) increase urinary flow in bladder outflow obstruction by relaxing the smooth muscle of the bladder neck and prostate.

Bladder pain

Bladder discomfort or pain presents in the suprapubic area and may be associated with other symptoms such as dysuria, frequency, nocturia, and urgency, as well as urine retention and/or incontinence. If the trigone is affected, the pain may radiate to the tip of the penis. Pain may be constant (e.g. urinary tract infection) or intermittent (e.g. bladder spasm). It may vary in intensity from a dull ache (e.g. urinary tract infection) to acute disabling pain (e.g. acute obstructive pathology causing retention of urine).

Commonest causes of bladder pain in palliative care

- urinary tract infection (UTI)
  - bacterial including tuberculous cystitis
  - fungal (immunocompromised patients)
  - urethritis
  - genital herpes
  - vaginitis
- anatomical
  - pelvic mass
  - urethral obstruction
  - cystocoele
- neoplastic
  - bladder cancer
  - urethral cancer
- foreign body
  - urethral or suprapubic catheter (usually comfortable unless infected or blocked)
  - bladder calculus
- bladder instability
  - bladder spasm may be idiopathic or more commonly due to contraction around the balloon of an indwelling catheter, blood clots, tumour, or infection
- inflammatory
  - radiotherapy
  - chemotherapy—cyclophosphamide
  - intravesical chemotherapy or immunotherapy for bladder cancer
  - interstitial and eosinophilic cystitis
  - amyloid

Treatment of bladder pain/irritability

Treat reversible causes.

Non-drug management

Regular toileting, maintaining adequate fluid intake (which may be difficult for the terminally ill), and avoiding caffeine and alcohol.

Drug management

- antimuscarinic drugs may be helpful but should be avoided in significant bladder outflow obstruction or urinary retention
- antispasmodics
  - oxybutynin 2.5–5mg b.d.–q.d.s. (also has a topical anaesthetic effect on the bladder mucosa and can be given intravesically as 5mg in 30mL o.d.–t.d.s.); modified preparations are available, including a transdermal patch
  - tolterodine 2mg b.d. (better tolerated than oxybutynin; use lower dose if hepatic impairment); modified release preparations are available
  - propiverine hydrochloride 15mg o.d.–t.d.s.
  - trospium chloride 20mg b.d.—undergoes negligible metabolism by cytochrome P450 (CYP450), and can therefore be useful in patients on drugs such as benzodiazepines which are also metabolized by CYP450
- tricyclic antidepressants
  - amitriptyline 25–50mg nocte
  - imipramine 25–50mg nocte
- NSAIDs may be useful
- Corticosteroids may reduce tumour-related inflammation of the bladder, thereby reducing pain associated with this.
- Local anaesthetic and opioids can be used intravesically although the evidence to support the effectiveness of this treatment is limited. Lidocaine 2% (diluted in sodium chloride 0.9%) can be instilled through an indwelling catheter, which should then be clamped for 20 min to 1h. Bupivacaine 0.5% can be combined with morphine 10–20mg and instilled t.d.s. through an indwelling catheter which should be clamped for 30 min.

Terminal situation

Antimuscarinics can be given via a CSCI: hyoscine butylbromide 60–120mg over 24h; glycopyrronium 0.2–0.4mg over 24h.

Blood supply of the bladder

The bladder has a considerable blood supply from the vesical arteries and from branches of the anterior division of the internal iliac arteries. This facilitates reconstructive surgery of the bladder but makes the management of haemorrhagic cystitis difficult.

Urinary tract infection (UTI)

UTI is common in palliative care patients and presentation may be non-specific. The clinical picture may vary from asymptomatic to severe symptoms and potentially septic shock.

Presentation

Dysuria, incontinence, urinary retention, haematuria, suprapubic pain, loin pain, pyrexia of unknown origin, confusion.

Risk factors

Low urinary output (dehydration), bladder dysfunction (outlet obstruction, neuropathic bladder), catheterization, atrophic vaginitis, renal calculi, diabetes mellitus, immunocompromise, vesical fistulae.

Pathogens

Escherichia coli commonest, also *Streptococcus faecalis* and *Proteus, Klebsiella,* and *Pseudomonas* spp.

Management

Bedside testing for protein, blood, leucocytes, and nitrites (any or all may be positive). UTI unlikely if all bedside tests negative. MSU for culture. Clinical diagnosis and positive bedside testing sufficient to start treatment in most patients. Catheter in situ—do not treat unless patient symptomatic or undergoing re-catheterization/instrumentation. Encourage increased fluid intake.

- Most clinical institutions have local antibiotic guidelines and if available these should be adhered to unless clinically indicated to do otherwise. Common antibiotic regimens include:
  - trimethoprim 200mg b.d. for 3 days is effective in most uncomplicated infections
  - ciprofloxacin 250–500mg b.d. p.o./ IV, co-amoxiclav 375mg t.d.s. p.o./ IV, cefalexin 250mg q.d.s. p.o., cefuroxime 125–250mg b.d. p.o./IV
  - prophylaxis is shown to be beneficial for those with recurrent symptomatic infections (proven on MSU)[1]

Reference

1. Albert X, Huertas I, Pereiróll, Sanfélix J, Gosalbes V, Perrota C. (2004) Antibiotics for preventing recurrent urinary tract infection in non-pregnant women. *Cochrane Database of Systematic Reviews*, 3:CD001209.

Renal pain

Renal pain is characteristically a dull ache in the loin caused by capsule distension, irritation, or obstruction.

Causes

- infection—pyelonephritis, abscess
- haematoma (trauma)
- infarct
- tumour—renal-cell carcinoma, transitional-cell carcinoma, oncocytoma, bleed into angiomyolipoma
- hydronephrosis
- renal vein thrombosis
- nephrolithiasis

Diagnosis

Urine culture, ultrasound scan, CT scan (MRI may be useful if contrast contraindicated)

Management

Treat the underlying cause if possible, consider dexamethasone 8–16mg for enlarging tumour, analgesics (WHO ladder)

Ureteric colic

Ureteric colic is a severe pain, usually located to the loin and may radiate to the ipsilateral groin and testicle. Its onset is typically over 15–20 min, building to an intense plateau of pain with fluctuations in intensity but never disappearing, as for example in small-bowel colic. It relates to acute ureteric obstruction, and, depending on the cause, may abate with a similar time course to its onset. The patient will become agitated and unable to settle, and will often roll around in agony.

Causes

Calculus, tumour, clot, renal papillae, fungal infection

Treatment

NSAIDs will inhibit the renal response to acute urinary obstruction (*avoid with impaired renal function*) and opioid analgesia may also help. Treating tumour-related oedema with dexamethasone 8–16mg may be useful. Anticholinergics (e.g. hyoscine butylbromide) play no role in the management of acute ureteric colic. Tamsulosin (400mcg o.d.) may be helpful in those with distal ureteric calculi.

Pelvic pain

Pelvic pain can be severely debilitating. It is a multifactorial symptom that can be challenging to manage. Assessment therefore needs a logical and thorough approach to ensure optimal symptom control for the patient.

Consider which structures may be the site of pain

- GU tract:
  - males: ureters, bladder, prostate, urethra, penis, testes
  - females: ureters, bladder, urethra, ovaries, uterus and fallopian tubes, vagina
- perineum
- GI tract: distal colon, rectum, anus
- bones: sacrum, pelvis

Consider the pathological process leading to pain

- cancer—can be nociceptive (visceral or somatic), musculoskeletal, or neuropathic and due to the tumour itself/local invasion/metastases/extrinsic compression of nearby structures
- concurrent non-cancer disease (e.g. UTI)
- iatrogenic (caused by cancer treatment or non-cancer treatment, e.g. radiotherapy, surgery, constipation)

Management

- treat underlying cause (e.g. antibiotics for infection)
- follow WHO ladder, adjuvant analgesia as appropriate to type of pain
- consider dexamethasone 8–16mg daily for extrinsic compression from tumour as a 3-day trial
- surgery: e.g. stabilization of fractures such as neck of femur
- oncological treatment: palliative chemotherapy or radiotherapy, hormone therapy (hormone-sensitive tumours)
- anaesthetic analgesic interventions: interruption of the pre-sacral sympathetic nerve supply may help relieve pelvic pain in those patients where analgesic drugs and adjuvants have not been successful in managing the symptom.[1] A caudal or lumbar epidural may be useful. **Note:** neurolytic techniques can have potentially serious side effects, including lower limb paralysis and double incontinence.
- non-physical treatments: complementary therapies, psychological support, spiritual input, social support

Reference

1. Chambers WA. (2008) Nerve blocks in palliative care. Br J Anaesth; 101(1):95.

Urinary retention

Urinary retention is common in palliative care patients and should always be considered in patients showing non-specific symptoms such as confusion, restlessness, and agitation. Patients presenting with retention often have a previous history of urological difficulties. Risk factors for retention include drugs (such as opioids, anticholinergics), constipation, poor mobility, and inadequate toileting facilities, and should be avoided as far as possible.

Causes

Drugs

Many of the drugs used in palliative care can affect bladder function and increase the risk of urinary retention):

- tricyclic antidepressants
- phenothiazines
- opioids
- anticholinergics, e.g. oxybutynin, hyoscine, glycopyrronium
- alpha-agonists (contained in some proprietary cough medicines)

Local

- urinary tract infection
- benign prostatic hypertrophy (BPH)
- pelvic tumours (any)—primary or secondary
- constipation
- urethral stricture—rare, since it usually presents with bad lower urinary tract symptoms first
- haematuria with clot retention

Neurological

- spinal cord compression
- pre-sacral plexopathy
- intrathecal/epidural anaesthesia

Debility

- immobility/weakness
- decreased conscious level

Acute obstruction

Symptoms: hesitancy and poor urinary stream, post micturition dribbling, early morning frequency and nocturia. Subacute symptoms may have been present previously but may be of sudden onset.

Diagnosis

- severe lower abdominal pain
- intense desire to urinate
- anxiety/irritability—may be the only symptom in the terminal or unconscious patient
- distended, tense bladder: tender to palpation, increases desire to urinate, dull to percussion

- bedside ultrasonography to assess bladder volume can negate the need for unnecessary catheterization and is becoming more commonplace in the hospice setting; training of clinicians in this modality of imaging can be hugely beneficial
- >500mL of urine on catheterization in presence of symptoms

Chronic obstruction

Symptoms: classic and cardinal symptom is nocturnal enuresis. The onset is often slow and insidious, and is often missed or misdiagnosed as incontinence.

Diagnosis

- dribbling incontinence
- large, non-tender bladder (low pressure chronic retention)
- dull percussion note in lower abdomen (may extend to above the umbilicus)
- high residual volume (>300mL) post-micturition (may otherwise be symptomless); acute on chronic volumes may be >800mL on catheterization

Complications

- urinary infection and bladder stones
- hydronephrosis and post-renal failure (high-pressure chronic retention)
- constipation refractory to laxatives
- agitation, confusion
- post-catheterization diuresis due to released pressure on the renal cortex and osmotic effects of high urinary urea
- record should be kept of urine output and if excessive (e.g. >200mL/h), intravenous fluid should be used for replacement. To avoid driving the high urine output, 80% of the output, on an hourly basis, can be replaced as a combination of oral ± IV fluids with measurement of serum biochemistry. It is no longer good practice to clamp catheters to allow slow drainage.

Treatment

Acute retention

- Immediately catheterize with a 12–16Fr gauge urethra catheter.
- Leave catheter in place if the patient is in agreement. There are risks of bacteraemia when catheters are both inserted and removed. In the terminally ill, this will prevent the risk of further retention and aid in nursing management.
- Measure residual volume.

If it is not possible to pass a urethral catheter, a suprapubic catheter will be needed. In a hospice setting in the terminally ill, a Bonanno catheter can be used. It should be inserted in the midline away from scars, two finger breadths above the symphysis pubis. This is a short-term measure, and the catheter should be changed by a urologist to a more appropriate tube if appropriate for the patient. A suprapubic catheter is contraindicated with clot retention.

Chronic retention

- catheterize—as previously
- check fluid balance and monitor electrolytes Na^+ and K^+
- consider IVI if needed to supplement oral intake

Clot retention

- Can be difficult to manage in the hospice setting. Ideally this should be managed by urologists who will use a stiff 22Fr catheter and may need to use an introducer. In a hospice setting with a terminally ill patient, an 18Fr catheter should be tried. It may be necessary to use a three-way catheter to irrigate the bladder.

Treat underlying cause as appropriate for the patient

- Give laxatives for constipation.
- Treat UTI.
- Review medication and reduce or stop drugs causing retention (if possible).
- Clot retention—stop anticoagulants and correct bleeding diathesis if possible. **Note**: tranexamic acid should be used with caution since it might exacerbate the situation.
- Consider and treat spinal cord compression. Investigate/treat pelvic tumour (surgery, radiotherapy, or chemotherapy according to type).
- Place urethral stent, e.g. in patients too unwell for surgery.
- Debilitated patient—ensure regular toileting, use commode rather than bedpan (women), sit/stand at edge of bed (men), privacy—anxiety will inhibit micturition.

Further investigations (consider whether appropriate based on clinical condition)

- CSU for culture and sensitivity.
- Urea and electrolytes, creatinine—uraemia not improving after catheterization may indicate other cause, e.g. NSAID nephropathy or a high obstruction not corrected by catheterization.
- Consider urinary imaging: IVU, USS, cystoscopy if patient is well and corrective treatment is contemplated.

Ureteric obstruction

This may be unilateral or bilateral and is caused, in palliative care, largely by pelvic tumours resulting in hydronephrosis, e.g. carcinoma of the cervix in women and carcinoma of the prostate in men. A reduction in urine volume, abdominal pain, and/or serial blood tests of deteriorating renal function alert the team to the possibility of bilateral obstruction and impending renal failure. Renal ultrasound will confirm the diagnosis of ureteric obstruction due to tumour and rule out other contributing factors.

In the case of ureteric obstruction without calculus involvement (extrinsic compression), an indwelling ureteric stent can be passed under cystoscopic control if there appears to be reasonable potential for regaining function. If this is not possible, a percutaneous nephrostomy could be considered under ultrasound guidance. This can sometimes be replaced by the antegrade insertion of ureteric stents. In some circumstances, antegrade ureteric insertion into an ileal conduit may be appropriate. With modern equipment and techniques, long-term nephrostomies are a possible option, but this needs very careful discussion with patients who may already be suffering from pelvic pain, fistulae, or other tumour-related problems. They may not want artificial prolongation of life at the expense of relentlessly distressing symptoms.

If a renal or ureteric calculus is suspected, the best imaging modality for diagnosis is non-contrast CT.[1] Ultrasound scan (USS) can be useful if radiation exposure is a concern, although diagnosis rates are lower. IV pyelograms are also less commonly used to diagnose renal calculi owing to potential contrast reactions, lower sensitivity, and increased radiation exposure.

Discussion with the patient and their family is crucial in helping guide the patient to determine the best management for them. The balance between the disruption caused by the intervention, the likely benefit from it, the patient's quality of life, and their potential prognosis all need to be considered. Finding the right path for your patient can be challenging. All patients are individuals, and their beliefs and experiences will shape their decisions. We as clinicians need to be able to understand what is important to them to help guide them through that process.

> The good physician treats the disease; the great physician treats the patient who has the disease.
>
> William Osler

Reference

1. Smith-Bindman R, et al. (2014) Ultrasonography versus computed tomography for suspected nephrolithiasis. *N Engl J Med*; 371(12):1100.

Urinary incontinence

Incontinence is a distressing symptom for patients, affecting their lives physically, psychologically, socially, and sexually. Patients may become isolated from family and friends as they try to maintain their own personal hygiene, fearing to lose their dignity in public. A good history is essential and may reveal the underlying cause, e.g. poor mobility resulting in an inability to reach the toilet in time, or known pelvic disease resulting in a vesicovaginal fistula resulting in constant drainage through the vagina.

Total urethral incontinence

This type of incontinence is relatively common for those patients with advanced malignant disease. An uncontrollable loss of urine occurs secondary to local incompetence of the urethral sphincter (due to direct tumour invasion or previous surgical intervention) or central loss of sphincter control (due to confusion or dementia).

Treatment includes regular toileting for the central loss of control to allow continence to be regained. Females will likely need a urethral catheter. A male sheath catheter can be tried first, but these can be problematic since they may be difficult to fit securely.

Neurological incontinence

Loss of neurological bladder control may be due to damage to the sacral plexus or spinal cord/cauda equina compression. A hypotonic neuropathic bladder may result in overflow incontinence while a reflex/automatic bladder empties automatically. Patients who are well, willing, and dextrous enough may be taught intermittent self-catheterization. Other patients will require long-term catheterization. Anticholinergics may help.

Overflow incontinence

This is associated with obstruction of the bladder outlet or a poorly contractile floppy bladder. Small volumes of 'overflow' urine may be passed without control. A palpable, distended bladder can alert the clinician to overflow incontinence, although this can be difficult to diagnose in patients with other abdominal or pelvic pathology. Ultrasound scan of the bladder to assess volume can be useful, if available, to aid diagnosis. Permanent catheterization will probably be necessary. Definitive treatment may be possible if the patient is well enough and if the obstruction is amenable to surgery or other intervention such as an intraurethral stent.

Urge incontinence

A sudden urge to urinate and subsequent urinary loss may be particularly distressing for patients with poor mobility who are unable to reach the toilet in time. The underlying cause should be treated; anticholinergic agents may help. Patients may be able to manage timed voiding.

Stress incontinence

The involuntary urethral loss of urine with increased intra-abdominal pressure from coughing, sneezing, laughing, jumping, or even walking in severe cases in the absence of bladder contraction may occur. It is more common in multiparous women and is associated with poor urethral support and reduced pelvic floor tone. In patients who are well enough to participate, management of stress incontinence includes lifestyle modifications such as reducing caffeine intake, smoking cessation, and weight loss, in conjunction with pelvic floor exercises. This may be unrealistic for many in our patient group and in these cases support prostheses (e.g. ring pessary) and urethral inserts may be a possibility in the absence of local tumour.

Haematuria

A normal urinary tract does not usually bleed, even if the patient is on warfarin. Haematuria is a frequent presentation of urological disease. It ranges from microscopic haematuria discovered incidentally on urinalysis to frank haematuria with the passage of clots and clot retention of urine. The extent of the bleeding does not always correlate with the severity of the underlying aetiology. The bladder is a very vascular organ and hence will not have a chance to stop bleeding unless it is collapsed. Some medications (such as phenytoin or rifampicin), food dyes, and foodstuffs (such as beetroot) can stain the urine red and may give a false impression of haematuria.

Causes

- tumour—renal, ureteric, bladder, prostate
- UTI
- drug-induced—aspirin or NSAIDs do not cause gross haematuria in a normal urinary tract, but any bleeding associated with surgical interventions may be exacerbated; cyclophosphamide, doxorubicin, and ifosfamide may cause haemorrhagic cystitis
- systemic coagulation disorder—usually evidence of bruising or bleeding elsewhere; platelets may be low owing to leucoerythroblastic anaemia and marrow infiltration
- radiation cystitis
- urinary calculus

Investigations

- urinalysis, microscopy, and urine culture
- CT urogram (has widely replaced IV urogram)
- ultrasound scan
- cystourethroscopy (visualizes the bladder and urethra)

Treatment

Treat any reversible causes, i.e. treat UTI and systemic coagulation disorder and stop precipitating drug.

General measures

- Encourage oral fluids to promote a good urine output (to avoid clot retention).
- Transfusion may improve symptoms due to anaemia.
- Etamsylate: reduces bleeding by enhancing platelet adhesion. The use of tranexamic acid (prevents fibrinolysis by inhibiting plasminogen activation) is controversial. It may result in the formation of hard clots, which then need to be irrigated cystoscopically; urological surgeons describe bladders lined with clots, which can be difficult to manage. But, as ever, the decision must be made on an individual basis. Terminally ill patients may prefer to risk clot retention than to continue with gross haematuria and significant blood loss.
- Palliative radiotherapy often reduces haematuria from a bleeding urinary tract cancer.

- Instilling 1% alum, formalin, 0.5–1.0% silver nitrate, or epsilon aminocaproic acid solutions may be tried. (Discuss with urologists.)
- Internal iliac artery embolization may provide effective relief from severe bladder haemorrhage; renal artery embolization may be useful in renal-cell carcinoma.
- Bleeding from the prostate in patients with benign prostatic hyperplasia may respond to finasteride 5mg o.d. (a specific inhibitor of 5 alpha-reductase which metabolizes testosterone to the more potent androgen, dihydrotestosterone), even if patients are on other drugs.
- Cystectomy may be the final option in a patient able to undergo the procedure, which, however, would be most unusual in the palliative care situation.

Clot retention

The principle in the management of clot retention is to evacuate the bladder clots. A non-distended bladder bleeds far less than a distended bladder. An 18Fr catheter will be needed. Patients may need referral to a urologist for insertion of a 3-lumen catheter (to permit irrigation with sodium chloride 0.9% and allow removal of clots), which is stiff. Cystoscopic bladder washouts may be necessary. Percutaneous insertion of a suprapubic catheter is contraindicated in the presence of clot retention since the catheter is of insufficient diameter to allow satisfactory irrigation; there is also the potential for seeding of bladder tumour through the percutaneous tract.

Haemorrhagic cystitis

Haemorrhagic cystitis may require clot evacuation and irrigation, and instillation of alum. Intravesical prostaglandin E2 may be helpful. In selected fit patients, urinary diversion, cystectomy, or selective embolization of the internal iliac artery may be appropriate, but this would be very rare in the palliative care population.

Catheterization

Indications

Urinary retention (acute and chronic), incontinence, patients in whom toileting is problematic, e.g. pathological fracture femur.

Indwelling urethral catheterization

The French scale of catheter size is measured in mm. A 12–16Fr (French gauge) silicone catheter is most commonly used in adults since smaller diameters tend to coil in the urethra. A larger size may be needed (e.g. 18Fr) if debris and infection are suspected. A size 18Fr will be needed for clot retention (see following). Long-term catheters should be changed based on clinical indication and type of catheter. Most can remain in situ up to 12 weeks but may need to be changed more frequently if clinically indicated, or per manufacturer guidelines.

The term 'French gauge' (Fr) is a unit of measurement designed by the Parisian maker of surgical instruments Joseph-Frédéric-Benoît Charrière. The French unit of measurement is three times the diameter in millimetres, i.e. a 12 French gauge catheter has a diameter of 4mm.

For male urethral catheterization

- Retract the foreskin to view the urethral meatus.
- Clean the glans and urethral meatus with sodium chloride 0.9% or aqueous chlorhexidine.
- Anaesthetize and lubricate via urethral meatus with 10mL lidocaine 2% gel via syringe.
- Wait for a few minutes and gently pass the catheter using an aseptic technique. Resistance may be encountered at the level of the distal sphincter complex or bladder neck. Sphincter spasm will diminish in a few minutes. Asking the patient to cough may facilitate passage of the catheter.
- A catheter introducer should only be used by experienced urological surgeons.
- If the catheter is bending and not passing easily, it may be appropriate to try a larger gauge catheter. After insertion and urine is draining, inflate the catheter with the required volume of saline to prevent the catheter dislodging.

For female catheterization

- The female meatus may be difficult to identify and is often situated in the vaginal introitus or along the anterior vaginal wall.

Urethral catheter problems

- Trauma and false passages—refer to urological team
- Haematuria
- Infection is extremely common with long-term catheterization. Catheter-associated UTIs are the leading cause of secondary healthcare-associated bacteraemia. Antibiotic treatment should be given if the patient is symptomatic (fever, urinary symptoms, delirium, etc.).

- Bladder spasm—caused by irritation of the trigone of the bladder by the balloon. Often this is relieved by removing water from the balloon, although most long-term silicone catheters have only a 10mL balloon and there is the risk that the problem will not be solved and the catheter will fall out. Antispasmodics (e.g. oxybutynin) may help.
- Blockage may occur from debris or clots. Flushing the catheter with a sodium chloride 0.9% 100mL bladder washout flush may relieve the blockage but at the risk of encouraging further infection.[1] This decision will depend on the particular clinical circumstances.
- Bypassing is due to a blocked catheter or bladder spasm.
- Paraphimosis—failure to reposition the foreskin may lead to constriction, causing swelling and pain in the glans penis. Reduction with gentle squeezing pressure over 30min using swabs soaked in 50% glucose may allow foreskin repositioning.
- Undeflated balloon—if the balloon will not deflate to allow removal of the catheter, it will need deflating with a wire, usually under ultrasound control.

Suprapubic catheter

A suprapubic catheter is indicated if passing a urethral catheter has failed. This may be due to a stricture, obstruction due to intrinsic or extrinsic compression, or distorted anatomy of the urethral meatus due to tumour or lymphoedema. It may also be used as an alternative to a urethral catheter in a patient with an unstable bladder in whom the balloon is constantly irritating the trigone. A suprapubic catheter is contraindicated in clot retention.

Intermittent self-catheterization is unusual in patients with palliative care needs. It may be used in patients with a neuropathic bladder, e.g. after spinal cord compression or in certain neurological conditions such as multisystem atrophy (MSA). Clean-catheter insertion at least four times daily frees patients from indwelling catheterization, gives them control, and prevents renal damage from urinary retention. Patients need to be highly motivated, have manual dexterity, and be well enough to perform the task. Refer to an incontinence adviser for counselling/instruction.

General management of catheters

Catheters (especially suprapubic) need skin-protective agents around the base of the catheter to stop leakage spilling directly onto the skin. Secretions around the catheter site should be removed with soap and water. Over-granulated areas can be removed with silver nitrate. Cleaning around the urethral meatus is necessary since secretions are increased due to urothelial irritation. The secretions form crusts which, when removed, form areas of exposed damage that are prone to bacterial colonization and which can then ascend into the bladder.

Reference

1. Gould, C, Umscheid, C, Agarwal, R. (2008) Guideline for the Prevention of Catheter-Associated Urinary Tract Infections 2008, HaH Services (ed.), Department of Health and Human Services, Centers for Disease Control and Prevention, Atlanta, GA. pp.1–47.

Genitourinary fistulae

A fistula is an abnormal communication between two hollow viscera or viscera and body surface. A genitourinary fistula is a communication between the genital tract and the bladder, ureter, or urethra. It can occur in patients with advanced cancer, causing considerable morbidity and distress. Fistulae may be caused by previous radiotherapy or direct tumour extension, and are best managed with bypass surgery, if possible and appropriate to do so.

General management

- Meticulous skin protection—barrier creams, e.g. zinc and castor oil, Sudocrem®, or Cavilon® (applied as a spray or stick protector and dries to form a protective membrane). Lutrol gel (solidifies when warmed in contact with skin, forming a protective layer) is not commercially manufactured but is usually accessible through specialist hospital pharmacies.
- Water-absorbent pads or tampons
- Treatment of odour: metronidazole 400mg t.d.s. may reduce odour from anaerobic infection. Charcoal dressings and charcoal placed in the room may have some effect. Masking the smell with lavender oil, etc., has been tried but is often ineffective.

Vesicoenteric fistulae

A vesiocoenteric fistula may develop between the bladder and any segment of bowel. The cause in palliative care is usually colonic malignancy, although diverticulitis or small bowel inflammatory disease may also be responsible. Vesicoenteric fistulae rarely occur secondary to bladder pathology. A characteristic symptom is pneumaturia (passage of gas or froth in the urine), and there may also be a foul odour to the urine, persistent urinary tract infections, and the presence of faecal matter in the urine (especially with large fistulae). Cystoscopy, contrast cystography, or intestinal barium studies will normally demonstrate the fistula. Ideally, the management is surgical removal of the segments of bowel and bladder, together with repair of the bowel and bladder. Otherwise a bypass procedure may be performed: a colostomy or ileostomy may provide complete relief. Some patients may be too unwell for surgery or prefer not to have a stoma.

Vesicovaginal fistulae

These are characterized by a continuous leakage of urine from the bladder into the vagina and need to be distinguished from total urethral incontinence. Cystoscopy and retrograde ureterography may be helpful, although pelvic MRI is becoming more commonly used and may be more sensitive in detecting a fistula. Surgical excision provides the most effective solution but is often not feasible. Urinary diversion, e.g. ileal conduit, may be necessary if the patient is well enough, but this is a formidable undertaking in patients who have had radiotherapy. Bilateral nephrostomy is a potential but radical alternative. As ever, the advantages and disadvantages of procedures need to be discussed with the patient.

Sexual health in advanced disease

Sexuality is the process of giving and receiving sexual pleasure and is closely connected to a sense of well-being.

Sexuality is a feeling of belonging, of being accepted by another, and the conviction that we are worthy to live and enjoy life.*

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Maintaining our sexual health is a key component of our well-being as humans. Sexuality will be different for every individual, and most importantly, as clinicians, we should not assume what our patients want or need from their sexual relationships. Crucially, we should explore how their illness is affecting their feelings about themselves, their relationships, and their sexuality. Patients facing the prospect of a terminal illness may find that their intimate and sexual relationships change as a result of their illness, and we need to support them through this.[1]

Individuals with advanced cancer may want to continue or commence a sexual relationship with a partner but may have physical, psychological, or relational difficulties. Exploring these areas will help ensure patients receive help from the correct professionals if needed and wanted by the patient. Patients are unlikely to broach sexuality and intimacy themselves for fear of it being deemed a less pressing issue than other difficulties they may be facing, but it may be a significant concern for them. Opening up the discussion about these issues may empower patients to know that both the decision to continue, or not continue, a sexual relationship is acceptable.

There are certain patient groups who have traditionally not been included in discussions or studies about sexual health and therefore have not benefitted from the potential services and help that are available. This includes patients who identify themselves as within the same-sex, bisexual, transsexual, or transgender population. Adolescent patients with life-limiting conditions may well have a different experience of sexual development, health, and intimacy than their peers. This is not commonly explored with them. Their medical condition may well have a negative impact on their well-being, body image, emotional development, and sense of self. Assumptions may be made about older patients, or patients who are single and not in a long-term relationship, regarding their need or want for an intimate or sexual relationship.

If patients are seeking help with their sexual relationship, it is important to consider the nature of the problem, and a thorough history will do this. This will ensure that referral to the appropriate service is made.

General advice

- Consider whether a referral to a specialist is needed, e.g. a clear history of psychological distress requiring a referral to a psychology team or a urological problem requiring intervention from a urology team.
- Manage other symptoms well. It may be that other symptoms are limiting the ability for sexual intimacy, e.g. dyspnoea.
- Consider medications that may be influential, e.g. hormone therapy affecting libido.

As clinicians, we are there to support our patients and help them optimize their quality of life. It is important that we are able to explore and discuss all aspects of their life, including their sexuality, in an open and non-judgemental manner.

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Chapter 12

Skin problems in palliative care

Wound care in cancer *408*
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Wound care in cancer

> The wound is granulating well, the matter formed is diminishing in quantity and is laudable. But the wound is still deep and must be dressed from the bottom to ensure sound healing.
>
> British Medical Journal (1901) on the postoperative recovery after appendicectomy of Edward VII

Background

Skin wounds are common in advanced malignancy. Pressure ulcers are most frequently seen, affecting an estimated one-third or more of patients in palliative care units. Malignant/fungating wounds occur in approximately 5–10% patients with metastatic cancer and are associated with significant physical and psychological distress.

Loco-regional skin involvement (e.g. breast fungation) should be distinguished from generalized skin metastases, which imply advanced disease.

Local extension of malignant tumours leads to embolization of blood and lymphatic vessels, which can compromise tissue viability. Tumour infarction leads to necrosis with subsequent infection.

Goals of treatment

The ideal aim of treatment is skin healing through local or systemic treatment, e.g. surgery, radiotherapy, hormonal manipulation, or chemotherapy. Electro-chemotherapy for patients with primary or metastatic skin lesions is a relatively new outpatient-delivered palliative treatment involving a single dose of chemotherapy followed by local application of electroporation pulses to lesion(s). Meta-analysis of 44 studies showed best response with small cutaneous lesions, with complete response of skin lesions in 59.3% of patients.[1] Retreatment is possible.

Unfortunately, complete healing is often not possible, and the primary aim is often comfort and the enhancement of quality of life.

> Palliative wound care needs to take account of the psychological impact of wounds on the individual as well as their family; it strives to reduce the impact of the wounds by managing the underlying cause, the wound-related symptoms, and the wound itself.

For all patients, irrespective of whether skin healing is possible, care should be directed to the minimization of:

- pain
- infection
- bleeding
- exudate
- odour
- psychological trauma

In the context of advancing disease, treatment should be realistic and acceptable to the patient.

Good skin care aims to maintain and replenish the skin by cleansing, hydrating, and protecting.

Continually re-evaluate

In relation to wound care, there are numerous commercially available products: hydrocolloids, hydrogels, alginates, semi-permeable films, cavity foams, de-sloughing agents, and charcoals. Despite the pressure to adopt the latest innovation, often the simplest products may be both very beneficial and the most cost-effective. If the first choice of dressing regimen is not right for a patient, try a different one. The key is in working with the patient and the family to come up with a plan which suits the individuals involved (see Box 12.1).

Box 12.1 Choosing a wound care regimen

Consider:

- Pain
- Comfort
- Exudate
- Odour
- Cosmesis
- Patient lifestyle
- Necrotic tissue
- Infection
- Psychological effects
- Bleeding

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Wound care management: symptom focus

Pain

It is important to ensure that neither infection nor the actual dressing is contributing to pain or distress. *First do no harm*.

Consider using a short-acting opioid for analgesia 15 minutes or so prior to initiating the dressing change. This may be in the form of liquid morphine or one of the fast-acting fentanyl preparations. Topical opioids—usually in the form of diamorphine or morphine, often mixed with lidocaine gel—have been shown to improve analgesia in some small studies and are usually well tolerated[1] (10mg mixed in 10mL of gel is a common concentration used). Non-stick dressings are often recommended as they do not impede the healing work of fibroblasts on the wound surface. Use of a hydrogel sheet dressing may provide topical analgesia and comfort by helping to keep a wound hydrated while at the same time encouraging the breakdown of slough and reducing bacterial growth.[2]

Exudate

A copious volume of exudate risks maceration to the peri-wound skin. If there are bleeding points within the wound, it may be necessary to apply a combination dressing—an absorbent primary dressing such as an alginate or methylcellulose which will not adhere as much to the wound—with a secondary absorbent or super-absorbent pad. Where wounds are very moist, specialist input may encourage the use of a topical negative pressure device.[3]

While it might seem economical and patient-friendly to change only the outer dressing when saturated, leaving the inner dressings on exposes the patient to potential skin maceration.

Protection of surrounding skin using a durable barrier cream, e.g. Cavilon®, or, if the skin is broken, Cavilon® No Sting Barrier Film, is very important.

Additional support may be gained by using flexible tubular bandaging (Netelast®), sports bra, or firm pants to avoid dressings sticking to the skin. (See also Table 12.1.)

Bleeding

Control of spontaneous bleeds:

- consider gentle pressure
- gauze soaked in adrenaline 1:1000
- tranexamic acid topically (+/-regular oral use for prevention of bleeding)
- topical sucralfate
- alginate dressings have haemostatic properties

Prevent trauma and hence bleeds by gentle removal of dressings with warm normal saline 0.9% or water irrigation. Alginate dressings may become a jelly-like substance and can be easily lifted off using forceps or gloved fingers. Sorbsan® dressings, made from the salt of alginic acid, become liquefied and can be washed off with sodium chloride 0.9%.

Odour

Wounds are naturally colonized with bacteria, and alteration in the balance of bacteria, particularly heavy anaerobic colonization, can cause significant odour. Patients' toleration of odour varies considerably, and there are patients who are convinced they smell bad even when reassured repeatedly that they do not.

The presence of necrotic tissue can also cause malodour and increases the risk of infection. Malodour can be the most distressing wound-related symptom for patients, particularly leading to isolation and withdrawal.

Management

- If necrotic tissue exists, consider debridement:
  - Surgical: not usually used in the palliative care population. Can be painful. Avoid if arterial bleeding risk/large wounds.
  - Mechanical, e.g. VAC dressings
  - Biological, e.g. larval therapy; occasionally can increase pain and bleeding
  - Autolytic: most common in the palliative care population. Can be slow. Occlusive moisture-retentive dressings assist, e.g. hydrocolloid: absorbs exudate on contact, forming a gel layer. Note that dressings may have brown colouring and malodour on removal. Avoid hydrocolloid dressings if there is copious exudate or if the wound is infected, as there may be a risk of skin maceration.
- Charcoal dressings—when dry—absorb odour before it reaches the air. Apply over primary absorbent dressing, prior to application of an outer adhesive dressing. Change once saturated to maintain odour control.
- Treat any infection. In the absence of infection, metronidazole intravenous solution or 0.75% gel applied topically to the wound weekly can control anaerobic colonization and reduce odour. Apply using gauze-soaked solution or filling cavity for 5–10min, then remove gauze or gently suction away fluid.
- Other topical antimicrobials can reduce odour: medical-grade honey, silver- and iodine-containing dressings, etc.

Infection

This is usually chronic and localized. The wound should be cleaned with running water or sodium chloride 0.9%. A swab should be taken and antibiotics commenced if infection is suspected, i.e.:

- if the surrounding areas are inflamed or cellulitic—not just a red rim
- if the wound is more smelly or painful, or discharging more
- if the patient is showing systemic signs of infection

The commonest organisms involved in wound contamination include coliforms, anaerobes, *Staphylococcus aureus*, and group G beta-haemolytic streptococci.

Antibiotics such as flucloxacillin, trimethoprim, and erythromicin cover the most common infections. Anaerobic infections may need to be treated with metronidazole: metronidazole topical gel can be applied daily for 7–14 days.

Table 12.1 TIME, wound bed preparation, interventions, methods, and generic products

TIME	Wound bed preparation palliative nursing	Methods and generic products
TISSUE Necrosis	Debride the necrotic tissue Consider promoting a dry scab when: life expectancy is short, multiple wounds, head and neck wounds.	Autolytic dressings—hydrogels Biological debridement—larva Mechanical—ultrasound and water Surgical—forceps scalpel (tissue viability nurse, TVN)
Granulating	Promote and protect fragile granulating tissue	Semi-occlusive dressings non-adherent (foam)
Epithelializing	Protect epithelializing cells	Low adherent moisture conserving soft silicone based
INFECTION and **I**NFLAMMATION	Debride dead tissue unless scab formation appropriate Apply antimicrobial dressings	Antimicrobial dressings may include medical honey, polyhexamethylene biguanide (PHMB)
MOISTURE	Remove exudate without drying the wound	Two-layer dressing system—low adherent primary dressing and secondary absorbent dressing, e.g. alginate or methycellulose dressing with secondary absorbent pad
EDGE	Edge of wound epithelialization will cover granulation tissue	Monitor the wound edge to ensure wound edge kept in optimal condition

Reproduced from Leaper DJ et al (2012) Extending the TIME concept: *International Wound Journal*, Volume 9, Supplement 2 pp 1–19 with permission from Wiley.

Meticillin-resistant *Staphylococcus aureus* (MRSA) is difficult to eradicate. Risk of transmission to other immunocompromised individuals means in-patients who are MRSA-infected or MRSA-colonized often require isolation precautions. Collaboration with your microbiology department, if you have access to one, is encouraged.

Psychosocial well-being

By trial and error, a combination of dressings that is tailored to be the most comfortable for the individual patient is the goal.

Patients may need different regimens for different occasions. For social occasions, for example, the avoidance of bulky unsightly dressings may be really important, but less so when not needing to go out.

Attention to detail, ensuring leak- and odour-proof appliances, and giving information and an explanation will lessen anxiety and reduce isolation, enhancing confidence and morale. Use minimal skin strapping by fixing dressings with vests, cling film, Netelast®, or incontinence pads (which may be more comfortable).

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Pruritus (itch)

Pruritus is defined as 'an unpleasant sensation that provokes the desire to scratch'.

The pathophysiology of itch is complex and depends on the cause.

Mediators, including cytokines, histamine, and neuropeptide substance P, are released from neuronal cells, which then interact with cutaneous cells, including keratinocytes, mast cells, and eosinophils.

Complications of pruritus

- excoriation +/- secondary infection
- lack of sleep
- social stigma
- interference with daily functioning
- depressive symptoms—in up to a third of patients with generalized pruritus

Assessment of the pruritic patient

- history: generalized or localized itch, exacerbating or relieving factors, drug history, past medical history
- use a measurement tool, e.g. visual analogue scale, to assess the impact on quality of life/severity and measure response to any treatment
- examination: skin integrity, dryness, and nature of any rash
- investigation: guided by history, likely cause, and potential treatment options; consider lab tests, e.g. TFTs, iron studies

Common causes (and prevalence where known) of pruritus in the palliative care population

- cholestasis (80%)—usually due to biliary obstruction; increased concentration of bile salts, histamine, progesterone metabolites, and endogenous opioids contribute to itch
- end-stage renal failure (ESRF)—(not dialysing: 30%; on haemodialysis 70–80%); uraemic toxins, altered levels of phosphate, systemic inflammation, and skin xerosis contribute
- hormone-related—thyrotoxicosis (up to 11%)
- elderly (50–70% in >70-year-olds); usually associated with skin xerosis and atrophy
- iron deficiency—even without anaemia; iron replacement can help symptoms
- iatrogenic—drug-related (e.g. penicillins, cephalosporins, sulfonamides, phenytoin, aspirin, opioids); pruritus related to opioid administration is most common when given intrathecally; intrathecal use in conjunction with local anaesthetic reduces the risk
- paraneoplastic itch—particularly common in haematological malignancies such as Hodgkin's lymphoma (30%)
- end-stage HIV (20%)
- at EOL, often multifactorial as multiple organs failing

Management of pruritus

This can be divided into general and cause-specific measures. Limited evidence exists for different systemic agents in pruritus, but specific drugs may help in specific situations.

General management

For intact skin

- ensure skin is not dry
- use soap substitute, e.g. emulsifying ointment/aqueous cream/O
- apply emollients b.d.—t.d.s. including after a bath
- avoid overheating and hot baths; bathe in cool/lukewarm water
- avoid exacerbating factors, e.g. heat, dehydration, anxiety, spicy food
- discourage scratching: short nails; allow gentle rubbing; cotton gloves at night
- consider behavioural or psychological therapies to break itch-scratch cycle
- consider aromatherapy or TENS machine therapy
- consider 1–2% menthol in aqueous cream or oily calamine lotion if itch persists

For macerated skin

- dry the skin and protect from excessive moisture
- use hairdryer on a cool setting
- apply wet compress t.d.s. and allow to dry completely
- if infected, use antifungal cream, e.g. clotrimazole
- if inflamed, use 1% hydrocortisone cream for 2–3 days
- avoid adsorbent powders, e.g. starch, talc, zinc oxide, which can be abrasive

General pharmacological measures

Consider trial of a sedating antihistamine, e.g. chlorphenamine 4mg t.d.s-12mg q.d.s. Stop if ineffective. Consider a sedative antihistamine, a benzodiazepine, or doxepin (10–75mg nocte) to help sleep.

Cause-specific management

For further information, see Xander C. et al.[1]

Cholestasis

- Treat cause if possible—for example, in biliary obstruction secondary to tumour, consider stenting of common bile duct +/– steroids, e.g. dexamethasone.
- Rifampicin (75mg o.d.–150mg b.d.) has been shown in several small RCTs to reduce itch. Colestyramine (4–16g/day) is an alternative, but is often unpalatable and ineffective in complete biliary obstruction. A small RCT showed sertraline (50–100mg/day) was effective compared to placebo.

Naltrexone, a mu-opioid receptor antagonist, effectively reduces cholestatic and uraemic pruritus, but is inappropriate in patients on opioids for pain where the analgesic benefit could be reversed.

Renal failure/uraemia

- If on dialysis: enhancing the dialysis regimen may help, and speaking with the dialysis team should be considered. Managing parathyroid hormone, calcium, and phosphate levels is easier to consider with ready access to hospital laboratory measurements.
- If localized itch: topical capsaicin cream or UVB phototherapy are options. Conflicting evidence exists regarding use of narrowband UVB phototherapy, with some small studies indicating benefit but others suggesting that this is marginal and not sustained.[2]
- Meta-analysis of small RCTs suggests gabapentin can be effective. Starting dose 50–100mg nocte or post-dialysis. Pregabalin is an alternative.
- Doxepin 10mg b.d. has also shown benefit.[3]
- Nalfurafine, a k-opioid receptor agonist, is another option. Side effects include insomnia and constipation, but have been found to be tolerable.
- Some evidence exists for erythropoietin, thalidomide, colestyramine, and oral cromoglicate sodium. However, the variety of different options underlies the great difficulty there is in relieving the symptoms of itch for many patients.

Paraneoplastic

- Treatment of underlying cancer. In itch associated with lymphoma, steroid treatment, e.g. prednisolone 10–20mg t.d.s., can be effective.
- Paroxetine has been recommended for pruritus in the palliative care population in general, based on a small RCT.[4] Start with low dose 5–10mg nocte. Benefit is usually seen within 24–48 hours. Side effects include nausea, vomiting, and sedation. Sertraline is an alternative and perhaps less likely to cause delirium in the elderly.
- Cimetidine (800mg/24 h) has been shown to be effective in case reports of patients with itch associated with Hodgkin's lymphoma and myeloproliferative disorders.

Opioid-induced

Consider antihistamines; if ineffective, opioid switch is usually necessary. Ondansetron at anti-emetic doses has been shown to be effective, probably owing to opioid interaction with 5HT3 receptor. Opioid antagonists could theoretically reduce pruritus, but may reverse essential analgesic benefit.

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Lymphoedema

Lymphoedema is an excess collection of interstitial fluid within soft tissue caused by lymphatic system disruption. It can occur in any part of the body, although usually in a limb. It is progressive and can become grossly debilitating, increasing psychological distress and reducing quality of life. In cancer, lymphatic system obstruction caused by malignancy, or by fibrosis due to previous radiotherapy or surgery, is the main cause.

Treatment aims to achieve maximum improvement and long-term control and to prevent complications developing. Its management is largely palliative in nature in that there are no treatments which can offer a cure in the majority of patients.

Success in management of lymphoedema should be seen as ensuring that patients are as little inhibited in their enjoyment of life as possible by their condition.

Full patient cooperation and treatment strategies overseen by a lymphoedema therapist (often a nurse or physiotherapist) offer the most opportunity for a good outcome.

Management

Decongestive lymphatic therapy (DLT) is gold standard management. It comprises two phases: intensive and maintenance.

- The intensive phase is indicated for those patients with moderate/severe lymphoedema and is a daily therapist-led treatment for 2–4 weeks. This phase includes manual lymphatic drainage (MLD), multilayer lymphoedema bandaging, skin care, and exercise.
- The maintenance phase focuses on self-management and includes simple lymphatic drainage (SLD), the use of compression hosiery, skin care, and exercise.

Additional management

- explanation, information, and encouragement
- scrupulous skin care
- avoidance of trauma, such as sunburn or venepuncture, to minimize infection risks
- MLD is undertaken by a skilled therapist using specialized hand movements to encourage lymph flow from congested areas to areas of normal lymphatic drainage
- SLD is a simplified form of MLD, taught to patients and carers, enabling them to self-administer this treatment
- compression pumps and intensive low-compression bandaging may also be used for slowly resolving oedema

Contraindications to compression include local extensive cutaneous metastases, truncal oedema (since fluid from a limb may be diverted to an already congested area), infection, and venous thrombosis. Caution is also warranted in impaired arterial circulation or sensation.

Chronic lymphoedema leads to changes in both subcutaneous tissue and skin, which increases the risk of infection, sometimes known as an acute inflammatory episodes (AIE). These usually present with flu-like symptoms, pain, redness, and increased swelling. Immediate administration of antibiotics is essential. Consider prophylactic cover if repeated infections.

Other therapies

- Diuretics are of limited value, unless the swelling has deteriorated due to a NSAID or systemic corticosteroid, or there is a cardiac or venous component.
- Drugs which influence capillary protein flux and filtration and reduce protein viscosity in interstitial spaces are currently under evaluation.
- Surgical techniques are rarely employed: liposuction; debulking; lymphatico-venular anastomosis (experimental).
- Subcutanous drainage of fluid using sterile needles inserted into skin: case studies suggest improved comfort, subjective volume reduction, and well tolerated.
- Kinesio taping:[1] tape is applied to skin, improving absorption and lymph flow by causing convolutions in the skin, increasing surface area of interstitial space.
- Low-level (low-powered) laser therapy[2] has been shown to reduce arm volume and pain in women with breast cancer–related lymphoedema.

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Chapter 13

Neurological problems in advanced cancer

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Local nerve damage

> Nerve endings. That's what it all comes down to. Billions of rooted synapses, like trees entwined in erratic soil. Lightning strikes every millionth of a second, the charges scattering across the gaps and down a spinal braid.
>
> Ryan Galloway, *Biome*

For spinal cord compression: ➔ see Chapter 29, Emergencies in palliative care.

Plexopathy

Definition

Plexopathy is a disorder affecting a network of nerves, commonly cervical, brachial, or lumbosacral.

Causes

- invasion or compression by tumour
- fibrosis secondary to radiotherapy
- ischaemia of small vessels
- metabolic abnormalities, for e.g. diabetes
- traumatic injury (major trauma to neck or shoulder)

Investigations

CT is useful for detecting bony abnormalities but MRI is often more helpful, if available, as it is more sensitive for structural abnormalities. Newer techniques, such as magnetic resonance neurography, are available and are useful in visualizing individual roots and peripheral nerves.

> Magnetic resonance neurography (MRN) is the direct imaging of nerves in the body using the unique MRI water properties of nerves. This technique yields a detailed image of a nerve from the resonance signal that arises from in the nerve itself rather than from surrounding tissues.

Management

Palliative radiotherapy or chemotherapy may reduce the pain if tumour is the cause, but there is rarely an improvement in function. Otherwise, appropriate analgesia, including an agent for neuropathic pain, will be necessary.

Cervical plexopathy

Clinical features

Cervical plexopathies may be due to a head or neck tumour or metastatic deposits within the lymph nodes. Pain can occur in periauricular, postauricular, or anterior regions of the neck. Pain can be referred to other areas of the face, head, and shoulder.

Brachial plexopathy

Clinical features

Patients with a brachial plexopathy often have an underlying diagnosis of lung or breast malignancy. Presentation includes pain in elbow, forearm, hand, or shoulder, followed by numbness, allodynia, muscle weakness, or atrophy. Horner's syndrome can occur.

Lumbosacral plexopathy

Clinical features

Symptoms depend on exact anatomical sites affected. Lumbosacral pain radiating into the legs is common. If sacral plexus is involved, bowel and bladder dysfunction can occur.

Paraneoplastic neurological syndromes

Definition

In patients with malignancy, paraneoplastic neurological syndromes are a group of disorders affecting the nervous system that are not caused by metastases, metabolic or nutritional deficiencies, infections, or side effects of cancer treatment.

These syndromes were first described by Guichard and Vignon in 1949 upon the study of three patients with metastatic neuropathies. On autopsy they discovered no malignant cells in the spinal cord or nerve roots of these patients. Guichard and Vignon coined the term 'paraneoplastic' to describe this group of disorders. The term was extrapolated to other non-neurological complications associated with, but not directly caused by, malignancy.

Pathogenesis

- differs amongst conditions, but involves antibody and T-cell responses against the nervous system
- antibodies identified target either intracellular neuronal proteins or neuronal cell surface and synaptic proteins
- some antibodies are associated with specific paraneoplastic disorders (although are not necessarily diagnostic for underlying malignancy, as they can occur in a non-paraneoplastic context), e.g.:
  - voltage-gated calcium channel antibodies in Lambert–Eaton myasthenic syndrome (LEMS)
  - acetylcholine receptor antibodies in myasthenic syndrome
  - NMDA receptor antibodies in anti-NMDA receptor encephalitis
- syndromes can occur as a presenting feature before the diagnosis of cancer is made
- the commonest implicated cancers include small-cell lung cancer (SCLC) (30%), breast and ovarian cancer, and lymphoma

Common neurological paraneoplastic disorders

Peripheral neuropathy

This can present with involvement of the distal sensory and/or motor or autonomic nerves. Common cancers associated with peripheral neuropathies include lung cancer and multiple myeloma. Neuropathies are also associated with monoclonal gammopathy, and a number of patients with this constellation of conditions will go on to develop a haematological malignancy.

Cerebellar degeneration

This disorder is most commonly associated with SCLC, gynaecological and breast cancers, and Hodgkin's lymphoma. It may present rapidly, sometimes before the primary tumour becomes apparent. Symptoms include ataxia, diplopia, dysarthria, and dysphagia. Early in the disease MRI may be normal, but over time reveals cerebellar atrophy. Treatment involves targeted treatment of the underlying malignancy. There are some case reports suggesting potential benefit from immunotherapy.[1]

Lambert-Eaton mysathenic syndrome (LEMS)

LEMS is a disorder of neuromuscular transmission occurring in 3% of patients with small-cell lung cancer, who account for the majority of cases. In patients presenting with LEMS, 50% will have an underlying malignancy, most commonly SCLC. It is a presynaptic deficit in neuromuscular transmission caused by a reduction in the amount of acetylcholine released at the motor nerve terminal.

There is evidence of an autoimmune aetiology, with the presence of autoantibodies to calcium channels at the neuromuscular junction. Common symptoms include proximal muscle weakness, particularly of the legs, and an associated waddling gait. Fatigue, diplopia, ptosis, and dysarthria may also be problems. Autonomic dysfunction is common, resulting in erectile impotence and dry mouth. Unlike classical myasthenia, weakness may be improved by repetitive activity; there is a poor response to edrophonium. Symptoms may improve with treatment of the underlying malignancy.

Limbic encephalitis

Limbic encephalitis occurs with inflammation of the limbic system of the brain. This can result in sleep disturbance, seizures, hallucinations, and memory loss. Cancers more commonly associated with limbic encephalitis are SCLC, testicular germ-cell cancer, thymoma, Hodgkin's lymphoma, and teratoma. MRI commonly reveals abnormal, hyper-intense signals in the temporal lobes.

Identifying antibodies can help during diagnosis and in some cases can aid towards treatment plans; for example, for those with SCLC and limbic encephalitis, prognosis is worse in those with anti-Hu antibodies. Those with anti-Ma2 antibodies can have encephalitis involving the hypothalamus, brainstem, and limbic system. This can result in a different presentation with symptoms of narcolepsy, hyperphagia, and excessive daytime sleepiness.

Other clinical presentations

Other presentations include, but are not limited to, the following:

- dementia
- opsoclonus-myoclonus syndrome (OMS)
- necrotizing myelopathy

Corticosteroid-induced proximal myopathy

- Corticosteroid-induced proximal myopathy can occur within a few weeks of starting dexamethasone—usually doses of 8–16mg a day.
- Patients experience difficulty in rising from a sitting position and in climbing stairs.
- Disabling symptoms may not be readily volunteered; direct questioning may be needed. Management includes reducing the dose of steroid to the minimum possible and considering a change to prednisolone, which may not cause as much muscle wasting (but is associated with more fluid retention).
- Weakness should improve in 3–4 weeks of steroid withdrawal.

Drug-induced movement disorders

- Certain drugs may induce extrapyramidal symptoms and signs.
- They include akathisia (motor restlessness in which the patient frequently changes position or paces up and down if able), dystonia, and parkinsonism.
- Implicated drugs are those which block dopamine receptors, such as antipsychotics (particularly haloperidol and the phenothiazines) and metoclopramide.
- Antidepressants and ondansetron may also cause problems.
- ❗ All these drugs should be avoided as far as possible in patients with Parkinson's disease.

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Convulsions and seizures

Descriptions of seizures and epilepsy have been found throughout history. In 'On Sacred Disease', written in 400 BC, Hippocrates challenged the previously held view that seizures originated from a magical or religious source.

Although Hippocrates' descriptions did not accurately explain what we commonly know now as the underlying pathophysiology, he shifted the discussion to understand that the origin of the disease was the body itself and not a result of divine intervention.

Common causes of seizures in palliative care include the following:

- brain tumour (primary or secondary)
- biochemical disturbance (e.g. severe hyponatraemia)
- previous cerebrovascular accident
- long-standing epilepsy

Partial seizures rarely last more than a few minutes. A tonic-clonic seizure can last longer and develop into a distressing event for family particularly.

If a patient develops a generalized convulsive seizure lasting ≥5 minutes or has ≥2 discrete seizures between which there is incomplete recovery, they need to be treated rapidly. This includes initial emergency assessment and treatment with benzodiazepines to terminate the seizure.

- midazolam 5–10mg buccal/SC or slow IV (dilute 10mg with water to 10mL) and repeat after 15 and 30 minutes if seizure has not terminated; a number of alternative benzodiazepines can be used:
  - lorazepam 2–4mg slow (no faster than 2mg/minute) IV or sublingually (IV dose can be repeated after 2min if no response)
  - diazepam solution 10mg p.r. or emulsion 2–10mg slow IV
  - clonazepam 1mg slow IV (into large vein)

If the patient has not responded to a repeated dose of benzodiazepine or seizures recur, consider:

- phenobarbital 100mg IM or IV after diluting 1 in 10 with water for injection
- repeat phenobarbital if necessary and set up a syringe driver with phenobarbital 200–600mg SC over 24h
- once seizures have been controlled, review anticonvulsant therapy

General notes

- For patients with intracranial tumours, consider starting, or review dose of, corticosteroids.
- Remember to advise the patient about restrictions on driving and to contact the DVLA.
- Consider parenteral thiamine if alcohol abuse is suspected.
- Consider and treat hypoglycaemia in at-risk patients.
- Consider drug interactions that alter anticonvulsant levels (e.g. steroids).
- Consider electrolyte abnormalities that may precipitate seizures, e.g. for hyponatraemia.

Initiating anti-epileptic drugs (AEDs)

- It is usually appropriate to initiate anticonvulsant therapy after one seizure in patients with terminal illness.
- Sodium valproate is an appropriate first-line anticonvulsant for almost all types of convulsions or seizures, including focal and partial seizures, and those caused by intracranial tumours. Levetiracetam is used when traditional first-line treatments are ineffective or unsuitable.
- Be aware that some AEDs have the potential to interact with some chemotherapeutic agents.[1]
- Some drugs commonly used in palliative care, such as levomepromazine and haloperidol, may lower seizure threshold.
- Aim to increase the dose to the lower end of the quoted 'usual maintenance dose' unless side effects occur or the patient is frail and elderly (doses given in following).

Patients unable to take oral medication

- Patients who are unable to take oral medication owing to dysphagia or vomiting, or because they are in the terminal stages, may need to be given anticonvulsants by another route.
- The half-life of most anticonvulsants is quite long (>24h), therefore no parenteral anticonvulsant is usually needed if there is a low risk of seizures, **and** only a **single dose** is missed.
- **The risk of seizures is higher if the patient:**
  - has decreased or stopped steroids (intracranial tumours)
  - has increasing headache, vomiting, or other signs, suggesting rising intracranial pressure (intracranial tumours)
  - exhibits myoclonus or other twitching
  - has a history of poor seizure control or recent seizures
  - has previously needed more than a single anticonvulsant to achieve control
  - is on other medication that may affect seizure threshold
- Because of the long half-life of anticonvulsants, parenteral treatment can be started at any time within 24h after the last oral dose.

Choice of non-oral anticonvulsant

Choice of non-oral anticonvulsant may be determined partly by availability (see Table 13.1).

Management of seizures at home

Most seizures are self-limiting and require only supportive care. For more prolonged seizures occurring at home, a number of measures can be arranged in anticipation, which can avoid inappropriate emergency admission to hospital.

- diazepam rectal solution 10mg p.r.—administered by district nurse or carer
- midazolam 5–10mg SC (or preferably IM)—administered by district nurse
- midazolam buccal 10mg/2mL can be administered by a carer if the rectal route for diazepam is unacceptable: it appears to be as effective and may be quicker-acting than rectal diazepam 10mg. Buccal and oral solutions are available or the injectable preparation can be used.

In an inpatient unit, midazolam 5–10mg SC (or preferably IM) may be given first before treating status epilepticus as earlier.

Table 13.1 Choice of non-oral anticonvulsant

Phenobarbital CSCI or daily SC	Well-proven anticonvulsant for all types of seizures. Experience suggests it is effective in doses of 200–600mg/24h. Phenobarbital is incompatible with most other drugs in a syringe driver; therefore a second syringe driver may be necessary. Stat doses of 100mg SC or IM can sting.
Midazolam CSCI	Midazolam is more useful as a sedative than as an anticonvulsant. Anticonvulsant efficacy of 'standard' doses is unknown, but probably requires 20–30mg/24h min. Unlicensed use. If low risk of seizures, and midazolam indicated for, for example, terminal agitation, then additional anticonvulsant probably unnecessary. If higher risk of seizures, use phenobarbital in addition.
Clonazepam CSCI	Main advantage is that clonazepam is compatible with many other drugs used in CSCI. Much less experience supporting its use in this way; doses recommended: 2–4mg/24h (4–8mg/24h if sedation acceptable or desired).
Carbamazepine or sodium valproate suppositories	Occasionally suitable for patients well-controlled on one of these drugs who develop a temporary inability to take oral medication (e.g. vomiting and who would find rectal administration acceptable).
Levetiracetam	Commonly used as a second-line oral agent, it has been used off-licence in a subcutaneous form in the palliative care setting for those who can no longer swallow. Some case studies have suggested potential benefit.[2, 3]

Non-convulsive status epilepticus

Non-convulsive status epilepticus (NCSE) is a possible cause of confusion or delirium in terminally ill patients. The clinical presentation varies from altered mental status to comatose patients, without visible convulsions. In comatose patients, unilateral tonic head and eye movement is often observed. Other symptoms include myoclonic contractions of the angle of the mouth, mild clonus of an extremity, or, rarely, epileptic nystagmus. EEG is the most important diagnostic tool to identify epileptiform activity. Treatment should be initiated following a stepwise model (e.g. phenytoin, sodium valproate, levetiracetam, together with benzodiazepines), avoiding intubation and transferral to the intensive care unit. Although mortality rates are high, in some patients NCSE can be reversed by treatment.

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Anticonvulsants

see Chapter 5, Principles of drug use in palliative care.

Carbamazepine and phenytoin levels are decreased (risk of fits) by corticosteroids. Carbamazepine, phenytoin, and phenobarbital can reduce the efficacy of corticosteroids.

This two-way interaction is common when managing patients with cerebral tumours. Carbamazepine, phenytoin, and phenobarbital plasma levels are also reduced by St John's wort (risk of fits).

Sodium valproate

- tabs, m/r tab, granules, liquid, injection available
- dose: start with 100–150mg m/r b.d.
- if necessary, increase by 150–200mg b.d. every 3 days
- usual maintenance dose 1–2g/24h; max 2.5g/24h in divided doses; suppositories available as special orders

Carbamazepine

- available as tabs/chewtab/liquid/supps
- dose: 100mg b.d. p.o.
- increase from initial dose by increments of 100mg every week; usual maintenance dose 0.8–1.2g/24h in two divided doses; max 1.6–2g/24h; equivalent rectal dosage: 125mg p.r. ≅ 100mg p.o.
- carbamazepine has numerous drug interactions—e.g. levels are increased (risk of toxicity) by clarithromycin, erythromicin, fluoxetine, and fluvoxamine

Phenytoin

- available as tabs/chewtab/liquid/caps/IV injection
- initially 3–4mg/kg/day with subsequent dosage adjustment if necessary; usual maintenance dose: 300–400mg daily; max 600mg/24h; single or two divided doses
- phenytoin levels are increased (risk of toxicity) by clarithromycin, metronidazole, trimethoprim, fluconazole, miconazole, omeprazole, fluoxetine, fluvoxamine, aspirin, diltiazem, nifedipine, and amiodarone
- because phenytoin has a very long and variable half-life, it can take several days and even up to 3–4 weeks for changes in dosage to take complete effect: this should be borne in mind in determining the interval after dosage is altered before measuring the plasma phenytoin concentration again

Levetiracetam

- available as tabs/granules/oral solution, IV injection or infusion
- start 250mg b.d., increasing stepwise by 250mg b.d. to a maximum dose 1.5mg b.d.
- can be given via CSCI using equivalent p.o. 24hr dose; use water or sodium chloride 0.9% as diluent
- levetiracetam is widely used in addition to phenytoin or sodium valproate, but it may also be used alone; no interactions with other antiepileptic drugs or other drugs have been reported

Barbiturates

Phenobarbital (phenobarbitone)

- p.o./IM/IV/CSCI
- avoid SC stat doses—can cause skin necrosis
- can be given undiluted IM; dilute adequately before giving IV or CSCI
- phenobarbital is a barbiturate with both sedative and anticonvulsant effects; rarely used nowadays as a first-line anticonvulsant, as it is too sedative.
- doses: see earlier

Benzodiazepines

Midazolam

- Inj: 1mg/1mL, 2mg/1mL, 5mg/1mL. ❗ Caution is needed to avoid confusion.
- typical starting dose 10–20mg/24h CSCI
- oromucosal solution (prefilled oral syringe) 5mg/mL, 2.5mg, 5mg, 7.5mg, and 10mg
- sedative effect markedly enhanced by itraconazole, ketoconazole, and possibly fluconazole

Lorazepam

- tabs: 1mg (oral or sublingual use), 2.5mg inj: 4mg/1mL
- dilute inj with an equal volume of water or saline for IM use

Diazepam

- tabs: 2mg, 5mg, 10mg; oral solution: 2mg/5mL, 5mg/5mL
- rectal tubes: 5mg/2.5mL, 10mg/2.5mL; supps: 10mg
- inj: (emulsion) 10mg/2mL (Diazemuls®)—IV use only
- inj: (solution) 10mg/2mL— IM use

Clonazepam

- tabs: 500mcg, 2mg; inj: 1mg/1mL
- starting dose: 1mg nocte
- increase gradually to usual maintenance dose of 4–8mg/24h; oral solutions in various strengths available from several sources

Further reading

Books

Back I. (2001) *Palliative Medicine Handbook* (3rd edn). Cardiff: BPM Books.

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Chapter 14

Palliation of head and neck cancer

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Basic epidemiology and pathology

Head and neck cancer makes up about 4% of all cancer cases and deaths in the UK. It is more common in France, Italy, Poland, Thailand, and the Indian subcontinent. About 50% of patients overall are cured. Although 50% die of their disease, mortality varies widely according to site, histology, stage at diagnosis, and degree of tumour differentiation. Most patients who survive 2 years without recurrence are likely to be cured. Second primaries are very common, occurring in around one in eight patients. The effects of second primaries on prognosis are often dire. Second primaries may be due to the following:

- field change: carcinogens produce widespread epithelial changes, which easily develop into malignancy
- clonal expansion and migration of malignant cells
- common aetiological factors include:
  - smoking
  - alcohol: these two factors have synergistic and dose-related effects[1]
  - HPV (human papilloma virus): HPV accounts for 46% of oropharyngeal, 24% of oral, and 22% of laryngeal cancer. The proportion of HPV-associated oropharyngeal cancers has increased from 40% to 72.2% in the last decade, but the proportion of HPV-related non-oropharyngeal cancers has remained stable.[2] The rise in HPV accounts for an increase in oropharyngeal cancer in young patients. The effect may be synergistic with smoking and alcohol.
- tumours at particular sites also have local risk factors:
  - betel nut chewing, vitamin deficiencies for oral cancer
  - nickel, chromate, hardwood dusts: for airway tumours
  - viruses: Epstein–Barr virus for nasopharyngeal carcinoma
  - iron deficiency: Patterson-Brown-Kelly syndrome (iron deficiency, koilonychia, glossitis, upper oesophageal web) are associated with postcricoid carcinoma
  - familial: increased risk of head and neck squamous cell carcinoma (HNSCC) if there are two or more first-degree relatives with HNSCC

Histology

- most tumours are squamous cell carcinomas
  - often moderately chemosensitive but not curable with chemotherapy
  - tend to develop hypercalcaemia, usually due to the secretion of parathyroid hormone-related peptide (PTHrP)
- less common tumours: adenocarcinomas, adenoid cystic carcinomas (salivary glands), anaplastic carcinomas, lymphomas, melanomas of the mucosa, and other rare tumours

Staging

Squamous cell carcinoma tends to progress from local disease, along lymph node levels in a stepwise manner, to distant disease quite late. This allows staging for radical treatment with treatment of the important lymph node groups, e.g. radical neck dissection. Treatment has now improved such that the cause of death is changing: as local control has

improved, distant metastases are the cause of death in perhaps one-third of patients and are found in many others. This has obvious implications for the likely problems to be encountered and the management of the terminal phase.

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The patient with head and neck cancer

Many patients with head and neck cancer will have a history of heavy alcohol and tobacco use. Those with a history of heavy alcohol intake may also have inadequate coping strategies, poor family and social networks to fall back upon, and sometimes very damaged close relationships. Understandably, the psychological toll can be considerable. All this has to be kept in mind during assessment, rehabilitation, and discharge planning, as well as the provision of psychosocial support to the patient and their family to help them cope with possible severe disfigurement, communication problems, and often frightening potential complications such as severe airway obstruction or bleeding. They need explanation, sensitively given information about the likely future, and special care for isolated relatives, young children, and those with severe health or other problems of their own.

Possible psychiatric complications

- Adjustment reactions (anxiety, depressive reactions, or mixed states) can occur around surgery or other treatment, as well as when function alters rapidly in advanced disease. Adjustment reactions are more common and more severe if severe disfigurement or communication problems are anticipated. They often settle with time, particularly in a supportive environment, but they need active management if severe.
- Depression has been found in over half the patients with advanced disease, and is a negative prognostic factor in oropharyngeal cancer. Counselling and antidepressants may be needed.[1, 2]
- Suicidal ideation: the suicide risk is said to be considerably higher than with other cancers (three times that of the general population in a recent study).[3] Professional psychiatric assessment (by a psychiatrist or social worker) should be sought. Uncontrolled pain is a major risk factor.
- Anxiety may be related to fears that one's airway is about to close off, or of an impending serious bleed or other catastrophe. The underlying fears, if any, need to be addressed. Always explain, and also consider counselling, cognitive therapy, relaxation training, and anxiolytics.
- Alcohol withdrawal can cause confusion and agitation. Detoxification, often under benzodiazepine cover, may be necessary.
- Sleep disturbance is common and severe.[4]

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Tumour treatment: implications for the palliative stage

Head and neck tumours can be treated by surgery, radiotherapy, or chemotherapy.[1]

Treatments

Surgical treatment

Surgical treatment operates on the principle that HNSCC spreads in an orderly manner through successive lymph node groups, so bloc dissection—taking out tumour, nodes, and intervening lymphatics—will control disease. Excision of structures invaded by tumour may be needed. Therefore, major reconstruction is frequently required. Cervical nodal metastases are found in 40% of patients with HNSCC at diagnosis. Surgery remains the primary treatment of choice for most oral cavity, salivary gland, thyroid, nasal, paranasal sinus, skull base, and skin tumours and sarcomas.

Radical neck dissection

Removes all the nodes on the side of the tumour, the sternomastoid, internal jugular vein, and spinal accessory nerve, which supplies the trapezius and sternomastoid. This is effective but disabling, and more limited forms of neck dissection are now employed when appropriate,[2] often associated with radiotherapy or chemotherapy. Damage to the axillary nerve can result in the 'shoulder syndrome'.

Radical radiotherapy

Radical radiotherapy often retains function better than surgery, but it has side effects: mucositis, dry mouth (xerostomia), tissue fibrosis, and complications to other organs within the radiotherapy field, e.g. the spinal cord. Radiotherapy can be given by external beam or brachytherapy (radioactive implants, e.g. needles in the tongue). Various fractionation regimens are used. In addition, radiotherapy can be given preoperatively (neoadjuvant), post-operatively (adjuvant), or as an accompaniment to chemotherapy. Here it can sterilize small neck nodes or those from certain tumours (nasopharynx, thyroid) effectively. Modern techniques such as intensity-modulated radiotherapy (IMRT) significantly reduce damage to surrounding tissue and thus complications.[3]

Palliative radiotherapy

Palliative radiotherapy can address various problems, such as bone pain, dysphagia, and stridor from paratracheal nodes, as well as bleeding or infection from fungating tumours.

Chemotherapy

Chemotherapy is potentially curative in some tumours, e.g. lymphomas, but never in HNSCC. However, adjuvant or neoadjuvant chemotherapy has a place alongside surgery and radiotherapy.

Chemoradiotherapy

Locally advanced squamous cell carcinomas of the head and neck (oral cavity, pharynx, larynx) respond better to cisplatin-based (and more recently less toxic gemcitabine-based) chemoradiotherapy than to radiotherapy alone,[4] and are an alternative to surgery for less fit patients.

Immunomodulators

Epidermal growth factor is overexpressed in most head and neck squamous cell carcinomas, and this is associated with poorer prognosis. The role of cetuximab, erlotinib, gefitinib, and other immunomodulators, especially in conjunction with radiotherapy, is being developed.

Some notes on specific tumours, with emphasis on advanced disease

Oral cavity tumours

- anterior two-thirds of the tongue
- lips
- buccal mucosa
- alveoli of the teeth
- hard palate
- floor of mouth
- retromolar trigone

These are the most frequent head and neck cancers. They are usually well-differentiated SCC, but tumours of minor salivary gland origin are also seen. Spread is predominantly local and to nodal groups in a stepwise manner. Larger tumours are more likely to have spread and have a poor prognosis. Midline tumours metastasize quickly to deeper cervical nodes. Anterior tongue carcinomas tend to spread or recur despite adequate primary treatment.

Oral tumours can initially be treated with surgery, with or without radical neck dissection. Radiotherapy causes less functional impairment, but mucositis and xerostomia are invariable. Dental care is essential with radiotherapy: dental sepsis can contribute to osteoradionecrosis. Late disease or treatment may cause dysarthria, dysphagia (if the tongue is not mobile), and local ulceration and extension. A third of patients with tongue tumours develop multiple primaries.

Carcinomas of the sinuses

Paranasal sinus tumours (maxillary, ethmoid, frontal, sphenoid) are commonly well-differentiated SCC. They present late with local swelling, pain, ocular symptoms if the orbit is involved, and nasal or palatal extension with dental symptoms. Treatment is a combination of surgery and radiotherapy.

Salivary gland tumours

Malignancy is likely if a parotid mass is associated with:

- facial palsy
- a salivary gland mass that is rapidly growing, hard, and infiltrative

Adenoid cystic carcinoma is the commonest salivary cancer. It is slow-growing and ulcerative. The tumour spreads along perineural sheaths, with the potential for neuropathic pain (squamous cell carcinoma also spreads perineurally, although slightly less often). It also infiltrates marrow cavities, so X-rays may miss its true extent.

Adenocarcinomas often have a relatively good prognosis because of their differentiation.

Squamous cell carcinomas are more aggressive, cause pain, and metastasize early. They are more often metastatic than primary.

Undifferentiated carcinomas progress rapidly, and may mimic sarcomas.

A small proportion of pleomorphic adenomas become malignant.

Management is usually surgical, with radiotherapy for residual or recurrent disease, high-grade tumours, or lymphomas.

Malignant melanoma

Malignant melanoma is commonest on the hard palate, but also occurs on lower jaw, lips, tongue, and buccal mucosa. It is infiltrative and metastasizes early to lymph nodes. It often ulcerates and bleeds.

Carcinoma of the larynx

Carcinoma of the larynx may present with voice changes, dysphagia, or stridor.

Glottic (vocal cord) carcinoma is the most common. Nodal metastases occur late. The main determinant of prognosis is the T stage. Initial treatment consists of radiotherapy or surgery. Combined radiosurgical or radiochemotherapeutic approaches are often needed in cases of advanced disease.

Supraglottic carcinoma presents late, with vague dysphagia, referred ear pain, or cervical lymphadenopathy; hoarseness may signify involvement of the vocal cords or adjacent structures. Progression is by local extension (to the oropharynx, especially posterior third of the tongue, hypopharynx, or glottis) or lymph node spread. Treatment is commonly by radical radiotherapy, and addition of chemotherapy can confer a survival advantage; surgery has to be radical (total laryngectomy[5]), but must be used in certain settings, e.g. airway obstruction. Radical neck dissection may be warranted. Restoration of the voice has to be considered after total laryngectomy. Various forms of partial laryngectomy have been developed.

Subglottic carcinomas are rare but highly invasive. Pyriform fossa tumours behave like supraglottic tumours and have a poor prognosis. Postcricoid tumours may be associated with iron deficiency (Patterson-Brown-Kelly syndrome) and invade the hypopharynx circumferentially. Radiotherapy, radical surgery (sometimes very radical), and chemotherapy have a role in management, depending on the exact site and stage.

Carcinomas of the pharynx

Carcinomas of the pharynx are usually squamous cell carcinomas, though lymphomas are fairly common, especially for the tonsils and nasopharynx.

Nasopharyngeal carcinomas cause nasal obstruction, epistaxis, and otitis media from eustachian tube obstruction. Lower cranial nerve palsies from base of skull extension, or third, fifth, and sixth nerve palsies from cavernous sinus invasion, signify advanced disease. Growth into the posterior orbit also takes place. These may spread haematogenously. Tumours are often anaplastic. Radiotherapy is the treatment of choice. Unusually for head and neck cancers, irradiation of the neck is as effective as radical neck dissection, though very occasionally may cause damage to the upper spinal cord. Xerostomia is common from salivary gland irradiation. Chemotherapy is sometimes very effective. Late recurrences (over 2 years) can be retreated.

Oropharyngeal carcinomas frequently present late. They produce dysarthria dysphagia, pain, and risk of aspiration. Radical radiotherapy is usual, often in conjunction with chemotherapy, but extensive surgery with radical neck dissection followed by RT may be indicated in locally advanced disease.

Hypopharyngeal carcinomas are uncommon but have a poor prognosis as they occur in a silent area with late diagnosis. Aggressive treatment has to be used judiciously.

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Pain

Pain is widely prevalent in head and neck cancer, particularly in those with advanced disease. With the complex anatomy of the head and neck, diverse anatomical structures are compressed or invaded by tumours in a small space (see Table 14.1). Thus, pain is often mixed somatic (bone, muscle, skin) and neuropathic, and treatment may need to combine the following:

- opioids
- NSAIDs
- antidepressants, anticonvulsants, etc., for neuropathic pain
- other drugs
- non-pharmacological techniques

Sources of pain in cancer of the head and neck

- local infiltration with tumour, e.g. ulceration, infection
- vascular and lymphatic occlusion producing oedema, lymphoedema, and sometimes pain
- bone invasion or extension of soft tissue infection causing osteomyelitis
- nerve involvement or pressure: adenoid cystic carcinoma in particular (but to a lesser extent most head and neck tumours) can show perineural invasion and extension
- referred pain is very common, e.g. earache from most structures in the face, neck, and mouth
- treatment-related, e.g. chemotherapy- or RT-induced mucositis[1]

Approach to pain assessment

- Take a detailed pain history, with special emphasis on character, exacerbating factors, and accompanying dysfunction; functional disturbances need treatment in their own right—they are distressing and disruptive to the patient.
- Examine the head and neck for masses and deformities.
- Check the movement of involved joints.
- Carry out a cranial nerve assessment.
- Radiology or other tests may elucidate the cause of pain.

Further pain management options

- Tumour mass reduction by surgery, radiotherapy, or chemotherapy is usually the best way of reducing pain.
- Radiotherapy is particularly useful for bone metastases, e.g. base of skull
- Steroids, e.g. dexamethasone 4–8mg p.o. daily, may contribute to analgesia by reducing swelling inside restricted fascial spaces; they are also useful temporizing measures while effective doses of other neuropathic analgesics are built up; doses are then usually able to be tailed off gradually.
- Antibiotics can relieve pain by reducing pressure in tight fascial compartments or by controlling osteomyelitis.
- Nerve blocks are often difficult owing to the distorted anatomy following disease or treatment.

Table 14.1 Specific pain syndrome

Syndrome	Location, features	Causes	Notes
Shoulder syndrome	Pain in shoulder, difficulty with certain movements, e.g. putting on jacket	• Radical neck dissection (due to axillary nerve sacrifice/damage)	Patient can only abduct arm to 75° and flex arm to 45°
Trigeminal neuralgia-like syndrome V_n	Lancinating, continuous/paroxysmal. Distribution of Va, Vb, and/or Vc, not crossing midline, though very occasionally bilateral	• Middle/posterior fossa tumours • Base of skull metastases • Meningeal metastases	Trigger areas or activities such as chewing, talking, breeze of air. May be accompanied by neurological signs ± diplopia, dysarthria, dysphagia, headache
Glosso-pharyngeal neuralgia	Severe unilateral paroxysmal pain in throat, or beneath the angle of the jaw, may radiate to ear, often precipitated by swallowing	• Meningeal metastases • Disease around jugular foramen • Local disease around the base of the tongue or oropharynx	Occasionally associated with syncope or postural hypotension
Jugular foramen syndrome	Pain occiput to vertex, ipsilateral shoulder, or neck	• Base of skull metastases[2] • Meningeal metastases	Horner's syndrome, lower cranial nerve signs ± local tenderness Worse on head movement
Clivus syndrome	Vertex headache worse on head flexion. ± cranial nerves VI–XII signs	• Base of skull metastases • Meningeal metastases	
Orbital syndrome	Retro-orbital/frontal headache	• Orbital metastases • Meningeal metastases • Metastases around sella turcica, with sphenoid bone or cavernous sinus invasion	± Diplopia, visual loss, proptosis, extraocular nerve palsies
Sphenoid sinus metastases	Bifrontal headache radiating to both temples, intermittent retro-orbital pain	• Base of skull metastases: sphenoid sinus • Meningeal metastases	± Nasal stuffiness, diplopia, cranial nerve VI palsy
Occipital condyle invasion	Severe occipital pain exacerbated by movement	• Occipital condyle invasion	± cranial nerve XII palsy

Mouth problems in head and neck cancer

Apart from disease and therapy, other contributory factors to mouth problems include the following:

- smoking and alcohol
- dry mouth: medication, treatment, dehydration
- poor dental hygiene—made difficult by, for example, intraoral mucosal tenderness or friable tumour
- infection and bleeding from fungating tumours
- trismus, restricting mouth opening
- vitamin deficiencies associated with poor nutrition
- underlying osteomyelitis

Dry mouth is extremely common, due to:

- radiotherapy involving salivary glands
- antimuscarinic drugs, opioids
- blocked nose leading to open-mouth breathing
- dehydration, including diuretics
- some immunomodulators, e.g. sorafenib

Xerostomia can lead to decreased taste perception and poor appetite; food becomes more difficult to swallow, and intraoral infections and dental caries become much more likely.

Management of xerostomia

- dental hygiene: may occasionally require specialist advice
- adequate hydration
- general measures, e.g. sucking on fruit drops, pineapple chunks
- synthetic salivas, e.g. Saliva Orthana: little evidence of effectiveness in these circumstances
- simple sialogogues, e.g. Salivix® tablets
- pilocarpine tablets[1] or eye drops instilled in the mouth: but can induce sweating or gastrointestinal complaints
- treat underlying causes when possible

Dribbling

Dribbling usually indicates either a problem with swallowing saliva or a mass in the mouth, such as an infected fungating tumour. It is also associated with poor lip closure, as in facial palsy, and with postural changes from neck weakness from accessory nerve damage by the tumour. This is managed by antimuscarinic drugs (e.g. transdermal or sublingual hyoscine), tricyclic antidepressants, and occasionally surgery. Antimuscarinics greatly increase the risk of confusion. Drugs that do not cross the blood-brain barrier (e.g. hyoscine butylbromide, glycopyrronium) should be chosen in those at special risk of such confusion.

Sticky, viscous saliva

Sticky and viscous saliva is common and under-reported. It is a frequent complication of radiotherapy, as serous salivary glands are more sensitive to its effects than the mucous glands. Antimuscarinics, apart from reducing the volume of saliva, also render it more viscous. Beta-blockers can make

saliva looser, as can hydration. Antibiotics for intraoral infections as well as frequent, meticulous oral hygiene help. Carbocysteine is used by some, although there is no published evidence of its usefulness in this context.

Mucositis

Mucositis usually follows radiotherapy or chemotherapy with certain agents, e.g. fluorouracil, methotrexate, or cyclophosphamide. There are reports of a reduction of mucositis by treating intraoral infections.

A number of prophylactic measures have been studied:

- sucralfate reduces mucositis severity
- reasonably good evidence for cryotherapy (ice chips) and keratinocyte growth factor
- weaker evidence for prophylactic aloe vera, amifostine, intravenous glutamate, granulocyte-colony stimulating factor, honey, laser, and antibiotic lozenges containing polymixin, tobramycin with amphotericin

Treatment of established mucositis usually requires a combination of oral analgesics and topically applied local anaesthetic agents or anti-inflammatories.[3] Benzydamine, an anti-inflammatory with local anaesthetic properties, is often used as a mouthwash, and has been claimed to reduce the duration of mucositis, as has sucralfate. However, a recent Cochrane review shows that neither of these drugs is effective. Low-level laser treatment and morphine were found to be effective for mucositis pain. However, it needs to be kept in mind that many of these studies were done in other contexts, and may not work in patients with head and neck cancer.

References

1. Cheng CQ, et al. (2015) Efficacy and safety of pilocarpine for radiation-induced xerostomia in patients with head and neck cancer: a systematic review and meta-analysis. J Am Dent Assoc. 147(4), 236–43.
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3. Clarkson JE, Worthington HV, Furness S, McCabe M, Khalid T, Meyer S. (2010) Interventions for treating oral mucositis for patients with cancer receiving treatment. Cochrane Database Syst Rev., Issue 8. Art. No.: CD001973.

Tracheostomy

Tracheostomies:
- relieve respiratory obstruction
- reduce anatomical dead space, improving respiratory failure
- aid removal of respiratory secretions
- can protect the airway in aspiration
- allow prolonged artificial ventilation with less trauma to the airways

Bypassing the nose and upper pharynx also impacts on the following:
- patient's voice
- warming and humidification of inspired air
- filtering function of the nose
- first line of the immune response: the tonsils
- the narrower bore of the tracheostomy tube compared to the natural airway increases airways resistance
- tracheostomies impair swallowing performance

To prevent drying and damage to the tracheal mucosa, an increase in sputum production, and tracheal or lung infection, the nasopharyngeal functions need to be compensated for by good tracheostomy care.

Types of tracheostomy

Most tracheostomies seen in palliative care will be established surgical tracheostomies, and this section concentrates on these. For percutaneous tracheostomy, used mostly in intensive care for airways management, and for the management of new surgical tracheostomies, refer to appropriate ENT texts.

A guide to types of tracheostomy tube

It is crucial to know what type of tracheostomy tube you are dealing with:

Metal or plastic: metal is less irritant, but is rarely used as prolonged intubation with plastic tubes is now possible. Metal tubes interfere with CT and MRI scans and radiotherapy.

Cuffed or uncuffed: an inflatable cuff at the lower end of the tracheostomy tube seals air leaks around the tube. This permits artificial ventilation and protects the airway if there is a risk of aspiration. However, prolonged cuff inflation causes ischaemic damage to the tracheal wall. Prevention requires frequent pressure checks (generally keeping a pressure of 25–34cm H_2O, as far at the lower end of this range as is safe) and periods of cuff deflation. Apart from some high aspiration risk patients, all patients seen in general wards, palliative care settings, or the home environment are almost certain to have uncuffed tubes.

NB: Please also consult your local NHS Trust guidelines.

Four essential warnings about cuffed tubes

1. For resuscitation, the cuff must be inflated for bag ventilation to be effective. In most palliative care patients, of course, resuscitation may be inappropriate.
2. If the tracheostomy is occluded, e.g. by secretions or a decannulation cap, and the balloon is inflated, the airway will be totally blocked

and the patient will suffocate. Open the cap, deflate the balloon, or remove the tracheostomy tube immediately.
3. Speaking valves should, in general, not be used with cuffed fenestrated tubes as the extra resistance increases the work of breathing considerably.
4. If a patient at risk of aspiration has debris (saliva, vomit, etc.) at the cuff, this needs to be removed by synchronized suction/cough deflation if the cuff needs to be deflated. This requires two practitioners to perform safely.

With or without inner cannula: a removable inner cannula is nowadays almost always used. This prolongs the life of the tube before it needs changing (30 days instead of 7–14 days with a single lumen tube), and allows cleaning to reduce risks of occlusion and infection. The inner cannula should be removed, inspected for encrustation, and cleaned every 4h or if respiratory distress develops.

Fenestrated tubes: fenestrated tubes have little windows in their wall to allow air flow round the tube as well as through it. **NB**: Patients at risk of aspiration should not have fenestrated tubes. If suctioning through a fenestrated tube, ensure there is a non-fenestrated inner cannula in situ, to avoid sucking the tracheal mucosa into the fenestrations.

Humidification: ventilated patients need heat-moisture exchanger devices. Long-term tracheostomy or laryngectomy patients will usually use a Buchanan bib or foam filter dressing, which needs changing every 24 hours. Regular saline nebulizers with tracheostomy fittings also help keep the mucosa healthy.

Suctioning: this can clear up excessive secretions but carries risks. Suction pressures should be between 10.6 and 20kPa. The suction catheter should not be inserted for more than a third of its length and should not make the patient cough; suctioning should not be used for longer than 15 seconds.

Signs of problems with a tracheostomy

- stridor, difficulty breathing
- bleeding
- increasing thickness and volume of sputum
- difficulty expectorating

If these develop, you may need specialist advice.

Reference

1. Kendall K. (1997) Dysphagia in head and neck surgery patients. In *Dysphagia Assessment and Treatment Planning: A Team Approach* (ed. R. Leonard, K. Kendall), pp. 19–27. San Diego, CA: Singular Publishing Group.

Swallowing problems

Swallowing requires the following:[1]

- good lip closure: prevents food leakage
- teeth: break down food
- mobile tongue: crushes bolus and pushes it back into the pharynx
- saliva: lubrication
- an intact palate
- functioning cheek musculature for food not to collect in gingival sulcus
- intact oral and pharyngeal musculature and cranial nerve innervation (V, VII, IX, X, XI, XII)

Remember innervation:

- lingual nerve, from Vc, supplies sensation
- chorda tympani (VII) supplies taste to anterior two-thirds of tongue
- glossopharyngeal (IX) supplies sensation and taste to posterior third of tongue
- hypoglossal (XII) supplies tongue musculature

A tongue lacking sensation produces more long-term swallowing difficulties than a tongue with restricted mobility. Obstruction by a mass, functional problems (muscle dysfunction, nerve damage), pain, dry mouth, and tooth loss contribute to dysphagia.

Improving swallowing

Perhaps the commonest cause of difficulty swallowing is dry mouth. For management, see pp. 321–2.

Other helpful manoeuvres

- Chilled food helps re-educate lost sensation, e.g. after surgery.
- Encouraging the patient to chew or even just manipulate the bolus in the mouth for a few seconds facilitates initiation of the swallow.
- Alternating the temperature, taste, and texture of food in a meal keeps awareness of the swallowing process high—important while the process has to be deliberate.
- Carbonated drinks increase the sensation of the liquid bolus.
- Placement of food boluses in parts of the mouth where sensation is still intact aids patients with diminished sensation.
- Viscous boluses, e.g. thickened liquids and purees, permit poorly co-ordinated muscles to mount a much more effective swallow than thin liquids.
- Head or body tilting in the appropriate direction can utilize gravity in the swallowing process and protect the airway.

Is the patient at risk of aspiration?

- wet or gurgling noises with breathing: fluid in the airways
- altered voice during eating: food on vocal folds
- cough associated with swallowing
- fatigue during a meal: leads to prolonged meal times
- lower cranial nerve palsies
- aspiration pneumonia

Seek a speech and language therapy (SALT) assessment if appropriate, considering the patient's clinical state.

Gastrostomies

Many patients come into palliative care with a gastrostomy tube (a feeding tube bypassing the mouth) in place.[1] In patients with advanced disease, inserting a gastrostomy has to be judged carefully, considering not only the small risks of the procedure itself but later risks as well; for example, diarrhoea, vomiting, or a feeling of fullness may occur especially in the first weeks after insertion. It is important to distinguish starvation, which responds to feeding, from cachexia, which does not respond to feeding alone. The latter is more likely in the presence of large tumour masses, metastatic disease, certain types of tumours, or ongoing sepsis.

Types of gastrostomy

- Nasogastric tubes (NGTs): can be used for feeding for up to 4 weeks.
- Percutaneous endoscopic gastrostomy (PEG): inserted under sedation and local anaesthetic using a 'pull' technique. Throughout its lifetime, the PEG tube should be rotated through 360° at least twice a week to prevent adhesion formation.
- Radiologically inserted gastrostomy (RIG): these are inserted in the radiology department without sedation by a 'push' technique under fluoroscopic control. The tube is thinner than a PEG tube, and is held in place by its pigtail shape; it should *not* therefore be rotated, or it will dislodge.
- Surgical gastrostomy: carried out under general anaesthetic, usually when it is impossible to insert a PEG or RIG.

Care of the gastrostomy tube

The fixation plate should be maintained at 1–1.5cm from the abdominal exit stoma. A 50mL flush of sterile water should be used before and after every feed or administration of medication, and regularly three times a day. Soda water, but not other fizzy drinks (too acidic), can be used to unblock stubborn blockages.

Feeding

Patients should be maintained at an angle of 30–45° during feeding and for 2 hours after to reduce the risk of aspiration. Many centres are less keen for feeding to occur during sleep because of the aspiration risk.

Problems with gastrostomies

- dislodgement
- leakage: chemical digestion of surrounding skin
- overgranulation
- infection
- blockage: more common with narrower-gauge tubes

Reference

1. National Institute for Health and Clinical Excellence (2006). Nutrition support for adults: oral nutrition support, enteral tube feeding and parenteral nutrition. NICE Guideline CG32, updated August 2017.

Speech problems

Head and neck cancer and its treatment impair communication in various ways:

- dysarthria, e.g. tongue fixed by tumour
- laryngectomy
- recurrent laryngeal nerve palsies
- loss of facial expression: VII nerve palsy, facial disfigurement
- kissing: tumour/body image problems
- reception of communication by others: hearing or visual impairment

Up to 92% of patients with head and neck cancer have difficulties, with speech the single most important correlation to quality of life after treatment.

Production and articulation of speech

The vocal cords produce sound which is then modified by the action of tongue, lips, and mouth to produce intelligible speech. For example, good lip closure is needed to say 'p' or 'b', while a mobile tongue is necessary to produce 't' and 's'. Thus problems with any part of this apparatus can produce difficulties with intelligible speech.

Laryngectomy

This produces the most profound speech deficit, as the production of sound is removed. Various techniques have been developed to address this:[1]

- Oesophageal speech: produced by swallowing air and then expelling it while mouthing the necessary sounds. Various techniques are available for learning this, and it is taught by a speech therapist. Only 25–50% of patients master this technique, and it is useless in noisy environments or from any distance.
- Speaking valves, e.g. Blom–Singer valve: opening is made between the larynx and oesophagus, and a valve is fitted which allows oesophageal air to be used to produce sound. Fluency rates of 70–90% have been reported. However, the dynamics of sound production may change again if there is major local disease recurrence.
- Electrolarynx: this produces clear intelligible words, although in an 'electronic' voice. It occupies one of the patient's hands to keep it against the neck while talking.

Recurrent laryngeal nerve palsy

If laryngeal nerve palsy is unilateral, it causes hoarseness, which sometimes becomes worse as the day wears on; if bilateral, it reduces the voice to a whisper. The recurrent laryngeal nerves are motor to the intrinsic muscles of the larynx; they also supply sensory fibres to the mucosa below the level of the vocal folds. Therefore, in bilateral palsy the sphincter effect of the vocal folds during swallowing is lost and aspiration can result from adductor paralysis. In addition, aspiration will not be detected owing to the sensory loss, and the risk of aspiration pneumonia is high. Bilateral abductor paralysis can produce stridor.

There are various techniques for treating vocal fold palsies:

- behavioural techniques and biofeedback may be taught by speech therapists
- injection of Teflon, fat, or collagen into a paralyzed vocal fold[2]

- more invasive techniques (thyroplasty, arytenoid adduction, re-innervation, vocal cord lateralization) are very rarely indicated in patients with advanced disease
- patients who aspirate from bilateral vocal fold paralysis are temporarily helped by vocal fold injection; more extensive surgery is unlikely to be indicated in this patient group with end-stage illness

Articulation problems

Articulation problems can result from the following:

- tongue problems: glossectomy, tumour
- facial palsy
- dry mouth
- poor lip closure
- poor control of jaw movement: e.g. trigeminal nerve palsy
- defect in palate (excision) or teeth
- other lower cranial nerve palsies: base of skull metastases

How to communicate with patients with articulation problems

- Choose a quiet place where you can hear better.
- Sit in a position where you can see the patient talk; make sure there is enough light to see properly.
- Sit close enough to hear.
- Take time: you get tuned in.
- Encourage the use of gestures, which give useful clues to the meaning.
- If necessary, remind the patient to keep their sentences short and uncomplicated.
- Encourage the patient to articulate each syllable clearly but not to overarticulate.
- Learn lip reading.
- Encourage the family to participate.
- Involve a speech and language therapist.
- Be aware of the range of procedures on offer.

Remember: lack of fluency does not just result in loss of ability to speak. Reduced communication from embarrassment may also impoverish the *content* of speech to deal only with the concrete. These patients need time to express their deeper thoughts, and utilize alternative means of communication, e.g. as stated previously, and pen and paper or tablet. Utilize non-verbal expression, e.g. art therapy, which can often express feelings better than words.

References

1. Blalock D. (1997) Speech rehabilitation after treatment of laryngeal carcinoma. Otolaryngol Clin North Am 30(2): 179–88.
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Infection and fistulae

Local infection

Local infection has devastating consequences in advanced tumours:

- septicaemia
- wound extension
- pain from inflammation, pressure build-up within fascial spaces, erosion into adjacent tissues, maceration, e.g. of skin by exudates
- fistula formation
- vascular erosion: catastrophic bleeds
- cachexia in unchecked sepsis
- thick saliva: heavy intraoral exudate makes speech and breathing difficult

Osteomyelitis

Particularly common in the jaw, osteomyelitis produces discharging sinuses, pain, and tooth loss; necrosis is particularly extensive in irradiated bone and after bisphosphonate or denosumab treatment. Two very rare localized infections deserve mention. First, base of skull infections spread via the retropharyngeal space to the anterior mediastinum (the cervical vertebrae are protected by thick fascia). Such infections are, however, commonly tubercular. Second, infections of the submental space (Ludwig's angina) cause pain, high fever, trismus, and hypersalivation; floor-of-the-mouth swelling occasionally causes respiratory obstruction.

Treatment

Most infections are caused by anaerobes and Gram-positive cocci, which are commensals in the mouth. Gram-negative bacteria are less frequently found. Options include metronidazole and a penicillin, or clindamycin (concentrated in bone, but remember risk of pseudomembranous colitis)—consult your microbiologist as this is a complex area. Do not ignore the indispensable role of antibiotics in analgesia and reduction of intraoral exudates: gratifyingly rapid effects are often seen in both, enabling the patient to communicate properly and breathe easily for the first time in months. The conditions which set off the infection in the first place usually persist, so consider continuous prophylactic antibiotics at a lower dose (little trial evidence, but clinical experience suggests it is a very effective ongoing symptomatic measure).

Fistulae

Once formed, fistulae are maintained because:

- There is something in the depths of the wound needing to be discharged—usually infectious exudates or bony sequestrae in chronic osteomyelitis.
- The chemical composition of the exudate prevents healing, e.g. saliva, small bowel fistulae.

In palliative care there is usually an untreatable deep necrotic tumour, but bear in mind drainable abscesses and osteomyelitis.

Exudates or saliva bathing the great vessels (e.g. in oropharyngocutaneous fistulas) greatly increases the risk of catastrophic bleeding. This risk can be reduced through the following:

- dressings
- drying up saliva (➔ see Mouth care, pp. 517–18)

- continuous antibiotics
- making a silicone elastomer plug to fit large fistulae—unfortunately, malignant fistulae enlarge, so this plug will need to be renewed regularly. Such plugs are only used in single, clean, open cavities: plugging complex cavities impedes drainage, extending deep infection, and encouraging new fistulae to form where they can drain freely.

Emergencies

Catastrophic bleeds*

Catastrophic bleeds are among the most feared complications of cancer of the head and neck, although they are rare.

Risk factors

- previous neck irradiation
- fungating tumour invading the artery
- post-operative: flap necrosis
- infection
- salivary fistula
- systemic factors, such as malnutrition, cachexia, increased age

Warning signs

- minor bleeding from wound, tracheostomy, or mouth
- 'pulsations' from artery or tracheostomy or flapsite—false aneurysm formation
- sternal or high epigastric pain several hours before rupture if carotid
- the patient may become restless and irritable

Management

- If the patient is thought to be at risk, discuss a plan within the multidisciplinary team. Can the risk be reduced, e.g. embolization[1], stenting, or ligation of the implicated artery?
- What should the patient and family be told?
  - Obviously, if the patient or family asks specifically about catastrophic bleeds, this should be discussed with them, giving information in small steps and letting them decide how much they want to know. It is also useful to ask in a general way if they have any special fears about how the patient will die, as this may bring out unspoken fears. Otherwise, one needs to be careful not to raise fears of unlikely complications, which are frightening and about which nothing may be able to be done.
- Stop anticoagulants, aspirin, NSAIDs (COX-2 inhibitors may be safe)—though this will make no difference to a major bleed. Correct any platelet abnormalities if warning bleeds occur.

To tell or not to tell about potential bleeding?

Consider:

- Bleeds are often feared, but rarely occur.
- No amount of preparation for a very severe bleed will make it any less frightening.
- Can the patient or family do anything to reduce the risk of bleeding, e.g. embolization?
- Are there special circumstances, e.g. children in the house, who would be especially traumatized by a catastrophic bleed?
- Is the patient doing anything that might increase the risk, e.g. neglecting an infection in a dangerous area?
- Has the patient had any warning bleeds or are there other severe risk factors which would indicate that a major bleed is more likely?

* This section based in part on British Association of Head and Neck Oncology Nurses guidelines.

Checklist

- Treat infection.
- Ensure the family and staff know whom to contact in an emergency.
- Have emergency sedative drugs in the home: morphine, midazolam.
- Ensure all professionals involved know the plan, e.g. district nurses, GP.
- If in a hospice or hospital, nurse the patient in a side room to avoid the potential distress of other patients or relatives.
- Discreetly have trolley available with blue towels, gloves, apron, and emergency drugs.
- If there is a bleed, a senior member of staff must stay with the patient. Nothing is as reassuring as a calm human presence; nothing as frightening as panic. Call for help.
- Be respectful of the family's wishes about whether they wish to stay with the patient. Support them.
- Apply towels to the bleeding site and absorb the bleeding if possible.
- Apply gentle suctioning to the mouth and trachea as necessary.
- Give IV/IM midazolam, e.g. 10mg; if necessary, repeat in 10–15 min. Subcutaneous drugs are poorly absorbed in shock.
- Occasionally, families might be taught to administer rectal diazepam or buccal midazolam. Few will be calm enough to do this, and, in most cases, it loads them with an extra responsibility they can do without.
- After the event, debrief the family and staff, and point them in the direction of their normal supportive networks. Extensive counselling just after an event has actually been shown to be more likely to do harm than good.
- Offer family and staff (including non-clinical involved staff, such as domestics) a chance for a follow-up meeting later to deal with any questions they might have.

Tracheostomy tube obstruction

Causes

- infection
- excessive mucus production
- pressure sores around the tracheostomy
- tube displacement
- granulation tissue

Management

- call for help
- reposition the patient in semi-recumbent position
- ask the patient to cough; use suction
- head positioning to reduce tube kinks
- give oxygen
- remove inner cannula
- suction
- resuscitate if appropriate
- if severe problems breathing, sedate as for haemorrhage

Reference

1. Haas, R., et al. (2013). Interventional management of head and neck emergencies: carotid blowout. Semin Intervent Radiol 30(3): 245–8.

Quality of life

Cancer of the head and neck not only has the usual overtones of any cancer but also has a major impact on appearance, communication, and the basic functions of life, e.g. feeding and breathing. It is, therefore, to be expected that it will have a massive impact on patients' quality of life.

There is a plethora of scales which look at quality of life in head and neck cancer. The most widely used are the following:

- EORTC QLQ-C30 and QLQ H&N35
- FACT G and FACT H&N ℘ http://www.facit.org/FACITOrg/Questionnaires
- UWQoL
- ℘ http://www.entnet.org/content/head-and-neck-surgery-outcome-tool-uw-qol-r4
- SEIQoL: the patient decides which domains of quality of life are most important for them in this scale
- HNQOL
- problem-specific scales—for a good summary, see Heutte et al. (2014)[1]

Before treatment, advanced tumour stage and performance status are the leading factors in establishing quality of life, but smoking at diagnosis, significant alcohol use, and polypharmacy also contribute. Socio-economic factors are key determinants of QoL in stable head and neck cancer 5 years after treatment, as is having a feeding tube or oral cancer. For a summary of factors affecting QoL in head and neck cancer, see Nelke et al. (2014).[2] The literature on quality of life in far-advanced head and neck cancer is extremely scanty.

It is impossible to summarize here all the key findings of the important studies,[3] but let us highlight one aspect. There is a subset population who judge their QoL to be very good despite major disease and deeply disfiguring treatment. It has become clear that what gives life quality can change as an illness progresses—the so-called *response shift*. Understanding this, and understanding how disability and disfigurement affect quality of life, will allow us both to adapt our management to promote a better life for patients, and to understand better the process of coping and adaptation to illness, which might in turn lead us to ways of helping people develop coping strategies.

References

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Body image and sexuality

Slade defined *body image* as the picture we have in our minds of the size, shape, and form of our bodies, and our feelings concerning these characteristics and our body parts. There is little gender or age difference in the impact of appearance changes on body image. The degree to which people can be rehabilitated after facial disfigurement also does not depend on the degree of disfigurement, but correlates with perceived social support and with the degree of dysfunction. Speech and swallowing problems correlate most strongly with body image concerns and social avoidance after surgery. Thus body image does not only depend on appearance but also on dysfunction.

Factors which have been associated with poor body image include the following:

- poor self-esteem
- social anxiety
- self-consciousness
- depressive features

Sexuality is a closely related field. One study found how, a year after head and neck surgery, marital and sexual relationships still suffer, and alcohol use (a marker of depression, particularly in men) is higher in a very significant number of patients. Almost half of patients at least a year after treatment in another small study had problems with libido, arousal, and sexual activity; a significant minority still never or almost never kissed and held hands with their partner.

see Chapter 11 for further information about sexual health in advanced disease. For a review of the literature, see Rhoten et al.[1]

Working with body image

It is obvious from the foregoing that body image depends more on perceived social support and the existence of supportive relationships than on the degree of disfigurement or disability. This effect is found in women but not in men. It again brings us back to one of the central, though often unsaid, tenets of palliative care: ultimately what matters most to people is being cared for, respected, and loved. There is now good work showing how after cancer treatment, social rehabilitation through a simple behavioural approach is effective. Poor body image is perpetuated by social avoidance and countered by social reintegration. Medical staff play an important role by modelling attitudes and allowing patients to practise new behaviours in a safe environment. For example, patients can be trained to prepare a number of responses for when people inevitably comment to them about their appearance, or when they walk into a pub and everyone stares. Changing Faces, a UK charity, runs courses about this.[2] But the situation in advanced cancer, where appearance rapidly worsens rather than being static as after surgery, where it is accompanied by generalized bodily deterioration and by a shrinking social world, has not been explored properly yet.

There are various tools available to assess body image.[3]

Clearly, management of body image starts from the treatment planning phase, by choosing treatments that preserve appearance and function as long as they are as safe. Psychological support at this stage is also needed,

mainly in the form of training to deal with awkward situations. Mood disorders also need to be dealt with actively.

In end-stage disease, the situation is complicated by ever more rapid change coupled with a loss of reserve, and often serious communication difficulties. This can be countered by strong social and medical support, by giving people a variety of ways to express themselves, and by making people feel safe and respected in their environment. This may involve work with families as well as the patient.

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2. http://www.changingfaces.org.uk
3. Fingeret, M., et al. (2015). Body image: a critical psychosocial issue for patients with head and neck cancer. *Current Oncology Reports*, **17**(1):422.

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Bressan, V., et al. (2017) The life experience of nutrition impact symptoms during treatment for head and neck cancer patients: a systematic review and meta-synthesis. *Supportive Care in Cancer*, **25**(5):1699–712.

Cocks, H., et al. (2016) Palliative and supportive care in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. *Journal of Laryngology and Otology*, **130**(S2):S198–S207.

General medical problems in patients with head and neck cancer

When one recalls that the main risk factors for head and neck cancer are smoking and alcohol, it is not surprising that concurrent medical problems are common in these patients:

- **Malignancies in other organs** are common, particularly lung, but also other smoking- or alcohol-related tumours: bladder, kidney, pancreas, liver. This may have both physical consequences to the patient, e.g. owing to metastatic disease from a distant malignancy, and a psychological toll on them. It should be kept in mind that many patients are more prone to other head and neck cancers too, so patients with a history of two or three head and neck primaries and a distant primary are encountered as well.
- **Ischaemic heart disease**: keep in mind that such patients are less tolerant of anaemia.
- **Alcohol-induced cardiomyopathies**: may limit the use of some agents for neuropathic pain.
- **Strokes**: if these are present in addition to neurological damage from the tumour, almost total disability can result.
- **Chronic obstructive airways disease**: airways problems from head and neck cancer can precipitate decompensation and respiratory failure.
- **Thromboembolic disease**: may necessitate difficult decisions about continuing anticoagulation if there is a risk of bleeding. Sometimes conversion to heparin will allow rapid responsiveness if bleeding occurs.
- **Alcoholic liver disease**: may contribute to clotting problems or to altered handling of medication.
- **Nutritional deficiencies**: from poor diet, dysphagia, alcohol, cachexia.
- **Psychiatric problems**: depression, anxiety.
- **Substance abuse**: watch out for alcohol withdrawal in particular.

Syncope

This is common among patients with cancer of the head and neck. It may be carotid sinus syncope from metastatic compression or post-radiotherapy fibrosis. Glossopharyngeal neuralgia can lead to sinus arrest, perhaps as intense glossopharyngeal nucleus stimulation overflows to the vagal nucleus, leading to parasympathetic suppression of the cardiac pacemaker.

Steroids

Do not ignore the fact that many patients will have been on high doses of steroids for prolonged periods. This may mean that if they are in crisis, steroids may need to be restarted if an acute and potentially fatal crisis is to be avoided.

Further reading

Books and book chapters

Cherny N. (2015) *Oxford textbook of palliative medicine* (5th edn). Oxford: Oxford University Press.

Devins G.M., Otto K.J., Irish J.C., Rodin, G. (2015) Head and neck cancer. In Holland J.C., et al. (eds) (2015) *Psycho-oncology* (3rd edn). Oxford: Oxford University Press.

Harrison L.B., Sessions, R.B., Kies M.S. (eds) (2013) *Head and neck cancer: a multidisciplinary approach* (4th edn). Philadelphia: Lippincott Williams & Wilkins.

Leonard R., Kendall K. (eds) (2013) *Dysphagia assessment and treatment planning: a team approach* (3rd edn). San Diego: Plural Publishing Inc.

Useful websites

- http://www.changingfaces.org.uk
- http://www.tracheostomy.org.uk/ has a number of e-learning modules and management algorithms.

Chapter 15

Endocrine and metabolic complications of advanced cancer

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Introduction

Hormones are drivers of behaviour, physiology, and personality; their fingerprints are on everything from blood pressure to attraction and appetite.

Metabolic and endocrinological disorders have a profound impact on a patient's physical and psychological well-being. These disorders are at times complex, but it is important to be aware of the associated endocrine and metabolic complications in advanced cancer as they can have a significant impact on morbidity and mortality. In addition, even when the underlying cancer may not be responsive to treatment, such symptoms may be reversible, which can have a significant benefit to the individual patient.

Malignancy affects endocrine systems in two ways:

- directly interfering with the function of endocrine glands by invasion or obstruction, or
- remotely producing effects without direct local spread—paraneoplastic syndromes

Paraneoplastic syndromes are caused by the following:

- tumour cells secreting hormones, cytokines, and growth factors
- normal cells secreting products in response to the presence of tumour cells (such as antibodies in the Lambert–Eaton myasthenic syndrome)

Paraneoplastic syndromes

- hypercalcaemia
- Cushing's syndrome
- syndrome of inappropriate antidiuresis
- hypoglycaemia (non-islet cell)
- carcinoid syndrome

Non-paraneoplastic syndromes

- diabetes mellitus

Paraneoplastic syndromes: hypercalcaemia

Definition: serum-corrected calcium >2.6mmol/L

Corrected calcium = measured calcium + [(40−serum albumin g/L) × 0.02]

Hypercalcaemia is common and potentially life threatening. It is usually treatable, if recognized, and therefore should always be considered as a possible cause of unexpected deterioration in patients with malignancy. The pathogenesis is complex and commonly involves increased bone resorption, decreased renal clearance of calcium, and increased absorption of calcium in the gut.

Epidemiology

- Some 10% of patients with cancer develop hypercalcaemia.
- Commonest cancers associated with hypercalcaemia include multiple myeloma, and breast and lung cancer.
- Malignancy is responsible for 50% of the patients with hypercalcaemia who are treated in hospital.
- Some patients develop hypercalcaemia without bone metastases. Pathogenesis involves ectopic secretion of factors, such as parathyroid hormone-related protein (PTHrP), which disrupt calcium homeostasis. An elevated level of PTHrP is associated with a very poor prognosis.
- Most patients with hypercalcaemia of malignancy have disseminated disease—80% will not survive beyond one year.
- The prognosis of hypercalcaemia of malignancy is poor, with a median survival of 3–4 months.

Features

- general: dehydration, myopathy, and polydipsia
- gastrointestinal: constipation, anorexia, weight loss, nausea, vomiting
- neurological: fatigue, confusion, psychosis, and seizures
- cardiological: bradycardia, arrhythmias, prolonged PR interval, reduced QT interval, wide T waves

Treatment

Management involves rehydration and use of calcium-lowering drugs. Drugs promoting hypercalcaemia (thiazide diuretics, vitamins A and D) should be withdrawn.

Most healthcare facilities will have local guidelines to follow for the management of hypercalcaemia associated with malignancy, which should be referred to.

Intravenous fluids

Dehydration due to polyuria and vomiting is a prominent feature of acute or symptomatic hypercalcaemia. While large fluid volumes will lower serum calcium, calcium levels will seldom return to normal by rehydration alone, and care to avoid fluid overload must be taken. Other electrolytes should also be monitored during this time. There is little evidence that there is any benefit in using diuretics in conjunction with rehydration; they should be avoided.

Bisphosphonates

Synthetic pyrophosphate analogues reduce bone resorption by inhibiting osteoclastic activity. They are highly effective at reducing hypercalcaemia. Treatment should be considered if the patient is symptomatic rather than based on absolute calcium levels. Symptoms are unlikely unless the corrected calcium is >2.8mmol/L.

Administration of a bisphosphonate following rehydration is the mainstay of hypercalcaemia treatment. Intravenous bisphosphonates are most commonly used to reduce serum calcium levels. Zoledronic acid is more effective in achieving normocalcaemia and has a longer duration of effect than pamidronate.[1]

Some 20% of patients with hypercalcaemia of malignancy will be resistant to bisphosphonate infusion therapy. If resistant to one intravenous treatment, it is reasonable to try the other before declaring the patient resistant to bisphosphonates.

One of the following intravenous bisphosphonates may be used:

- disodium pamidronate 60–90mg IV over 2–4h
- zoledronic acid 4mg IV over 15min
- sodium clodronate (not UK) 1.5g over 4h
- ibandronic acid 2–4mg IV over 2h

In mild–moderate renal impairment, no dosage adjustment is necessary when treating tumour-induced hypercalcaemia. In severe renal impairment, the use of bisphosphonates is complex, and specialist renal/endocrinological advice should be sought.

Complications of bisphosphonates

There has been an increase in reports of osteonecrosis of the jaw with intravenous bisphosphonates. Updated guidance indicates that early diagnosis and management are optimal. If possible, patients who need intravenous bisphosphonates should have a dental assessment and complete procedures prior to commencing treatment. Good oral hygiene with regular dental visits should be advised. Exposed bone in the mouth should be reported with urgency to a dental professional.[2]

Bisphosphonates can cause renal toxicity. This risk is reduced by ensuring adequate hydration, monitoring renal function, and adhering to the recommended infusion rate and dose.

Corticosteroids

Prior to the advent of bisphosphonates, corticosteroids were the mainstay of treatment. They are now less commonly used owing to the effectiveness of newer drugs. They are most useful in haematological malignancies when oral prednisolone 40–100mg/day is often effective.

Calcitonin

Calcitonin inhibits osteoclastic bone resorption and encourages calcium excretion. It is effective in around one-third of patients and usually causes a fall in calcium within 4h.

Doses of salmon calcitonin can be used subcutaneously every 6–8h. The dose is weight-dependent. It is rarely used in palliative care since it needs frequent administration, and correction of hypercalcaemia is short-lasting.

Denosumab

Denosumab is a monoclonal antibody that specifically targets RANKL, a transmembrane protein essential for the formation, function, and survival of osteoclasts, the cells responsible for bone resorption, thereby modulating calcium release from bone. It has been used in hypercalcaemia refractory to bisphosphonate treatment, although this is an unlicensed indication. Seek specialist advice.

References

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2. Weitzman R, et al. (2007) Critical review: updated recommendations for the prevention, diagnosis, and treatment of osteonecrosis of the jaw in cancer patients—May 2006. Critical Reviews in Oncology/Hematology, 62(2): 148–52.

Paraneoplastic syndromes: Cushing's syndrome

- Cushing's syndrome results from an excess of glucocorticoid, with chronic glucocorticoid therapy being the commonest cause.
- Ectopic secretion of corticotrophin (ACTH) by non-endocrine tumours is rare but can occur with some solid tumours, particularly bronchial and small-cell lung cancer.
- Associated pro-peptide secretion is more common, producing a more complex mosaic of symptoms.
- Up to 20% of cases of Cushing's syndrome are caused by ectopic ACTH, often from an occult tumour.
- Some 15% of ectopic ACTH secretion is due to carcinoid and neural crest tumours.
- Long-term survivors of malignancies with associated ectopic ACTH secretion will often continue to have elevated ACTH levels.
- See Table 15.1.

Investigations

- increased free urinary cortisol
- loss of diurnal variation of plasma cortisol
- failure of cortisol suppression in low-dose (2mg) dexamethasone test
- failure of cortisol to suppress ACTH levels following high-dose dexamethasone (2mg q.d.s. or 8mg nocte)

When the foregoing investigations are still equivocal, more complex imaging techniques are available at specialist centres, and advice from a local endocrinology team should be sought if appropriate.

Treatment

If an ACTH-secreting tumour is localized, surgery may be an appropriate option. If this is not possible, the mainstay of treatment is inhibition of steroid synthesis. Ketoconazole, metyrapone, and etomidate have been used to manage Cushing's syndrome through adrenal enzyme inhibition. These drugs are often used in combination as they work synergistically. Be vigilant of side effects, particularly in patients with metastatic disease, as ketoconazole can cause liver toxicity and metyrapone can cause nausea and vomiting.

Treatment efficacy should be monitored by measuring 24h urinary cortisol excretion. As levels return to normal, hormone replacement therapy, as in Addison's disease, may be required.

Table 15.1 Clinical features

Hypokalaemic metabolic alkalosis	Mental changes
Weak muscles	Glucose intolerance
Oedema	Weight loss
Raised blood pressure	

Paraneoplastic syndromes: syndrome of inappropriate antidiuresis (SIAD)

Hyponatraemia (serum sodium of <135mmol/L) is common in patients with advanced malignancy due to many factors, including cardiac and hepatic failure, hyperglycaemia, diuretics, and sick-cell syndrome. However, the presence of concentrated urine in conjunction with hypo-osmolar plasma suggests abnormal free-water excretion and the presence of the syndrome of inappropriate antidiuresis. (The SIAD acronym is more appropriate than SIADH, as there is no vasopressin hormone secretion in approximately 15% of cases.)

The vasopressin gene codes for peptide products, including arginine vasopressin (AVP) and vasopressin-specific neurophysin II (NP II). In malignancy-related SIAD, tumours secrete ectopic AVP, increasing the numbers of aquaporin channels in the collecting ducts. This results in increased water reabsorption and reduced free-water excretion and ultimately hypo-osmolar plasma and concentrated urine.

SIAD is most frequently associated with small-cell lung carcinoma or carcinoid tumours, but has also been noted in pancreatic, oesophageal, prostatic, and haematological cancers.

Causes of SIAD

- ectopic AVP
- infections
  - lung, cerebral and meningeal
- drugs
  - morphine
  - phenothiazines
  - tricyclic antidepressants
  - NSAIDs
  - vincristine
  - cyclophosphamide

Clinical features

Significant symptoms of hyponatraemia develop at plasma sodium levels below 125mmol/L, with confusion progressing to stupor, coma, and seizures. Nausea, vomiting, and focal neurological signs may also develop.

The clinical features depend on both the levels of plasma sodium and the rate of decline. With gradual falls, the brain cells can compensate against cerebral oedema by secreting potassium. Asymptomatic hyponatraemia suggests chronic SIAD, whereas symptomatic hyponatraemia suggests acute SIAD.

Diagnosis

Initially it is important to exclude three other reversible causes of hyponatraemia: hypothyroidism, hypoadrenalism, and diuretic use.

Essential criteria

- plasma hypo-osmolality (plasma osmolality <275mosmol/kg H_2O and plasma sodium <135 mmol/L)
- concentrated urine (with plasma osmolality >100mosmol/kg H_2O)
- normal plasma/extracellular fluid volume
- high urinary sodium (urine sodium >20mEq/L) on a normal salt and water intake

Management

Management depends on the rate of onset of symptoms and neurological complications. The aim of treatment will vary depending on the patient's overall condition. For some, normo-traemia may be the ultimate target, and for others, focusing on symptom reduction may be the most appropriate goal.

Acute symptomatic hyponatraemia has a mortality rate of 5–8%, and patients will need prompt correction with intravenous hypertonic saline with meticulous monitoring, as over-rapid correction can lead to central pontine myelinosis with quadriparesis and bulbar palsy.

Chronic asymptomatic hyponatraemia is best treated with fluid restriction. In effect, this means reducing dietary input or urinary output to less than 500mL/day, which may take several days to produce an effect. This may not be appropriate in the terminal care setting, when patients may prefer to eat and drink what they like without strict regimens.

Drug treatments involve the use of distal nephron inhibitors that prevent water reabsorption (e.g. demeclocycline) and oral osmotic diuretics (e.g. urea).

Demeclocycline (desmethylchlortetracycline) inhibits vasopressin and causes nephrogenic diabetes insipidus: 900–1200mg/day will reverse chronic SIAD over 3–4 days and should be followed by a maintenance dose of 600–900mg/day. Side effects include gastrointestinal disturbances, hypersensitivity reactions, and reversible nephrotoxicity.

Urea is effective in controlling SIAD by both intravenous and oral routes. Oral urea, 30g dissolved in orange juice to mask the taste, is the daily dose. (Using urea obviates the need to fluid-restrict the patient, but oral urea is often poorly tolerated.)

Paraneoplastic syndromes: non-islet cell tumour hypoglycaemia

Tumours that secrete insulin, such as beta-cell tumours (insulinomas), often cause hypoglycaemia. More rarely, non-islet cell tumours cause hypoglycaemia by increased tumour usage of glucose, secretion of insulin-like growth factors (IGFs), and disruption of the balance maintaining normal homeostasis.

Increased use of glucose by tumours has been clearly documented, with daily consumption sometimes reaching levels of 200g/kg per day. Hepatic glucose production may also fall, and suppression of compensatory growth hormone and glucagon also contribute to the hypoglycaemic state.

It is important to remember that the commonest cause of hypoglycaemia in advanced cancer is use of hypoglycaemic medications.

Epidemiology

Insulin-secreting tumours are usually large (average 2.4kg), and often retroperitoneal or intrathoracic with liver invasion. The tumours may be growing over a relatively longer time course than many other cancers (often several years). Patients with IGF2-producing tumours will often first present with hypoglycaemia.

- approximately 60% are mesenchymal tumours (mesothelioma, neurofibroma, leiomyosarcoma, etc.)
  - 20% are hepatomas
  - 10% are adrenal carcinomas
  - 10% are gastrointestinal tumours

Clinical features

Hypoglycaemic symptoms often present in the fasting state or in advanced disease. Symptoms are associated with cerebral hypoglycaemia and the associated secondary response of catecholamine secretion. The neurological features include agitation, stupor, coma, and seizures, usually following exercise or fasting, and occur most often in the early morning or late afternoon. Other causes of hypoglycaemia should be excluded, such as overtreatment of diabetes.

Treatment

The reversal of symptomatic hypoglycaemia initially requires intravenous glucose infusion. Central lines may be needed for hyperosmolar glucose solutions. Up to 2000g/day of glucose may occasionally be needed. Frequent feeding, including during the night, and steroids may be helpful.

Debulking surgery, arterial embolization of tumours, and chemotherapy can all have a place in the palliation of tumour-related hypoglycaemia.

Clinicians can be faced with an ethically challenging situation in patients with advanced cancer and recurrent hypoglycaemia. The need for repeated re-cannulation, resultant sleep disturbance with frequent blood sugar monitoring, and measures to maintain normo-glycaemic state can all be an overwhelming burden for some patients, resulting in an unacceptable quality of life. It is important this is recognized, particularly in those with advanced disease, as the level of medical intervention required to maintain adequate blood sugar levels is significant for some patients.

Paraneoplastic syndromes: carcinoid syndrome

Carcinoid tumours are a diverse group of tumours of enterochromaffin-cell origin. The incidence is 1.5 per 100,000. The carcinoid syndrome develops in up to 18% of patients with such tumours, and these patients almost invariably have hepatic metastases.

The commonest site of origin is the appendix (25%) and rectum, but they have also been reported in the pancreas, lungs, thymus, and gonads. Tumours may be benign, but 80% that are greater than 2cm in diameter metastasize.

Clinical features

- Flushing and diarrhoea occur in at least 75% of patients.
- Cardiac manifestations involving the right side of the heart are late manifestations in one-third of patients.
- Wheeze/right ventricular heart failure (RVF) (tricuspid valve regurgitation or stenosis and pulmonary valve stenosis) are seen.
- Asthma and pellagra are less common.

Clinical features are mediated by several active substances secreted by tumours:

- serotonin (5HT), 5-hydroxytryptophan (5HTP)
- prostaglandins
- catecholamines
- tachykinins (substance P, neuropeptide K)
- histamine
- alcohol or psychological stress may precipitate symptoms

The features of carcinoid tumours vary by their sites of origin (Table 15.2).

Diagnosis

Diagnosis is usually established by:

- measuring urinary excretion of 5HIAA (metabolite of 5HT)
- platelet 5HT levels (unaffected by diet)

Tumour localization may be achieved with somatostatin scintography or PET scanning.

Management

The aim of management is to suppress circulating hormones and chemicals produced by the tumour. Palliative debulking surgery, hepatic artery embolization, somatostatin analogues, and chemotherapy may be appropriate palliative treatment for selected patients. Somatostatin analogues reduce 5HT secretion and thereby symptoms. Octreotide and lanreotide are both commonly used, although octreotide is short-acting and therefore may need to be given via multiple daily doses, a syringe driver, or depot injection. More recent trials have suggested that as well as symptom management, somatostatin analogues are likely to have a significant impact on survival[1, 2]

Symptomatic treatment of diarrhoea and wheezing, using more traditional agents, also has a place in the management of patients with advanced carcinoid tumours.

Table 15.2 Comparison of carcinoid tumours by site of origin

	Foregut	Midgut	Hindgut
Site	Resp. tract, pancreas, stomach, proximal duodenum	Jejunum, ileum, appendix, Meckel's diverticulum, ascending colon	Transverse and descending colon, rectum
Tumour products	Low 5HTP, multihormones	High 5HTP, multihormones	Rarely 5HTP, multihormones
Blood	5HTP, histamine, multihormones	5HT, rarely ACTH, multihormones	
Urine	5HTP, 5HT, 5HIAA, histamine	5HT, 5HIAA	Rarely 5HT or ACTH
Carcinoid syndrome	Atypical	Frequently with metastases	Rarely occurs
Metastases to bone	Common	Rare	Common

Data sourced from Cherny, N. et al (2015) Endocrine and metabolic complications of advanced cancer—Oxford Textbook of Palliative Medicine Oxford Medicine. (5th ed).

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2. Rinke, A., et al. (2009). Placebo-controlled, double-blind, prospective, randomized study on the effect of octreotide LAR in the control of tumor growth in patients with metastatic neuroendocrine midgut tumors: a report from the PROMID Study Group. Journal of Clinical Oncology, 27(28), 4656–63.

Non-paraneoplastic complications: hyperglycaemia and hypoglycaemia

The incidence of hyperglycaemia in patients with cancer is higher than in the general population. Several theories to account for this have been postulated:

- increased gluconeogenesis
- increased conversion of lactate to glucose
- diminished glucose tolerance
- insulin resistance
- increased use of medications such as corticosteroids promoting hyperglycaemia

These changes may arise as a result of liver damage, altered glucose metabolism by tumour cells, or secretion of insulin antagonists. Studies have established that diabetes is a risk factor for some cancers and has also been associated with increased mortality. The mechanism by which this occurs is complex.[1]

Diabetes mellitus

Management of diabetes in palliative care

Diabetes UK has published recommendations on end-of-life diabetes care. These guidelines are available at http://www.diabetes.org.uk

Aims of treatment may vary depending on the patient's clinical condition. Tight glycaemic control and regular monitoring may not be appropriate where a patient is entering the last days of life. As prognosis shortens, the emphasis on reducing the long-term sequelae of diabetes becomes less significant.

However, it is important to be cognizant of hyperglycaemia as a potential contributing factor to symptoms such as thirst, nausea, polyuria, and thrush. Avoidance of hyperglycaemia may be important for reducing these symptoms if patients are symptomatic. It is important that patients and families understand this if the goal of treatment changes, as many patients have spent years striving to maintain very strict glycaemic control.

Changes in the patient's condition, cachexia, anorexia, infection, nausea and vomiting, and particular treatments (e.g. corticosteroids) alter the diabetic treatment needed—the management may have to change rapidly at different phases of the illness.

Aim in patients with diabetes and advanced malignancy

- to prevent symptoms
  - maintaining the blood glucose at <15mmol/L is usually sufficient to prevent symptoms of hyperglycaemia

To prevent hypoglycaemia occurring, treatment options for diabetes include:

Oral hypoglycaemic drugs

- Used in the context of non-insulin-dependent diabetes. Gliclazide is a short-acting hypoglycaemic agent. It may be given once or twice daily at a starting dose of 40–80mg o.m.
- Increase as required to a maximum total dose of 160mg b.d. If uncontrolled on oral hypoglycaemics, may need to start insulin.
- Avoid starting metformin in patients with advanced cancer.

Insulin

For patients with pre-existing insulin-dependent diabetes, a regimen will likely be established. If patients are relatively well and glycaemic control is maintained, it is often most acceptable to patients to continue on their current regimen initially. The chosen regimen will have taken account of patient preferences, lifestyle, and adequacy of glycaemic control. Potential regimens may include the following insulins:

- long-acting: human insulin glargine (e.g. Lantus®)
- intermediate-acting: human isophane insulin (e.g. Insulatard®, Humulin® I, or Insuman Basal®)
- short-acting: human soluble insulin (e.g. human Actrapid® or Humulin® S)

Sliding-scale insulin regimen

Sliding-scale insulin may have a particular place, particularly as a short-term measure whilst establishing a more sustained regimen in insulin-dependent patients with unstable blood sugars or whilst managing an acute episode that has disrupted the regular diabetic regimen. Blood glucose must be monitored regularly and short-acting insulin given 8-hourly if the patient not eating, or before mealtimes. Sliding-scale doses can be adjusted according to response. Most healthcare facilities have agreed protocols for the use of sliding scales or correction-dose insulin.

Management of vomiting

Patients who are vomiting will likely need changes to their diabetic regimen (see Table 15.3). If on oral hypoglycaemics, the risk of hypoglycaemia needs to be managed by reducing the dose. If patients are insulin-dependent, a hyper-osmolar state needs to be avoided by continuing with insulin. Insulin can be more easily titrated using IV insulin regimens (not commonly used in non-specialist settings, and may require admission to acute medical unit if appropriate), or sliding-scale insulin with close blood glucose monitoring. Specialist advice may be sought from a local diabetic or endocrine team if management is complex or challenging.

Management in terminal phase

In the last days of life, the emphasis will be focused on symptom control and therefore it may be appropriate to rationalize a patient's insulin regimen to minimize monitoring and frequency of insulin administration (outlined in Table 15.4).

Hyperglycaemia in advanced malignancy

In addition to pre-existing diabetes mellitus (including previously undiagnosed cases, which may present in the terminal stages), there are two particular causes of hyperglycaemia that may occur in patients with advanced malignancy:

- corticosteroid-induced diabetes
- insulin deficiency/resistance in pancreatic cancer

Corticosteroids

Corticosteroids are commonly used in advanced malignancy. They have a direct metabolic hyperglycaemic effect, and may also increase appetite, sometimes dramatically.

Table 15.3 Managing diabetes when vomiting or not eating

Diabetes type	Action
Oral hypoglycaemics	Reduce dose by 50% if oral intake reduced, or discontinue if no oral intake
Insulin-dependent	Insulin is required to prevent ketosis even with no oral intake. Use the IV regimen if intensive control is appropriate, or use sliding scale of human soluble insulin 8h

Table 15.4 Managing diabetes in the terminal days

Diabetes type	Action
Oral hypoglycaemics	Discontinue when unable to take orally

Insulin-dependent	Insulin is required to prevent ketosis, even with no oral intake
	• If patient unconscious/unaware, discontinue insulin and monitoring
	• If the patient is still aware/conscious, several strategies may be appropriate, depending on the patient's/relatives' attitude to burden of treatment (and monitoring) and prognosis:
	  ◦ use sliding-scale soluble insulin 8h
	  ◦ give approximately half of the patient's recent insulin requirement as a single dose of human glargine as a single daily injection, with or without blood sugar monitoring

Hyperglycaemia is a dose-related side effect of steroids in any patient (one in five patients on high doses will develop steroid-induced diabetes), but there is wide variability between patients in their response. Patients with sustained hyperglycaemia will need to start an oral hypoglycaemic drug, commonly gliclazide, and occasionally may require insulin. The dose of steroids should be reduced to the minimum possible.

Initiating treatment in a new diagnosis of hyperglycaemia

- See Table 15.5 for example of a potential treatment plan.
- Most healthcare facilities have a local policy on management of steroid-induced hyperglycaemia, which should be referred to if available.
- Restrict diet *if overeating*: do not impose a strict diet on a patient with advanced illness. It is more important to try to achieve a regular caloric input from one day to the next.
- If on steroids and appropriate, consider reducing the dose.
- Consider infection as a factor causing the hyperglycaemia.
- Thin, cachectic patients are less likely to respond to oral hypoglycaemic drugs, and insulin should be considered early if not responding to simple measures, e.g. gliclazide 80mg o.d.

Table 15.5 Management of hyperglycaemia

Blood sugar (mmol/L)	Action
11–17	• Dietary advice • Reduce steroids if possible • Start gliclazide 40mg daily and increase as necessary every few days
17–27	• Start gliclazide 80mg mane if no or mild ketonuria • If moderate or severe ketonuria, the patient will need insulin—start human glargine 10 units nocte • If ketonuria and symptomatic, consider reducing blood glucose more rapidly using human soluble insulin 4–8units every 4h until glucose <17mmol/L, or IV regimen below
>27	• Consider whether admission to acute medical unit is appropriate, especially if ketonuria present • Use IV regimen if intensive treatment appropriate, or human soluble insulin 4–8units every 4h until glucose <17mmol/L

Hypoglycaemia

Common clinical changes that occur in patients with advanced malignancy may result in a need to reduce insulin or oral antidiabetic drugs. These include the following:

- cancer cachexia in advanced illness (reduced body mass)
- reduced food intake due to anorexia, dysphagia, 'squashed stomach', or nausea/vomiting, etc.
- liver replacement by tumour causing low glycogen stores and limited gluconeogenesis

Drugs used in hypoglycaemia

Glucagon

- inj. 1mg
- dose: 1mg IM (<12years, 0.5mg)
- do not give by SC route, as the patient may be peripherally vasoconstricted
- Glucagon may be ineffective in a starved patient, as it depends on an adequate liver glycogen level.

Glucose/dextrose

- oral options include 150mL non-diet cola drink, four teaspoons of sugar dissolved in water, or five glucose tablets
- IV: give 75–80mL of 20% glucose (over 10–15min)

Further reading

Books

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Chapter 16

Paediatric palliative care

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Who needs paediatric palliative care?

> There can be no doubt that a perfect Cure of the Diseases of Children is as much desired by all, as anything else whatsoever in the whole art of physick.
>
> Walter Harris, 1698

The emergence of a new specialty

- Advances in the treatment of life-threatening neonatal and paediatric conditions have dramatically improved survival rates over recent years.
- One of the most striking reductions in mortality has been achieved for children with malignant conditions, although there remain certain forms of cancer for which the prognosis remains extremely poor.
- Similarly, despite advances, there is a range of non-malignant conditions which continue to be life-limiting.
- The patient population in paediatric palliative care is quite different from that encountered in adult practice. Approximately 25–30% of children with palliative care needs have a malignancy.
- A larger group have a variety of conditions including congenital abnormalities and neurodegenerative disorders.
- Modern pharmacological and technical approaches now make it possible for some children, who would previously not have survived at all, to live longer, sometimes into adulthood. Many of these children have long illness trajectories which see them deteriorate slowly and inexorably toward a state of high dependency and disability.
- It can be difficult to identify a point where treatment becomes exclusively palliative, and this presents a major challenge to service providers.
- Many conditions are rare and the prognosis is often unpredictable—the child could die at any time or may live a number of years. These children often have multiple symptoms requiring frequent medical intervention, in addition to complex psychological needs.
- The parents, siblings, and grandparents of such children also need support in adjusting to the diagnosis and ongoing care of the child.

Specialist paediatric palliative care services have recently been established in a number of centres throughout the world and focus variably on the three main care settings: home, hospice, and hospital. Families will generally move between the various settings according to need, but it has become clear that where home care is offered as a realistic option, most families will wish to care for their child at home. Children's home care teams and outreach nurses are becoming more common, and are often able to take on a palliative care role, providing support for children with life-limiting diseases and their families in their own homes.

In addition, children's hospices are also being established, providing an option for respite and terminal care. Specialist palliative care services for children in hospitals are not as widely available away from major centres, although adult palliative care teams are available for advice in many.

Box 16.1 is taken from *A Guide to the Development of Children's Palliative Care Services* and lists the four main groups of conditions that may affect the child in palliative care.[1]

Box 16.1 Four main conditions affecting the child in palliative care

1. Conditions for which curative treatment is possible but may fail, e.g. leukaemia.
2. Diseases where premature death is likely but intensive treatments may prolong good quality life, e.g. cystic fibrosis, muscular dystrophy.
3. Progressive conditions where treatment is exclusively palliative and may extend for many years, e.g. mucopolysaccharidoses, other neurodegenerative conditions.
4. Conditions, often with neurological impairment, causing weakness and susceptibility to complications, e.g. non-progressive CNS disease.

Reprinted from Association for Children with Life-threatening or Terminal Conditions and their Families and the Royal College of Paediatrics and Child Health (2003) A Guide to the Development of Children's Palliative Care Services (2nd edn). Bristol: ACT, with permission.

Background

Children in the terminal phase of illness are known to suffer significantly from the inadequate recognition and treatment of symptoms, aggressive attempts at cure, fear, and sadness. Any child's death is experienced as a profound loss by parents, siblings, their extended family, and the wider community. Bereaved parents suffer intense grief and may be at increased risk of death themselves from both natural and unnatural causes.[2]

For those living in developed nations, child mortality has fallen to such an extent that the death of a child seems an utterly unnatural and devastating affront. It is now so uncommon as to create a sense of alienation for families who are caring for a dying child or whose child has died. This increases the importance of support for the family throughout the child's illness, from diagnosis and treatment through terminal care to bereavement.

Provision of paediatric palliative care

The provision of paediatric palliative care is patchy and the structure of specialist teams variable. Before thinking about service provision, it may be helpful to consider what and who surrounds a family in this situation.

A large number of agencies and individuals may be involved in supporting children and families, and although this is appropriate, there is the potential for confusion, intrusion, and replication of services. It is often helpful to nominate a *key worker* who can coordinate the various services involved and act as a first point of call for families. Through effective communication, including regular meetings, a comprehensive management plan can be created for the child in question. However, it is also important that all the professionals involved are supported themselves, as this can be a demanding and unfamiliar area of practice. A specialist paediatric palliative care team can support the agencies and individuals involved in caring for the family.

References

1. Association for Children with Life-threatening or Terminal Conditions and their Families and the Royal College of Paediatrics and Child Health (2003) A Guide to the Development of Children's Palliative Care Services (2nd edn). Bristol: ACT.
2. Li J., Precht D.H., Mortensen P.B., Olsen J. (2003) Mortality in parents after death of a child in Denmark: a nationwide follow-up study. Lancet, 361: 363–7.

Differences between paediatric and adult palliative care

Developmental factors

An understanding of developmental issues is essential to the management of a child with palliative care needs. Infants and young children are completely dependent on the adults in their lives for providing care and protection. They also depend on others to make decisions on their behalf.

As children grow and develop, their capacity to care and decide for themselves increases. Indeed, the emergence of autonomy is a central developmental task of adolescence. In this way, care that is appropriate for a child of 11 may be inappropriate two years later, as the need grows for independence, privacy, and control. This can be difficult for both parents and healthcare professionals to accept. The natural desire to protect a child who is experiencing a devastating illness can lead to that child feeling stifled.

The relationship between development and illness is bidirectional. The changing developmental status of the child influences the way in which they experience illness, and illness, in turn, influences the child's development. Chronic illness can delay development, but the life experience it brings may also make a child seem old beyond their years.

The child's developmental level will influence all aspects of palliative care, but the following issues are worth highlighting:

- communication of wishes, fears, and symptoms
- understanding of illness and death
- assessment of symptoms
- management of symptoms
- decision-making
- importance of play as a means of understanding the world
- importance of school and education

Approach to consultation

Developmental level and cognitive ability will vary widely and are not necessarily related to age, so an appraisal of the child's level of understanding will need to be made early in the consultation. While not unique to the paediatric setting, the child's and family's previous experience with medical procedures and staff will strongly influence their attitude to professionals. Honest communication and the development of trust early in the course of the illness will provide a solid foundation on which to face the challenges of palliative care. Conversely, long-term intense treatment involving repeated hospitalization and painful procedures may make a child wary of health professionals. Therefore, consultation and communication style need to be highly flexible and adapted to each individual child and their family. A great deal of patience may be required.

Physiology/pharmacokinetics

Physiology and pharmacokinetics change as the child grows and develops. Neonates have a higher relative volume of distribution and lower clearance than adults, so the half-life of many drugs is prolonged. Conversely, infants and young children may metabolize certain drugs more quickly than adults.

Children over six months of age, for example, may need higher doses of morphine than expected for their size.

Differences in family structure and function

Parents are socially and biologically invested with the responsibility of caring for and protecting their child. Consequently, the development of a fatal illness in the child leads many parents to feel they have failed in this important role. Denial is a common reaction and, despite advice to the contrary, parents may feel compelled to try everything and do anything to find a cure. This can be a difficult time for the child, the family, and the staff caring for them. Staff may feel the child is being subjected to overly burdensome treatment and may also worry that the child is unable to talk about the reality of what is happening. Maintaining hope and a supportive presence while advocating strongly for the child's needs are important elements in managing such situations. A 'hope for the best, prepare for the worst' approach is often helpful.

Whilst the management of the patient is foremost, involving the family in decisions and information-sharing is extremely important. Families will often have a great deal of knowledge about their child's medical condition and, in the case of a child with a rare disease, often know more about it than many professionals. In addition, parents may have already been heavily involved in treatment decisions, and will expect this level of involvement to continue.

The structure of families in the UK may now include the natural parents, step-parents, partners, foster parents, and siblings not directly related to the child. Organizing effective communication amongst these groups is sometimes challenging, but is extremely important, particularly towards the end of life.

Siblings require special consideration in paediatric palliative care. They are almost universally distressed, but often feel unable to share this with their parents. Negative outcomes such as developmental regression, school failure, and behavioural problems may be seen if the needs of siblings are not adequately addressed.

School

The centre of a child's day-to-day life is school, and any disruption of this routine can add to a child's sense of isolation and substantiate their feelings of being 'different' from their friends. Peer groups can be an enormous source of support for a child living with a life-limiting disease. For these reasons, children often remain in school during treatment and even as death approaches. Keeping schools informed (with the permission of the parents and child) is important so that practical arrangements regarding the support required in school and flexibility of school hours can be discussed.

Medical staff can facilitate school attendance by scheduling elective and semi-elective treatments appropriately. As death approaches, the school staff may need support. A plan for supporting staff and pupils through bereavement may also be helpful.

Illness trajectory

Illness trajectory will vary with the particular diagnosis. Often the palliative phase of care in children is much longer than for adults. Indeed, it may even extend from the time of diagnosis. There is also commonly a great deal of uncertainty surrounding the prognosis. Children in advanced states of disability and dependence are at high risk of dying from complications such as respiratory infections, but also have the potential to live many years. Families can find this extremely difficult to cope with, and they may experience negative thoughts and feelings about their situation and about their child.

Physical and emotional exhaustion, as well as concern for the child's suffering, may see them wishing it would all be over. Parents often feel alone with these thoughts, believing they are too terrible to share. The protracted nature of many illness trajectories presents challenges in planning support for the child and their family in terms of both symptom management and psychological support.

Ethical issues in paediatric palliative care

Medical ethics involves the application of ethical principles to medical practice and research.

In palliative care, most dilemmas relate to end-of-life situations. In paediatric palliative care, the inability of the child to act autonomously adds an extra dimension to the decision-making process.

Autonomy

In order to act autonomously:

- one must act with intention and understanding, and without controlling influences
- individuals must demonstrate an understanding of their situation and the implications of their decisions
- individuals must be able to communicate their decisions

Children represent a continuum in this regard, from the non-verbal infant to the adolescent striving for self-determination. Thus, a child's ability to make informed choices depends on their developmental level and life experience. For example, an eight-year-old child with a chronic illness may, through their own experience and that of fellow patients, be better positioned to participate in decision-making than an older child with no previous medical history.

Children may be able to make some decisions about their medical care even where major decisions are made by others. They may, for example, make choices regarding pain control and venepuncture sites. Empowering children in this way gives them a sense of control that impacts positively on their experience of care. Furthermore, even if not deemed sufficiently competent to act autonomously, a child's preferences and insights may guide decision-making by others and should be sought actively.

Decision-making in the palliative care setting

Decision-making requires the following:

- the ability to understand one's illness in physiological terms and to conceptualize death as an irreversible phenomenon
- the capacity to reason and consider future implications (formal operations stage of cognitive development)
- the ability to act autonomously and not acquiesce to the authority of doctors and parents[1]

The Royal College of Paediatrics and Child Health (UK) describes four levels of child involvement in decision-making:[2]

1 being informed
2 being consulted
3 having views taken into account in decision-making
4 being respected as the main decision-maker

Age is not necessarily a good measure of capacity, although an arbitrary distinction is drawn for legal purposes.

Competence

Even young children have the right to be informed regarding decisions which affect their future. Both the Royal College of Paediatrics and Child Health and the American Academy of Pediatrics advocate strongly for the participation of children in decision-making to the extent that their ability allows.

Competence is assessed according to the following criteria:

- Cognitive ability: this may be reflected in young patients' ability to provide a clinical history as well as their understanding of the condition, treatment options, and the consequences of choosing one option over another. Other factors to consider include their level of schooling, verbal skills, and demonstrated capacity to make decisions.
- Presence or absence of disturbed thinking (e.g. in the setting of psychiatric disorder).

Treatment should be discussed with parents and child if appropriate; ideally both will have an understanding of what is involved. Where this is not the case, providing more time for families to think about issues may help. In extreme circumstances, a court of law can be asked to decide what is best.

Decision-making regarding life-sustaining treatment

Doctors, children, and informed parents share the decision regarding life-sustaining treatment, with doctors taking the lead in judging the clinical factors and parents the lead in determining best interests more generally.[3]

Decisions are made on the grounds of benefit/burden proportionality. In order to justify a particular intervention, the expected benefits of that intervention must outweigh the burdens.

End-of-life decision-making is a collaborative process. It should involve the child (where possible), the family, and all the health professionals involved in providing care to the child. An important underlying principle of the process is open communication between staff and families. See Box 16.2.

Box 16.2 A practical approach to decision-making—questions to be answered

- Is this intervention going to cure the disease?
- Is this intervention going to prevent progression of the disease?
- What impact will the intervention have on the child's quality of life?
- Will the intervention improve the child's symptoms?
- Will the intervention make the child feel worse?
- How long will the child feel worse for?
- What will happen without the intervention?
- How will the intervention change the outcome?

Data sourced from Frager G. (1997) Palliative care and terminal care of children. Child and Adolescent Psychiatric Clinics of North America, 6: 889–909.

> Physicians should do more than offer a 'menu' of choices—they should recommend what they believe is the best option for the patient under the circumstances and give any reasons, based on medical, experiential, or moral factors, for such judgements.
>
> American Academy of Paediatrics (1994) Guidelines on forgoing life-sustaining medical treatment. Pediatrics, 93: 532–6.

The Royal College of Paediatrics and Child Health outlines five circumstances under which withholding or withdrawing curative medical treatment may be considered:

- The child has been diagnosed as brain dead according to standard criteria.
- Permanent vegetative state: these children have 'a permanent and irreversible lack of awareness of themselves and their surroundings and no ability to interact at any level with those around them'.
- 'No-chance situation': life-sustaining treatment simply delays death without providing other benefits in terms of relief of suffering.
- 'No-purpose' situation: the child may be able to survive with treatment but the degree of mental or physical impairment would be so great that it would be unreasonable to ask the child to bear it.
- The 'unbearable' situation: in the face of progressive, irreversible illness, the burden of further treatment is more than can be borne.

Disagreement

Society invests parents with the responsibility of acting on behalf of their children. There are occasions however, where parents insist on what staff may view as inappropriate treatment. Conversely, parents may refuse treatment that is of potential benefit to the child. It is important that the best interests of the child are advocated for and that decision-making is shared between the family and the healthcare team.

Families often need time to absorb and process difficult information, and decision-making should be viewed as a process, not an event. Most disagreements can usually be resolved by regular open and honest communication. Where conflict cannot be resolved, it may be helpful to request a second opinion from an independent practitioner. It may also be beneficial to include other family members or cultural and religious leaders from the local community. In extreme circumstances where agreement cannot be reached despite these interventions, it may be necessary to seek legal judgement. See Box 16.3.

Advance care planning

Where children have an existing condition, then a gradual or sudden deterioration may be anticipated. It is helpful for health professionals to assist families in planning for crises so that interventions considered unhelpful to the child are not initiated. Written documentation in the medical record as well as a copy for the family to have with them is required.

Advance care plans should record

- what has been discussed
- who was present
- what decisions were made
- what the child's and family's wishes are regarding various interventions
- who should be called in case of a crisis

Provision of hydration and nutrition

- Food and fluid should always be offered if the child is able to take it by mouth.
- Most authors consider the provision of nutrition and hydration by artificial means to be a medical intervention subject to the same assessment of benefits/burdens as any other.
- The insertion of tubes into the gastrointestinal tract carries with it the burdens of discomfort and the potential for complications, and therefore needs to be justified on the grounds of the benefits it may provide to the patient.
- Some argue, however, that the provision of food and fluid constitutes a basic component of humane care and can never be withdrawn or withheld.
- In the paediatric setting, this concept is extended by the centrality of feeding to the parental role and the vulnerability of infants and small children.
- Children in the terminal phase of illness will naturally cease eating and drinking as their requirements decrease, and it is not necessary in these circumstances to provide fluid and nutrition by artificial means.

Medical ethics in different cultures

It is important to understand the limitations of Western ethics. The beliefs, values, and conceptual frameworks used by other cultures must be considered when making decisions with families. The most appropriate source of information is the family itself, as there will be considerable variability within cultural groups.

Box 16.3 Case study—Charlie Gard

Charlie Gard was born at full term, apparently healthy, in August 2016. At a few weeks of age his parents noticed early signs of muscle weakness. By two months of age, he was admitted to Great Ormond St Hospital (GOSH) with poor feeding, failure to thrive, and respiratory failure. He was admitted to intensive care, where investigations led to diagnosis of a rare severe mitochondrial disorder—infantile onset encephalomyopathic mitochondrial DNA depletion syndrome (MDDS).

The specific genetic form of MDDS in Charlie Gard (RRM2B) had previously been reported in approximately 15 infants, with typical clinical features including early onset, rapid progression, and death in infancy. By that point, he was paralyzed and unable to breathe without respiratory support. He was found to have congenital deafness, and his heart, liver, and kidneys were affected by the disorder.

In early 2017, Charlie's parents identified an experimental treatment, previously used in a different form of MDDS, which they hoped might benefit Charlie. In mouse models of a myopathic form of MDDS (TK2), early supplementation with deoxypyrimidine nucleosides apparently bypasses the genetic defect and leads to reduction in the biochemical defect and severity of clinical phenotype 22 23. Doctors at GOSH initially planned to use nucleoside treatment in Charlie; however, in January he developed evidence of electrical seizures, and clinicians became convinced that treatment, both continued intensive care and the requested nucleoside therapy, would be futile. A US physician involved in the nucleoside research offered to provide treatment, and Charlie's parents raised funds for him to travel to the US.

However, doctors at GOSH were not happy with Charlie being transferred overseas for treatment. They applied to the Family Division of the High Court on 28 February for permission to withdraw life support and to provide palliative care. Charlie's parents opposed this plan. On 11 April, Justice Francis ruled in favour of the hospital. Charlie's family appealed, and the decision was reviewed (and upheld) in the Court of Appeal (23 May), Supreme Court (8 June), and European Court of Human Rights (20 June).

Appeals. At that stage, all avenues of legal appeal had been exhausted, and plans were made to withdraw medical treatment.

Following widespread public and media attention, including statements of support by President Trump and Pope Francis, a number of international medical and scientific experts came forward offering treatment and presenting apparently new evidence allegedly increasing the chance of benefit from nucleoside treatment. On 10 July, Great Ormond Street Hospital elected to bring this evidence back to the high court. The court arranged for the US mitochondrial specialist to review Charlie in London. Following a multidisciplinary meeting and new evidence of the severity of Charlie's illness, including the results of a full-body MRI, on 24 July his parents accepted that further treatment could not help him and withdrew their application to the court.

Reproduced from Wilkinson D, Savulescu J. Hard lessons: learning from the Charlie Gard case. Practical Ethics blog, University of Oxford. Accessed from http://blog.practicalethics.ox.ac.uk/2017/07/hard-lessons-learning-from-the-charlie-gard-case/

Psychosocial needs in paediatric palliative care

Physical, emotional, and spiritual needs cannot be addressed in isolation, as each affects the other. For example, a child's pain can heighten parental anxiety, and family distress may adversely affect pain control. A multidisciplinary approach to palliative care is required; therefore a large number of individuals and services can potentially become involved in the care of the child. Coordination of these professionals and the services each is providing is essential to avoid replication or omission, or disempowerment of the family. This can be achieved by regular communication between team members and the appointment of a key worker for each child. This person may be a general practitioner, paediatrician, nurse, or an allied health worker.

Providing emotional and psychological support for the sick child is as essential as providing relief of physical symptoms.

Communicating with children about death and dying

A child can live through anything so long as he or she is told the truth and is allowed to share with loved ones the natural feelings people have when they are suffering.

From Hebert M. (1996) *Supporting Bereaved and Dying Children and their Parents*. Leicester: BPS Books.

Parents may instinctively want to protect their children from 'bad news'. However, children very often know a great deal about their illness and prognosis. Children may not reveal what they know for fear of upsetting their parents, who then falsely assume their child knows very little. Children are very sensitive to discrepancies between verbal and non-verbal information. They readily sense distress in those around them and may feel anxious and isolated as a result. They may also generate fantasies to explain unusual behaviour in their parents (e.g. 'I have been bad', 'Mummy and Daddy don't love me any more'). These notions may be more frightening than death and dying to a young child. This is particularly true of younger children, who are naturally egocentric and believe that the world revolves around them, and hence personalize other people's emotional and behavioural reactions.

- Parents' reluctance to talk to their child about dying usually stems from an erroneous belief that their child's concept of death is similar to that of an adult's, and their consequent desire to protect them from emotional pain.
- Younger children's greatest fear is usually around immobility and separation from loved ones during their illness and after. Opening up discussions about death can help allay these fears and provide the child with reassurance.

- School-aged children frequently have worries about experiencing pain, and can be greatly reassured by discussions about pain control. They may also ask questions about what will happen after their death, and can receive great comfort from religious or family beliefs.
- Just as parents and siblings need to plan the time they have left with the sick child in order to build memories and have as few regrets as possible, the dying child may also wish to prioritize the time left to do special activities or spend time with loved ones.

Children very often ask staff questions about their illness and prognosis. When confronted by a difficult question, staff may be uncertain as to how best to respond. Questions often come unexpectedly, when the staff member is especially busy or distracted. Children generally know the answer to the question before they ask it.

In this way the child who asks, 'Am I dying?' may already know the answer. What they seek is a person who can be trusted to speak honestly with them. Responding with a question such as 'What makes you ask me that?' or 'What is it that makes you think you are going to die?' may elicit information on which to base a response. The real question may be something completely different. Of course, children, just like adults, are very individual in how they respond, and while some children may ask plenty of questions and request lots of information, other children may wish to hear limited information. It is important to be guided by the child, and also to remind them that they can ask questions whenever they wish.

Supporting the sick child

These ideas mirror the supportive measures used in adult palliative care.

- Listen
  - Ask the child how they would like to be supported.
  - Find out exactly what it is the child wants to know.
  - Let the child set the pace.
- Allow the child to make choices where possible.
- Explain things in simple language appropriate to the child's development and cognitive ability.
- Wherever possible, answer questions honestly.
- Answer the question that is being asked. Try not to burden the child with too much unsolicited information.
- Children may find it easier to talk while drawing or doing some other activity. They may also find it helpful to talk in an abstract way, e.g. about a character in a story or during play with dolls.
- Artwork, play, story writing, music, and other creative activities may provide an outlet for emotion.
- Normalize feelings of fear, anger, and sadness.
- Try not to dismiss a child's beliefs unless they are potentially damaging.
- Model and encourage expression of emotion. Children need to know they can express their feelings without alienating those around them.
- Provide physical contact and comfort.
- Maintain routine to the greatest extent possible.
- Involve the child's friends in visits. If this is not possible, encourage letters, photos, emails, videos, etc. Discourage social isolation but do allow time for privacy.

Recruit the child's school teacher to help—this may be helpful even where children are not able to attend school.[1]

Reference

1. Hebert M. (1996) *Supporting Bereaved and Dying Children and their Parents*. Leicester: BPS Books.

Supporting parents

Communicating difficult information to parents

The way in which difficult information is communicated is important and sets the stage for the working relationship between professionals and family. Health professionals need to be aware of how their own feelings of anxiety, sadness, and impotence may influence this process. Most parents desire a realistic appraisal of their child's condition delivered empathically and with a sense of hope. Realistic hope can be offered in terms of ongoing support from the team, attention to symptoms, and help to maximize the child's quality of life. In situations where the family is pursuing curative treatment, hope can be maintained by 'hoping for the best but preparing for the worst'.

How should difficult news be delivered?

- empathically
- in person, face-to-face
- allow plenty of time
- establish what the parents know or suspect, e.g. 'How do you think things are going?'
- allow the family to set the pace
- respect silence and do not feel compelled to fill it
- allow expression of emotion
- avoid being evasive
- offer to help inform other family members, e.g. siblings, grandparents
- offer to meet again soon

What information should be given?

- honest, accurate information devoid of technical jargon
- Try to determine what the family wish to know, e.g. 'Are you the sort of person who likes to know everything or just the basic information?'.
- simple language—there will be time later to explore details
- Avoid ambiguous language such as 'We might lose the battle' or 'He's passed away'. The words 'death' and 'dying' should be used.

A brief outline of the expected disease course should be given and expected symptoms mentioned. It may also be helpful for some families to understand what can be done for these symptoms. Many parents have not experienced the death of a relative or friend and may be frightened at the prospect of seeing someone die. Information about the bodily changes that accompany death may be helpful, and it is possible to be very reassuring about the process because—for most children who are managed carefully—it is very peaceful. Families may be worried about pain and distress or a final dramatic event. In most cases, however, the terminal phase is characterized by the progressive shutdown of the various organ systems.

Parental reaction to bad news

Parents are often so shocked on being told that their child is dying, even if this is confirmation of their own suspicions, that they cannot assimilate any other information at that moment. It is important to slow the process

down, provide multiple opportunities to speak with the family, repeat information where necessary, and provide written information. Following the initial shock, parents may feel confused and overwhelmed. They may be frightened that they will not be able to cope with the child's physical care or be unable to control their emotions. Parents also experience feelings of uncertainty. They may have difficulty making sense of what is happening and are unsure of what to do first.

Denial occurs occasionally. For some parents it may be an adaptive defence and does not always need to be 'broken down'. In fact, great caution should be exercised in confronting denial. Where denial is impairing optimal care and family functioning, however, it may be helpful to gently challenge inconsistencies and explore underlying concerns. Asking a question like, 'Is there ever a time even for a few seconds where you worry things might not turn out the way you hope?', may provide a window of opportunity for the parent to work through the issues confronting them.

Anger may arise from fear and confusion, often as an expression of despair. Parents feel an enormous loss of power and control in their lives. Their sense of justice is rocked. The struggle to understand, make sense of the situation, and control emotions can produce anger. This may be directed at staff. In managing angry parents, it is important to keep in mind the following:

- to acknowledge the anger, e.g. 'I can see you're very angry'
- not to take it personally
- not to be defensive
- to allow venting of the anger: 'Can you tell me more about what you're feeling?'
- not to dismiss the complaint or try to explain the situation logically
- to set limits: 'I can see you are angry and I am willing to speak with you about it, but I cannot let you damage property/threaten me, etc'.

Guilt is another common reaction amongst parents of dying children. They may feel that they failed to recognize and respond effectively to the symptoms of the child's illness. They may feel responsible because the illness is inherited. They may experience 'survivor guilt', believing that children are not supposed to die before their parents. They may believe that their action or inaction somehow triggered the illness. Parents may externalize these feelings and blame others. Staff members occasionally find themselves unfairly blamed for a child's illness or death. This may feel hurtful, but it is important not to become defensive or allow this to impact on the care of the child. Any inclination to label the family as 'bad' should also be avoided.

What parents need to know

Explaining to parents that children often ask questions about their illness and prognosis provides a key opportunity for them to consider how they might deal with these themselves.

Planning in advance is helpful, and a team approach, with parents forming part of the team, essential. Parents bring particular knowledge of their child as a unique individual. Staff bring knowledge of the literature in this area and experience with other families in similar circumstances.

Families need to know that

- Children are generally more aware of their prognosis than those around them believe.
- If a child does not ask questions or speak about their illness, it does not mean that they are oblivious or indifferent. Children often protect parents by feigning ignorance—'mutual pretence'.
- The anxiety generated by misinformation is potentially more harmful than any arising from the truth. Children may have all sorts of worries and fantasies, many of which an adult might not expect, e.g.: 'What will happen to the cat?'; 'Will my school friends forget me?'; 'Will somebody be with me?'; 'Are Mummy and Daddy breaking up?'; 'Are Mummy and Daddy cross with me?'; 'Did I get sick because I was bad?'; 'Will it hurt?'. To a young child, abandonment and withdrawal of their parent's love may be more frightening than the notion of death because they have not yet acquired a full understanding of death. An environment of honesty provides the child with opportunities to share these worries. They need to feel they can trust those around them.
- A dying child may be better able to cope with news of their impending death than their parents.
- Parents are important role models. Children look to their parents for cues regarding the appropriate way of reacting to a given situation. While courage and calm will help reassure a child, it is also reasonable for parents to show their sadness. It is helpful for children to understand why their parents are upset so that they do not make incorrect assumptions. An honest explanation may be reassuring.

In extreme cases where parents still insist that information is withheld but the child is clearly distressed by this approach, the health professional's duty is to the child.

While, in general, honesty is the best approach, it is important to recognize that not all children benefit from detailed information and not all parents feel able to communicate openly with their child. The best interests of the child are what is important. Cultural factors also require careful consideration.

Parents' needs and the role of the health professional

Information

Parents generally want information so that they know what to expect. They may also want to discuss treatment options and plans for symptom control. Parents say that full information allows them to make decisions and helps them plan for the remaining time they have with their child. In general, it is best to be open and honest, as a trusting relationship between parents and healthcare workers provides a solid foundation for the challenges of palliative care. It is also helpful to regularly check that families are not being overwhelmed with too much information (e.g. 'I know this is a lot of information for you to hear all at once. We can talk in more detail a little bit later on if you would prefer').

Time to be listened to

Many parents want to discuss their situation with the many healthcare workers involved in their child's care. They may need to speak about their concerns, fears, hopes, and expectations on numerous occasions to clarify and make sense of a world gone awry. The healthcare worker (whether it be a paediatrician, social worker, or nurse) needs to provide time and opportunities for parents to share these concerns. By listening to the concerns of parents, providing guidance, affirming their skills and resources, and staying with them, staff can make a major difference to how a family copes. It is important to remember that some parents do not wish to have such discussions, and individual coping styles should be respected.

Control

Parents talk of losing control of their lives. The healthcare worker can assist parents to regain a sense of control by providing them with information, including them in discussions regarding care, allowing them to decide who is allowed to visit and when, and so on. Making decisions for (rather than with) a family can be deskilling and destructive. Parents need to be viewed as competent partners in their child's care.

Emotional support

Parents with a sick child grieve for the 'normal' child they no longer have. With this grief comes a range of strong feelings and emotions which add to the task of caring. Parents need acknowledgement, compassion, empathy, and non-judgemental understanding. Spiritual support may or may not be part of a family's support system when their child becomes sick. The child's illness may cause parents to question their faith, renew their faith, or explore new avenues. Spirituality includes, but is not restricted to, religion. Local clergy, ministers of all faiths, and other spiritual leaders are available to help during this confusing time.

Amidst major changes to their routines and view of the world, the family may, however, try to hang on to some sense of normality. Health professionals can facilitate this by scheduling treatment around important activities and school attendance, and encouraging the family to maintain routines and activities.

Practical support

Parents need advice and guidance from various professionals in order to learn what is available to help them. Most parents would not know where to begin if they have had no previous experience. Therefore, liaison between the hospital and community team is a helpful step.

Medical equipment may be required as part of the child's care, either routinely or in an emergency. It is possible to have equipment items on loan from a hospital or community agency, e.g. a palliative care service. Health professionals, including social workers, occupational therapists, and physiotherapists, may be needed to make assessments of the child's and family's needs.

Sibling needs

The needs of siblings are very similar to those of the dying child.[1]

Relationships within families and communication patterns are important factors in determining how siblings react to a brother or sister's illness. It may be easier for children to adapt to having a sick sibling in a family where it is usual to discuss matters openly and to share their feelings and emotions.

Physical symptoms may develop, such as nausea, vomiting, diarrhoea, constipation, headache, and aching limbs. Symptoms similar to those experienced by the sick sibling may also be reported.

Behavioural changes may also occur, including unusual aggression, temper tantrums, withdrawal from family or friends, rudeness, bullying, and demanding attention. Regression in the form of thumb-sucking, enuresis, toileting problems, or school refusal may occur. Sleeping problems include a fear of the dark, nightmares, waking in the night, and wanting to sleep in the parents' bed. Older children and adolescents may withdraw completely or indulge in risk-taking behaviour.

It is also important to note that some siblings will experience none of the above.

Information

Parents should be encouraged to be honest with siblings and to provide them with information at a level appropriate to their developmental stage. This might include facts about the illness, what treatment is being given, and what to expect. They may need reassurance that they and their parents are not likely to become ill and that nothing they did or said caused the illness. Siblings may have concerns regarding their own health, and if they are reporting symptoms, may benefit from the reassurance of a thorough physical examination by their doctor.

Routine

Whilst it is difficult to maintain routine at a time of such upheaval, the familiar routines are important for a child's sense of security. These include going to school, continuing with extracurricular activities, and maintaining contact with their own peer group. Siblings may need to know that it is acceptable to have fun.

Emotional support

Siblings may try to protect their parents from added distress by not burdening them with their own worries. Many are known to suffer in silence. Unexpressed emotion may manifest as school failure, behavioural problems, and physical symptoms. Siblings may also try to excel at school to 'cheer their parents up'. Feelings of resentment, jealousy, isolation, fear, guilt, anger, and despair need to be explored, acknowledged, and normalized. It is helpful if parents are able to dedicate special time to be with their well children. Some parents may need permission to do this, as they feel guilty if they leave the sick child's side.

Contact with the sick child

Regular visits to the sick child in hospital allow siblings to see what is happening for themselves. It is important, however, that they are adequately prepared for what they might see, e.g. 'John is very sleepy. He might not be able to talk to you but he will know you are there. He has medicine running into his body through a tube in his arm—this doesn't hurt', etc. In the rare circumstance where siblings cannot visit, regular updates, videos, and photos can be helpful. Siblings can feel included by sending drawings, favourite toys, photos, and videos to their brother or sister.

Inclusion in the care of the sick child

Siblings may benefit from the opportunity to be included in the care of the sick child and in the family's experience. Children can help by taking a drink to the child, changing the channel on the TV, reading a story, playing games, and taking the cat in to visit.

School

It is helpful if the sibling's school teachers are kept informed (with the family's permission) of the sick child's condition. Schools can also help by identifying one person to whom the sibling can go if they need help.

Further reading

Hain R, Jassal S. (2010) Paediatric Palliative Medicine. Oxford: Oxford University Press.

Community-based care

Most children who need palliative care will be looked after in, and by, their local community. It makes sense then that the community team is involved from early in the child's illness so that relationships are well established by the time the child's care needs to be increased. Resources available to families may include the following:

- general practitioner who will often know the child and family
- community-based paediatrician
- palliative care services
- paediatric palliative care services
- domiciliary nursing
- respite
- children's hospices
- counselling
- religious groups
- family and friends
- community agencies (which may offer the family support and financial assistance)

Since children will often move between hospital and community settings, it is important that there is a collaborative approach to care and that communication flows easily and appropriately. The use of a key worker can facilitate such communication.

The nature of the care available in a particular situation will vary a great deal depending on the particular community services available. Services are changing rapidly and it is important to check on current service availability before planning community care. Non-evidence-based optimism or pessimism about the community service availability can cause much needless distress for the child and family.

Bereavement

- Most adult palliative care programmes become involved with patients towards the end of life.
- In contrast, children's programmes aim to identify children close to the time of diagnosis and provide services and support to the family as they progress through the disease process and eventual death.
- Most children and their families wish to spend as much time at home as possible, and many hope to be able to care for their child during the terminal phase, provided adequate support is available.
- Some families will find this task extremely difficult and will wish to return to a hospital or hospice environment close to the time of death.
- This should not be viewed as a failure of home care.

The dying process

The actual dying process is usually an orderly and undramatic progressive series of physical changes which are not medical emergencies requiring invasive interventions. Parents need to know that these physical changes are a normal part of the dying process. It is very important that families are well supported at this time. If the child is dying at home, 24-hour support from experienced staff whom they know and trust can make an enormous difference. Home visits by the GP, domiciliary nurse, and oncology liaison nurse, where appropriate—to assist with managing the child's symptoms—are greatly appreciated by the family. This is a very emotional and difficult time for the whole family.

Staff support

The death of a child is a relatively unusual event, so that the modern paediatrician is more familiar with cure and prevention than with death and dying. While advances in medicine have led to happier outcomes for the majority of children, there remains a group for whom cure is impossible. The relative infrequency with which death occurs in childhood has implications for those caring for this group of children. Staff may feel a sense of failure and impotence. A lack of exposure to dying children may leave them feeling ill-equipped to support a child and family through this phase of their care. They may also have become very attached to the child and family and experience their own grief. All these responses are normal, but in the absence of adequate self-awareness and support, health professionals may, over time, become 'burnt out'.

Burn-out is 'the progressive loss of idealism, energy, and purpose experienced by people in the helping professions as a result of the conditions of their work'.[1] This may manifest as excessive cynicism, a loss of interest in work, and a sense of 'going through the motions'.

Other features include fatigue, difficulty concentrating, depression, anxiety, insomnia, irritability, and the inappropriate use of drugs or alcohol. The consequences for families are significant, as staff affected in this way may

- avoid families or blame them for difficult situations
- be unable to help families define treatment goals and make optimal decisions
- experience physical signs of stress when seeing families

The quality of care may be compromised, and families may become disenchanted with the health professional and seek help elsewhere, sometimes from inappropriate sources.

Risk factors

There are a number of risk factors for the development of behaviours and responses that may impact upon patient care, and these can be categorized in the following way:

- clinician-related
  - identification with the family or situation
  - unresolved loss and grief in own past
  - fear of death and disability
  - psychiatric disorder
  - inability to tolerate uncertainty
- family-related
  - anger, depression
  - uncooperative families
  - family member is a health professional
  - complex or dysfunctional family dynamics
  - well-known to staff (e.g. friends, relatives, colleagues)
  - intractable pain or difficult symptoms
- situation-related
  - family member/s are friends or relatives of the clinician
  - uncertainty/ambiguity
- disagreement about goals of care
  - patient/clinician
  - team
- protracted hospitalization[2]

While it is common for health professionals to experience emotions such as anger and sadness in the course of clinical care,[3] it is important that these do not result in behaviours that could compromise the quality of care. Recognition of the emotion helps control it to some extent, as does accepting the normality of experiencing emotion. It may also be helpful to seek out a trusted colleague to whom you can talk.

References

1. Edelwich J., Brodsky A. (1980) Burn-out: Stages of Disillusionment in the Helping Professions. New York: Human Sciences PR.
2. Meier D.E., Back A.L., Morrison S. (2001) The inner life of physicians and care of the seriously ill. Journal of the American Medical Association, 286: 3007–14.
3. Vachon M.L.S. (1995) Staff stress in hospice/palliative care: a review. Palliative Medicine, 9: 91–122.

Strategies for self-care

Stress amongst staff who provide palliative care for children, in any setting, is likely to be great, and the stresses involved in providing palliative care for children may affect the caregiver's ability to provide care in a sensitive and professional manner. Regular supervision and access to professional expertise by staff in areas where long-term relationships with patients and families are built up are important, and should ideally be written into job descriptions.[1]

There are a number of ways in which staff may be supported:

- Formal support through regular team meetings reduces conflict between staff members as long as open discussion is encouraged. This is dependent on the structure of the team and the quality of facilitation.
- Formal support at an individual level is beneficial for some. It is particularly useful in circumstances where concerns cannot be raised in the group context.
- Informal peer support is generally regarded by staff as being most effective.[2]
- Support from family and friends.
- Maintaining perspective through involvement in outside activities. Formal supervision may assist in developing the self-awareness necessary to achieve this.
- Education provides staff with the skills they require to overcome feelings of impotence. In a recent survey of resident medical officers in the United Kingdom, lack of training in the breaking of bad news was identified as a serious deficiency in their education.[3]

The care of the dying child presents enormous challenges, but if done well has the potential to bring lasting benefits to both the family and the health professional.

References

1. Association for Children with Life-threatening or Terminal Conditions and their Families and the Royal College of Paediatrics and Child Health (2003) A Guide to the Development of Children's Palliative Care Services (2nd edn). Bristol: ACT.
2. Woolley H., Stein A., Forrest G.C., Baum J.D. (1989) Staff stress and job satisfaction at a children's hospice. Archives of Disease in Childhood, 64: 114–18.
3. Dent A., Condon L., Blair P., Fleming P. (1996) A study of bereavement care after a sudden and unexpected death. Archives of Disease in Childhood, 74: 522–6.

Drugs and doses

The following section is divided into the common symptoms experienced by very ill children, and outlines a management strategy for each.

- agitation
- anorexia
- bleeding
- breathlessness
- constipation
- convulsions
- cough
- gastro-oesophageal reflux
- gastrostomy care
- hiccup
- infection
- mouth care
- muscle spasm
- nausea and vomiting
- noisy breathing
- pain
- other pain syndromes
- psychological issues
- raised intracranial pressure
- skin
- sleeplessness
- terminal restlessness
- ventilation at home

Introduction to drugs and doses

The approach to the care of a dying child and their family greatly influences the quality of their lives and the ability of the parents and siblings to cope with the child's death. Most symptoms are readily amenable to effective management. It is important, however, to adopt an individualized approach, taking into account the unique circumstances of each child and family.

Drug information

Drug information for paediatric palliative medicine is changing all the time. The lead-in time for books is such that information is often out of date. To get the latest information on medication and dosage, we would strongly recommend you refer to the following resources:

- **Association of Paediatric Palliative Medicine Formulary** http://www.appm.org.uk/10.html or the
- **Rainbows Symptom Control Manual** http://www.togetherforshortlives.org.uk/professionals/resources/2434_basic_symptom_control_in_paediatric_palliative_care_free_download

Planning care

Medical assessment

- Make sure you are armed with as much information about the child and their family as possible.
- Make sure you involve all the right people: this might include parents, siblings, grandparents, and other carers. Whether you involve the child themself will depend on the child's age, understanding, and state of health, and the parents' wishes. It is often helpful to have another involved professional present, e.g. the district nurse in the community setting, so that someone else is fully aware of the discussion and can answer any questions the family might have after you have left.
- Try to arrange things so that you are not in a hurry and are unlikely to be disturbed.
- Be methodical: take a thorough history and perform a full examination. Allow the child and parents time to voice their concerns as fully as possible.

Explanations

- Explain symptoms and management options.
- Identify any concerns the child or family may have and address these (e.g. concerns about the use of strong opioids).
- You may not have all the answers: if not, say so.

Plans

- Identify, articulate, and document the current goals of care.
- Formulate a plan of action in consultation with the parents and/or child.
- Listen to any concerns that arise from this, and be prepared to compromise on a management plan if the parents or child want something different.

- Ensure there is a plan for the exacerbation of current symptoms and the development of new ones. Knowledge of the child's condition will be important here, and expertise may be required from sub-specialists.
- Run over the plan at the end of the consultation in language the parents and/or the child can understand.
- It may be helpful to write the plan down and give a copy to the family.

Communication

- Families need access to advice and support around the clock: make sure family members/carers know how to contact professionals, particularly out of normal working hours.
- Liaise with relevant professionals and carers—leave clear written instructions in medical records or contact the community team to discuss directly—many different healthcare professionals may be involved, particularly in the community, and it is important that everyone is aware of any changes in management.
- A key worker can be invaluable.

Review

- Make a time and date when the management plan will be reviewed, and by whom.

Routes for drug administration

According to the bioavailability of the drug and patient preference, different routes of administration should be considered for each drug prescribed. These include routes not normally used in adult care:

- oral
- sublingual
- buccal
- nasal
- intravenous
- subcutaneous
- transdermal
- rectal
- epidural/spinal

Agitation/delirium

Consider the following causes:

- terminal restlessness
- uncontrolled pain
- medication (e.g. benzodiazepines, polypharmacy)
- gastro-oesophageal reflux
- urinary retention
- constipation
- dehydration
- sepsis
- cerebral causes: raised intracranial pressure, intracranial bleed
- hypoxia
- environmental irritation: too hot/cold/bright light
- fear/anxiety
- nausea
- positioning

Management

General measures

- Treat any reversible cause if possible and appropriate (make sure the child is not in pain).
- Nurse the child in a quiet and safe environment surrounded by familiar people and objects.
- If other measures are unsuccessful, pharmacological intervention may be necessary.
- Benzodiazepines are the most commonly used medication in this setting.
- Many children with neurological disease will have been on benzodiazepines for muscle spasm or seizures, and will therefore need and tolerate higher doses.
- Benzodiazepines are generally very effective, but occasionally a paradoxical increase in irritability may be seen.
- Haloperidol is less frequently used but may also be helpful, and is not too sedating. It may cause extrapyramidal side effects at higher doses.
- Families may need to understand that the child may not be as responsive once medication is given, but that the priority is the child's comfort.

Medication

The choice of medication will depend on the circumstance for which it is being prescribed, duration of action required, and the location of care. Children experiencing brief periods of anxiety or panic attacks may benefit from a benzodiazepine that has a short half-life, such as midazolam or lorazepam. Children needing a longer duration of action may do better with diazepam or clonazepam.

In the community, lorazepam, midazolam, and clonazepam may all be given via the buccal or sublingual routes, and are easy for families to use. Levomepromazine may be an appropriate agent for children who also have nausea. Midazolam is the benzodiazepine of choice for use in a syringe pump. Both midazolam and levomepromazine are useful if deeper levels of sedation are required. Lorazepam or midazolam can be used in combination with haloperidol in severe agitation.

Anorexia

Poor appetite and weight loss are common in children with terminal illness, particularly towards the end of life. This causes a great deal of anxiety amongst many parents and carers for the following reasons:

- They may consider one of their main caring roles is to keep their child well-fed.
- They often perceive eating as a road to recovery.
- Acceptance that their child doesn't want to eat may go hand-in-hand with acceptance that the terminal phase is approaching.

Consider reversible causes

- oral candidiasis
- pain (in mouth or elsewhere)
- gastro-oesophageal reflux
- nausea/vomiting
- constipation
- medication

Management

General measures

- Explanation and discussion with the family may be helpful. Listen to parents' concerns and reassure as appropriate. It may be helpful for families to understand that as the child becomes less mobile and as the body winds down, the child's need for fluid and food diminishes.
- Provide small meals on small plates. The child may prefer to snack through the day rather than sit down to a meal.
- Make food less effort to eat (e.g. by providing mashed meals or wholesome soups, ice cream, and rice pudding).
- Offer 'favourite' meals.
- Offer supplementary high-calorie/high-protein drinks.
- Try not to make an issue out of mealtimes.
- Low-dose steroids will stimulate the appetite but will not change the course of the disease and may have harmful side effects. They are almost never given for this indication.

Bleeding

Management

General measures

- Consider a platelet transfusion if bleeding is problematic and related to low platelet count in a child with a reasonable prognosis where a transfusion would improve quality of life.
- Unfortunately, as there are few options for dealing effectively with large bleeds in the palliative stages, focus should instead be on anticipation and relief of anxiety and pain.
- If bleeding is likely, explain this to the parents and prepare a management plan.
- If a significant bleed is a possibility, then benzodiazepines should be readily available and the use of dark towels and blankets may be helpful.

Medication

Bleeding gums

- Use a soft toothbrush if possible. If not, avoid brushes altogether. Consider gentle regular antibacterial mouthwash to prevent secondary infection. Absorbable haemostatic agents such as Gelfoam® may be useful.

Tranexamic acid

- Tranexamic acid is an antifibrinolytic agent that will help to stabilize blood clots and reduce oozing from the mouth and other mucosal surfaces. Commence treatment at the onset of bleeding and continue for 72h after bleeding has stopped.

Topical adrenaline

- form: 1:1000 solution
- small external bleeds: soak gauze, apply directly to bleeding point

Sorbsan dressing

- haemostatic dressing: apply directly to the bleeding point

Vitamin K

- consider in liver dysfunction with coagulation abnormalities

Vaginal bleeding

- may respond to oral progesterone

Catastrophic haemorrhage

An anxiolytic or sedative drug such as midazolam or diamorphine is useful, as a large haemorrhage is likely to be very frightening if the patient is conscious. If haemorrhage is likely, then an anxiolytic in a suitable form (e.g. subcutaneous or buccal) should be readily available, and all carers/staff should be aware of how to administer it. A rapid onset of action may be desirable, so provision should be made for parenteral administration.

Terminal haemorrhage may not always be painful, and the 'traditional' use of diamorphine in this instance may not be appropriate. However, some bleeds are undoubtedly painful, and diamorphine should be available if this is a possibility.

Breathlessness

Dyspnoea, like pain, is a subjective symptom and may not correlate with objective signs.

Consider causes and treat reversible factors as appropriate:

- anaemia
- airway obstruction
- anxiety
- ascites causing elevated diaphragm
- bronchospasm
- cerebral tumours
- chest pain (musculoskeletal or pleuritic)
- congenital heart disease
- cystic fibrosis
- infection
- metabolic disorders, including uraemia
- raised intracranial pressure
- respiratory muscle dysfunction, e.g. neurodegenerative disorders
- primary or secondary tumours within lung fields or abdomen causing elevated diaphragm
- pleural effusion/pneumothorax*/haemothorax
- pulmonary fibrosis
- superior vena cava (SVC) obstruction*
- increased secretions
- pulmonary oedema
- pulmonary embolism*
- pericardial effusion*

*❗These are **medical emergencies** that may require specialist intervention. Swift treatment of these conditions can significantly reduce symptoms.

Management

General measures

- Anxiety is likely to be an associated feature. Try reassurance, relaxation techniques, distraction, and anxiolytics where necessary.
- Provide a flow of fresh air—fan/window.
- Try not to overcrowd the room.
- Optimize position.
- Excess secretions may respond to gentle physiotherapy and suction.

Oxygen

May be helpful in hypoxic patients but is not without consequences (e.g. wearing a mask can be uncomfortable and interfere with the ability of the child to be close to parents and carers; equipment can also compromise mobility). The benefits of this intervention need to outweigh the burdens.

Children often refuse masks but may tolerate nasal specs. Consider humidifying oxygen, which will dry the mouth less.

Caution is needed in circumstances where chronic hypercapnia has left the child dependent on hypoxic respiratory drive. Too much oxygen will result in hypoventilation, so titrate carefully.

Medication

The choice of medication will depend on the underlying cause. Bronchospasm will respond to a bronchodilator. Anxiety that is unresponsive to reassurance, distraction, or relaxation techniques may require treatment with a benzodiazepine. Excessive secretions may respond to physiotherapy and/or mucolytic agents. Opioids, however, are generally very effective.

Morphine

Morphine is effective in treating dyspnoea, although there may be no measurable effect on respiratory rate or oximetry. Morphine reduces anxiety, pain, and pulmonary artery pressure. Begin with half the paediatric analgesic dose and titrate to effect.

Benzodiazepines

Many children will be frightened by dyspnoea. In addition to relaxation techniques and guided imagery, benzodiazepines may be helpful. The choice of benzodiazepine will depend on the circumstance for which it is being prescribed. Children experiencing brief periods of anxiety or panic attacks in association with dyspnoea may benefit from a benzodiazepine with a very short half-life, such as midazolam, given buccally or subcutaneously. Sublingual lorazepam is another option for panic attacks or anxiety related to dyspnoea. Children needing a longer duration of action may do better with diazepam, clonazepam, or a subcutaneous midazolam infusion.

Dexamethasone

Dexamethasone may be helpful in circumstances such as bronchospasm, bronchial obstruction, lymphangitis carcinomatosa, SVCO, and raised intracranial pressure. Administration requires careful consideration, as steroids may produce potentially distressing side effects in children if given for more than a few days. To avoid this, it is preferable to prescribe short courses (3–5 days) of steroids. These can be repeated if necessary.

Radiotherapy

In cases where dyspnoea is secondary to malignant chest disease, radiotherapy should be considered, although the burden of treatment needs to be weighed against the potential benefits. It is more likely to be beneficial if tumour bulk is close to the major airways rather than distal to them. Radiotherapy also has an important role in managing breathlessness secondary to SVC obstruction, carrying the added advantage of controlling haemoptysis—which, even in small volumes, can be upsetting for the child and family.

Constipation

Prophylaxis and early intervention are important in managing this distressing symptom. A laxative should always be considered when opioids are commenced.

- What are the child's usual bowel habits?—children vary a lot; what is constipation for one may be a normal pattern for another.
- Has there been a change in the usual pattern?

Consider cause

- inactivity
- metabolic: dehydration, hypercalcaemia, hypokalaemia
- cystic fibrosis
- reduced oral intake
- spinal cord/cauda equina compression
- bowel obstruction
- fear of pain on defaecation: secondary to hard stools, rectal/anal grazes and tears
- drugs: opioids, anticholinergics, anticonvulsants, vincristine chemotherapy
- social: shy about using toilets away from home, not knowing where the toilets are, etc. Liaise with parents.

Management

General measures

- Check for bowel obstruction, faecal impaction, and rectal/anal grazes/tears (NB: only conduct a rectal examination if absolutely necessary).
- Consider the underlying cause and address it if appropriate/possible.
- Increase fluid intake where possible and appropriate.
- If parenterally fed, consider altering the feed.
- Increase mobility if possible.
- Optimize access to the toilet.
- Encourage regular toileting, especially after meals.
- Try oral medication first, then proceed to rectal preparations if necessary.

Medication

Many children with non-malignant conditions will have been on laxatives for some time. Parents often know which laxatives are most effective for their child.

It is generally helpful to use a combination of a stimulant laxative (e.g. senna, bisacodyl, docusate, or sodium picosulfate) and a softening agent (e.g. macrogols, magnesium hydroxide).

Paediatric Movicol® (polyethylene glycol) is an iso-osmotic laxative, better tolerated than older osmotic laxatives, and increasingly considered the laxative of choice in children. If constipation is morphine-related and resistant to the usual measures, it may be helpful to change to another opioid such as fentanyl.

Convulsions

Convulsions are most commonly seen in the palliative care setting in children with neurodegenerative disorders or intracranial malignancies.

Children with neurodegenerative disorders will often already be on multiple anticonvulsant medications and their parents/carers will be knowledgeable about recognizing and treating fits. For these children, fits are often variable in type and may become more frequent, severe, and difficult to control towards the end of life.

Children with intracranial malignancy will not necessarily develop fits. However, for those who do, it is a frightening new symptom for the child and carers to learn how to manage. If fits are likely, then prophylactic anticonvulsants should be considered and parents warned about what to expect. They should be given a clear plan of what to do in the event of a convulsion. The mainstay of medical treatment, a benzodiazepine (lorazepam, midazolam, or diazepam), should be readily available with clear instructions as to how and when it should be administered.

Not all fits are grand mal: more subtle behaviours (e.g. grimacing or coughing) may also represent seizure activity. These may not require treatment if they are not troubling the child.

Investigation and treatment of persistent fits should be tailored to the child's stage of illness, and discussion will be required with the appropriate paediatric neurology teams and the family.

Consider causes and treat as appropriate

The emergence, or increasing frequency or severity, of fits may be caused by worsening disease, but other potentially reversible factors should be considered:

- hypoglycaemia
- electrolyte imbalance
- sub-therapeutic anticonvulsant medication
- infection, e.g. UTI
- raised intracranial pressure/other intracranial pathology

Management

- Not all fits require treatment.
- Where treatment is required, the choice of anticonvulsant depends on the type of fit. Advice from the paediatric neurology unit where the child is being managed should be sought.
- Single-agent therapy is ideal. Where children are already on multiple medications, reducing the number of different anticonvulsants may improve seizure control.
- Withdrawal or addition of anticonvulsants should be done cautiously, as most agents need to be tailed off or titrated down.
- Relatively higher doses of anticonvulsants are required for children <3yrs because of a higher metabolic rate and more efficient drug clearance.
- In difficult cases, an SC infusion of midazolam or phenobarbital may be used to enable a child to stay at home. Clonazepam can be used as an alternative to midazolam.

The management of seizures will depend on the goals of care at the time. A child who is enjoying a reasonable quality of life and is in the early stages of a life-limiting illness should be treated as any other. Children in the terminal phase of illness should be kept comfortable, and this will include reasonable efforts to abort the seizure.

Acute management of a fit

- Place the child on their side in a place where they cannot fall or be injured.
- If the fit lasts longer than 5min, prepare to give buccal midazolam, sublingual/intranasal lorazepam, or rectal diazepam (avoid the SC or IM routes where possible).

Medications used for emergency management of seizures do not have a prolonged effect, and if fitting is likely to be an ongoing problem, maintenance treatment is indicated. In most cases, management is straightforward and successful. For the minority, fits are persistent and difficult to control, but even the most persistent fits can usually be controlled in the home environment provided there is good multidisciplinary support.

The administration of antiepileptics for children with no oral route (or other enteral route such as a PEG) becomes more of a challenge. If a permanent intravenous route is available, then phenytoin can be administered via this route. Carbamazepine can be given rectally. Other alternatives are phenobarbital, midazolam, and clonazepam, which can all be given by subcutaneous infusion, but they are relatively sedative compared to the other medications mentioned. Rectal paraldehyde may also be helpful.

Provision should be made for breakthrough seizures, which may be managed with buccal or subcutaneous midazolam, rectal diazepam, or rectal paraldehyde.

Cough

Coughing can be a distressing symptom for child and carers alike if it is impacting on sleep, play, or eating. If persistent, it can precipitate pain, vomiting, and seizure activity in the predisposed child. The primary aim should always be to treat underlying causes, but if this is not possible or is more of a burden than benefit, cough suppressants can be used.

Consider causes and treat reversible factors if appropriate:

- infection
- bronchospasm
- gastro-oesophageal reflux
- aspiration
- drug-induced (e.g. ACE inhibitors) or treatment-related (e.g. total body irradiation)
- malignant bronchial obstruction/lung metastases
- heart failure
- secretions
- cystic fibrosis
- subclinical seizures

Management

General measures

- Keep child as upright as possible.
- Raise head of bed: use blocks under head end of cot/bed, or pillows.
- Consider physiotherapy, or suction for children with secretions. Modified physiotherapy is the mainstay of treatment for children with thick secretions.
- Consider a trial of humidified air/oxygen.
- Trial of nebulized saline.

Medication

The choice of medication will depend upon the underlying cause. A dry throat may respond to simple linctus. Bronchospasm will respond to bronchodilator therapy. If the underlying cause cannot be reversed, a suppressant such as an opioid will be required.

Gastro-oesophageal reflux

Many neurologically impaired children suffer with gastro-oesophageal reflux. Consider reflux if the child refuses food; vomits; has dysphagia, abnormal movements (Sandiffer's syndrome or extensor posturing), cough, intractable hiccups, or aspiration pneumonia; or is irritable when supine.

Management

General measures

- Check for overfeeding.
- If nasogastric/gastrostomy-fed, consider changing regimen from large bolus to smaller, more frequent volumes. Continuous feeding is another option.
- Thicken feeds.
- Ensure optimal posture for feeds.
- Adjust posture overnight to keep child more upright: use blocks under cot/bed, or use pillows.
- Surgery can be considered in children with a longer prognosis. Gastrostomy and fundoplication is effective in 80% but is not without complications. Gastrostomy alone will increase the likelihood of reflux, as will nasogastric feeding.
- Postpyloric tube feeding is a better option than nasogastric tube feeding.

Medication

Omeprazole

- Omeprazole is the drug of choice for reflux oesophagitis. It is more effective than ranitidine and has a good safety profile. Individuals vary in their response, and doses will need to be titrated to achieve effective acid suppression.
- It easily blocks feeding tubes, so if a child is enterally fed, dissolve in sodium bicarbonate (see following) or consider lansoprazole as an alternative.

Lansoprazole

- Lansoprazole is as effective as omeprazole, but orodispersible tablets dissolve better in water and do not block tubes as readily.

Ranitidine

- Ranitidine is often used alone or in conjunction with a proton pump inhibitor.

Antacids

- To be really effective, antacids should be given 4-hourly. This may limit their usefulness.

Metoclopramide and domperidone

Metoclopramide and domperidone are prokinetic drugs that are very effective for GORD. However, their use is now limited following a European safety warning recommending short-term use only, owing to cardiac side-effect concerns. Recent amendments to the initial guidance now allow longer-term use in paediatric palliative care.

Gastrostomy care

Children with life-limiting illnesses commonly have gastrostomy tubes in situ, either a PEG (percutaneous endoscopic gastrostomy) or a MIC-KEY* (Medical Innovations Corporation, UK) gastrostomy button. These allow feeding in the presence of disordered swallowing and ease the administration of medication.

Considerations

- Daily cleaning of the skin around the stoma site will help prevent irritation and infection.
- Formation of granulation tissue is reduced by the regular rotation of the tube by 360° daily.
- Ensure all connections and tubings are comfortable for the child and not in a position where they can be easily pulled at or dislodged.

Blockage

- Gastrostomy tubes block easily. They should be flushed before and after all feeds and medications. Some drugs are notorious for causing blockages, and alternatives should be considered (e.g. lansoprazole instead of omeprazole).
- If blocked, flushing with a large (50mL) syringe of pineapple juice may help dissolve the blockage. If not successful, Pancrex V® (a pancreatic enzyme) can be instilled into the tube for 30 minutes.

Granulation tissue

- Apply topical steroid-based, antifungal cream twice daily for up to ten days.
- May need second course, but prolonged use not advised.
- If not resolving, swab and exclude infection.

Infection

- Indicated by erythema, swelling, tenderness, and oozing around the tubing. Swab before treating.
- Sodium fusidate cream topically may be sufficient.
- Consider systemic antibiotics.

Dislodged tubes

- Most families will keep spare MIC-KEY* or gastrostomy tubes with them, which are easily replaced. If not available, a size 12G Foley catheter can be used to keep the stoma patent until stocks are found.

Infection at the end of life

Management of infection at the end of life needs careful consideration, and, if possible, forward planning. This avoids decisions being made in a crisis, and may spare the child from intrusive and futile interventions. Discussing and recording a preferred course of action with the parents (and, where appropriate, the child) in advance of the terminal phase is ideal. Such plans should always be open for further discussion and revision should this be necessary. Treating infection, even at the end of life, should always be considered in terms of benefit and burden. For example, if antibiotics reduce symptoms and make the child more comfortable, the benefits may outweigh the burden of the treatment. Each case must be considered on an individual basis.

Mouth care

A painful mouth can cause anorexia, discomfort, and difficulties eating. It can also make it difficult for the child to take oral medication. Good mouth care can significantly enhance quality of life for children in the palliative care setting.

A general examination should always include inspection of the mouth, as oral problems are readily overlooked but can usually be easily managed.

Consider cause and treat as appropriate

- oral candidiasis
- dry mouth
- ulcers
- bleeding gums
- dental caries
- impacted teeth
- gum hyperplasia
- medications, e.g. morphine, antidepressants, antihistamines, anticholinergics

Management

General measures

- If using oxygen, try humidifying it or using nasal prongs.
- Keep mouth clean and moist.
- Rinse mouth after vomiting.
- If possible, brush teeth, gums, and tongue and other mucous membranes two or three times a day with a soft toothbrush.
- Clear a coated tongue by gently brushing with a soft toothbrush, or by using effervescent vitamin C.
- Sucking pineapple chunks will help maintain a clean mouth, but avoid if there is ulceration in the mouth because of pain and mucosal breakdown with pineapple.
- If the mouth is too painful to brush, regularly clean with pink sponges dipped in water or mouthwash, particularly after eating or drinking.
- Avoid preparations containing alcohol.
- Try water sprays or atomizers.
- Ice chips may be helpful.
- Artificial saliva: a number of preparations are available.
- Moisten lips with white soft paraffin or lip balm.
- Refer to dentist if appropriate; consider a specialist dentist for children with severe neurodisability.

Oral candidiasis

- Oral candidiasis may present as classic white plaques or less commonly as atrophic candidiasis with a red glossy tongue.
- Remember that candidiasis may extend beyond the line of vision to the oesophagus.

Ulcers/mucositis

- Ulcers and mucositis are often related to neutropenia resulting from high-dose chemotherapy or radiotherapy.
- Mouthwash: type will depend on the severity of the mucositis. Chlorhexidine 0.2% (swished for 1min or swabbed 3 times daily) is generally adequate for those children with mild-to-moderate mucositis. Hydrogen peroxide mouth rinse (diluted 1 in 8 with water or saline and used 2–3 times daily) may need to be used in addition to chlorhexidine in children with severe mucositis.
- An antifungal agent should be used. This should be given 20–30min after chlorhexidine.
- Mucositis can be extremely painful and analgesia appropriate to the degree of pain should be given. For children with severe mucositis, opioid analgesia may be required.

Muscle spasm

Muscle spasm, commonly experienced by children with neurodegenerative conditions, can cause significant pain and distress. It may also interfere with positioning and activities. Spasms themselves cause pain, leading to further spasms, and a distressing cycle of symptoms can evolve. Muscle spasms may be difficult to distinguish from movement disorders or convulsions, and therefore a good history and examination are imperative.

Management

General measures

- Early involvement of physiotherapy and occupational therapy teams is invaluable for advice on moving, handling, positioning, and seating, and is essential to prevent the problem worsening.
- Long-standing contractures in a child with a relatively long prognosis can inhibit daily caring and may be managed surgically or with botulinum toxin injection. This should be assessed by an orthopaedic surgeon and can now be done under local anaesthetic.
- Discussion with a paediatric neurologist may also be helpful.
- Baclofen and benzodiazepines are the most commonly used drugs, with dantrolene and tizanidine being increasingly used by paediatric neurologists.
- More invasive techniques, such as intrathecal baclofen pumps, may be considered if the benefits outweigh the burdens of the initial surgery and the necessary follow-up.
- While it is generally possible to reduce muscle spasm, it may not be possible to abolish it altogether.

Caution

- High tone and muscle spasm may be the only things that allow a child to sit or stand. Therefore, treating spasms will require careful assessment as it may impact on the child's mobility and also on their independence.
- Many of the effective drug therapies may also cause significant sedation.

Nausea and vomiting

See Fig 16.1 and Table 16.1.

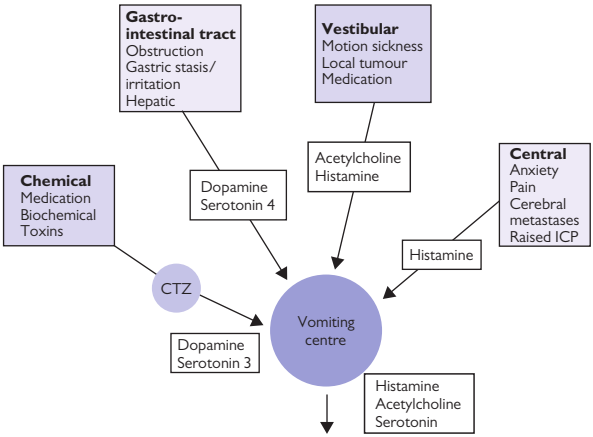


Fig 16.1 Suspected causes of nausea and vomiting and suggested receptors/ neurotransmitters involved.

Table 16.1 Receptor site affinities of anti-emetics*

	D_2 antagonist	H_1 antagonist	ACh antagonist	5-HT_3 antagonist
Metoclopramide	++	0	0	(+)
Ondansetron	0	0	0	+++
Cyclizine	0	++	++	0
Hyoscine hydrobromide	0	0	+++	0
Haloperidol	+++	0	0	0
Prochlorperazine	++	+	0	0
Chlorpromazine	++	++	+	0
Levomepromazine	++	+++	++	0

D_2 = dopamine; H_1 = histamine 1'; ACh = muscarinic, cholinergic; 5-HT_3 = serotonin group 3.

*Data sourced from Twycross R, Back I. (1998) Nausea and vomiting in advanced cancer. *European Journal of Palliative Care*, **5**: 39–45.

Consider cause

- obstruction: gastric outflow/bowel
- constipation
- uraemia/deranged electrolytes/hypercalcaemia
- raised intracranial pressure
- upper gastrointestinal tract irritation
- anxiety
- cough
- pain
- drugs: opioids, chemotherapy, carbamazepine, NSAIDs
- intercurrent illness, e.g. gastroenteritis, urinary tract infection

Management

General measures

- Treat the underlying cause if possible.
- Ensure optimal pain management.
- Avoid strong food smells and perfumes—may antagonize nausea.
- Keep meals small and remove leftover food quickly.

Medication

- Give an appropriate anti-emetic according to suspected cause (see following). If this is ineffective or the cause is unclear, a phenothiazine such as levomepromazine will usually be effective.
- Non-oral routes should be used if a child is vomiting (e.g. subcutaneous, parenteral, or rectal routes) until symptoms are under control and the oral route can be re-established.
- Review: if treatment is not successful, reconsider cause.
- Levomepromazine is an effective anti-emetic with anticholinergic, antihistaminergic, and antidopaminergic actions.
- Haloperidol is a dopamine antagonist which acts centrally. It is more potent in this action than metoclopramide.
- The MHRA in 2014 gave warnings on the use of metoclopramide and domperidone, restricting them to short duration only and contraindicating them in certain cardiac conditions. It is now recommended that domperidone is contraindicated in those with underlying cardiac disorders, severe hepatic impairment, or concurrently receiving drugs known to be CYP3A4 inhibitors and/or cause QT prolongation. A subsequent amendment allowed use of metoclopramide for longer-term use in palliative care.
- Metoclopramide is a dopamine antagonist and acts on both the CTZ and the gastrointestinal tract (prokinetic action).
- Domperidone is available for oral administration and does not cross the blood-brain barrier. Therefore, it is less effective than metoclopramide and haloperidol, but it is also less likely to cause extrapyramidal side effects.
- Dexamethasone may be a useful adjuvant agent. Caution is required when treating children with steroids. Side effects include weight gain and distressing behavioural and emotional changes if steroids are used for more than a few days. For this reason, it is preferable to prescribe

steroids in short courses (3–5 days) and to repeat courses if necessary. Monitoring blood/urinary glucose may be necessary, and is advised in prolonged courses. Try to avoid prescribing after 3 p.m. as this may affect sleep.

- 5-HT_3 antagonists (e.g. ondansetron) are very effective in relieving nausea and vomiting associated with chemotherapy. Since they are constipating, adjuvant laxatives may be necessary. In refractory cases, dexamethasone can be used as a second-line agent, in combination. Levomepromazine is recommended as the third-line agent. High-dose metoclopramide is used in some centres.
- Cyclizine possesses anticholinergic and antihistamine activity. Where raised intracranial pressure is a major factor in generating nausea and vomiting, cyclizine is often helpful. Drowsiness is a common side effect, but may be desirable in some circumstances.
- Cyclizine can be given subcutaneously. Although it does have the potential to crystallize in syringe drivers, this is an uncommon problem in practice. It may cause redness at the infusion site.

Noisy breathing

Excessive respiratory secretions more often cause distress to parents and carers than to the child. Reassurance may be all that is required, but pharmacological intervention may be warranted where the child is distressed. Suction may be helpful, if carefully done, although it is not always available.

Drug treatment is more effective when started before or immediately after the secretions are evident.

Antisecretory agents may cause drowsiness and anticholinergic side effects: glycopyrronium has fewer CNS side effects than hyoscine hydrobromide because it does not cross the blood–brain barrier. Sometimes, however, a sedative effect may be desirable.

Pain

- Adequate pain control can be achieved for the vast majority of children, but requires careful attention to recognition, assessment, treatment, and review.
- Assessment should include a careful history and examination to elucidate the exact nature and likely cause(s) of pain so that the most effective management can be initiated.
- Assessment should include discussion with parents/carers and staff as well as the child if possible.
- A number of pain assessment tools are available to aid diagnosis and monitor pain and the analgesic effect.
- Assessment of pain in children, particularly young infants and non-verbal children, may be difficult.
- Pain may be under-diagnosed and therefore inadequately treated in children, particularly those who are unable to communicate readily.
- Pain is closely associated with fear and anxiety.

Recognizing pain in children with communication difficulties

- Discuss with family/carers who know the child well.
- Look for signs, including crying, becoming withdrawn, increased flexion or extension, hypersensitivity, frowning/grimacing on passive movement, poor sleep, increasing frequency of fits.

Management

General measures

- Management should include reducing stress and anxiety as far as possible, as well as analgesic measures.
- Analgesics should be used in conjunction with non-pharmacological techniques.
- Explanations and discussion often help to reduce anxiety.
- A calm, quiet environment may help to reduce anxiety.
- Distraction is a useful tool, but should not replace consideration of pharmacological intervention.
- A formal record of pain scores is helpful when introducing a new intervention, particularly when many carers are involved or when the child's communication is limited. Such a record may reassure or indicate that further measures are required, and allows comparison between different interventions to be made in a robust manner.
- Carefully recording all information in medical records on a regular basis is essential to enable anyone who consults the records to easily recognize changes and assess the success of previous interventions.

Medication

Choosing an analgesic:

- For mild-to-moderate pain, it is usual to start by using a non-opioid analgesic on a p.r.n. basis, progressing to regular use.
- Some non-opioid analgesics may be used in conjunction with one another or in conjunction with opioids for added analgesic effect.

- If non-opioid analgesics do not control pain effectively, then opioid analgesics will usually be helpful.
- The oral route is preferred; adequate pain relief can be achieved using this route for most children.
- In the palliative care setting where pain is constant, analgesics should be given regularly rather than p.r.n.
- Codeine is no longer recommended by the WHO owing to issues around its metabolism. The WHO now recommends using low-dose major opioids as a second step in its ladder of pain control.
- If a patient is having regular analgesia of any kind, it is important to prescribe additional p.r.n. analgesia for breakthrough pain.
- Once stable, it may be possible to change to a slow-release form of medication.
- Discuss the management plan with the family. If opioids are to be used, a careful explanation is required so that families are prepared for drowsiness, understand that laxatives are necessary, and are reassured about issues relating to addiction and dependence.
- Plan for exacerbations and crises. Make sure appropriate medications and plans for their use are available to the family. This may include parenteral forms of medication for children on oral opioids.
- All analgesic regimens should be regularly reviewed, particularly during titration.
- Seek advice from appropriately skilled staff if you are unsure or analgesia is not quickly achieved.

Non-opioid analgesics for mild/moderate pain

Paracetamol should be prescribed at a dose based on weight rather than age.

Non-steroidal anti-inflammatory drugs (NSAIDs)

- Possess analgesic and antipyretic properties.
- Are particularly useful for bone pain.
- Individuals may respond better to one agent than another.
- Should not be given to children with thrombocytopenia or with coagulation disorders.
- Can be combined with paracetamol or opioids for additive analgesia.
- If GI side effects are likely, it may be useful to prescribe antacids and/or a proton pump inhibitor.

Opioid analgesics for moderate/severe pain

- Usually commenced when non-opioid analgesics have been tried and have not been fully effective or if pain is severe at presentation.
- Always co-prescribe a regular laxative: opioids can be expected to cause constipation, and it is better to prevent this from the outset.

Other side effects which should be anticipated and promptly managed

- drowsiness: usually wears off after 3–5 days; families may need forewarning as they may interpret drowsiness as a severe decline in the child's condition
- nausea and vomiting (➔ see section on nausea and vomiting, pp. 520–2)

- pruritus: topical measures and antihistamines; ondansetron may be effective
- urinary retention: check that constipation is not a contributory factor; bethanechol may be helpful; catheterization is required infrequently
- respiratory depression: this is very unlikely if the dose is titrated appropriately; naloxone will reverse respiratory depression, but this may be at the cost of analgesic effect if not administered carefully
- euphoria, dysphoria
- nightmares: a night-time dose of haloperidol may be useful
- physical dependence: opioids should be weaned and not ceased abruptly or a withdrawal reaction may occur
- tolerance: this is the need for escalating doses to achieve the same therapeutic effect; tolerance is managed by increasing the dose; families may need to be reassured that tolerance is rare and does not necessarily imply disease progression

Strong opioids

Morphine sulfate

- prescribing regimen
  - always prescribe breakthrough doses (total dose/24h ÷ by 6)
  - if pain not controlled, increase dose by 25–50%
  - use 4h dosing until pain well controlled, then convert to m/r preparation and prescribe 12h (total dose/24h ÷ by 2)
  - slow-release preparations normally given b.d. may need to be given t.d.s. in some children
  - keep required dose under constant review and adjust to give optimum pain control

Diamorphine hydrochloride

- conversion
  - the dose of parenteral diamorphine is one-third the dose of oral morphine, so if converting directly from oral dose: total dose oral morphine sulfate over 24h ÷ by 3
- high solubility makes it very useful in paediatrics
- can be given intranasally and buccally

Fentanyl

Fentanyl is less sedating and less constipating than morphine, but it is more difficult to adjust the dose in response to unstable pain when used transdermally. Unless contraindicated, it is generally better to stabilize the pain using an oral or parenteral opioid before changing to fentanyl patches.

Converting from oral morphine sulfate:

- Continue oral morphine preparation for up to 12h after first fentanyl patch applied as patch will take 6–12h to reach therapeutic levels.
- Wait 24–48h after application before evaluating analgesic effect or changing dose.
- Always provide p.r.n. doses of oral morphine for breakthrough pain.
- Use new area of skin with each patch change.
- Avoid exposure of patch to excessive heat (sunbathing; hot-water bottle, etc.) as heat will increase absorption.

- Dose (buccal)
  - useful for incident and breakthrough pain
  - Start with 200mcg lozenge and adjust dose according to response. These lozenges are only suitable if the background opioid dose is equivalent to 60mg oral morphine or more. Their usefulness is also limited by their availability.
- Although fentanyl may be less constipating than morphine, a laxative should be co-prescribed.
- Fentanyl is less problematic in renal failure than diamorphine.

Buprenorphine

Buprenorphine is available in both patch and sublingual formulations. Its advantage over fentanyl is the lower morphine equivalency at which buprenorphine patches can be used. Buprenorphine is a partial mu-agonist and has a ceiling dose—in practice, this is rarely an issue. Theoretically, buprenorphine can block opioid receptors to the effects of other strong opioids, and therefore it should not be used at high dose alongside these.

Oxycodone

- Oxycodone has no benefits over morphine and is more expensive. It should be used as a second-line strong opioid when the patient is unable to tolerate morphine or opioid rotation is required.

Other opioids such as hydromorphone and methadone are available, but their use should be discussed with a paediatric pain or palliative care specialist.

Pain syndromes and adjuvant therapy

Bone pain

Radiotherapy

- useful for discrete bone metastases
- may be given as a short course or single dose
- effective treatment with minimal side effects

Non-steroidal anti-inflammatory drugs (NSAIDs)

When used in combination with opioids, NSAIDs may lower the dose of opioid required for effective analgesia. Common choice is ibuprofen. Diclofenac can also be used, but requires caution in view of the MRHA (2015) guidance on its cardiac risks. Naproxen can be used, but is limited by a lack of formulations.

Selective COX-2 inhibitors

Selective COX-2 (cyclo-oxygenase 2) inhibitors are not widely used because of the associated risk of cardiovascular and cerebrovascular disease. COX-2 inhibitors such as celecoxib are equianalgesic when compared with non-selective NSAIDs. They offer certain advantages: the risk of gastrointestinal bleeding is reduced, and they have no effect on platelet function.

Bisphosphonates

Bisphosphonates have been shown to reduce bone pain related to both malignant and non-malignant causes in adults. They have been used in children. Seek advice before using.

'Resistant' and neuropathic pain

Most pain can be controlled with adequate doses of opioid medication, and much of what is regarded as 'resistant' pain can be managed with a dose increase or an alternative route of delivery (e.g. parenteral, spinal) or opioid switch (changing to an alternative strong opioid).

In some instances, however, adding an adjuvant agent which targets a particular pain mechanism or pathway may be helpful. Neuropathic pain has particular features, including a lancinating or burning quality, shock-like features, or associated paraesthesiae.

Furthermore, antidepressants or antiepileptic medications may be a useful addition to the regimen where these features are present. The choice between the two classes of drug will depend on the child's other symptoms. For example, a child with sleeping difficulties might benefit from a tricyclic antidepressant, whereas one with a coexistent seizure disorder will benefit from an anticonvulsant.

Tricyclic antidepressants

Tricyclic antidepressants can enhance opioid-induced analgesia and improve sleep. Amitriptyline, nortriptyline, and imipramine can be used.

Anticonvulsants

- Carbamazepine, sodium valproate, and gabapentin are the three main medications used. The medications should be started at the lower end of the dose range and slowly titrated until therapeutic levels are achieved, symptoms are relieved, and side effects are limited (e.g. ataxia, drowsiness, nausea). Titrating slowly minimizes side effects.
- Doses should be increased and decreased slowly.

Ketamine

Ketamine is a useful adjuvant agent for patients with neuropathic pain, perhaps because of its action on NMDA receptors. It has a tendency to cause agitation and hallucinations in higher doses. Seek specialist advice before using.

Methadone

Methadone can be very helpful in neuropathic pain, particularly when associated with solid tumours. Its use should be limited to specialist units only.

Nerve blocks, spinal administration, and other neuroanaesthetic approaches

Nerve blocks, spinal administration, and other neuroanaesthetic approaches may be helpful for children who do not respond to any of the foregoing measures, or for whom regular medication is practically difficult or poorly tolerated. Commonly used drugs are opioid analgesics and anaesthetic agents, or a combination of the two. Availability of such interventions varies widely across the world, and early consultation with your local anaesthetic team is advisable before options are discussed with the patient/parents. Spinal infusions can be managed in the community if appropriately trained staff members are available. If this is not possible, single-dose epidural/spinal analgesia may be a more practical alternative, and would allow some assessment of whether a continuous infusion is likely to be beneficial in the longer term.

Pain associated with tumour-related oedema

Pain associated with tumour-related oedema includes pain related to intracranial tumours and nerve plexus compression.

Steroids

- Should be used with caution in children.
- Short courses (up to 5 days) can be very effective for this type of pain.
- Potential problems include insomnia, mood and behaviour changes, and, in longer-term use, rapid weight gain, body image changes, and reduced mobility caused by proximal myopathy. Dyspepsia can be anticipated and prophylaxis should be prescribed.
- Give entire dose before midday to reduce the likelihood of sleep disturbance at night.
- Dexamethasone is the steroid of choice.

Painful procedures

- If a procedure is likely to cause discomfort, take preventive action!
- Explain all procedures to parents and children as appropriate to reduce anxiety.
- Undertake procedures in friendly, if not familiar, surroundings.
- Have parents/carers or the nurse who know the child best present.
- Use anaesthetic creams and distraction techniques appropriate to the age of the child.
- For more difficult procedures, benzodiazepines are often employed in small doses in conjunction with analgesia; e.g. midazolam given buccally, IV, or intranasally gives light sedation and some amnesia.

Nitrous oxide

- Inhaled nitrous oxide has analgesic and amnesic properties but is non-sedating, so is generally used in co-operative children aged 5 years or older. It requires a child to have sufficient respiratory abilities to trigger the valve. Careful supervision is needed.

Ketamine

- Ketamine is another useful agent but requires careful supervision by trained staff and is usually started in an inpatient setting. We suggest contacting the nearest specialist palliative care team for further advice.

Psychological issues—anxiety and depression

Management

General measures

- Provide an environment and the opportunity for the child to raise their concerns and fears.
- Children often find relaxation techniques such as guided imagery very helpful.
- Complementary therapies (e.g. music therapy) may be useful, particularly in non-verbal children.
- Counselling and complementary therapies should ideally also be available to parents/primary carers.
- Formal psychotherapeutic techniques may also be helpful.

Anxiety

Medication

- Medication should be used in combination with non-pharmacological techniques.
- Anxiety may be a manifestation of depression, in which case an antidepressant may be more appropriate.
- The choice of benzodiazepine will depend on the circumstance for which it is being prescribed. Children experiencing brief periods of anxiety or panic attacks may benefit from a benzodiazepine with a short half-life, such as midazolam, given buccally or subcutaneously. Sublingual lorazepam is another option for short-lived anxiety, panic attacks, or anxiety related to dyspnoea. Those children who need a longer duration of action may prefer diazepam.

Depression

The incidence of depression in terminally ill children is unknown, but it is likely that for many it remains unrecognized and untreated.

The clinical picture will depend on the age and developmental stage of the child, but the expected features of depressed mood—anhedonia, social withdrawal, and disturbed sleep and appetite—may be present. The diagnosis is less dependent on somatic symptomatology because of the coexistence of illness.

Diagnosis may be difficult: trust the instincts of parents and carers and consult a child psychologist at an early stage. The initiation of antidepressant medication to children under the age of 18 years is limited to a paediatric psychiatrist only. Fluoxetine is the only selective serotonin reuptake inhibitor (SSRI) licensed for use in children for depression.

Raised intracranial pressure

Consider raised intracranial pressure if the child shows evidence of any of the following:

- confusion
- personality change
- drowsiness
- vomiting
- headache (especially on waking)
- focal neurology

Management

General measures

- Investigation should be considered only if it will contribute to management decisions.
- Reduction of tumour bulk may improve symptoms, e.g. cranial irradiation and chemotherapy.
- In some circumstances, a ventricular shunt may be helpful.
- Symptomatic management may include analgesia (➔ see section on pain, pp. 524–7), anti-emetics, and steroids.

Skin

Management

General measures

- Like adults, children with terminal illnesses have skin that is susceptible to breakdown with poor healing abilities.
- Good nursing care is required to predict and prevent problems, which, once established, may be more difficult to treat.
- Frequent and appropriate turning is essential to avoid pressure areas breaking down.
- The use of suitable mattresses and mobility aids should be considered.
- Consult the tissue-viability nurse if available.
- Dressing changes can be very painful. Consider the use of a short-acting analgesic such as buccal diamorphine, Entonox®, and/or topical anaesthetic agents such as lidocaine.

Medication

- at-risk areas:
  - protect with adhesive film dressings
- broken areas:
  - use hydrocolloid or foam dressings
- infection:
  - send swab for culture; use IntraSite hydrogel, cadexomer iodine paste covered with adhesive film dressing, and consider antibiotics
- cavities:
  - pack with alginate dressing
- fungating tumours and odour:
  - use topical metronidazole gel, oral metronidazole, charcoal dressings, or honey and sugar
- painful ulcers:
  - consider anaesthetic preparations, e.g. lidocaine/prilocaine EMLA or a topical morphine gel
- associated cellulites or discharge:
  - consider antibiotics (oral is usually sufficient)
- ➔ see also Chapter 12, Skin problems in palliative care.

Sleeplessness

Disturbed sleep has a major impact upon the child and family's quality of life. Adequate sleep may be the difference between a family's ability to cope with the stresses placed upon them or not.

Many children with neurodisability have poor sleep patterns related to underlying brain maldevelopment or associated problems such as seizures, reflux, visual impairment, or medication.

Management

General measures

- Address the child's fears and concerns.
- Consider the sleep pattern: the child may be sleeping a lot in the day and may be reversing the day/night pattern. It may be appropriate to keep the child awake more in the day or to provide extra stimulation during the day—this will depend on the child's stage of illness. The child may be unaware of when they are expected to sleep if intervention is needed around the clock.
- Optimize bedtime routine: bath if possible, story, hot drink if appropriate, lights low.
- Increase exposure to light in the mornings.
- Consider complementary therapies to aid relaxation.
- Try to disturb the child as little as possible during the night: this may mean re-scheduling medications.
- Medications include melatonin, temazepam, choral hydrate, and promethazine.

Terminal restlessness

Restlessness and agitation are not uncommon during the terminal phase. Nursing the child in a calm, peaceful, and preferably familiar environment is helpful, as is having a parent or other trusted adult present. Supporting the parents and carers at this point is fundamental, and helpful support will impact on the child indirectly. From the child's perspective, it is important to exclude poorly controlled pain, other symptoms, and inadequate positioning as causes of distress. Hypoxia may also be a factor.

Supporting and nursing a family in this circumstance is extremely challenging, particularly for staff who have established strong bonds. It is important for staff to actively seek their preferred support in order to optimize their ability to function effectively during care-giving and to protect coping mechanisms for the future.

The choice of medication to alleviate the restlessness will depend on the clinical circumstances. Midazolam is very effective and can be given via a continuous subcutaneous infusion combined with other medication such as diamorphine as necessary. Levomepromazine is also compatible with these medications and is an appropriate choice for children who have coexistent nausea.

Ventilation at home

Increasing numbers of children with life-limiting or life-threatening illnesses are accessing home ventilation. Most commonly, these children have neuromuscular diseases (e.g. Duchenne muscular dystrophy). Ventilation may also be required for children with craniofacial abnormalities, spinal injuries, and congenital central hypoventilation syndrome (Ondine's curse).

Levels of ventilation

Nocturnal ventilation

Most children will start with ventilatory support overnight, this may be:

- continuous positive airway pressure (CPAP) via a face or nasal mask
- positive pressure ventilation (PPV), delivered via a face or nasal mask or via a tracheostomy

24h ventilation

- Children may continue to use CPAP or PPV via their mask system, but a tracheostomy may be more practical if ventilation is a long-term option.
- The commonest home ventilation devices encountered in the UK are the Nippead ventilator and the Breas ventilator. Children requiring such support usually have respiratory home support teams who can offer advice if difficulties are encountered with the machines.
- During acute exacerbations of illness, increased ventilation may be required, necessitating alterations in the duration or pressures of ventilation. Consultation and continued communication with a respiratory physician are essential when caring for such children at home.

General measures

- Feelings of claustrophobia are common when nocturnal ventilation is first experienced. Thus, adequate explanation and reassurance is essential. Different masks exist with differing fixings that may allow the child some input into the decision-making process.
- The masks are tight-fitting and can become uncomfortable, particularly if the child is hot or sweating. Ensure that the environmental temperature and humidification are appropriate.
- Pressure marks are common, and care is needed to prevent skin breakdown. Consider gauze over the ears and hydrocolloid dressing Duoderm under the edge of the mask.
- Water may accumulate in the tubing, causing the ventilator to alarm. This can be removed easily by suction or the tubing can be changed before seeking further advice.
- Ventilators either have an inbuilt battery backup or else a separate battery pack for use in an emergency. These usually last 2–3h. Alternatives should always be available, and those caring for a child should be appropriately trained to provide care during a power cut.

Further reading

Books

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Chapter 17

Heart failure

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Definition of heart failure

Chronic heart failure is a progressive, terminal syndrome and is the final common pathway of many cardiovascular diseases. There is difficulty in defining heart failure as there are many different criteria around the world used to define it. However, common criteria usually include history, physical examination, chest radiography, and echocardiography. The European Society of Cardiology defines heart failure as the presence of symptoms of heart failure at rest or during exercise, and objective evidence of cardiac dysfunction (usually on echocardiography).

Epidemiology

Heart failure is the only major cardiovascular disease with increasing incidence. Approximately 1–2% of the adult population in developed countries has heart failure;[1] it is predominantly a disease of old age (mean 75 years). There are 67,000 new cases per annum in the UK.[2] The majority of cases are a result of coronary artery disease, with hypertension and diabetes common contributing factors. A diagnosis of heart failure has huge cost implications: patients with heart failure occupy up to 2% of all inpatient bed days and account for up to 2% of NHS costs (most of which are hospital, not community).

Prognosis

An estimated 5% of all deaths in the UK (24,000 per annum) are from heart failure. (Death certification explicitly discourages doctors from recording heart failure as a cause of death—the true number may be much higher.) Some 40% of patients die within one year of diagnosis; 50% of patients with heart failure die suddenly; 25% without worsening of heart failure symptoms. There are no reliable prognostic models as yet.

Relevant pathology and physiology

The direct insult is of mechanical pump failure; however, the pathophysiology is more complex, as pump failure initiates an ongoing, complex cascade of haemodynamic, metabolic, neuroendocrine, and renal dysfunction that is the syndrome of chronic heart failure. Depending on the underlying cause—e.g. valve dysfunction or hypertension—the exact pathophysiology by which heart failure occurs is different and may affect treatment options.

Clinical features

See Table 17.1.

- symptoms include:
  - breathlessness, orthopnoea, ankle swelling, fatigue
- signs include:
  - elevated JVP, pulmonary crackles, and displaced apex beat
- clinicians need to be aware of less commonly recognized symptoms as they can be distressing:
  - pain that may be multifactorial; possible causes include angina, liver capsule distension, lower limb swelling, and co-morbid disease, e.g. arthritis
  - anxiety and depression (severe in one-third of hospitalized patients); depression adversely affects mortality and hospital readmission[3, 4]

Table 17.1 New York Heart Association (NYHA) functional classification (summary)

Class	Symptoms
I	Heart disease present, but no undue dyspnoea
II	Comfortable at rest; dyspnoea on ordinary activities
III	Less than ordinary activity causes dyspnoea, which is limiting
IV	Dyspnoea present at rest; all activity causes discomfort

Data sourced from Criteria Committee, New York Heart Association, Inc. Diseases of the Heart and Blood Vessels. Nomenclature and Criteria for diagnosis, 6th edition Boston, Little, Brown and Co. 1964, p 114.

- disordered sleep
- memory loss and confusion
- anorexia, nausea, vomiting, and constipation (secondary to medications and disordered fluid balance)
- weight loss (usually mild, but severe cachexia is a poor prognostic sign)
- loss of libido

Functional impairment in activities of daily living and social isolation are common, long before the end of life. Despite this, there can be challenges accessing social and therapeutic services. The pattern of functional decline is slow and often unpredictable when compared to the classic patient with cancer who exhibits a precipitous decline before death.[5]

Disease burden

The burden of chronic heart failure has physical, psychological, and social dimensions. These needs have been demonstrated to be prevalent, severe, and prolonged, and often go unrecognized and unrelieved.

Traditionally there has been a disparity in symptom control and support offered to those dying from heart failure when compared to those with cancer. This has been recognized, and several initiatives have attempted to broaden access to palliative services for those with non-malignant disease.

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Management of heart failure

Principles of management

Ultimately heart failure is a progressive, symptomatic disease. Therefore treatment plans need to be developed around patient goals, symptom management, and quality of life. A key element of the management of heart failure is including the patient in education about their condition and potential future outcomes. This allows patient and families an element of preparedness and allows for advanced care planning to be initiated at an appropriate time. Gaining an understanding of a patient's values, and regular review of clinical status, current treatments, and future options, are crucial to making an appropriate care plan for a patient and identifying potential future problems that are likely to arise.

Disease-specific management

Heart failure results in reduced cardiac output that prompts retention of sodium and water. Treatment is therefore focused on optimizing fluid balance, removing exacerbating factors, and optimizing cardiac performance.

The cornerstones of drug treatment include the following:

- angiotensin-converting enzyme (ACE) inhibitors
- aldosterone antagonist (usually spironolactone)
- beta-blockers

These drugs aim to modify systolic function. Angiotensin-II antagonists and digoxin are used where appropriate. Diuretics are used to control fluid overload. Furosemide is less effective when given orally rather than parenterally in heart failure, cirrhosis, and probably any hypoalbuminaemic state. It is more affected by food intake than bumetanide, which may be better absorbed orally than furosemide. Continuous infusion of furosemide may be given IV and has been given by CSCI. Metolazone has a similar mechanism of action to thiazide diuretics and can be used alone, but it is often used with furosemide and has a synergistic effect. Management of fluid balance is also dependent upon patient diet and compliance with salt and fluid restriction.

Avoid, where possible, drugs that may worsen cardiac function. These include some drugs commonly prescribed in cancer palliative care practice. See Table 17.2.

Management of associated symptoms

Actively seek out and manage other symptoms. Consider that symptoms may relate to other underlying pathology. For example, renal failure is common in patients with heart failure, and this may be causing other symptoms such as itch.

- **Pain**: follow the WHO ladder. Avoid NSAIDs and alter opioid choice according to renal function.
- **Nausea**: try haloperidol for a biochemical cause and metoclopramide for gastric stasis.
- **Anxiety and depression**: treat conventionally (with or without drugs). Newer classes of antidepressant such as sertraline (an SSRI) and mirtazapine are safer than tricyclics. Both of these are less likely to affect cardiac conduction, cause postural hypotension, or interact with other drugs.

- **Breathlessness management**: may include correction of anaemia, low-dose opioids, and the non-pharmacological approaches used in respiratory rehabilitation and lung cancer management.
- **Adopt a palliative approach**: to psychological, social, spiritual, information, and communication needs, actively pursuing and managing identified needs. Patients and carers may need help to manage the uncertainty of a future with a high chance of sudden death.

Table 17.2 Key drugs to avoid in heart failure patients

Drugs	Reason for avoidance
Non-steroidal anti-inflammatory (NSAID)	Salt and water retention and worsen renal function
Tricyclic antidepressants	Cardiotoxic
Lithium	Salt and water retention
Cyclizine	Probably cardiotoxic
Steroids	Water retention
Progestogens	Water retention
Flecainide/mexiletine	Depress myocardial function

End-of-life care

Diagnosing dying in heart failure is extremely difficult. The last year of life is often marked by repeated hospital admission with acute exacerbations, increasing frailty, and reduced function and ability to participate in activities of daily living (ADLs). Patients and families have to deal with the unpredictability of the condition with the ongoing decline in symptoms and function. However, it is still very difficult to prognosticate, and the risk of sudden death remains high.

Features suggested as characterizing a subgroup of patients with a poor prognosis include the following:[1]

- previous admissions with worsening heart failure
- no identifiable reversible precipitant
- optimum tolerated conventional drugs
- deteriorating renal function
- failure to respond soon after admission to changes in vasodilators or diuretics

In these patients, invasive treatments and monitoring should be reviewed. Discontinuing some cardiac drugs that are not beneficial for symptom control may be appropriate (see Table 17.3).

Implantable cardioverter defibrillator

- If the patient has an implantable cardioverter defibrillator (ICD) in place, it is important to consider when it would be an appropriate time for a technician to switch it off. Ideally this would be an ongoing discussion with patient and family over time, but in an emergency situation an ICD can be deactivated by applying a large magnet to the area of the chest overlying the ICD.

Table 17.3 Heart failure drugs discontinuation strategy

Continue drugs for short-term benefit (morbidity)	Weigh up advantages/disadvantages of continuing drugs with medium-term benefits (morbidity/mortality)	Discontinue drugs with only long-term benefit (mortality)

• Loop and thiazide diuretics
• Digoxin/ beta-blockers in AF
• Antianginals
	• ACE inhibiter/A2A
	• Beta-blockers
	• Spironolactone
	• Drugs for co-morbidities:
	  • hypoglycaemics
	  • antihypertensives
	  • levothyroxine
	  • warfarin
		• Statins
		• Digoxin in sinus rhythm

A2A = angiotensin-II antagonist.

Decreasingly important for symptom control GIBBS (2006)

Useful resources

- British Heart Foundation (2007) discussion document on 'Implantable cardioverter defibrillators in patients who are reaching the end of life' https://www.bhf.org.uk/informationsupport/publications/living-with-a-heart-condition/icd-deactivation-at-the-end-life
- British Heart Foundation: https://www.bhf.org.uk/informationsupport/treatments/implantable-cardioverter-defibrillator

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Complex decision-making

In the era of modern medicine, there are constantly new innovations, and no more so than in the field of cardiology. Technology has developed rapidly, and with it so has the complexity of the decisions that must be made by clinicians and patients.

There are invasive treatment options that can be offered to patients with heart failure that prolong life that previously wouldn't have been an option. This means that discussions around the balance between quality of life, improvement in symptoms, and the intention to prolong life are increasingly brought to the fore.

For example, an ICD may prolong life by reducing the risk of sudden death, but it won't improve symptoms of heart failure. In the case of cardiac surgery, e.g. valve replacement, symptoms and prognosis may improve, but it is associated with a significant short-term morbidity post-operatively, and for some patients this will not be acceptable. Some patients may be eligible for heart transplantation or mechanical cardiac assist devices. These are invasive procedures which themselves are associated with significant morbidity and a new set of medical challenges. In addition to treatments for heart failure itself, these patients are often older and have other co-morbidities such as osteoarthritis. Discussions need to be had as to the benefit of treatment, e.g. hip replacement vs the burden of surgery, post-operative recovery time, prognosis, and improvement in quality of life.

In patients who have an ICD, left ventricular assist device (LVAD), or permanent pacemaker (PPM), a decision can arise towards the end of life regarding the choice to turn a device off. In these situations, it is important to know what the likely outcome from this will be when counselling patients and also to predict potential symptoms that will need to be pre-emptively accounted for if possible. Some devices are essential for ongoing cardiac functioning, and the implications of turning off the device are significant and immediate. In the case of a LVAD, it is likely that a patient will die quickly once this has been turned off, but for an individual with an ICD that has not been activated recently, it is unlikely to have any immediate repercussions. Patients and families need to be guided through these decisions and be empowered to make decisions that respect their autonomy. There is rarely a clear right answer. However, it is important that a collaborative approach is taken with these decisions to ensure the best outcome for the patient.

Models of care

Chronic heart failure is increasingly being managed across the community/hospital interface by multiprofessional heart failure teams. These teams should aim to address the disease management and supportive and palliative care needs of the majority of patients with heart failure. A smaller group of patients with challenging palliative needs may need to have direct involvement from specialist palliative care services, often in collaboration with heart failure team management. Mutual support and education, plus joint management by heart failure and specialist palliative care teams, should be objectives for the future.

Further reading

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Chapter 18

Renal failure

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Introduction

As obesity and diabetes increase, so does the incidence of chronic renal disease and end-stage renal failure. Determining the exact number of patients dying of renal failure is challenging. Often the cause of death will be ascribed to an associated contributing factor, e.g. diabetes mellitus, or the final acute event resulting in death, e.g. myocardial infarction. However, we know that renal failure is an independent risk factor for cardiovascular disease and is associated with a high all-cause mortality.[1] In addition, patients with end-stage renal failure have a significant symptom burden and therefore it is important that patients have access to palliative care services to assist with symptom management, advanced care planning, and, where appropriate, decisions around dialysis and transplantation.

Causes of death in renal failure are as follows:

- cardiovascular causes (commonest)
- cerebrovascular disease, including stroke
- infection (20%), including dialysis and transplant-related infection
- cancer
- stopping dialysis

Definition

There have been controversies as to the exact definition of 'renal failure', but a consensus from the international guideline group, Kidney Disease Improving Global Outcomes (KDIGO), was published to attempt to define this.[2] Debate continues.

KDIGO defined chronic kidney disease (CKD) as follows:

- presence of kidney damage (pathological abnormalities) or
- presence of decreased kidney function for ≥3 months (as defined by GFR)

Kidney failure was defined as GFR <15 mL/min/1.73 m^2.

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Decisions regarding dialysis

The decision when to start dialysis is a complex one. The decision depends on the rate of decline of renal function, symptom burden, patient choice, and clinical situation. Communication is, as ever, the key factor in arriving at an appropriate and satisfactory decision.

Factors that would prompt consideration of dialysis are as follows:

- eGFR <15 mL/min/1.73 m^2
- uncontrolled symptoms related to kidney failure
- inability to control volume status or blood pressure
- progressive deterioration in nutritional status refractory to dietary intervention
- cognitive impairment

Recent research assessing mortality, symptom burden, and quality of life of those on dialysis vs conservative management has shown interesting results, which may influence the choices patients and clinicians make regarding dialysis. Studies assessing patient perception of dialysis revealed that in a significant number of cases, patients regretted the decision to start dialysis.[1] Those with multiple co-morbidities who are older and frailer may not see significant improvement in mortality from dialysis vs conservative management.[2] Some studies have even revealed that the benefit of dialysis in improving symptoms may not be as great as once thought. This, in conjunction with the time commitment needed to attend dialysis, means that for some people dialysis is not the right answer. Input and guidance from a specialist is crucial to allow fully informed decisions to be made about future treatment plans. The decision to start or not to start dialysis should be made with the patient, considering their lifestyle, goals, and aims for the future.

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Symptom control in renal failure

As with palliative care for other illnesses, the management of the disease and concurrent symptom control should not be mutually exclusive. Unpleasant symptoms experienced by patients in renal failure should be palliated whether or not dialysis is being offered. Symptoms include the following:

- pain
- fatigue/weakness
- pruritus
- anorexia
- sleep disturbance
- anxiety
- dyspnoea
- nausea
- restless legs
- depression

The principles of symptom control remain the same as with cancer and other non-cancer diagnoses. The aim must be to determine the cause of the symptom prior to treatment. Any other approach fails to make the best use of the therapeutics available.

Causes of pain in renal failure

- concurrent co-morbidity is common; may include diabetic neuropathy, peripheral vascular disease, arthritis, pressure sores
- primary renal disease is less common, but may include adult polycystic kidney disease and renal calculi
- complications of renal failure such as renal osteodystrophy, gout, calciphylaxis, dialysis amyloid arthropathy
- infection, including septic arthritis, peritonitis following peritoneal dialysis, and discitis with epidural abscess
- dialysis-related pain, such as 'steal syndrome' from AV fistulae, cramp, headache, abdominal pain with peritoneal dialysis

Prescribing in renal failure

The kidneys are involved in filtration, secretion, and/or reabsorption of drugs. If renal function is impaired, drugs, or their metabolites, that are normally excreted in the urine may accumulate and take longer to clear. It is worth noting that some drugs will be cleared well by dialysis, and so will have to be given post-dialysis to maintain their effectiveness. Others will not be cleared by dialysis, thereby accumulating. Increased dosing intervals or smaller daily dosing of the drug may be needed.

Factors associated with altered handling of drugs in renal failure

- Oral absorption of drugs may be reduced because of vomiting, diarrhoea, and gastrointestinal oedema.
- Changes in hydration may affect the distribution of drugs in the body, leading to excessive drug levels.
- Loss of plasma protein-binding capacity may occur due to uraemia. This may increase the plasma levels of drugs that are highly protein-bound, e.g. diazepam.
- Increased permeability of the blood–brain barrier may occur, which may exaggerate the unwanted CNS effects associated with certain drugs.

Pain management in renal failure

The absorption, metabolism, and clearance of opioid drugs is complex in renal failure. Individual analgesics are affected by renal failure in different ways. Additional factors must also be considered if the patient is receiving dialysis. However, it is possible to ensure adequate analgesia if opioids are carefully selected and titrated.

Opioids

The choice of opioid will be made based on several factors, one being renal function. Information outlined in the following gives guidance on prescribing in renal failure, but it is important to remember that patients are individuals, and consideration needs to be taken of their drug history, pain history, clinical needs, and co-morbidities as these factors will also impact on the opioids selected.

- **Alfentanil** is highly protein-bound and metabolized in the liver. Because it has a very short serum half-life, it can be difficult to use for breakthrough pain and procedures. It can, however, be delivered very effectively via a SC syringe driver or as an intranasal spray. It is considered by many to be the opioid of choice in the end-of-life care of patients in renal failure. The conversion ratios between alfentanil and morphine vary between units, so refer to local guidelines if in doubt.
- **Fentanyl** is mainly metabolized in the liver to inactive metabolites, and is therefore considered to be relatively safe in renal impairment. Although there are some reports of the parent compound accumulating in renal failure, its clinical effect is unclear. Fentanyl is not dialysable because of high protein binding and a high volume of distribution, so dose adjustment is not necessary for patients on dialysis. However, it may adsorb onto one type of filter, and specialist advice should be sought before use.
- **Buprenorphine** appears to be a relatively safe opioid for use in renal failure. One study compared buprenorphine kinetics between healthy patients and those with renal failure (all dialysis-dependent with creatinine clearances of less than 5mL/min). It found that buprenorphine clearances and dose-corrected plasma concentrations were similar in the two groups, but metabolites were increased in the group of patients with renal failure. Another study, which measured only buprenorphine (not its metabolites) over a 3-hour sampling period, reported that the disposition of buprenorphine was similar in patients with end-stage renal failure compared to healthy controls. The patients with renal failure showed no clinical evidence of sedation or respiratory depression. The effects of haemodialysis on transdermal buprenorphine have been studied in a case series of ten patients. Elevated levels of buprenorphine or norbuprenorphine were *not* found. Furthermore, haemodialysis did not affect buprenorphine levels, leading to stable analgesic effects during therapy.
- **Oxycodone** undergoes hepatic metabolism, but up to 19% is excreted unchanged in the urine. Toxicity caused by the accumulation of both the parent compound and its metabolites has been reported in renal failure. If used in patients in renal impairment, then dose reduction and careful titration are advised. Although oxycodone has a large volume of

distribution, it is only 50% protein-bound and is water-soluble, making it likely to be dialysable. However, pharmacokinetic data on its use in dialysis is lacking, and other opioids should be used in its place where possible.

- **Morphine** (and its prodrug **diamorphine**) is not recommended in renal failure owing to the accumulation of neurotoxic, active metabolites. The use of other opioids is preferred. If clinically indicated and deemed essential, long-acting preparations should be avoided and the patient closely monitored for toxicity. Both morphine and its metabolites can be removed by dialysis, but 'rebound' can occur as drugs and metabolites re-equilibrate between the CNS and plasma, and can lead to unpredictable analgesia and sedation.
- **Hydromorphone** has been reportedly used safely in patients with renal failure, but caution is still advised because the 3-glucuronide metabolite is neuroexcitatory and can accumulate. Dose reduction and careful titration is advised. Hydromorphone has also been used safely in patients receiving haemodialysis, but dose reduction and careful monitoring are required. It is water-soluble, and has a small volume of distribution and a low molecular weight. Studies have shown that plasma levels decrease to 60% of the pre-dialysis levels during treatment.
- **Methadone** undergoes hepatic metabolism, and its metabolites appear to be inactive. The parent compound and its metabolites are mainly excreted in the gut, and so methadone is considered to be a relatively safe drug in renal impairment. Methadone is not dialysable, and therefore no dose adjustments are required.

Adjuvants

- **Paracetamol** is safe in renal failure but should be reduced to 3g every 24h if the patient has severe renal impairment. Paracetamol is dialysed by haemodialysis but not by peritoneal dialysis.
- **Codeine** should be avoided because of reports of profound toxicity, which may be delayed and can occur after even small doses.
- **Non-steroidal anti-inflammatory drugs (NSAIDs)** should be avoided in patients with any degree of renal impairment, although in some contexts cautious use may be appropriate, particularly in the palliative care setting. If patients are on dialysis, NSAIDs can be used as there is no residual renal function. Gastro-protection is recommended.
- **Pregabalin and gabapentin** are commonly used drugs, particularly in the palliative care setting where they are useful neuropathic agents. Both require dose reduction in renal failure as they are renally excreted. Patients receiving dialysis may require an additional dose post-dialysis, as both pregabalin and gabapentin are removed through haemodialysis (pregabalin particularly). Studies that include patients with renal failure are limited, but there are recommendations for dosing in renal failure which should be used as a guide.[1] In patients with GFR <15mL/min, maximum dose of pregabalin is 75mg once daily and gabapentin 300mg once daily.

Reference

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Other symptoms in renal failure

As with pain management, other symptom control measures demand careful assessment of the causes. The specific hazards of drug usage in renal failure must be considered.

The early stages of chronic kidney disease are often asymptomatic; however, patients with stages 3–5 will often experience symptoms:

- CKD 3 (GFR 30–59mL/min): fatigue due to anaemia, muscle cramps
- CKD 4 (GFR 15–29mL/min): above plus nausea, oedema, anorexia, insomnia, poor concentration, neuropathy
- CKD 5 (GFR <15mL/min): above plus headache, pruritus, encephalopathy leading to death

Fatigue, daytime somnolence, and weakness

Fatigue, daytime somnolence, and weakness are common symptoms in patients in renal failure. The causes are usually multiple, and include anaemia due to a low erythropoietin level and iron deficiency, poor nutrition, inadequate dialysis, biochemical disturbances, insomnia, depression, and immobility because of uncontrolled pain. Severe fatigue can also be a feature of the immediate post-dialysis period, probably due to rapid changes in fluid volume, blood pressure, and electrolytes.

Management

Management depends on the likely prognosis and potential benefit of an intervention. Non-drug measures include anaemia correction, improved nutrition, physiotherapy, a good night's sleep, and increased social supportive care. Drug measures include the use of better analgesia, erythropoietin, iron, electrolyte correction, and antidepressants.

Anorexia and weight loss

Like cancer and cardiac cachexia, renal failure can lead to anorexia and weight loss due to fundamental metabolic changes; they are part of the symptomatic spiral experienced in end-stage disease. Only some causes are correctable. Protein malnutrition may occur, especially in patients receiving dialysis.

Other factors include the following:

- chronic nausea
- altered taste
- dry mouth
- gastric stasis due to diabetic neuropathy or opioids
- constipation
- social isolation
- depression
- abdominal discomfort in peritoneal dialysis (PD) patients

Management

- attention to improved nutrition
- treatment of oral infections, especially Candida
- trial of metoclopramide as a prokinetic anti-emetic
- treatment of constipation
- treatment of depression

Appetite stimulation with corticosteroids may temporarily improve appetite, but long-term use is likely to exacerbate muscle wasting and fluid retention.

Pruritus

Pruritus has an incidence of over 50% in patients with end-stage renal disease, whether they are being dialysed or not. The pathophysiology is complex and likely mediated through several pathways. The hypothesis of an *inflammatory* pathway is supported by the effectiveness of immunomodulating therapies such as phototherapy. On the other hand, according to the *opioid* hypothesis, an imbalance in opioid receptors is responsible for pruritus.

Management

Treatment options will depend on patient preference, stage of disease, and likely prognosis. Optimizing existing treatments, if possible, is important. Dialysis modification, treatment of hyperparathyroidism, hyperphosphataemia, and hypermagnesaemia all may improve symptoms of itch. In general, pruritus is usually less problematical after dialysis. Avoidance of dry skin and excessive hot baths, and reduction of alcohol intake, are all simple measures. Short, clean fingernails will reduce secondary infection following scratching. Topical capsaicin cream has been advocated, but topical steroids are unhelpful. Specific measures include ultraviolet B phototherapy, which is effective but burdensome. Oral antihistamines are worth trialling, although caution needs to be taken of their potential sedative effect. Gabapentin and pregabalin have both been shown to be helpful. Sertraline has been shown to be effective in management of pruritus.

Nausea

Nausea is present in 25–33% of patients. The cause may be rising levels of blood urea, but it may also be due to other non-renal causes such as medication, constipation, delayed gastric emptying due to diabetic neuropathy, and fluid and electrolyte changes. As ever, the best treatment is to define and correct the cause if possible. In general, the standard anti-emetics used in palliative care can be used in renal failure at normal dosage. However, caution is always required for untoward side effects such as extrapyramidal syndromes, constipation, and hypotension.

Restless legs syndrome (RLS)

This is an unpleasant 'crawling' sensation felt in the legs. It is more common at night and may be relieved by movement. It occurs in 2–15% of the general population, but may occur in up to 30% of patients in renal failure. It is thought to be connected with dopaminergic dysfunction, iron metabolism, and, possibly, uraemic neuropathy. RLS may be worse with anaemia, low ferritin and PTH levels, as well as with medication such as tricyclics, caffeine, and neuroleptics. It is associated with pruritus, diabetes, and the elderly.

Management

Management with adequate dialysis may help, as will treating anaemia and withdrawing offending medication. Specific drug treatment includes dopamine agonists such as pramipexole, ropinirole, pergolide, and cabergoline, but they may all cause sleepiness and require slow titration. Benzodiazepines such as clonazepam at night are useful, as are opioids and gabapentin. The latter two will both require dose modification in patients in renal failure.

Calciphylaxis and muscle cramps

Calciphylaxis and muscle cramps are two other symptoms of end-stage renal failure. The former is a very rare, painful condition caused by small artery calcification resulting in necrosis and ischaemia of the skin. It carries a poor prognosis and requires careful management with both analgesia and explanation. The high incidence of cramps is due to water and electrolyte imbalance. This may be correctable by adjustment of the dialysis regimen. Preventing weight gain between dialysis treatments has been shown to be helpful. Both quinine and vitamin E have been shown to be useful in small RCTs.

Formulary

See Table 18.1.

Table 18.1 Dose reduction of commonly used drugs in renal failure

DRUG	Mild	Moderate	Severe
Creat.	150–300	300–700	>700μmol/L
GFR	20–50mL/min	10–20mL/min	<10mL/min
Paracetamol	ND	ND	Reduce to 1g 8h
NSAIDs	ND	Avoid if possible	Avoid unless on dialysis
WEAK OPIOIDS			
Co-codamol	ND	1–2 tab q.d.s.	1–2 tab q.d.s.
Co-dydramol	ND	**6** tab in 24h	**4** tab in 24h
Tramadol	ND	50–100mg t.d.s.	50mg t.d.s.
STRONG OPIOIDS			
Alfentanil	ND	ND	ND
Buprenorphine	ND	ND	ND
Diamorphine	75% of ND	2mg SC 6h*	2mg SC 8h*
Fentanyl	ND	75% of ND*	50% of ND*
Hydromorphone	ND	**1.3mg** 6h*	**1.3mg** 8–12h*
Methadone	ND	ND	50% of ND
Morphine	75% of ND	2.5–5mg 6h*	1–2mg 6–8h*
Oxycodone	ND	ND	1–2mg 6h*
ANTI-EMETICS			
Cyclizine	ND	ND	ND
Domperidone	ND	ND	ND
Haloperidol	ND	ND	Reduce dose
Levomepromazine	ND	ND	Caution
Metoclopramide	ND	ND	ND
Ondansetron	ND	ND	ND
ANTICHOLINERGICS			
Hyoscine butylbromide	ND	ND	ND
Hyoscine hydrobromide	ND	ND	ND
CENTRAL NERVOUS SYSTEM MODULATORS			
Amitriptyline	ND	ND	ND
Baclofen	5mg t.d.s.*	5mg b.d.*	5mg o.d.

(*Continued*)

Table 18.1 (*Contd.*)

DRUG	Mild	Moderate	Severe
Benzodiazepines. Start with small doses. Increased cerebral sensitivity.			
Citalopram	ND	ND	ND (caution)
Pregabalin	75mg o.d.*	25–50mg o.d.*	25mg o.d.*
Fluoxetine	ND	ND or alternate days	Low dose or alternate days
Gabapentin	300mg b.d.*	300mg o.d.*	100mg nocte*
Mirtazapine	ND	ND	15mg nocte

*titrate

ND = normal dose

With permission from Andrew Hoy

General considerations

As with the application of palliative care principles to any non-cancer illness, the philosophy that has proved helpful in the past has been to place the patient at the centre of all decision-making. Adaptations may well be required for the specific application of symptom management techniques to end-stage renal failure, not least the modification of drug dosage where renal excretion is important. Any palliative care specialist healthcare professional will need to learn from their colleagues in renal medicine, as well as contribute to innovative thinking in the care of this difficult group of patients.

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Chapter 19

HIV and palliative care

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Introduction

> I'm one of the millions of people around the world living with HIV. I know many of you are probably asking yourselves how I got infected—you're wondering how a 63-year-old grandmother could have been exposed to HIV. Well, the answer is simple: it just doesn't matter.
>
> Doreen Millman, opening the 11th International Conference on AIDS (1996)

HIV disease and treatment have undergone a revolution in the past 35 years, which has taken the diagnosis of HIV from a death sentence to a chronic illness. This chapter reviews the natural history of HIV before discussing the place of palliative care in HIV. The chapter focuses on HIV in the UK.

A brief history of HIV

Human immunodeficiency virus (HIV) was first identified in 1983, following the recognition of acquired immune deficiency syndrome (AIDS) in the early 1980s. There are historical accounts suggesting viral transmission to humans may have occurred as far back as the 1920s. HIV-1 is closely related to the simian immunodeficiency virus (SIV) in chimpanzees and gorillas in Central and West Africa. HIV-2, a less virulent virus, is closely related to a strain of SIV found in West African monkeys called sooty mangabeys.

In 1986, the first therapy for HIV (zidovudine) was trialled in clinical studies, but it wasn't until 1996 when the benefits of triple antiretroviral (ARV) therapy were presented at the 11th International Conference on AIDS. This has dramatically changed the prognosis for those living with HIV. Over the last 30 years, incredible advances have been made in the treatments for HIV, and the average life expectancy for people living with HIV (PLWH) is near normal in the UK. Depending on the age of acquisition, the life expectancy for PLWH is 68, 73, and 77 years at ages 20, 35, and 50 years, respectively, compared with 77, 78, and 79 years in the general population. For men who have sex with men (MSM), the average life expectancy is 75 years for those living with HIV, but the range is wider for women living with HIV, with expected age at death to be 69, 74, and 78 years, compared with 81, 82, and 83 years in the general population.

Further reading

May, M.T., et al. (2014). Impact on life expectancy of HIV-1 positive individuals of CD4+ cell count and viral load response to antiretroviral therapy. AIDS, 28(8): 1193–1202.

Epidemiology

Worldwide there are 36.7 million PLWH; 69.8% are living in Central and Southern Africa and 66% of new infections per year occur in this region. In the UK, an estimated 107,800 people were living with HIV by the end of 2013, but 13% were unaware of their diagnosis.

Late diagnosis of HIV still exists in the UK, with 39% of all new diagnoses per year presenting with CD4 counts less than 350 cells/mm^3. The normal absolute CD4 count in adolescents and adults ranges from 500 to 1500 cells per mm^3 of blood. In general, the CD4 (%CD4+ or absolute count) progressively decreases as HIV disease advances. The impact of presenting late on morbidity and mortality rates is high, particularly within the first year of diagnosis. In the UK, 24% of deaths amongst people living with HIV were related to a late diagnosis. Early recognition and treatment is key to improving health outcomes. The National Institute for Health and Care Excellence (NICE) recommend routine HIV testing in regions where there is an HIV prevalence of >2 per 1000 and in all high-risk groups. The highest risk group in the UK are MSMs, but other risk groups include sex workers, injecting drug users, patients known to be from a high-prevalence country or have sexual contacts abroad, and females with MSM partners.

Natural history

The natural history of HIV and progression of illness are variable. Seroconversion illnesses occur in 80% of PLWH, 2–4 weeks after infection. For many, there are relatively few symptoms for a few years before they acquire opportunistic infections; for others, it may take another 10 years before this stage develops.

Mechanism

HIV targets CD4, a glycoprotein, found on the surface of immune cells, particularly T-lymphocytes, but also present in monocytes and macrophages. The virus uses cytokine receptors (CCR5 and CXCR4) to allow fusion of the viral envelope with the host cell membrane and to gain entry into the cell. Within the cell, HIV reverse transcriptase converts HIV RNA into HIV DNA, which enters the cell nucleus. Once inside the nucleus, HIV integrase inserts the HIV DNA into the host's DNA for replication. HIV proteins are produced from the DNA and are cleaved by HIV protease, allowing new virus particles to be produced.

The discovery of the life cycle was important for the development of therapies to combat the viral replication. Each of the foregoing enzymes is targeted by different classes of ARVs to inhibit virus production.

The virus causes destruction of the cell as it replicates and emerges from the host cell, damaging the host's immunity. The virus, without ARVs, will produce 10 billion virus particles per day. The CD4 count will decline as the viral load increases, and provides a biomarker for monitoring patients.

Classification

Historically, people with advanced HIV (those who had a CD4 count less than 200 cells/mm^3 or had contracted one of a list of conditions identified by the Centre for Disease Control) were referred to as having acquired immune deficiency syndrome (AIDS). This carried prognostic importance prior to effective ARV treatment because the average life expectancy was 2 years after an AIDS-defining illness. AIDS-defining illnesses no longer carry such a poor prognosis as effective ART can be given even when immunity is severely suppressed, with good return of immune function. HIV is now classified either by degree of immunosuppression using the CD4 count as a marker (Table 19.1) or by clinical stage (Box 19.1). The term 'advanced HIV' is now more commonly used than 'AIDS' in the UK.

Table 19.1 World Health Organization immunological classification for established HIV infection in people over 5yo

HIV-related immunodeficiency	CD4 cells/mm^3
None or not significant	>500
Mild	350–499
Advanced	200–349
Severe	<200 or <15%

Adapted from WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children © 2007, Word Health Organization. Geneva, with kind permission from the WHO.

Box 19.1 WHO clinical staging of HIV/AIDS for adults and adolescents with confirmed HIV infection

Clinical stage 1
Asymptomatic
Persistent generalized lymphadenopathy

Clinical stage 2
Moderate unexplained weight loss (<10% of presumed or measured body weight)
Recurrent respiratory tract infections, sinusitis, tonsillitis, otitis media, and pharyngitis)
Herpes zoster
Angular cheilitis
Recurrent oral ulceration
Papular pruritic eruptions
Seborrhoeic dermatitis
Fungal nail infections

Clinical stage 3
Unexplained severe weight loss (>10% of presumed or measured body weight)
Unexplained chronic diarrhoea for longer than one month
Unexplained persistent fever (above 37.6°C intermittent or constant, for longer than one month)
Persistent oral candidiasis
Oral hairy leukoplakia
Pulmonary tuberculosis (current)
Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis, or bacteraemia)
Acute necrotizing ulcerative stomatitis, gingivitis, or periodontitis
Unexplained anaemia (<8 g/dL), neutropenia ($<0.5 \times 10^9$ per litre) or chronic thrombocytopenia ($<50 \times 10^9$ per litre)

Clinical stage 4
HIV wasting syndrome
Pneumocystis pneumonia
Recurrent severe bacterial pneumonia
Chronic herpes simplex infection (orolabial, genital, or anorectal of more than one month's duration or visceral at any site)
Oesophageal candidiasis (or candidiasis of trachea, bronchi, or lungs)
Extrapulmonary tuberculosis
Kaposi's sarcoma
Cytomegalovirus infection (retinitis or infection of other organs)
Central nervous system toxoplasmosis
HIV encephalopathy
Extrapulmonary cryptococcosis including meningitis
Disseminated non-tuberculous mycobacterial infection
Progressive multifocal leukoencephalopathy
Chronic cryptosporidiosis (with diarrhoea)
Chronic isosporiasis

Box 19.1 (*Contd.*)

Disseminated mycosis (coccidiomycosis or histoplasmosis)
Recurrent non-typhoidal Salmonella bacteraemia
Lymphoma (cerebral or B-cell non-Hodgkin's) or other solid HIV-associated tumours
Invasive cervical carcinoma
Atypical disseminated leishmaniasis
Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

Adapted from WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children © 2007, Word Health Organization. Geneva, with kind permission from the WHO.

Further reading

WHO (2007). WHO case definitions of HIV surveillance and revised clinical staging and immunological classification of HIV-related disease. http://www.who.int/hiv/pub/guidelines/HIVstaging150307.pdf

Antiretroviral medication

There are five major classes of ARVs (Table 19.2).

Table 19.2 Commonly used ARVs in the UK

Nucleoside Reverse Transcriptase Inhibitors (NRTIs)	Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)	Protease Inhibitors (PIs)	CCR5 Inhibitors	Integrase Inhibitors (INIs)
Abacavir (ABC)	Efavirenz (EFV)	Atazanavir (ATV)	Maraviroc (MVC)	Dolutegravir (DTG)
Emtricitabine (FTC)	Etravirine (ETR)	Darunavir (DRV)	Enfuvirtide (T-20)	Elvitegravir (EVG)
Lamivudine (3TC)	Nevirapine (NVP)	Evotaz® (ATV + **cobi)		Raltegravir (RAL)
Tenofovir disoproxil fumarate (TDF) or Tenofovir alafenamide (TAF)	Rilpivirine (RPV)	Rezolsta® (DRV + **cobi)		
Zidovudine (AZT)		Ritonavir *(RTV)		

*Ritonavir is a PI, but is only given in combination with ATV or DRV to boost drug levels

**Cobicistat (cobi) is a non-PI, acting as a booster for ATV or DRV

ARVs are given in combinations to reduce the incidence of drug resistance. Ritonavir is a protease inhibitor (PI), but is now mostly used to potentiate the effect of other ARVs by inhibiting their metabolism through cytochrome P450-3A4. These treatment combinations are said to be ritonavir 'boosted'. Cobicistat is also used as a booster for PIs and elvitegravir.

Many combinations are available in single tablet formulations to ease compliance. These are known by their trade names, and it is important to look up which drugs they contain (Table 19.3).

Starting ARVs

The British HIV Association (BHIVA) recommends starting ARV treatment as soon as the patient is committed to taking daily medication, regardless of their CD4 count. This is based on evidence seen in the START study involving 4685 patients across 35 countries. The study found a 57% reduction of AIDS-related events or AIDS-related death in those who started treatment immediately vs those who deferred treatment until CD4 counts dropped to 350 cells/mm^3.

Recommendations in the UK suggest initiating ARV treatment with two nucleoside reverse transcriptase inhibitors (NRTIs) plus one of the following: a boosted protease inhibitor (PI/RTV or PI/cobi), non-nucleoside reverse transcriptase inhibitor (NNRTI), or integrase inhibitor (INI).

Table 19.3 Some combination formulations with trade names

Trade name	Contains
Truvada®	Tenofovir disoproxil fumarate, emtricitabine
Atripla®	Efavirenz, emtricitabine, tenofovir disoproxil fumarate
Eviplera®	Rilpivirine, emtricitabine, tenofovir disoproxil fumarate
Kivexa®	Abacavir, lamivudine
Stribild®	Tenofovir disoproxil fumarate, emtricitabine, elvitegravir, cobicistat
Triumeq®	Abacavir, lamivudine, dolutegravir
Odefsey®	Rilpivirine, emtricitabine, tenofovir alafenamide
Genvoya®	Tenofovir alafenamide, emtricitabine, elvitegravir, cobicistat
Descovy®	Tenofovir alafenamide, emtricitabine

Post-exposure prophylaxis and pre-exposure prophylaxis

In cases of emergency exposure to HIV either through unprotected sex, sharing needles, or needle-stick injury, ARVs can be started within 72 hours to reduce the risk of HIV infection. ARVs will be continued for 28 days as post-exposure prophylaxis (PEP). The effectiveness of PEP is not known as it has been considered unethical to do a randomized trial.

For non-emergency exposure to HIV, prophylaxis can be used, e.g. for those who are HIV-negative and are engaging in high-risk sexual activity. Studies in 2014 and 2015 found pre-exposure prophylaxis (PrEP) to reduce HIV transmission by 86% in serodiscordant couples. In the UK, PrEP is not available on the NHS, but sexual health clinics have been offering monitoring and support for this treatment, if procured independently by patients.

Major side effects of ARVs

Liver toxicity

Liver toxicity is rare with modern ARVs, but efavirenz and nevirapine have a low risk of developing hepatitis. Didanosine (ddI) is a first-generation NRTI which is no longer used in the UK due to its adverse effect of non-cirrhotic portal hypertension. Whilst this medication is no longer in use, the side effects are irreversible and therefore patients are being managed for this condition years later. Atazanavir causes a benign hyperbilirubinaemia.

Renal toxicity

Tenofovir disoproxil fumarate (TDF) has been associated with renal toxicity, Fanconi's syndrome, and osteoporosis. Tenofovir alafenamide (TAF) is a prodrug that provides a reduced extracellular availability and increased intracellular concentrations which reduces the adverse impact on bone and kidneys. Atazanavir has been associated with renal stones.

Peripheral neuropathy

Peripheral neuropathy can be related to the HIV virus or ARVs, especially with some of the older drugs (e.g. zalcitabine, didanosine, and lamuvidine). ARV histories are important to review in patients presenting with peripheral neuropathy or with patients who may have started treatment in developing countries. Peripheral neuropathy is not reducing in incidence in PLWH, and some of the newer ARVs may be implicated.

Rash and hypersensitivity reactions

A rash can occur in 10–15% of patients starting these medications, which can mostly be managed symptomatically with antihistamines +/– steroids. Rarely, Steven-Johnson syndrome can occur with ARV initiation. Fatal hypersensitivity reactions can occur with abacavir. All patients should be tested for HLA 5701 to reduce this risk, and a positive HLA is a contraindication to starting this treatment.

Lipodystrophy and metabolic abnormalities

Lipodystrophy is a range of symptoms which include abnormal central fat accumulation and loss of fat tissue (lipoatrophy). Lipoatrophy can cause stigmatizing facial thinning and painful loss of fat in the feet and buttocks. Lipodystrophy is most associated with PIs. PIs have also been associated with increases in blood sugar.

CNS side effects

Efavirenz has been linked to central nervous system side effects, including vivid dreams and anxiety. In patients with a previous psychiatry history, efavirenz has a ten-fold increase in suicide.

Bone marrow suppression

Bone marrow suppression and anaemias are a common side effect of zidovudine and need to be monitored during its use. Zidovudine is a first-generation ARV which is still used for HIV vertical transmission prophylaxis in babies, post-natally. Whilst its use in adults is rare, it is sometimes prescribed in cases that require intensification of ARVs to penetrate the central nervous system.

Further reading

BHIVA. Current clinical guidelines. http://www.bhiva.org/guidelines.aspx

HIV and ageing

Despite full viral suppression by HAART, premature ageing in PLWH is an area of interest and is likely to be multifactorial. The direct viral impact on the immune system causes a systemic low-grade inflammation that accelerates ageing and increases the risk of co-morbidities. Lifestyle factors play a role in ageing and co-morbidities, with high levels of smoking, alcohol consumption, and illicit drug use in HIV cohorts. These lifestyle factors can influence adherence to antiretroviral medication. The side effects of HIV treatment also play a role. HAART can cause a range of adverse effects, including mitochondrial toxicity, abnormal lipid metabolism, osteoporosis, and renal impairment. Consequently, cardiovascular, neurocognitive, and metabolic disorders can present earlier in PLWH.

Palliative care for PLWH

As a consequence of the effectiveness of antiretroviral therapy, PLWH in the UK can have a near-normal life expectancy. As a result, it would seem that palliative care may have little relevance to such a group, and it is true that the numbers of PLWH who require palliative care are small. Deaths from HIV are low in the UK, with 594 people dying from HIV in 2015. However, there is a role for palliative care for some PLWH:

- A small number of people will develop advanced HIV disease because of issues with adherence to medication. For them, the natural history of their disease is as for untreated infection, with progressive immunosuppression, opportunistic infections, weight loss, and death.
- There are a significant number of late diagnoses, with individuals presenting with consequences of advanced immunosuppression and an uncertain prognosis.
- There are patients who develop cancers which are not amenable or do not respond to curative treatment, such as non-Hodgkin's lymphoma.
- There are patients with symptomatic complications of their HIV or its treatment, such as those with (or 'patients with') painful sensory neuropathy, that may be supported by palliative care clinicians.

Differences in palliative care in PLWH

- In the UK, most PLWH are men who have sex with men, with the second largest group being African women.
- PLWH tend to move to larger urban centres to access treatment and support.
- Patients accessing palliative care with HIV are likely to be younger than the general palliative care population.
- PLWH may have young families, some of whom may also be affected by HIV.
- There may be issues of confidentiality within the family and outside it because of the stigma still associated with HIV.
- Drug interactions and side effects of ART cause additional complexity for the palliative care clinician.

Symptom control in HIV

Despite advances in HIV treatment and prevention of consequences of immunosuppression, symptom surveys in the last ten years continue to demonstrate a high prevalence of symptoms in outpatients living with HIV, even in resource-rich countries. For instance, a study of ambulatory HIV patients in an urban hospital–based clinic found moderate-to-severe fatigue in 43%, insomnia in 35%, anxiety in 34%, and pain in 31%. Psychological issues are common, as are lack of energy, drowsiness, and difficulty sleeping. Many patients describe more than one symptom (Table 19.4).

Symptom control may have hidden benefits in that symptoms may impact on the patient's ability or willingness to adhere to treatment, including ARVs. Symptoms increase in prevalence with advanced disease; examples are given in Table 19.5.

Table 19.4 Symptoms in PLWH

Cause	Example
Directly related to HIV	Colitis Sensory neuropathy
Due to adverse effects of drugs	Nausea Rash Sensory neuropathy
Consequence of immunosuppression	Herpes simplex Toxoplasmosis *Pneumocystis carinii* pneumonia
Co-infection with carcinogenic virus	Anal squamous cell carcinoma Non-Hodgkin's lymphoma

Table 19.5 Symptoms in advanced HIV

Symptom	Possible cause
Severe, unintended weight loss, fevers	HIV itself Mycobacterium avium complex (MAC) tuberculosis
Night sweats	Mycobacterium avium complex (MAC) tuberculosis Parvovirus infection of bone marrow
Dry cough, shortness of breath	Pneumocystis jiroveci pneumonia (*Pneumocystis carinii* pneumonia, PCP)
Genital pain	Herpes simplex
Oral pain or pain on swallowing	Herpes simplex Oropharyngeal candidiasis
Persistent headaches	Cryptococcal meningitis Cerebral toxoplasmosis Cerebral lymphoma
Persistent fatigue	Atypical mycobacterial infection/tuberculosis, HIV infection
Lymphadenopathy	HIV infection, lymphoma, cytomegalovirus
Chronic diarrhoea	HIV colitis Cryptosporidiosis Salmonella
Rapid progressive neurological decline	Progressive multifocal leukoencephalopathy

Table 19.6 Examples of pain in HIV/AIDS

Type of pain	Diagnosis	Cause
Bilateral symmetrical neuropathic pain in sock or stocking distribution of lower legs	Sensory neuropathy	HIV or ART (could also be other causes such as diabetes)
Headache	Headache	ART
	Migraine	Unknown
	Encephalitis/meningitis	Opportunistic infection
	Toxoplasmosis	Opportunistic infection
Abdominal pain	Lactic acidosis	ART
	Pancreatitis	ART
	Gynaecological pain	Unknown
	Abdominal cramps	ART
Musculoskeletal pain	Arthralgia	Hepatitis C Statins
	Avascular necrosis of the femoral head	HIV Steroid treatment
	Fibromyalgia	Unknown

Pain

Around half of PLWH experience moderate or severe pain and it is the most prevalent symptom for this group. The most common sites of pain are in the lower limbs, head, muscles, and joints, and PLWH often report multiple pain sites (Table 19.6). Pain in PLWH can also be from unrelated causes.

Despite effective HIV treatment, the prevalence of pain in PLWH is not decreasing. In fact, the prevalence of some pain is increasing, notably painful HIV-associated sensory neuropathy. Musculoskeletal pain, including fibromyalgia syndrome, also persists despite effective suppression of HIV.

Pain in PLWH appears to be more common in women, those with a history of IV recreational drug use, with advancing age, and in advanced HIV. In this group, pain is associated with significant absence from work and reduced mobility and function. Severity of pain is associated with severity of emotional problems and psychological distress, including suicidal ideation and psychiatric illness. PLWH in pain are more likely to experience lack of social support and more likely to be involved in risky behaviours such as alcohol use, intravenous drug use (IVDU), and sexual risk-taking. Pain can influence adherence to ART and can be a reason for changes in treatment regimens.

Studies reporting on adequacy of pain management suggest pain in PLWH is under-treated. There is some suggestion that PLWH are reluctant to report pain, that there is little focus on symptoms in busy HIV clinics, that there is a reluctance to prescribe analgesics for those with a history of IVDU, and that HIV doctors do not have the necessary training in symptom management.

HIV-associated sensory neuropathy

Neuropathies are a major source of pain in HIV, especially in the context of advanced disease. Of these, the peripheral sensory neuropathy caused by HIV or antiretroviral therapy is the most common. PLWH are also susceptible to the neuropathies suffered by the general population, including acute zoster infections, postherpetic neuropathy, diabetic neuropathy, and painful neuropathy from B12 deficiency.

HIV-associated sensory neuropathy (SN) is one the most important causes of pain in PLWH. There is a strong association between advanced HIV and SN, with a prevalence rate of 35% in one study of hospitalized patients with an AIDS diagnosis. Unsuppressed HIV virus has a neurotoxic effect which is experienced most on longer peripheral nerves, but can also be a result of ARVs. The prevalence of SN remains about 32% despite better treatment of HIV and less frequent use of ARVs which were most commonly implicated.

Principles of pain control in PLWH

For palliative care patients

- Use principles of WHO analgesic ladder, including opioids, NSAIDs, and co-analgesics.
- Methadone bioavailability is reduced by ritonavir, and doses may need to be increased.

For chronic pain in HIV

- Refer to chronic pain teams or use principles of treatment of chronic pain.
- Avoid strong opioids if possible (little evidence of long-term efficacy but significant side effects, risk of depression of testosterone/FSH and LH, causing symptoms).
- Particularly avoid short-acting strong opioids (increased potential for addiction).

For sensory neuropathy

- Exclude other causes (IDDM, B12 deficiency, syphilis, etc).
- Counsel patient about care of feet which may be insensitive to pain or extremes of temperature (test hot baths with an elbow; look at soles of feet weekly; beware new shoes as ulcers can quickly develop; beware uneven ground or stairs in the dark).
- There is no effective remedy for numbness which patients may describe as unpleasant.
- Pain from HIV-associated SN does not respond to TCAs or pregabalin/gabapentin.
- Some evidence for high-dose topical capsaicin patches, which must be applied in specialist clinics.

Drug-drug interactions (DDIs) and palliative care medications

Drug-drug interactions need to be carefully considered in patients taking ARVs. Numerous interactions occur, particularly with drugs which induce or inhibit cytochrome P450 enzymes—especially boosted PIs, cobicistat, efavirenz, and etravirine. It is important to check for interactions when prescribing any new drug in PLWH on ARVs, and this can easily be done on the University of Liverpool drug interactions website (http://www.hiv-druginteractions.org).

Many interactions occur with palliative care medications which are not clinically significant. However, methadone levels will be significantly reduced by many ARV drugs, particularly PIs. Increased bioavailability of non-steroidal anti-inflammatory drugs occurs with some ARVs and may lead to gastric or renal toxicity. Benzodiazepine and tricyclic antidepressant levels may be increased.

Steroid levels are significantly increased by ritonavir to the extent that Cushing's syndrome has been reported with PLWH on ritonavir and using steroid inhalers. The effect of steroids by any route can be augmented, and there is a greater risk of adrenal suppression and insufficiency once the steroid has been stopped.

There are also important effects of non-HIV medications on ARVs. For instance, antacids will decrease the levels of some ARVs. Proton-pump inhibitors and H2 blockers should be avoided with certain ARVs.

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University of Liverpool Drug Interaction website. http://www.hiv-druginteractions.org

HIV-associated malignancies

HIV-associated malignancies are caused by oncoviruses which are enabled to cause cancer after immunosuppression from HIV. They include cervical cancer, Kaposi's sarcoma, and non-Hodgkin's lymphoma. Risk factors for developing HIV-related cancers include older age, a low CD4 count, and no prior treatment with ARVs. Factors affecting prognosis can be found in the International Prognostic Index (IPI) score. HIV malignancies should be managed in centres with expertise in managing these conditions. During treatment with chemotherapy, PLWH are at increased risk of developing opportunistic infections and should be started on prophylaxis for *Pneumocystis jirovecii* pneumonia, candidiasis, mycobacterium avium complex, and herpes simplex virus.

Kaposi's sarcoma

Kaposi's sarcoma is a skin cancer which occurs in certain populations, including Mediterranean Jews and immunocompromised individuals who are co-infected with human herpesvirus 8 (HHV-8). PLWH who have immunosuppression and HHV-8 can develop Kaposi's sarcoma on the skin and in lymph nodes, but also in solid organs, including liver, spleen, lungs, and digestive tract. Kaposi's sarcoma often responds to active management of the HIV infection with ARVs.

Non-Hodgkin's lymphoma

Between 4% and 10% of all PLWH will develop non-Hodgkin's lymphoma (NHL) which may be intermediate- or high-grade lymphoma (80%), primary central nervous system NHL (20% of NHL in PLWH), or, less commonly, primary effusion lymphoma. Certain types of NHL are associated with co-infection with Epstein–Barr virus (EBV). Non-Hodgkin's lymphoma can occur in PLWH with relatively well preserved immune function.

Anal/cervical cancer

PLWH co-infected with human papilloma virus (HPV) are susceptible to developing anal cancer or, in women, cervical cancer.

Other malignancies in PLWH

PLWH are also more likely than non-infected individuals to be diagnosed with liver cancer (through co-infection with hepatitis C) and Hodgkin's lymphoma (co-infection with EBV). Lung cancer is also more common, but here the causation is less clear, and it is possible that a higher rate of smoking in PLWH is responsible.

Further reading

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Confidentiality

HIV still carries a stigma which makes confidentiality an issue for some PLWH. There may not be disclosure between family members. The treating team should communicate sufficiently well between themselves so that confidentiality is maintained.

Death certification

The GMC is clear that a doctor's duty is to provide full and frank information on the death certificate. However, a doctor also has a duty to respect their patient's confidentiality. In the event of a death when there is non-disclosure of HIV with the next of kin, an ethical dilemma arises in death certification. The doctor needs to weigh up the conflicting duty to respect the patient's confidentiality and to record full information on the death certificate.

Chapter 20

Dementia and frailty

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Introduction

As we live longer, dementia is replacing cancer as the most feared disease. Dementia affects 5–7% of those over 60 and 20% over 80 years.[1] The worldwide population with dementia was estimated in 2014 as 47.5 million.[2] At the current rate there will be 850,000 people with dementia in the UK by 2015, and this number is forecast to increase to over 1 million by 2025 and over 2 million by 2051.[3] This is contributing to one in four hospital admissions, with the health and social costs of dementia estimated to be more than stroke, heart disease, and cancer combined. Along with these worrying progressive epidemiological figures, we need to take into account the immense caring burden for families, carers, and society.

End-stage dementia often falls between the cracks of specialization, with professionals feeling under-prepared for the intricacies of end-stage dementia management strategies.[4] Palliative care has been slow in its involvement for multiple reasons, but primarily because dementia has a much slower disease trajectory than cancer, with an unclear prognosis. In recent years palliative care has become more involved in the complex end-stage dementia patient owing in part to greater publicity of this condition and a political climate to improve dementia care as a result of our ageing population.[5]

There is a need for improvement in current care to develop compassionate, dignity-enhancing care for end-stage dementia. Palliative care with its holistic management of symptoms, care of the supporting family, and awareness of the process of dying is in an ideal position to provide support for the complex end-stage dementia patient.

End-stage dementia often follows a longer time course, and social problems tend to be the predominant feature for admission in comparison to other palliative care admissions.

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What is dementia?

Pray, do not mock me.
I am a very foolish fond old man,
Fourscore and upward, not an hour more nor less;
And, to deal plainly,
I fear I am not in my perfect mind.

Shakespeare, *King Lear*, 4.7.69–73

It has always been thought that as we age we lose faculties, and this elderly group have traditionally been labelled as 'senile'. In the 1960s and 1970s, research showed the degree of cognitive decline was related to pathological lesions in the brain and the decrease in the neurotransmitter acetylcholine (ACh). Alzheimer's disease was found as the most common cause of dementia, and the term is used by lay people synonymously with the umbrella term 'dementia'.

Dementia is a progressive broad deterioration of intellectual functionality. Dementia is a clinical diagnosis. This requires memory impairment to be present along with at least one other associated impairment, such as aphasia, apraxia, agnosia, or deterioration of executive function (planning, initiating, sequencing, monitoring, abstract thought, and complex behaviour). The condition must be severe enough to interfere with social circumstances, relationships, or work performance, and it must represent a decline from a previous level of performance.[1]

Subtypes

See Table 20.1.

Differentiating between the different dementia syndromes can be challenging owing to the overlapping clinical features and obscure underlying pathology. Other rarer causes of dementia exist predominantly in younger age groups, such as Creutzfeldt–Jakob disease and Parkinson's, plus syndromes such as progressive supranuclear palsy and corticobasal degeneration.

Prognosis of dementia

Much individual variability is seen with people with dementia. Median survival with Alzheimer's disease has been estimated at 7.1 years (6.7–7.5 years), while vascular dementia has been estimated at 3.9 years (3.5–4.2 years). Increasing age and male gender are associated with higher rates of mortality in dementia.[2] Co-morbidities which may or may not be related to dementia often exist, making it difficult to determine the contribution of dementia to mortality.

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Table 20.1 Main dementia subtypes

Alzheimer's dementia	Insidious onset with changes in memory, personality, communication, and mood. Alzheimer's is estimated to account for 60% of dementia cases.
Vascular dementia	Often stepwise decline in cognitive processing, language, decision-making, and visuospatial ability. Memory loss is often less noticeable than in Alzheimer's. There are often concurrent vascular problems, especially transient ischaemic attacks (TIAs).
Mixed dementia	The majority of dementia patients often have an element of both vascular and Alzheimer components that are difficult to quantify.
Lewy body dementia	Complex visual hallucinations are a key feature, as well as sleep disturbances and fluctuations in cognition. There are often symptoms of Parkinson's disease. It is estimated that 80% of Parkinson's disease patients develop dementia.
Frontotemporal dementia (Pick's disease)	A rarer form with marked changes in personality and behaviour including disinhibition and impulsiveness. Memory is preserved in the early stages and aphasia is a later feature. This is more common in younger groups (aged 50–60 years).
Huntington's disease	A rarer autosomal dominant disease caused by CAG (cytosine-adenine-guanine) triplet repeat stretch within the Huntington gene. Symptoms include writhing (chorea) movements, progressive dementia, and behavioural problems.

Diagnosis of dementia

The diagnosis of dementia is difficult. It is estimated that only 50% of patients are formally diagnosed. In England, the National Dementia Strategy from the Department of Health, which was updated in 2015, encourages early diagnosis, as do many independent and governmental bodies.[1]

Diagnostic tests

The diagnosis is based on cognitive testing, although brain imaging may help. Many tests have been studied, but the Mini-Mental State Examination (MMSE) is the best validated, and most studied and commonly used.

Other tests include the Addenbrooke's Cognitive Examination (ACE-R), Abbreviated Mental Test Score (AMTS), the General Practitioner Assessment of Cognition (GPCOG), the seven-minute screen (7MS), the Modified Mini-Mental State Examination (3MS), and the Cognitive Abilities Screening Instrument (CASI). The MOCA (Montreal Cognitive Assessment) is a further reliable screening test and is available online for free in 35 different languages.[2] The MOCA has also been shown to be somewhat better at detecting mild cognitive impairment than the MMSE.[3]

Population screening for dementia is unreliable owing to the poor predictive value of the mental assessments, so the current strategy focuses on case-by-case assessment for at-risk groups. Because of the push for early diagnosis and early intervention (Table 20.2), there have been discussions regarding strategies on how to do this.[3]

Table 20.2 Arguments for and against early diagnosis

Argument for early case finding	Argument against early case finding
Early diagnosis allows: • Advanced planning at a stage when the patient is able • Treatment of other risk factors (lifestyle, vascular disease, etc.) • Exclusion of reversible causes (see below) • Early support if appropriate	• Lack of evidence that the early identification improves outcomes • Concern regarding potentially distressing the patient • Often uncertainty as to clear diagnosis • Lack of services available to offer adequate response • Over-medicalizing patients

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Mild cognitive impairment

The diagnosis of mild cognitive impairment (MCI) is a likely consequence of increased awareness and case finding of dementia. MCI is defined as impaired memory for age and education, but with preservation of general cognitive function and functional status. MCI patients are at increased risk of developing dementia; however, MCI fluctuates, with 25–30% of patients improving. There is no evidence that acetylcholinesterase inhibitors reduce progression; they should not be used. This group of patients should be monitored by primary care and re-referral for specialist assessment if symptoms deteriorate. There is an increased cardiovascular risk in this population and this should be addressed. There is some evidence that cognitive stimulation is effective at delaying progression.[1, 2]

Management

Statins, HRT, vitamin E, and NSAIDs should not be prescribed as primary prevention against dementia.[3]

The VITACOG study is a small study on patients with cognitive impairment/dementia showing that B-vitamins may reduce progression of cerebral atrophy, and improve memory scores and cognitive function compared to controls (Table 20.3). This is a small study and needs larger confirmatory studies. B-vitamins are readily available over the counter should patients wish to take them.

Table 20.3 VITACOG B vitamin recommendation for 'MCI' in the A/W log

Oral folic acid	0.8mg OD
Oral B12	0.5mg OD
Oral B6	20mg OD

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Aetiology of dementia

Dementia is a term incorporating a collection of symptoms with variable aetiology. Any mechanism which causes a progressive cognitive impairment and associated functional loss is a potential cause. This differential is wide, including medication, infections, structural brain lesions, metabolic disorders, toxic chemicals, autoimmune disorders, and para-neoplastic and psychiatric disorders.

Alzheimer's disease currently has an unknown aetiology with a variety of models proposed. It appears that it is due to a slow inflammatory process altering the brain chemistry and structure, including the development of amyloid plaques and tau protein dysfunction on the background of genetic predisposition.

It is always important to create a differential diagnosis and review regularly as the disease progresses. Some of the secondary/differential causes of dementia are treatable, as are some diseases that imitate dementia, even in the perceived late stages of the disease (see Table 20.4).

The degree of reversibility varies depending upon the underlying cause, with some being completely reversible whilst others have only small components of reversibility. For example, treating vascular dementia with anti-platelets may not only improve prognosis but may also allow some recovery in cognition.

With ongoing future advances in treatment of dementias, the distinction between reversible and non-reversible may blur further, and eventually alleviate, arrest, or even reverse the cognitive decline.

Table 20.4 Potentially reversible differential diagnosis

Depression	Depression should *always* be considered as it is treatable and the most common disease masquerading as dementia. In comparison with dementia, the onset of depressive symptoms may be more rapid. Depression may be the first symptom of a dementia illness. Older people who were treated for depression showed improvement in cognition without reversibility of dementia, indicating a possible overlap between the two conditions. Depression is more common in vascular dementia.
Infection	Delirium is one of the most important reversibilities to recognize early because it is common and treatable. Delirium follows a fluctuating course and can be hypo- or hyper-active. Lyme disease (*Borrelia burgdorferi*) has been proposed to be linked with Alzheimer's dementia. This is through increased production of amyloid beta and tau proteins in tissue cell cultures, but has not been demonstrated in vivo. There is no current evidence to conclusively link the two diseases. Tertiary syphilis can cause late neurosyphilis, which can manifest as dementia. Treating the underlying infection often produces a partial improvement. HIV dementia is a heterogenous condition requiring HIV antiretroviral treatment.

(*Continued*)

Table 20.4 (*Contd.*)

Nutritional disorders	Vitamin B12 deficiency may cause sub-acute combined degeneration, multiple sclerosis–like syndrome, delirium, psychiatric symptoms, and dementia. It was originally thought that B12 supplementation would resolve or improve the dementia. However, there is little evidence to support this, and it is proposed that vitamin B12 deficiency may be an epiphenomenon of dementia rather than a cause of cognitive deterioration. Wernicke's encephalopathy and Korsakoff's syndrome are potentially treatable thiamine deficiencies. Wernicke's encephalopathy is characterized by the triad of ophthalmoparesis, ataxia, and confusion.
Alcohol-related	Chronic alcohol abuse is well known to result in deterioration in cognition, behavioural changes, and personality changes. The role of alcohol in the dementia process is still debated, as it is not clear whether there is a direct toxic effect or a secondary cognitive decline due to other factors related to alcohol consumption. Abstinence may improve cognition, but true reversibility is uncertain.
Endocrine disorders	Thyroid disturbances can cause depression and memory dysfunction. With the stabilization of thyroid function, memory and mood may return to normal. Idiopathic hypoparathyroidism is a rare disorder that can cause Fahr's disease (idiopathic basal ganglia calcification). The disease causes dementia, together with other neurological complications (epilepsy, parkinsonism, raised intracranial pressure). Treatment is symptomatic.
Metabolic disorders	Multiple electrolyte disturbances, and renal, hepatic, or pulmonary insufficiency, may present as a transient cognitive impairment or delirium that can mimic dementia with or without sepsis. Cognition often is restored after treatment of the underlying disorder. Wilson's disease is an autosomal recessive disorder causing copper accumulation and toxicity. It presents with psychiatric and movement abnormalities. Treatment is through chelation with penicillamine. Cognitive symptoms are also common and improve with therapy.
Poisoning	Lead exposure can cause lead encephalopathy, often presenting in industrial workers. Metals such as mercury, bismuth, arsenic, manganese, and aluminium have also been implicated in dementia. Carbon monoxide intoxication can present with confusion and altered memory. These symptoms may not be reversible even after cessation of the offending agent, though this may prevent further clinical decline.

Table 20.4 (*Contd.*)

Medications—adverse effects and drug interactions	Psychoactive drugs are the most common cause of drug-induced cognitive impairment (e.g. benzodiazepines, antidepressants, analgesics, anticonvulsants, antipsychotics, and anti-parkinsonian drugs). Non-psychoactive drugs are harder to identify as they are often idiosyncratic reactions (e.g. proton pump inhibitors, digoxin, calcium antagonists, corticosteroids, and some antibiotics). Anticholinergic burden: medications with a high anticholinergic burden score can increase the risk of cognitive impairment and delirium in those over 65 years. Examples are tricyclic antidepressants, antipsychotics (olanzapine and quetiapine), and antimuscarinic drugs (oxybutynin, tolterodine, darifenacin).
Brain lesions	Normal pressure hydrocephalus presents with the classical triad of gait apraxia, dementia, and urinary incontinence. Depending on the time of shunt insertion, urinary incontinence and gait apraxia may resolve and memory may improve. After surgical intervention, patients with haematomas and brain tumours can often see a resolution of their cognitive symptoms.
Miscellaneous	Radiation therapy of the brain can cause a dementia. Dialysis has been reported to cause a dementia-like syndrome. These often reverse after cessation of therapy or appropriate treatment, and should be considered in patients undergoing these procedures.

Treatment of dementia

There are no interventions that cure or alter the long-term progression of dementia.

There are currently four drugs licensed for treatment with modest overall benefit; a small minority can give a substantial benefit and therefore a trial of treatment is recommended (Table 20.5). NICE guidance recommends that these drugs should be started by a specialist.[1]

Combination therapy using an AChEI initially with the later addition of memantine can be considered with specialist advice, particularly as the dementia advances. These medications do not currently have licences for other types of dementia; however, in practice, because vascular dementia and Alzheimer's disease are often mixed, a trial of treatment is often performed.

Table 20.5 Acetylcholinesterase inhibitors (AChEIs) in mild-to-moderate Alzheimer's dementia

Medication	Side effect	Evidence
Donepezil, galantamine, rivastigmine	Cholinergic stimulation is often dose-related and titration regimes can minimize side effects. **Mild** Nausea, vomiting, diarrhoea, anorexia, headaches, insomnia **Severe** Tremor, agitation, bradycardia, hallucinations, urinary incontinence Caution in patients with urinary retention, asthma, COPD, seizures, and peptic/duodenal ulcer disease. Patients with sick sinus syndrome or supraventricular cardiac conduction disturbances require monthly monitoring at onset, stop if HR<50. Caution in patients with liver impairment as excreted via the liver.	Level 1a evidence from a systemic review of trials. Modest improvement in cognitive function compared to placebo in mild, moderate, and severe disease (NICE). NNT is 12 to achieve a significant benefit in cognitive function over 12 weeks. The NNH is also 12 to cause an adverse effect.
NMDA antagonists—moderate-to-severe Alzheimer's dementia		
Memantine	Fewer and less severe side-effect profile than cholinergic drugs. Sedation, dizziness, somnolence, dizziness, constipation, hypertension, and headache. Caution with epilepsy or a history of seizures. Check renal function as excreted via the kidney.	Level 1a evidence There is a small beneficial effect in moderate-to-severe Alzheimer's disease in cognition, mood, behaviours, and activities of daily living. No evidence of benefit in mild dementia but is frequently used off-label.

Reprinted from Prescribing drugs for Alzheimer's disease in primary care: managing cognitive symptoms DTB 2014;52:69–72 with permission from the BMJ Publishing Group.

There is evidence for benefit in using AChEIs in Lewy body dementia and Parkinson's disease.

There is evidence that these medications are *not* beneficial in frontotemporal dementia and MCI.

When should the dementia medications be stopped?

Dementia medications should only be continued when they are considered to be having a worthwhile positive global effect on cognition, behavioural, and/or functional status. This benefit should be reviewed on a regular basis (initially around 3 months) and the decision should also take into account the holistic picture incorporating the patient's, carers', and family's views. If medication is discontinued, often repeat cognitive assessments 4–6 weeks are performed to assess deterioration, and if significant deterioration occurs during this short period, consideration should be given to restarting therapy.

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Advanced dementia

Advanced dementia indicates disease progression leading to total dependence upon others. The patient either requires 24-hour care provided by carers at home or admission into an institution (such as a nursing home). The former often has a pronounced burden on the patient's carers and the latter may lead to institutionalization.

It is the advanced dementia patients who are most likely to benefit from specialist palliative care services. There are often psychobehavioural symptoms in this patient group along with the patient's loss in their ability to communicate their needs and wishes unambiguously.

Advanced dementia can be defined by multiple scoring systems not limited to, but including, the following:

- <10 on the Mini-Mental State Examination (MMSE)
- Stage 3 (some would include stage 2) on the clinical dementia rating (CDR)
- Stages 6–7 on the FAST score of the Global Deterioration Scale (GDS)

Advanced dementia changes

In advanced dementia, not only is cognitive function impaired, but commonly there are many other changes:

- **Physical changes**—including weight loss, recurrent falls, frailty, epilepsy
- **Behavioural changes**—frequently agitation, but many other neuropsychiatric symptoms
- **Advanced cognitive deterioration**—changes in not only memory, but also thinking and reasoning, perception, attention, executive functioning, emotional behaviour, and loss of practical skills

Discussing the future

While patients with dementia still have mental capacity, it is important to try to discuss personal wishes for future care, including who should make decisions when the patient is no longer able to do so (advanced care planning). Owing to this being a difficult discussion for all involved, it is frequently put off until it is too late, and there is a lack of guidance as to patient preferences.

Discussions about advance care planning require compassion, sensitivity, and honesty. Those medical professionals who have an established relationship with the patient are best placed to undertake these discussions and commonly find the patient has already thought about such topics. After such conversations, patients can formally record their wishes in several ways.

Outcomes of advance care planning discussions and terminology

See Table 20.6.

Table 20.6 Advance care planning discussion outcomes

Statement of wishes and preferences/ advanced statement	This statement is the patient's wishes for future care and provides a framework by which decisions can be based in the event of capacity being lost. It is not legally binding.
An advance directive for refusal of treatment (or 'living will')	This statement is the patient's refusal to receive specific medical treatment in a predefined future situation. It is legally binding and comes into effect when a person loses mental capacity. It has to include the phraseology acknowledging the awareness this decision could result in death. It cannot demand treatments.
A proxy decision-maker/lasting power of attorney for health and welfare (England and Wales), welfare power of attorney (Scotland)	This is a legally binding document whereby the patient ('donor') nominates another ('attorney' or 'attorneys') to make decisions on their behalf should they lose capacity. In England, following the Mental Capacity Act, there are two separate aspects to lasting power of attorney, one for an individual's health and welfare and a second for property and financial affairs. In Scotland, this is similar to 'welfare power of attorney' for health decisions and 'continuing power of attorney' for financial affairs. Within Northern Ireland it follows common law and can use an 'enduring power of attorney' form for financial affairs.

Identifying the need for palliative care

Identifying the need for specialized input from palliative care clinicians in dementia patients is difficult. Unlike cancer, there are no clear 'curative' and 'palliative' phases. No treatment cures dementia (with the exception of the rare reversible causes discussed earlier). All treatment is essentially palliative, aimed at symptom control. All dementia management needs to be infused with a palliative ethos.

There are two fundamental questions which need to be answered regarding the referral to palliative care:

1. Is the patient in the advanced stages of the disease requiring complex symptom control?
2. Is the patient dying?

Other situations may include providing psychosocial support for the patient or family, respite admissions, rehabilitation, terminal care, and staff support in particularly difficult situations.

There have been a variety of models and criteria suggested to help generalists and other specialists identify who should receive specialist palliative care for dementia.

The surprise question

The SPICT (Supportive & Palliative Care Indicators Tool) recommends a simple question to ask yourself: 'Would you be surprised if this patient were to die in the next 6–12 months?'.

This question works well at an intuitive level, with a 'No' answer being surprisingly accurate at around seven times out of ten for all causes. However, this tool is not a specific tool for dementia, and has yet to be tested exclusively for this population. Dementia patients' prognosis can be difficult to estimate, but this is nevertheless a very useful tool.

The Gold Standards Framework

http://www.goldstandardsframework.org.uk

The Gold Standards Framework (GSF) is a systematic, evidence-based approach to optimizing care for all patients approaching the end of life, delivered by primary care providers. It is for patients considered to be at any stage in the final years of life. The GSF involves the following:

- identify patients in need of special care
- assess and record their needs
- plan and provide their care

These criteria are not specific for dementia patients; however, there are specific indicators for dementia.

Indicators for palliative care under the GSF

- co-morbidities or other general predictors of end-stage illness
  - general physical decline
  - reducing performance status: the Outcome Assessment and Complexity Collaborative (OACC project)/Eastern Cooperative Oncology Group (ECOG)
  - dependence in most activities of daily living (ADLs)

Specific indicators for dementia

- unable to walk without assistance
- urinary and faecal incontinence
- no consistently meaningful verbal communication
- Barthel score <3
- unable to dress without assistance
- reduced ability to perform activities of daily living
- plus any one of the following:
  - 10% weight loss in previous 6 months without other causes
  - pyelonephritis or UTI
  - serum albumin <25g/L
  - severe pressure sores, e.g. stage III/IV
  - recurrent fevers
  - reduced oral intake/weight loss
  - aspiration pneumonia

Needs-based criteria

Given that there are no nationally agreed criteria for accessing specialist palliative care, the National Council for Palliative Care (NCPC)[1] has suggested pointers which should trigger serious consideration:

1. Does the patient have moderately severe or severe dementia?
2. Does the patient also have severe distress (mental or physical) which is not easily amenable to treatment?
   - or severe physical frailty which is not amenable to treatment?
   - or another condition (e.g. co-morbid cancer) which merits palliative care services in its own right?

If criteria (1) and (2) co-exist, then the patient ought to have full assessment of need and a focused analysis of why they are in distress and how best their symptoms can be improved and distress reduced.

Recognizing approaching death

This is not easy, especially for those who rarely witness dying, and even more difficult in the case of the dementia patient who often already has many of the signs of approaching death owing to the pre-existing dementia symptoms. Always take seriously any relatives/carers noting a change in the patient.

Premonitory signs

- often these are already established in advanced dementia
- increasing weakness and lethargy
- sleeping throughout the day
- loss of interest in feeding and drinking
- withdrawal from social interaction
- reduced communication
- terminal restlessness/agitation

As the dying process becomes increasingly established

- deteriorating consciousness
- breathing patterns change
- sometimes newly developed incontinence of faeces and urine
- peripherally shutting down

Challenging behaviours in dementia

Patients with dementia often have many challenging behaviours and may become agitated for many reasons, including inappropriate responses to distressing situations.

There is overall broad agreement with the current guidelines for the management of behavioural and psychological symptoms of dementia, including those of NICE, the American Psychiatric Association, the BMJ, and the American Geriatrics Society.[1-4] All recommend the use of non-pharmacological behavioural strategies as first-line, but none recommend a particular evidence-based non-pharmacological approach over another. The NICE guideline offers the most comprehensive approach to assessment of underlying causes.

As with all medical quandaries, there needs to be an examination as to the suspected underlying cause. Dementia patients are no different, albeit often requiring a more patient and systematic approach. There needs to be clear consideration given to possible reversible causes.

- Consider using a 'This is me' tool, or similar.
  - Royal College of Nursing, Alzheimer's Society (2015) https://www.alzheimers.org.uk/site/scripts/download_info.php?downloadID=399

Potentially reversible considerations

- infections
- pain and/or other distressing symptoms
- environmental factors

Infections

Infections are common in this group and are often the cause of a rapid decline or sudden change, with or without delirium. There should be a low threshold for investigating infection if suspicion is raised. Common infections include UTIs, chest infections, cellulitis, and, often missed, dental infections. The patient's co-morbidities often provide clues as to the source. Treatment of infection often provides better symptom control than resorting to antipsychotic medication, which has many additional problems. Having a low threshold for investigation into infection (MSU, sputum culture, inflammatory markers) is recommended.

Pain and/or other distressing symptoms

Please see section on pain and other distressing symptoms in dementia, pp. 607–10. A common, often missed cause is constipation.

Environmental factors

The environment in which we reside influences every aspect of our being. The environment should provide a peaceful, relaxing atmosphere with capacity for privacy and socializing. A lack of meaningful stimulation is linked to behavioural issues. People *need* to engage in constructive activities and social interaction. Within care homes this is increasingly recognized, with regular organized activities often arranged; however, there remains a need to improve the level of stimulation available.

At the opposite end of the spectrum, overstimulation can sometimes cause confusion to the patient. There needs to be a constant routine with expected periods of stimulation built into that routine. This balance is individually assessed and should be based on the patient's preferences and interests and suited to their capabilities.

References

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Neuropsychiatric symptoms of dementia

Neuropsychiatric symptoms are non-cognitive symptoms which are generally recognized as being beyond the former 'in-character' nature of the patient. If other reversible causes are ruled out, and the symptoms are deemed part of the dementia process, they are commonly known as behavioural and psychological symptoms of dementia (BPSD). They often occur in clusters or syndromes identified into groups by the neuropsychiatric inventory (NPI) and are outlined in Table 20.7.

The term 'BPSD' arose from the literature; the classification as such does not specify many other specific symptoms. Specific symptoms include the following: easily upset, repeating questions, arguing or complaining, hoarding, pacing, inappropriate screaming (also crying out, disruptive sounds), rejection of care (e.g. bathing, dressing, grooming), worrying, shadowing (following caregiver), sexually inappropriate behaviour, wandering, and rummaging.[1]

Principles in management of behavioural and psychological symptoms of dementia

Over 75% of people with dementia develop behavioural problems or psychiatric symptoms at some point during their illness. In those patients able to express themselves, it will be easier to identify whether or not the

Table 20.7 Neuropsychiatric inventory (NPI)

Delusions	Psychosis	The NPI was developed as a research tool for application to patients with Alzheimer's disease and other dementias. Note: with a predominance of the dementia being characterized by vivid visual hallucinations, delusions, and fluctuating cognition, consider Lewy body or Parkinson's dementia. This can respond well to AChEIs (e.g. rivastigmine).
Hallucinations		
Depression/dysphoria	Mood	
Anxiety		
Elation/euphoria		
Apathy/indifference		
Agitation/aggression	Agitation	
Disinhibition (socially and sexually inappropriate behaviours)		
Irritability/liability		
Aberrant motor behaviour (repetitive activities without a purpose)		
Sleep disorders (day-night reversal)		Ten behavioural and two neurovegetative areas are included in the NPI. This is further divided into three main syndromes: psychosis, mood, and agitation.
Appetite and eating disorders		

Based on modified neuropsychiatric inventory-Q categories. The NPI is scored by the caregiver according to frequency, severity, and caregiver distress at symptoms.

cause of distress is physical pain or mental incapacity; however, this ability diminishes as the disease progresses. BPSD occurs most commonly in the middle-to-late stages of dementia. Depressive and apathetic symptoms are usually the earliest to appear. Hallucinations, elation/euphoria, and aberrant motor behaviour are usually later. Apathy is the most common persistent symptom (reported in 75% of cases), and delusional symptoms the least persistent.[2,3]

Low-dose antipsychotics have been historically the choice to manage BPSD; however, antipsychotics (typical and atypical) have been shown to be only of limited benefit in BPSD, with a real risk of increased mortality and unfavourable side effects.

A very simple but useful tool in understanding the origin of BPSD is the ABC chart (antecedents, behaviour, consequences). This should not be used routinely, but for specific behaviours which are proving difficult to understand. See Fig 20.1.

Try to view the situation from the perspective of the dementia patient. Has anything changed? Look for patterns which occur (is it with a particular activity/time of day?) Often what appears as insignificant changes to routine or carers involved can upset the proverbial apple cart.

➢e.g. In Fig 20.1, is the common denominator the new carer (Ben), and is the patient upset with this change?

Fig 20.1 ABC Chart example

Patient's name, identification, date, and reported behaviour

Antecedents	**Behaviour**	**Consequences**
Sharon was upset today during breakfast	*Refused to eat and appeared agitated despite Ben helping*	*Did not eat*
Sharon was agitated at dinner	*Threw her spoon at Henry, shouted at Toby when Ben entered*	*Upset all evening*

Name and signature of person completing chart

Try to view the situation from the perspective of the dementia patient. Has anything changed? Look for patterns which occur (is it with a particular activity. time of day?) Often what appears as insignificant changes to routine or carers involved can upset the proverbial apple cart.

➢ e.g. Is the common dominator the new carer (Ben) and the patient is upset with this change?

Fig 20.1 ABC Chart example.

Acute distress

If a patient is at immediate risk of harm to self or to others or in severe distress, medications should be used to manage the behaviour and not the underlying dementia.[4]

Options here include IM lorazepam, haloperidol, or olanzapine. IM haloperidol and IM lorazepam could be used in combination if rapid sedation is required, but generally a single agent is favoured. IM diazepam or IM chlorpromazine are not recommended for use in challenging behaviour in dementia patients.

References

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Non-pharmacological measures

It has been shown that non-drug management of behavioural disturbances reduces the need for psychotropic medications.[1] These options should be tried first wherever possible. They are often perceived to be time- and labour-consuming, and on occasion are difficult to implement; however, often simple adjustments to social interactions and environment can make a large difference. One should not prescribe antipsychotics without due consideration and preferably a trial of non-pharmacological approaches.

Interventions should be tailored to the person's preferences, skills, and abilities. For example, a male farmer may respond better to reminiscing and music than a massage, which may be alien to him. Patiently monitor response and adapt the care plan as needed. Depending upon availability, some options are outlined in Table 20.8.

A helpful article is published by the Alzheimer's Society called 'Non-pharmacological therapies for the treatment of behavioural symptoms in people with dementia' https://www.alzheimers.org.uk/

It is also important to focus on training care staff to understand and manage BPSD. Encourage active engagement from all of the professional teams in the patient's life story. Often a change in staff culture is needed, with less focus on getting practical jobs performed to an emphasis on individual personal care. Strong positive encouragement is required throughout the multidisciplinary team to pursue this aim.

Namaste care programme

'Namaste' means 'honouring the spirit within' and this programme has quantitative and qualitative evidence to support its implementation.[2] To qualify for its use, there are entry criteria of one or more of the following:

- MMSE 0–7
- non-ambulatory
- sleeps a great deal of the time
- limited vocalization
- total care
- unable to actively participate in activities

Table 20.8 Potential interventions in behavioural management in dementia

Active interventions	Environmental interventions
• Aromatherapy • Reflexology • Multisensory stimulation • Animal-assisted therapy • Massage • Behavioural therapies • Reminiscence therapy • Simulated patient therapy • Therapeutic use of music or dancing	• Clear clock visible • Day and night cues • Calm environment • Familiar surroundings/people/voices • Quiet/peaceful • Furniture placement not cluttered; lighting appropriate • Placement of family photos/mementos • Respect privacy

Its principles are based on centring on the patient through sensory stimulation (stimulating all five senses) and the patient's individual story.

Methods

- meaningful interaction and activity
  - based on life story
  - being interested in the patient
  - reminiscing
  - giving time
- environmental
  - not isolated in bedrooms or inappropriately mixed with those residents who are more able to engage
  - no TV (or appropriate music and TV)
  - calm atmosphere
  - green plants (flowers and seasonal reminders)
  - waking up for lunch/tea 20min beforehand
- interventions
  - hand massage
  - doll therapy (not child-like)
  - animals
  - appropriate treats
  - nature, smells, textures
  - therapeutic touch—*not* using gloves, but 'like a mother would', on daily interactions and personal care (often an area of resistance)

Entry into Namaste triggers a family meeting to open conversation about the person's future planning, establishing goals of care, and beginning the process of getting to know their likes, dislikes, and personality. This requires significant care staff engagement and often further education (designating 'champions' of Namaste to maintain and engage the wider team). Feedback from staff, patients, and families has been very positive. Patients had fewer infections and falls and appeared more responsive, communicative, happier, and 'alive'.

Further psychobehavioural approaches to BPSD can be found in Table 20.9.

Table 20.9 Psychobehavioural approaches to BPSD

Correcting sensory impairment	Acceptance
Non-confrontation	Optimal autonomy
Simplification	Structuring
Multiple cueing	Repetition
Guiding and demonstration	Reinforcement
Reducing choices	Optimal stimulation
Avoiding new learning	Minimizing anxiety
Determining and using overlearned skills	Using redirection

Data sourced from Zec RF, Burkett NR (2008) Non-pharmacological and pharmacological treatment of the cognitive and behavioural symptoms of Alzheimer's disease. NeuroRehabilitation 23(5), 425–38 with permission of IOS Press.

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Complementary therapy

The use of complementary therapies has increased progressively in recent years. These include aromatherapy, massage, reflexology, reiki, hypnotherapy, acupuncture, and homeopathy.

The amount of quantitative and qualitative research conducted into various complementary therapies is small; however, evidence suggests that patient demand and satisfaction are high. There is some evidence of benefit from the use of aromatherapy and massage in dementia[1-3] and also dance therapy.[4]

There is often scepticism about such treatments; however, it is important to remember that the key element is physical contact through touch and the physical and psychological benefits that this creates, not only for the patient but often for the carer. At the end stages of the disease, the carer can often feel excluded or helpless and no longer able to participate in the process of caring. Simple hand massages that they can be taught to carry out with the patient provide comfort and awareness for the carer and the patient.

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Pharmacological measures

There is scanty evidence for the use of medication in BPSD. The management of delirium or psychosis should be distinguished from the long-term treatment of behavioural disturbances in dementia. Reversible causes should always be considered, investigated, and treated appropriately before resorting to pharmacological measures. Medication is advocated only when non-pharmacological methods are insufficient and the safety of the patient or others is at risk. Whichever medication is chosen, it should be guided by the individual patient and their symptoms and co-morbidities, and the physician's familiarity with the agent.

Dementia medications

Donepezil and memantine have been widely used to treat behavioural symptoms, with variable results. They may reduce the development of agitation, but they appear not to significantly affect agitation already present. They are generally very well tolerated and therefore commonly used.[1]

Antidepressants

SSRIs (citalopram, sertraline, trazodone) reduce symptoms of agitation compared to placebo and appear reasonably well tolerated.[2]

Mirtazapine is considered a second-line agent, but is a good first-line option for anxiety and agitation, and can cause drowsiness, which may be useful.

Anticonvulsants

There is limited evidence for the use of anticonvulsants (gabapentin, lamotrigine, topiramate, carbamazepine), but some patients may benefit.

Benzodiazepines

Advice is to avoid these medications if possible as their use is associated with further cognitive decline, increased risk of falls and fractures, and in some cases, paradoxically, agitation. They are, however, the preferred medication for delirium secondary to alcohol withdrawal, neuroleptic malignant syndrome, and Parkinson's disease. Z-drugs (e.g. zolpidem, zopiclone) and sedating antihistamines have been associated with cognitive decline and should be avoided.

Antipsychotics

A large RCT for agitation psychosis in patients with dementia found both atypical and typical antipsychotics no better than placebo in all but a few secondary outcomes.[3] Taken together with other studies, the efficacy of antipsychotics in dementia is at best modest.[4]

Antipsychotic drugs increase mortality in patients with dementia. The mechanism is unknown; however, the risk of stroke with olanzapine and risperidone is 2–3 times higher than with placebo.

Antipsychotics are generally not indicated for behavioural disturbances in dementia and should only be used as a last resort. It is advised to use the lowest effective dose for the shortest possible duration. The efficacy and tolerability of haloperidol, olanzapine, risperidone, and quetiapine are comparable.

All antipsychotics can cause extrapyramidal side effects, such as akathisia, parkinsonism, and tardive dyskinesia (long-term use). In patients with Parkinson's disease or Lewy body dementia, these medications are relatively contraindicated. It is important to look for extrapyramidal side effects regularly with these medications.

Risperidone

Risperidone is a potent D2 and 5HT2A antagonist. Low-dose risperidone is licensed for short-term use in the situation of persistent severe symptoms of psychosis, agitation, and aggression in patients with moderate-to-severe Alzheimer's who are unresponsive to non-pharmacological approaches and who are at risk of harm to themselves or others (see Table 20.10). Risperidone has the lowest risk of extrapyramidal side effects compared with the other antipsychotics.

Haloperidol

Haloperidol is a typical antipsychotic D2 antagonist. It is widely used in palliative care for delirium and as an anti-emetic (see Table 20.11).

There is a risk of QT interval prolongation and 'torsade de pointes' (particularly if given IV). Caution is required in patients with cardiac abnormalities, hypothyroidism, familial long QT syndrome, or electrolyte imbalance, or if given with other drugs also causing prolonged QT. ECG monitoring is recommended, although in practice is often very difficult.

Table 20.10 Risperidone in severe Alzheimer's

250 micrograms BD	Increase after every 2–4 days to usual dose 500mcg BD	Maximum dose 1mg BD. It should be withdrawn after 6–12 weeks

Table 20.11 Haloperidol in palliative care

Mild-to-moderate patient distress	Start with 500 micrograms stat and q2h p.r.n.	Increase the dose progressively (e.g. 1mg–1.5mg, etc.)
Severe distress or immediate danger to self or others	Start with 1.5mg–3mg stat, possibly combined with a benzodiazepine, and q2h p.r.n.	If necessary increase the dose further, e.g. 5mg

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Stopping medications

BPSD can be made worse by drugs with anticholinergic properties. There should be due consideration to stopping these medications. Please note some of these medications are commonly prescribed in this group, including oxybutynin, antihistamines, and tricyclics.

The higher the serum anticholinergic activity (SAA), the greater the anticholinergic effect, and therefore the greater the risk to the patient. See Table 20.12.

Table 20.12 Medications, commonly prescribed to elderly patients, that have the highest estimated serum anticholinergic activity (SAA)

High SAA (>15 pmol/mL)	Moderate SAA (5–15 pmol/mL)	Mild SAA (0.5–<5pmol/mL)
Amitriptyline	Nortriptyline	Citalopram
Doxepin	Paroxetine	Escitalopram
Clozapine	Sertraline	Fluoxetine
Thioridazine	Olanzapine	Mirtazapine
Atropine	Clozapine	Quetiapine
Tolterodine	Cetirizine	Temazepam
Chlorpromazine	Loratadine	Ranitidine
Imipramine	Prochlorperazine	Lithium
Chlorphenamine	Baclofen	Haloperidol
Hydroxyzine	Cimetidine	Paroxetine
Dicycloverine	Oxybutynin	Trazodone
L-hyoscyamine		Lofepramine

Data sourced from Gerretsen, P., Pollock, B.G. (2011). Re-discovering adverse anticholinergic effects. J. Clinical Psychiatry, 72(6), 869; and Chew, M.L. et al. (2008). Anticholinergic activity of 107 medications commonly used by older adults. J. Am. Geriatrics Society, 56(7), 1333–41.

Process of care

See Fig 20.2.

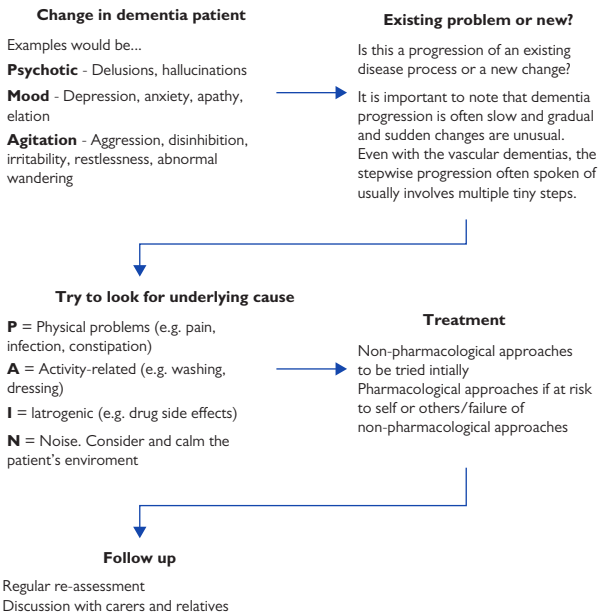


Fig 20.2 Flow chart illustrating process of care in dementia patients.

Pain and other distressing symptoms in dementia

Physical/psychological pain

Physical pain is a common cause of distress. It is difficult to detect and frequently underdiagnosed in the advanced dementia group. The difficulty in communication or the cognitive processing and conceptualizing of the experience of pain often manifests as agitation, but equally can pass unnoticed owing to subtle signs.

One of the most common requests by patients and relatives is to be pain-free. We can normally communicate the experience of pain through verbalizing, facial expression, and behaviour. These all become increasingly difficult to interpret in advanced dementia. Pain assessment tools may be useful, especially earlier in the disease process; however, they commonly lose effectiveness further in the illness, and pain assessment is purely based on behaviour and observations from the carers.

The dementia process alters the patient's experience of pain and is likely to affect nociception, cognition, and the emotive components of pain. see Table 20.13.

Despite these difficulties, experienced carers who know the patient well often can understand the patient's communications usefully.

Treatment

With the identification of pain, the usual principles of pain management apply, with escalation up the WHO analgesic ladder. As with all pain management, trying to understand the type of pain (neuropathic, nociceptive, visceral, somatic, bone) is helpful in alleviating the pain effectively.

If it is unclear as to the cause of the distress with no obvious source of pain, but if pain is suspected, consider an empirical trial of paracetamol. In an RCT, an empirical stepwise trial of analgesia (paracetamol—opioid—pregabalin) reduced agitation in unselected patients without a specific indicator of pain.[1]

Table 20.13 Dementia and pain

Effect on nociception	The dementia process damages the nervous system and may have a direct effect on pain pathways. This may decrease, increase, or alter the sensation of pain.
Effect on cognition of pain	Dementia damages all aspects of cognition from the memory in relation to the conceptualization of pain.
Effect on emotional response to pain	Dementia can damage appropriate emotional responses and can have effects as varied as indifference to disinhibition.

Common causes of pain in dementia

- arthritis—osteoarthritis and less commonly rheumatoid or seronegative spondyloarthropathies
- pressure sores—always check skin and common sites
- constipation—monitor bowel movements
- gastro-oesophageal reflux
- back pain—many causes
- headache—tension, migraine, raised intracranial pressure
- joint contractures
- muscle spasticity
- thrombosis

Pain scores

- The Doloplus-2 pain scale is a behavioural assessment of pain used in the elderly or in those with cognitive impairment. It has three domains: somatic, psychosocial, and psychomotor. A score of 5 or more indicates pain is present. Scores between patients cannot be compared. http://prc.coh.org/PainNOA/Doloplus%202_Tool.pdf
- The Abbey pain scale is a scoring system for measurement of pain in those who cannot verbalize. Domains include vocalization, body language, facial expression, behavioural change, physiological change, and physical change. A score of 3 or more indicates pain. http://www.wales.nhs.uk/sitesplus/documents/862/FOI-286f-13.pdf

State of mind and pain

Pain is subjective; only the person experiencing it knows what the pain is like. The physiological experience of pain is inseparable from the accompanying psychological and emotional experience.

Dementia affects all aspects of this experience and consequently affects its treatment. An interesting study has shown that Alzheimer's patients with prefrontal impairment lost their placebo response to analgesia.[2] Therefore, along with the likely increased psychological burden on dementia patients, there appears to be a corresponding loss of psychological relief with the placebo contribution. What the patient describes as pain can be the manifestation of these psychological factors or a combination of physical and mental anguish. This overlaps heavily with BPSD, but in holistically managing the patient, we are more likely to be successful if we consider this.

Mental pain examples

- depression
- psychosis
- fear and anxiety
- insomnia
- hunger and diet
- boredom, isolation
- spiritual pain

Other physical symptoms

There are a large number of symptoms other than pain which can be present in advanced dementia patients. These are addressed individually in the

same way as with every other patient, but with the framing of the difficulties in communication and understanding that dementia entails. As with pain scores, all validated methods of measuring the severity of each individual symptom are severely limited, and often judgement as to symptom severity is based upon astute carers' observations.

There are a few peculiarities which, although not unique to dementia patients, occur more frequently within this group.

Mouth care

Oral problems cause significant distress, and problems in this group of patient frequently go unnoticed. Xerostomia (sensation of dry mouth), painful mouth, oral thrush, and denture problems are common and require active treatment and close monitoring.

Swallowing problems

Dysphagia (and odynophagia/sticking) are a common symptom with end-stage Alzheimer's and sometimes earlier in other dementias. Dysphagia can become a problem very gradually and can remain unnoticed for prolonged periods of time. There is a significant risk of aspiration of food contents into the lungs, and aspiration pneumonia is a common terminal event. The speech and language therapist may be able to analyse the cause of the difficulty and provide useful advice. The occupational therapist can help by providing appropriate feeding implements. Drooling may be an early sign.

- If this occurs in Parkinson's disease dementia patients, it is important to switch their oral levodopa medications to patch form and not discontinue.

Patients with dementia should be helped to eat and drink for as long as they are able to. Enteral feeding and hydration may be considered in certain circumstances (e.g. if dysphagia is transient). However, where inability to eat is a progression of advanced dementia, enteral feeding or hydration is generally not felt appropriate (NICE).

This topic of discussion is often difficult for family and carers when their loved one loses the oral route. Each case is taken individually with a multidisciplinary approach. Seek expert advice, as enteral feeding is often not the most appropriate course of action. There is some evidence of improved nutrition with enteral feeding, but there appears to be little to no survival benefit, and there is a long complication list. There are patients in which it is entirely appropriate, such as when dysphagia occurs early in the disease process. It is often a good opening to explore the family's and carers' expectations of the disease process.

Nausea

Nausea with or without vomiting is a common and distressing symptom. Diagnosis of nausea without vomiting is difficult: food refusal could make you suspect, however, this is not specific. If there is suspicion, a trial of anti-emetic may be appropriate. An alternative is regurgitation, which classically does not respond to anti-emetics and may be related to dysphagia.

Constipation

Constipation is uncomfortable, common, and often missed. It is often under-reported for many reasons, but largely because of the nature and perceived embarrassment of the condition. Bowel movements should

always be monitored with a stool chart. A pleasant, private toilet with no time pressure should be provided, and discussions regarding laxatives or suppositories should be made early. Per rectum (PR) intervention is sometimes beyond the understanding of the dementia patient, and if required has a lower success rate and requires careful consideration. Often fluid intake is poor in this group of patients, and therefore encouraging increased fluid intake and stimulant laxatives is generally preferred.

Faecal incontinence

Faecal incontinence is very common in advanced dementia. This increases the risk of skin sores and infections such as UTIs. Faecal incontinence should be differentiated from overflow diarrhoea due to constipation. Management is nursing care, incontinence pads when appropriate, consideration of bulking agents, and skin barrier creams (e.g. zinc oxide). Occasionally, once these measures have been taken, diarrhoea can be managed with loperamide or somatostatin analogues can be useful, though there is the risk of constipation.

Hunger/thirst

With immobility and inability to communicate, these simple sensations can become distressing. Dehydration is a common finding in dementia patients, indicating improvements could be made in general care. Eating and drinking is a slower process in these patients, and due time and care need to be given. Discussions early regarding enteral feeding/fluids is often required. Often it is not appropriate; however, each case should be taken on an individual basis and with careful consideration of the whole multidisciplinary team.

Pressure sores

Pressure and bed sores remain a significant cause of morbidity in dementia patients. They require vigilance and meticulous care with appropriate equipment to prevent and to treat. A multidisciplinary approach with medical and nursing staff and occupational therapists is important. When severe or complex, specialist input is needed.

Frailty

See also the section on frailty, pp. 614–17.

'Frailty' is used commonly to indicate the overall health state of the patient, including the deterioration of the body systems and the gradual loss of in-built reserves. This is accepted as being related to the normal ageing process (British Geriatrics Society, 2014). Irrespective of the age of the dementia patient, there is an accelerated process of increasing frailty and an increase of associated risks such as falls. There should be awareness of and measures put in place to help manage these increasing needs.

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Care for the carer

When a person can no longer communicate verbally, is reliant on others for all personal care, and is often immobile, it can become difficult to see what quality of life remains. Those who work closely with people in the severe stages of dementia will be able to point to numerous ways in which the person demonstrates individuality and quality of life. In particular, carers will be aware of when the dementia patient is distressed or calm, content or discontent. The carers often become the advocate for the patient and often devote their lives to fine-tuning the care for their loved one.

As the disease progresses, management of the patient becomes more difficult and often requires professional care. It is often assumed that when a patient is admitted into long-term care that this largely resolves the carers of 'burden' and stress. This is often not the case, and the carer is left with feelings of guilt at 'giving up', as this may have gone against the expressed wishes of the loved one. This is further amplified when the patient inevitably dies. It is important to recognize the massive changes and emotional turmoil that carers go through. This is often under-recognized and the carers can feel that they have been left unsupported.

The best approach to trying to alleviate some of the carers' stress is to treat the patient with the dignity, respect, and care the carer has often been doing in isolation. Allowing the carer to participate in, and add pointers in, the patient's care so that a trusting relationship can be built helps. Until the carer has trust in the care being given, they will be unable to properly relax.

It is useful to highlight the many (often local) support networks available for carers. The social worker or GP usually has a list of local contacts. Financial and legal issues may also need to be addressed.

A useful scale for assessing carer burden is the Caregiver Burden Inventory (see Fig 20.3).

Caregiver Burden Inventory
(Novak and Guest, 1989)

The Case Manager will administer the inventory by reading the statement and marking the responses.
Choose the number that best represents how often the statement describes your feelings.

0 – Never
1 – Rarely
2 – Sometimes
3 – Quite Frequently
4 – Nearly Always

Client Name_____ Caregiver Name_____ Date_____

Time Dependence Items	
He/she needs my help to perform many daily tasks	⓪①②③④
He/she is dependent on me	⓪①②③④
I have to watch him/her constantly	⓪①②③④
I have to help him/her with many basic functions	⓪①②③④
I don't have a minute's break from his/her chores	⓪①②③④

Emotional Health Items	
I feel embarrassed over his/her behaviour	⓪①②③④
I feel ashamed of him/her	⓪①②③④
I resent him/her	⓪①②③④
I feel uncomfortable when I have friends over	⓪①②③④
I feel angry about my interactions with him/her	⓪①②③④

Development Items	
I feel that I am missing out on life	⓪①②③④
I wish I could escape from this situation	⓪①②③④
My social life has suffered	⓪①②③④
I feel emotionally drained due to caring for him/her	⓪①②③④
I expected that things would be different at this point in my life	⓪①②③④

Social Relationships Items	
I don't get along with other family members as well as I used to	⓪①②③④
My care giving efforts aren't appreciated by others in my family	⓪①②③④
I've had problems with my marriage (or other significant relationship)	⓪①②③④
I don't get along as well as I used to with others	⓪①②③④
I feel resentful of other relatives who could but do not help	⓪①②③④

Physical Health Items	
I'm not getting enough sleep	⓪①②③④
My health has suffered	⓪①②③④
Care giving has made me physically sick	⓪①②③④
I'm physically tired	⓪①②③④

Total Score:

Scores near or above 36 indicates a greater need for respite and other services.

It is important to seriously look at any item on the burden scale where the answer was scored as a 3 or 4 ('quite frequently' or 'nearly always'). If you have a 3 or 4 as an answer, give careful thought about why the caregiver scored so high on the question and see if you can find a way to reduce the stress.

Comments:_____

_____

_____

_____

_____

Fig 20.3 Caregiver Burden Inventory. Adapted from Novak and Guest (1989) Application of a multidimensional caregiver burden inventory, The Gerontologist © 1989 The Gerontological Society of America with permission from Oxford University Press.

The terminal phase

Owing to their disease, it is impossible to know how aware of impending death the dementia patient is. However, this should not change how you would treat the patient, and good practice is to always assume they can hear and understand you.

There is little specific advice on managing the terminal phase in an advanced dementia patient, but one area worth concentrating on is advanced planning. By anticipating any issues and problems, they can hopefully be avoided. Examples would include enteral feeding or capping recurrent courses of IV antibiotics. These issues could be discussed and agreed in advance of the problems occurring, allowing for a smoother, more controlled progression for all as change occurs.

Along with the medical aspects of future planning, it is worth considering and addressing potential emotional and social issues. There has often been a long course leading up to this point and a lot of conversations have likely occurred. Getting to know the family and exploring the patient's and family's wishes and fears about death allows everyone to plan and contribute to the process. Explore any religious, spiritual, and/or cultural needs and rituals. Never assume somebody's religious or cultural background, as it can cause offence. Always ask.

Frailty

Frailty is one of the major causes of morbidity and mortality in older people in the UK. Although it is very common, it has not been given due importance, in part because it is poorly understood and poorly defined.

Frailty is something that most people who live to an advanced age will probably face. Frailty is not really a disease but rather a mixture of the natural ageing process and common medical problems.

Frailty affects how an elderly person will respond to medical treatment, as well as how long and how well they will live.

Definition of frailty

- If an individual has three or more of the following, they should be considered 'frail':
  - unintentional weight loss (10 pounds or more in a year)
  - general feeling of exhaustion
  - weakness (as measured by grip strength)
  - slow walking speed
  - low level of physical activity

Source: the Fried Framework, after Dr Linda Fried

Frailty is a reliable predictor of declining health; in particular, the frail are at risk from falls, deteriorating mobility, disability, hospitalization, and death.

By the Fried definition, frailty is not a disease but rather a vulnerable state between being functional and non-functional, and between health and sickness.

Assessment

Once frailty has developed, it is much harder to reverse than if becoming frail is prevented. To reduce the speed of onset of frailty, it is important to regularly assess for key factors which contribute to becoming frail:

- anorexia, or loss of appetite
- sarcopenia, or loss of body mass
- immobility or decreased physical activity
- atherosclerosis
- balance impairment
- depression
- cognitive impairment

Anorexia

The elderly may develop loss of appetite as a natural part of the ageing process, but it may also be due to an illness or other factors, and it should never be assumed to be due to 'just getting old'. The result can be chronic undernutrition and, eventually, fatigue, weakness, cachexia, and micronutrient (vitamins and minerals) deficiencies. Hormone problems such as thyroid or testosterone deficiency can make things worse.

Sarcopenia

Sarcopenia is defined as an excessive loss of muscle, and may be associated with ageing. While genetically predetermined to some extent, several factors can accelerate the process, including decreased physical activity and hormonal deficiencies.

Immobility

Immobility can be caused by illnesses such as arthritis, which decreases the ability to move a joint. Joint pain can also lead to frailty through not wanting to be active.

Atherosclerosis

Atherosclerosis contributes to frailty as less oxygen reaches the tissues and organs. Clogging of the arteries can also cause small strokes, which, in turn, can lead to cognitive impairment. In the legs, vascular disease caused by atherosclerosis can result in decreased mobility and sarcopenia.

Balance impairment

Balance deteriorates naturally over a person's lifetime. Decreased balance can initiate a vicious cycle in which accidental falls lead to a fear of falling, which leads to decreased mobility, which makes frailty worse.

Maintaining balance through the use of exercise has been shown to help, and there has been interest in the use of techniques as diverse as tai chi, fencing, and computer sports programmes to help maintain balance in older people.

Depression

Depression can result in a reduction in mobility and a feeling of fatigue. Depression also produces a slowing of thought processes. Depressed people are more likely to develop major illnesses, such as myocardial infarction, and to have more difficult, slower recoveries. Depression is also a major cause of anorexia and weight loss in the elderly.

Depression in the elderly is often missed or misdiagnosed as dementia.

Cognitive impairment

Cognitive impairment can lead to a decline in mental processing time and reaction speed, resulting in more frequent falls.

Management options

Frailty prevention

While some aspects of frailty are age-related and irreversible, others are not. Frailty should be seen as treatable and as an important stage on the road to disability and serious illness.

The following list of measures can help reduce frailty, or at least reduce the speed of its onset:

- food intake maintained
- resistance exercises
- atherosclerosis prevention
- isolation avoidance (i.e. go out and do things)
- limit pain
- tai chi or other balance exercises
- yearly check for hormone problems

Managing the frail

The best treatment for frailty will vary because frailty has different causes in different people.

The first step is to get the best assessment and treatment for any physical or mental diseases that may be contributing to frailty. This may require referral to the Medicine for Older People service at your nearest hospital. After such an assessment, a plan can be devised to meet the particular resident's needs:

- resistance exercises three times a week, unless major cardiovascular problems
- pain control for pains that inhibit mobility or exercise
- maintain food intake by promoting appetite and serving tasty food in small portions, and consider the advice of a community dietician
- encourage mental stimulation through activities and stimulation

End-of-life care and frailty

When the frail are dying, they require particular care and attention to protect their skin from developing pressure sores due to loss of subcutaneous fat. This will require regular turning and the use of air mattresses.

With loss of muscle, the frail can develop contractures which are painful, and so keeping joints moving with passive exercises can be very important right up to the last few days. If residents are dying and their joints are stiff, an NSAID such as ibuprofen may be useful in reducing the pain of stiffness.

Relatives often ask about prognosis in such residents, and it is notoriously difficult to predict. The focus has to be on keeping the resident as comfortable as possible on a day-to-day basis.

Frailty should be managed actively.
It should not be assumed that frailty is just 'normal ageing'.

TRIAGE: care home, GP, or hospital

Deciding where best to manage residents when they develop clinical problems can be difficult and stressful for staff. Sending every resident to hospital is clearly not good care, nor is keeping every resident who develops new problems in the care home.

Some suggestions to help assess where best to manage residents with frailty in UK settings are given in Table 20.14.

Table 20.14 Assessing management location for frailty

Suitable place of care	Example of resident symptoms
Manage in the care home	Frailty has been assessed and reversible causes excluded: in dying phase
Manage with help of GP	Unknown cause of frailty, requesting GP assessment: family worried—suffering with frailty but resident has made it clear does not want to go to hospital or too frail to benefit from hospital treatment
Manage with transfer to hospital	Rapid development of frailty, having been previously well

Summary

Frailty has always been with us, though today it is increasingly seen not as an inevitable part of ageing but as a condition that in many cases can and should be treated aggressively. Many of the causes of frailty, such as depression, vascular disease, and vitamin deficiency, are treatable and even reversible through a combination of appropriate medical treatment, maintenance of a good diet, and a good exercise regimen.

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Chapter 21

Palliative care in non-malignant neurological disease

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Multiple sclerosis

Multiple sclerosis (MS) is a disease characterized by inflammation and demyelination affecting the central nervous system and ultimately injury and gliosis.

There are an estimated 100 000 to 110 000 people with multiple sclerosis in the UK, with a higher prevalence in northern Scotland. In the majority (70–80%), the course of the disease is relapsing and remitting in nature at the outset. Half of these patients will enter a progressive phase within ten years (secondary progressive MS). In a smaller group of patients (7–15%), the disease is progressive from the onset. Approximately 20–30% of patients will have marked paraparesis, hemiparesis, or paraplegia; 15% are wheelchair-bound and 5% have severe cognitive impairment. It is estimated that only about 25% of patients who are severely disabled are alive at ten years.

Death is commonly due to various secondary complications of MS (e.g. aspiration pneumonia, pulmonary embolus). If an unexpected neurological deterioration occurs, precipitating factors such as infection should be looked for. Disease-modifying therapies may be used in certain situations to reduce the number of MS relapses. Relapses are managed with courses of steroids; MS, however, is currently incurable and the mainstay of treatment is the control of symptoms.

Symptom management

Immobility

If the disease is progressive, walking is usually affected, via a combination of weakness, spasticity, fatigue, disuse, pain, cerebellar ataxia, and sensory loss, particularly proprioception. Immobility inevitably becomes difficult towards the end of life. This can lead to problems such as pain, pressure areas, and issues with continence, and therefore it is important that all members of the multidisciplinary team are involved in management.

Pain

The incidence of chronic pain in patients with MS is difficult to estimate, but may be as high as 86% of patients. It has been demonstrated that pain has significant adverse effects on quality of life.[1] Patients with MS will often have pain from different sources, and as such treatments should be targeted to treat the underlying cause if possible. Patients may well experience 'mixed' pain syndromes.[2]

Musculoskeletal pain is common, particularly back pain, and results from prolonged immobility, poor posture, and gait abnormalities. It is probably caused by a combination of spasticity leading to muscular pain and abnormal stresses resulting in mechanical pain. Simple analgesics or NSAIDs can be prescribed. Physiotherapy and occupational therapy (OT) are important for optimizing seating position and posture, and thereby ensuring that appropriate adaptations are carried out. Passive and active exercises, TENS, massage, and acupuncture may also be helpful.

Neuropathic pain, which may present as a persistent burning discomfort often affecting the lower limbs, is usually treated with standard agents for neuropathic pain, such as the tricyclic antidepressants, gabapentin, or pregabalin.

Lhermitte's sign is a syndrome of intermittent burning sensations or 'electric shocks' occurring on neck flexion. In the case of MS, it is due to

demyelination in the posterior columns of the spinal cord. It is often self-limiting, but if persistent, a cervical collar and carbamazepine may be needed.

Trigeminal neuralgia is more common in patients with MS than the general population. First-line treatment is with carbamazepine. There is a significant side-effect profile identified with this treatment, and other non-pharmacological interventions such as nerve blocks or microvascular decompression may be suitable.[3]

> Sufferers of depression have 'episodes' the same way those who suffer from multiple sclerosis do. It comes, wipes the floor with you, and then somehow returns you to the world. But it comes back.
>
> Michael Redhill

Spasticity

Increased muscle tone occurs in the majority of patients with MS. It may cause difficulty with function of the affected limb, painful muscle spasms, and, when severe, difficulties in nursing care. Neuro-physiotherapists can teach patients and their carers stretching techniques for shortened spastic muscles and passive joint exercises to maintain movement, which should be carried out regularly. Splints may be used and TENS may alleviate the frequency of painful muscle spasms and improve sleep. Aggravating factors such as urinary tract infections, pressure sores, and constipation should be avoided or treated.

Management

Baclofen can be built up slowly by 5mg every few days starting from 5mg t.d.s. up to a maximum of 80mg daily. Transient neuropsychiatric and gastrointestinal symptoms may occur. Reduction of baclofen should be gradual to avoid fits or hallucinations. Intrathecal baclofen has been shown to be effective in patients with severe spasticity in reducing pain and spasticity.[4]

Benzodiazepines such as diazepam can be given at night if painful spasms disturb sleep.

Dantrolene is less sedating than other muscle relaxants but can further weaken muscles, and is therefore often reserved for those patients who are wheelchair-bound. Liver function should be monitored.

Tizanidine, an alternative to baclofen, is associated with less muscle weakness than baclofen or diazepam. The starting dose is 2mg, increased every 3–4 days in 2mg increments up to 24mg daily in divided doses. It can cause sedation and dry mouth, and liver function should be monitored for the first 4 months. Gabapentin is an alternative.

Cannabinoids have also been used for refractory spasticity and pain in MS, although their role is less certain. RCTs have not shown a consistent benefit. Cannabis extract containing delta-9-tetrahydrocannabinol (dronabinol) and cannabidiol are the principal extracts from the cannabis plant present in a licensed preparation, Sativex®. It is the first cannabinoid preparation to be approved for medical use. It is licensed for symptom improvement in adult patients with moderate-to-severe spasticity due to MS who have not responded adequately to other anti-spasticity medication and who demonstrate clinically significant improvement in spasticity-related symptoms during an initial trial of therapy.

Intramuscular botulinum toxin can be effective for focal spasticity. It is generally only used when maintenance of function is less important, and should always be accompanied by a physiotherapy regimen of passive stretching.

Tenotomies (surgical release of tendons) or nerve blocks—most commonly obturator, perineal, adductor, or pudendal—are an option if non-invasive management has not been successful.

Ataxia and tremor

Ataxia is common in patients with MS. Feeding, correct seating, and head control can be very difficult. The role of the occupational therapist is crucial. There is little good evidence for pharmacological interventions that are helpful in reducing ataxia and tremor in MS.[5] The long-term benefits of thalamotomy or deep brain stimulation in treating tremor are also unproven.

Urinary system

Assessment and treatment are important in order to improve symptoms and to minimize complications such as pressure atrophy of the kidneys, urinary tract infections, and skin breakdown secondary to incontinence. Incontinence can lead to profound embarrassment and social isolation. Adequate fluid intake, bladder emptying (particularly if residual volume is more than 100mL), and treatment of infection are the principal priorities.

Hyperreflexia of the bladder is associated with a low-capacity bladder and possible symptoms of mild urgency, frequency, and incontinence. Treatment is usually with anticholinergic drugs such as oxybutynin or tolterodine. Incomplete bladder emptying, induced by these drugs, may require intermittent self-catheterization. Nocturnal incontinence may be relieved with desmopressin nasal spray 10–40mcg at night. Intradetrusor botulinum injection has been used with success in patients with overactive bladder symptoms.[6]

Bladder hypotonia and sphincter dyssynergia (sphincter contracts when voiding) result in incomplete emptying, of which the patient may be unaware. Catheterization will be needed. Intermittent catheterization is associated with less risk of UTI than a permanent indwelling catheter. However, the latter may be needed if all other methods fail to fully empty the bladder frequently enough to avoid problems, or if the patient is not able to self-catheterize. Even with a permanent catheter, an anticholinergic may still be needed for bladder spasm and urinary bypassing.

Constipation

Constipation is common owing, in large part, to delayed gut transit time, immobility, and anticholinergic medication. Adequate dietary fibre and fluid intake are important, and regular oral laxatives or suppositories/enemas are frequently needed.

Fatigue

Fatigue is severe and disabling in the many patients, reflecting muscle weakness and sleep interruption (e.g. from nocturia or spasms). Energy conservation, exercise, and psycho-behavioural techniques (cognitive behavioural therapy) are important non-pharmacological aspects of management of fatigue in patients with MS.

Precipitants such as exposure to hot baths and hot weather should be avoided. Amantadine or modafanil may be helpful for refractory MS-related fatigue, although RCTs have shown conflicting results.

Mood/cognitive disturbance

Clinical depression is common in MS. The estimated lifetime risk of developing depression is 50% and the risk of suicide is 7.5 times that of the healthy population. Antidepressants should be selected according to their side-effect profile; for example, a tricyclic antidepressant might be used if an overactive bladder and neuropathic pain are additional problems. Conversely, an SSRI, which is less sedating than a tricyclic, would be preferable if the patient feels fatigued. The positive effects need to be balanced against the potential side effects.

There is some degree of cognitive impairment in the majority of patients. The most common deficits relate to short-term memory, attention, speed of processing information, and impaired learning. Personality and behaviour may change. Moderate-to-severe dementia is seen in 10% of patients with long-standing MS. Treatment with donepezil and cognitive rehabilitation may give some benefit.

Usually MS is only managed in late advanced-stage disease by specialist palliative care teams, although they may have an earlier role in providing respite. The principles of palliative care apply through the illness trajectory, and should aim to provide the best and most acceptable quality of life for the individual. Therefore, good symptom control and support for families are paramount.

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Parkinson's disease

Parkinson's disease (PD) is the commonest neurodegenerative disease after Alzheimer's disease, with an estimated incidence of 2/1000. It affects just under 1% of people over the age of 65 years. PD is probably not one disease but several with common clinical features.

Criteria for the diagnosis of Parkinson's disease

Bradykinesia (slowness and progressive decrease of amplitude of movement) plus at least one of the following:

- tremor (frequently 'pill rolling')
- rigidity (often cogwheeling in nature)
- disorders of posture (flexion of neck and trunk)
- disorders of balance (loss of righting reflexes)
- disorders of gait (short steps, shuffling, festination, and freezing)

Classical pathological lesions seen in PD include loss of dopaminergic neurones in the substantia nigra and locus coeruleus with formation of Lewy bodies in the cytoplasm. Degeneration of the nigrostriatal pathway leads to depletion of the neurotransmitter dopamine.

Management

Research is underway into transplantation of human and animal fetal cells, allogeneic stem cells or retinal dopaminergic cells, and therapy with nerve growth factors.

Surgical options, such as targeting subthalamic nucleus (STN) lesions, may be effective for disabling dyskinesias (abnormal, involuntary movements) and relieving rigidity and tremor. Alternatively, deep brain stimulation using implantable electrodes and a pacemaker-like generator may be used, allowing flexibility to modify the response and reduce side effects.

The mainstay of management is the pharmacological control of symptoms with the aim of achieving optimal quality of life. Patients with PD should be monitored by a team specializing in the condition. If there are any changes to the baseline function or symptoms, reversible factors should be looked for and treated, and the specialist team informed as changes to medications may be needed in the short term.

Motor symptoms

Levodopa preparations

Dopamine does not cross the blood–brain barrier (BBB). To circumvent this problem, levodopa, which is able to cross the BBB, is used. Levodopa is converted to dopamine by the enzyme aromatic-L-amino-acid decarboxylase. The striatum is thus provided with the essential dopamine. However, the presence of too much dopamine outside the blood–brain barrier causes side effects such as nausea. To circumvent this problem, inhibitors of the converting enzyme, which do not cross the BBB, are given to reduce peripheral dopamine. Carbidopa and benserazide are used in this way and combined with levodopa as the preparations co-careldopa and co-beneldopa, respectively.

These compounds are available as modified-release and immediate-release preparations. They are also available in a dispersible form to aid administration with an oral syringe or through a nasogastric or gastrostomy tube where necessary. The timing of medication and dose is individualized, some patients

benefiting from a 'kick-start' dose in the mornings and others by avoiding late-night medication which may interfere with sleep. Others benefit from long-acting medication at night to reduce painful stiffness. Any changes in dose should be undertaken slowly, allowing several weeks for the change in regimen to stabilize. The drugs should never be withdrawn unless severe side effects develop, since withdrawal may render patients unable to move and swallow, and may result in a profound worsening of symptoms. Some patients will have significant escalation of symptoms even with a delay in dose.

Unfortunately, the efficacy of levodopa is marred by unwanted side effects. Patients may develop severe drug-induced dyskinesia, often alternating with sudden unpredictable loss of mobility (i.e. freezing and hesitancy).

Dopamine agonists

Dopamine agonists act directly on dopamine receptors; they include bromocriptine, pergolide, ropinirole, pramipexole, and cabergoline. Lisuride is rarely used in the UK. The new dopamine agonist rotigotine is available as a transdermal patch, which may be helpful if a patient is no longer able to swallow their current oral therapy. However, these drugs are more likely than levodopa to cause dopaminergic side effects such as nausea, vomiting, drowsiness, hallucinations, and confusion, and should be titrated up slowly; cover with domperidone may be needed to treat the nausea.

Apomorphine is usually administered subcutaneously, either as boluses or as a continuous infusion using a portable minipump. Its rapid onset of action can 'rescue' patients from sudden 'off' periods. This drug is most commonly reserved for patients experiencing severe and frequent motor fluctuations despite adequate trials with other oral medications, or as an alternative in patients who are unable to swallow. Domperidone is needed for 3 days prior to starting treatment to prevent nausea. Painful nodules which ulcerate may develop, and sites of injection should be changed daily. Apomorphine treatment should be guided by a specialist in PD.

Drugs that delay the breakdown of levodopa

Entacapone and tolcapone delay levodopa breakdown by inhibiting the enzyme catechol-O-methyl transferase (COMT). They used to relieve motor fluctuations, and allow dose reduction of levodopa-containing drugs.

Anticholinergics

Anticholinergics are sometimes effective for tremor, but not bradykinesia and rigidity. The benefit of such drugs needs to be balanced against the side effects of dry mouth, urinary retention, drowsiness, and confusion, which often limit their usefulness.

Glutamate inhibitors (e.g. amantadine)

Amantadine may help rigidity and bradykinesia. It can be useful as an adjunctive therapy and may be beneficial in reducing levodopa-induced dyskinesias. Possible side effects include confusion, hallucinations, peripheral oedema, and livedo reticularis.

Monoamine oxidase type B selective inhibitor (selegiline, rasagiline)

This inhibitor boosts the dopamine available in the brain by reducing its metabolism, and may be useful symptomatically. It seems that rasagiline has a neuroprotective role. Selegiline is available as both an oral and a buccal melt preparation.

Other general measures for management of motor symptoms include input from members of the multidisciplinary team, particularly the physiotherapist, occupational therapist, speech therapist, and dietician.

Nausea and vomiting

Nausea and vomiting may be due to drug treatment for PD, or for another unrelated reason. Avoid dopamine antagonists, e.g. haloperidol, metoclopramide, prochlorperazine, and levomepromazine. The safest drug to use is domperidone, which can be given orally or rectally. Cyclizine or a 5-HT_3 inhibitor such as ondansetron is also well tolerated.

Depression

Depression may occur in 40% of patients with PD. It is not known whether it is an inherent feature of PD or secondary to the disability caused by PD. Therapy should start with a selective serotonin reuptake inhibitor (SSRI) in a low dose. However, it may worsen symptoms of PD and can cause postural hypotension. Mirtazapine has proved helpful in relieving depression and anxiety and reducing tremor. Tricyclic antidepressants are less used because of their cognitive side effects.

Constipation

Constipation may be caused by a lack of adequate neurotransmitter in the myenteric plexus. Advice on diet, adequate fluids, and exercise should be given. Aperients are usually needed.

Swallowing difficulties

The ability to take food, chew, and swallow may vary during the day, especially in more advanced disease. A speech and language therapist, occupational therapist, and dietician will all be helpful in providing useful advice.

Patients often lose a significant amount of weight in late-stage PD, since the severe dyskinesias use up a significant amount of calorific energy. Feeding difficulties are often associated with periods of motor disability. Patients may choose to use their good functional moments to attend to activities of daily living (ADLs) or to pursue what they want to do, rather than wasting these precious moments on eating. They should be advised to eat little and often to make efficient use of time and energy intake. A deterioration of PD can be triggered by minimal dehydration, and patients should be encouraged to drink adequately, especially in hot weather. High calorific drinks and other nutritional additives are useful to supplement an often inadequate diet.

Postural hypotension

Patients should be given general advice on rising carefully from a lying or sitting position. It may be helpful to raise the head of the bed, and some patients may tolerate compression stockings. If symptoms are severe, fludrocortisone may be needed. If dizziness is experienced, encourage the patient to take a full glass of water with medication, especially with the first dose of the day.

Sleep

Sleep disorders are very common in patients with PD, and are distressing for patients and carers alike. The patient may be awoken by motor

fluctuations; they may wake up and be unable to move, and any effort to turn may cause painful muscle spasms; painful neck extension and leg cramp may occur. Attempts should be made to maintain nocturnal levels of levodopa, including avoiding high-protein meals in the late evening (amino acids compete with dopamine for receptor sites) and by giving domperidone in the evenings (if needed) to avoid a delay in gastric emptying. Restless legs syndrome (RLS)—characterized by an urge to move the legs, with painful cramps, paraesthesiae, and a burning sensation in the calves—may be relieved by standard levodopa therapy and dopamine agonists.

Amantadine and selegiline are stimulants and should be avoided if possible in the evenings. If PD is associated with dementia, a reversal of the sleep–wake cycle may occur. Short-acting hypnotics can be used if necessary. Hallucinations and panic attacks may also keep patients awake at night, which may be due to dopamine agonists and other anti-parkinsonian medication therapy (➔ see the Confusion/hallucinations section, below).

Communication

Difficulties in communication can be very distressing, especially if the patient is cognitively intact but has unpredictable episodes of being unable to communicate adequately. As with other symptoms in PD, it may worsen in stressful situations. Impaired emotional facial expression, a common characteristic of PD, impairs the very important non-verbal aspects of communication and should be recognized. Speech therapists can be helpful in finding alternative forms of communication where appropriate.

Dementia

Dementia may occur in up to 40% of patients. The deficiency of acetylcholine has provided a rationale for the use of acetylcholinesterase inhibitors. Modest improvement is seen with use of donezepil and rivastigmine.

Confusion/hallucinations

Confusion and hallucinations may occur as part of PD itself or as a result of medication. Nocturnal hallucinations are a particular problem but may improve if medication is avoided just prior to sleep. Patients will sometimes tolerate a degree of hallucinosis provided that the other features of the disease, such as motor disability, are reasonably well controlled. The newer antipsychotic agents such as clozapine (beware agranulocytosis), risperidone, or olanzapine may help, although they should be avoided if there is cerebrovascular disease. Quetiapine is a very useful medication and may be the drug of choice in this regard, but for some is too sedating. Antimuscarinics should be avoided if possible. The anti-dementia drugs—such as donepezil, rivastigmine, galantamine, and memantine—are being used to suppress drug-induced hallucinations and confusion.

Pain

Pain is a feature of PD, and may be relieved by treating the stiffness with levodopa or dopamine agonists. Pain of a sensory nature often occurs in PD, and should be treated appropriately. It is important to remember that if patients have dementia, they may not be able to communicate the presence of pain. Opioids should be used as appropriate, while recognizing the increased risk of constipation.

Anxiety

Anxiety occurs in 40% of patients but in over 90% of depressed patients with PD. Symptoms of PD such as tremor and dyskinesia often worsen in situations induced by anxiety or emotional excitement (even by watching a television programme). Although a benzodiazepine may help, it may result in muscle weakness and falls due to loss of muscle tone. Start with a very small dose of benzodiazepines, such as diazepam 1mg b.d. or lorazepam. This may be effective in helping alleviate an element of anxiety.

The terminal phase

PD may worsen with infection, dehydration, or other illnesses. Any reversible factors should be corrected where appropriate, alongside the management of the disease itself, preferably in a specialist centre. Care and consideration need to be given to continuing on the anti-parkinsonian drugs for as long as possible in order to keep patients as comfortable as possible and to maintain the ability to communicate and swallow. However, if the patient develops distressing side effects from the medication, reduction or withdrawal of therapy may be in the patient's best interests.

All patients should be encouraged, with help from the family and professionals, to discuss their attitudes and wishes for the management of acute life-threatening medical problems that may occur, such as pneumonia. An advance decision may be helpful in ascertaining patients' wishes for interventions (➔ see Chapter 34: Miscellaneous, for legal and professional standards of care, p. 866).

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Multiple system atrophy

Multiple system atrophy (MSA) is a progressive neurodegenerative disorder characterized by parkinsonian features, plus autonomic dysfunction in the form of orthostatic hypotension, and/or urogenital dysfunction in the form of incontinence and incomplete bladder emptying. At times it can also include cerebellar symptoms. It is not hereditary, and affects adults usually in the fourth or fifth decade. Post-mortem studies of patients diagnosed with PD indicate that 10–25% had multiple system atrophy. It is poorly responsive to levodopa. The mean survival is 9 years. As with PD, a multidisciplinary approach is essential.

Progressive supranuclear palsy

Progressive supranuclear palsy (PSP) is the most common cause of an atypical parkinsonian syndrome with dementia. It occurs more commonly in men than women, with a peak incidence in the early 60s. PSP criteria comprise a combination of postural instability associated with parkinsonism, vertical gaze palsy, bradyphrenia, abnormal neck posturing, and poor response to levodopa. Patients are limited in their ability to move their eyes downwards on request, although the eyes are able to move downwards reflexively, such as when a patient is asked to stare at a stationary object and the head is gently rotated backwards.

Within 1 year of diagnosis, the majority of patients have frequent falls, are slow in performing ADLs (bradykinesia), and have speech difficulties. The mean duration of the illness is 4–6 years.

Motor neurone disease

> Indignity is to be given a bedpan by a stranger who calls you by your first name.
>
> Maggie Kuhn

Motor neurone disease (MND) is a family of diseases of unknown aetiology in which there is progressive degeneration of upper and/or lower motor neurones, leading to wasting of muscles and weakness. The average survival is 40% at 5 years, although older patients presenting predominantly with bulbar signs may have a worse prognosis and, conversely, younger patients with largely lower motor neurone involvement may have a better-than-average prognosis. The mean age of onset is 56 years.

> Upper motor neurone involvement leads to generalized spasticity, hyperreflexia, pathological reflexes, and often emotional lability (i.e. pseudobulbar affect).
>
> Lower motor neurone involvement leads to weakness, muscle wasting, reduced muscle tone, hyporeflexia, and fasciculation.
>
> Involvement of bulbar-innervated muscles leads to dysarthria and dysphagia.

Common symptoms in MND include the following:

- weakness (100%)
- constipation
- pain
- cough
- insomnia
- breathlessness
- dribbling
- anxiety and depression

In addition, problems related to mobility and communication, as well as psychosocial issues, both for the patient and their families, must be addressed, necessitating a fully multidisciplinary approach.

Management

Extensive research has been conducted into stem-cell transplantation, autologous mesenchymal stem cells, and allogeneic haemopoietic stem cells, but the therapeutic potential remains uncertain.

Riluzole, the only drug approved for the treatment of MND, slows the disease progression and extends survival and tracheotomy-free life by an average of 3 months.

Symptoms

Weakness

Attention to individual needs for maximum comfort is crucial in order to prevent pain and other problems such as contractures and joint dislocation. The role of the physiotherapist is important, not only for the patient,

but also to educate and advise relatives. It is important to maintain muscle function and to keep joints mobile in a way that also conserves energy for important activities.

Insomnia

It is important to ascertain the cause of insomnia, which may range from pain and depression to the overwhelming anxieties of choking and the fear of dying. There is a general reluctance to prescribe night sedatives to patients with MND for fear of respiratory depression. In practice, this rarely happens, and the risk of sedation needs to be weighed against the detrimental impact of long-term insomnia.

Respiratory insufficiency

Hypoventilation develops owing to diaphragmatic and intercostal muscle weakness. The symptoms of respiratory insufficiency are dyspnoea, daytime sleepiness, and weak cough. Non-invasive positive pressure ventilation (NIPPV) has been shown to improve quality of life and prolong survival. Bilevel positive air pressure (BiPAP) reduces the breathing work by regulating the positive end-expiratory pressure in response to the patient's initial breaths. Generally, it is used initially during sleep time. Respiratory infections should be treated, and a cough-assist device can be used to clear secretions.

Pseudobulbar affect

Pseudobulbar affect, also known as 'uncontrolled laughing or crying', is present in up to 50% of patients. The patient and the family find this symptom quite disturbing. A selective serotonin reuptake inhibitor (SSRI) might be effective as early as 48 hours after beginning the therapy. Amitriptyline may also provide some improvement.

Pain

Management of the cause of pain

- stiff joints—careful positioning/physiotherapy
- inflammation—NSAID
- joint pains—intra-articular steroid injections
- muscle cramp—quinine sulphate
- muscle spasm—diazepam/baclofen
- skin pressure—regular turning/turning beds, analgesic ladder

Neuropathic pain is not a common feature of MND. However, patients may complain of pain associated with sensory disturbance, in which case tricyclic antidepressants may help.

The use of opioids in MND

There has been a reluctance to prescribe opioids for fear of causing respiratory depression in patients whose lung function may already be compromised. However, it is important to balance the small potential harmful impact against the benefit that could be gleaned from opioid use. Proportional, cautious use is advised.

Dysphagia

A speech therapist will help in analysing the exact cause of dysphagia in order to recommend specific techniques to aid swallowing. Spasticity of

the tongue, causing difficulty in propelling a food bolus to the pharynx, is a common cause.

Ice packs applied to the neck or chips of ice placed in the mouth may result in relaxation of the tongue and ease swallowing.

The subject of artificial feeding via a gastrostomy tube should be discussed with the patient, and the advantages and disadvantages outlined. In end-stage disease, tube-feeding may not necessarily prolong life. However, earlier in the disease, particularly if the patient is ambulant, gastrostomy feeding may slow the inevitable weight loss and its associated weakness and depression. The decision for artificial feeding needs to be made in conjunction with the patient and the MDT.

Dysarthria

The speech therapist should be involved early on to teach the patient various techniques relevant to their own special needs. Various aids are available, including Lightwriters with or without synthesized voice function. Other computerized systems are available from specialized centres, including electronic equipment, telephone devices, and communication boards, which may be adapted to the physical abilities of the individual patient. It is essential to plan ahead since motor function may deteriorate rapidly.

Breathlessness

Breathlessness is due to diaphragmatic and respiratory muscle weakness. The physiotherapist may suggest breathing techniques and help with chest drainage if appropriate.

Nocturnal hypoventilation is characterized by poor sleep, nightmares, early morning headaches, and daytime tiredness, with subsequent impaired concentration. In early stage disease, it may be appropriate to consider some form of limited assisted ventilation, such as NIPPV, to aid ventilation at night time. As breathing becomes weaker, this form of ventilation may continue during the day.

Patients must be fully informed of the pros and cons of assisted ventilation. More invasive ventilation through a tracheostomy is generally not used in the UK. The wishes of patients for respiratory support should be discussed well in advance of acute problems arising. Patients with MND may die suddenly and unexpectedly with respiratory failure.

Choking

The normal reflexes which protect the airway are impaired so that swallowing food or saliva may result in choking. Although it is a common fear, patients rarely die as a result of choking. Speech therapists may help by advising different techniques for protecting the airway, such as chewing carefully and slowly, breathing in, swallowing, and then deliberately coughing. This technique serves to clear the larynx and to minimize the possibility of choking.

Some patients find suction to the upper airways useful. For others it is avoided, since it not only causes trauma, fright, and discomfort, but may also be very distressing for the relatives to witness.

The multidisciplinary team

All members of the team will have been involved in the care of a patient with MND at some time. These include the neurologist, physiotherapist, occupational therapist, speech therapist, dietician, case manager, GP, district nurse, social worker, palliative physician, palliative home care team, and, of course, the family or carer. The MDT approach is particularly important in maintaining a patient's ability to communicate for as long as possible and to support families and patients through complex decision-making around ceilings and goals of care.

The MNDA provides an invaluable service not only in terms of liaising, supporting, and educating patients and carers, but also in facilitating the loan of equipment and helping financially.

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Creutzfeldt–Jakob disease

Creutzfeldt–Jakob disease (CJD) is a rare degenerative disorder of the central nervous system. Prion proteins occur naturally, but it is the abnormal development and accumulation of rogue prion proteins in brain cells that leads to the development of CJD.

The most common form of the disease, accounting for 80% of all cases, is *sporadic*, presenting as a rapidly progressive multifocal dementia with poor memory and cognition, impaired balance and mobility, myoclonic jerks, slurred speech, and visual problems. The incidence of sporadic CJD is 0.5–1 new case/million population per year.

Inherited prion disease, accounting for around 10% of cases, is due to autosomal dominant inheritance of a genetically mutated prion protein. The clinical course of inherited forms is usually more protracted than that of other forms.

Acquired prion disease occurs when rogue proteins have inadvertently been introduced into the individual (e.g. secondary to treatment with human-derived growth hormone, following the transplant of infected organs such as corneas, or the inadvertent use of contaminated neurosurgical instruments).

Variant (vCJD) was first described in 1996, and has been linked to the UK bovine spongiform encephalopathy (BSE) epidemic of the 1980s. The median age at onset is younger than for patients with the sporadic disease, at 26 years. Common early features are dysphoria, withdrawal, anxiety, and hallucinations, with subsequent neurological decline. The time course is longer than for sporadic disease (14.5 months mean duration compared with 4 months).

Key issues around the management of patients towards the end of life include the following:

- managing agitation and movement disorders
- issues around impaired communication
- dilemmas associated with end-of-life decisions

Frequently there is a high level of distress amongst those emotionally close to the patient, in keeping with the younger age of patients, the distressing nature of the illness, and its high media profile.

Following the death of a patient, the case should be discussed with the coroner, who may require a post-mortem. As with any coroner's case, a post-mortem can be carried out without permission from the next of kin, which may cause great distress, particularly with those from particular cultural backgrounds or with particular religious beliefs. Post-mortems for CJD are usually carried out in designated neuropathology institutions. Following removal of the brain and spinal cord, families are able to view the body again if they wish. There is usually no visual evidence that the body has been tampered with. The brain and spinal tissue are then sent to the CJD surveillance unit, where a formal tissue diagnosis may take months. The unit has information for relatives and handles the situation sensitively, organizing the return of body parts to the family's funeral director for cremation or burial when the tests are completed.

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Useful contacts

MS-UK

7 Peartree Business Centre
Peartree Road
Stanway
Colchester
Essex CO3 5JN
Freephone: 0800 783 0518
Website: http://www.ms-uk.org
Also provides a 24-h MS telephone counselling service: 0800 783 0518

Multiple Sclerosis Society

MS National Centre
372 Edgware Road
London NW2 6ND
Tel: 020 8438 0700
MS Helpline: Freephone 0808 800 8000, 9 a.m.–9 p.m.
E-mail: info@mssociety.org.uk
Website: http://www.mssociety.org.uk
Provides information, support, and practical help to anyone affected by MS and to those working with them. Also provides respite care centres and holiday homes.

Motor Neurone Disease Association

p.o. Box 246
Northampton NN1 2PR
Tel: 01604 250505
Helpline: 0808 802 6262
E-mail: enquiries@mndassociation.org
Website: http://www.mndassociation.org
Links to other sites and documents can be accessed through this site.

The National CJD Surveillance Unit

Western General Hospital
Crewe Road
Edinburgh EH4 2XU
Tel: 0131 537 2128
Website: http://www.cjd.ed.ac.uk

NHS National Prion Clinic

Box 98
National Hospital for Neurology and Neurosurgery
Queen Square
London WCIN 3BG
Tel: 020 3448 4037/020 3448 4038
E-mail: help.prion@uclh.nhs.uk
Website: http://www.uclh.nhs.uk

Chapter 22

Psychiatric symptoms in palliative care

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Introduction

Palliative care is the provision of holisitic management to individuals and their carers/families who are facing issues associated with life-limiting illness. It embraces a biopsychosociocultural and spiritual approach with emphasis on quality of life. Consequently, the maintenance of psychological and emotional health and well-being is an essential component in the provision of comprehensive care.

Initial diagnosis—and the circumstances surrounding this—is a time of great challenge for most patients, and the potential for strong emotional reactions and intense feelings of distress is heightened. How this information is processed and integrated into an individual's life experience varies significantly and will depend on the interplay of a number of factors, such as personal beliefs, attitudes, previous life and sickness experiences, family dynamics, and social supports. Consequently, healthcare professionals and support workers should be alert to the signs and symptoms of emotional distress, coping difficulties, and the emergence of mental health disorders.

It is important to consider that psychological and psychiatric symptoms can arise for various reasons:

- in response to the diagnosis of life-limiting illness
- as a direct consequence of disease (e.g. CNS tumour) or the treatment of that disease (e.g. neurosurgery)
- as an indirect consequence of disease (e.g. metastases) or complications (e.g. anaemia)
- as a result of adverse effects, toxicities, or withdrawal/discontinuation effects of medications or other substances

In addition, as part of comprehensive assessment and management, it is essential that *pre-existing* mental health and psychiatric disorders are identified, and that they are subject to ongoing monitoring and management to ensure optimal well-being throughout the illness trajectory.

Consultation and close collaboration and liaison with specialist mental health providers will assist in tailoring interventions best suited to the patient's needs.

Adjustment disorders

Adjustment disorders are a group of stress-related reactions which result in the development of emotional or behavioural symptoms, and are associated with marked distress and impairment in functioning. Generally they are considered to evolve within 3 months of the onset of the stressor, and they do not persist beyond 6 months once the stressor and its consequences have terminated.[1] Worry, nervousness, low mood, sadness, despondency, anger, tearfulness, insomnia, and other changes in behaviour may arise and can impact on day-to-day functioning, occupational performance, and social relationships, including relationships with carers and healthcare providers. Changes in behaviour may include self-medication with alcohol or drugs, impaired decision-making, and refusal to engage with treatments, which may compromise total patient care. Prevalence has been variously reported as between 10 and 36% depending on clinical setting.[2, 3]

Management

In the context of life-limiting illness, the specific stressor may be persistent and have little likelihood of resolving. However, there is wide variation in how individuals adapt to their circumstances; many are able to adjust to the 'new normal' in their lives, either through their own coping strategies or with assistance from others, including their own networks of support, counsellors and mental health professionals, and spiritual and pastoral care advisers.

There is currently no consensus as to what constitutes optimal therapy. Levels of distress, severity of symptoms, degree of functional impairment, and presence or absence of support networks are guides to intervention options and strategies. Practical support, psycho-education, and specific psychological therapies—either individual or group-based—may all have a role to play in assisting with transition to a new level of adaptation.

The use of medication may provide benefit in modifying specific symptoms such as insomnia and anxiety. Intermittent or short-term use can be made of benzodiazepines. Alternatively, antidepressants with sedative properties, or mildly anxiolytic antihistamines (e.g. hydroxyzine) may be considered. Etifoxine (not UK), a non-benzodiazepine anxiolytic, and sedating herbal remedies (e.g. valerian, kava-kava) have been used in clinical studies, but further studies are required to assess benefit.[3] Failure to improve or worsening of symptoms should trigger review and reconsideration of the diagnosis and management plan.

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Anxiety

Anxiety is a symptom or state, and in the context of palliative care it is virtually ubiquitous. Fear and anxiety are common experiences throughout the clinical trajectory. They reflect the unique concerns of the individual and their carers. Whilst anxiety in palliative care is often generated by death-related issues, it may also arise owing to concerns about quality of life, practical concerns (e.g. finances, housing), interpersonal relationships, unresolved conflicts, increased dependency, loss of dignity, spiritual concerns, or existential issues such as meaning and purpose. Exploration of these fears and anxieties helps to deepen understanding of a person and their carer/family context and enables service providers to tailor management to an individual's needs. Anxiety can also be a presenting feature of a wide range of medical conditions, substance withdrawal, toxicity states, and psychiatric disorders, such as specific anxiety disorders (e.g. panic disorder, phobia, generalized anxiety disorder), depression, delirium, and dementia. The accurate identification and more specialized management of these conditions is likely to result in anxiety reduction. Hence, thorough assessment of anxiety will assist in determining appropriate intervention and management strategies.

Anxiety assessment

- What are the characteristics of the anxiety?
  - episodic/intermittent/continuous
  - duration
  - unexpected/situational—are there patterns?
  - triggers/precipitants
  - alleviating/exacerbating factors
- What have you found helpful in the past? (past coping strategies)
- When you get these feelings, what do you think will happen? (cognitions, ideas, beliefs)
- Look for changes
  - physical condition
  - medications (increases/decreases/starts/stops)
- Basic observations
  - respiration rate, pulse, BP, temperature, pupils

Comprehensive assessment should also include past medical history, past psychiatric history (formal/informal), pre-morbid personality (what were you like before?), other stressors and life events, sleep patterns, diet, alcohol intake, caffeine intake (tea, coffee, and other caffeinated beverages), and smoking and drugs (prescribed, non-prescribed, over-the-counter, herbal preparations, illicit), with particular reference to onset of anxiety symptoms and drug intake or cessation. Thorough physical examination is essential.

Evaluation may be further enhanced by the use of objective assessment tools such as simple visual analogue symptom and quality of life scales (0–10 rating), the NCCN Distress Thermometer,[1] Patient Health Questionnaire for Depression and Anxiety,[2] and the Hospital Anxiety and Depression Scale.[3]

Non-pharmacological treatment of anxiety

Generally supportive actions include

- active listening
- acknowledging the patient's concerns
- working together with the patient to alleviate sources of distress and concern
- clarifying goals of care for the patient and carers
- providing information (take time to explain; use diagrams and pictures) and education (access to relevant materials, e.g. brochures, books, CDs, internet)
- practical advice—including lifestyle management such as diet, exercise, and sleep hygiene
- patient and/or carer advocacy
- ensuring timely referrals are made to the appropriate specialist providers

Additional interventions

- breathing techniques—diaphragmatic; pursed lip
- relaxation exercises—progressive muscle relaxation; guided visual imagery
- mindfulness meditation
- substitute activities and distraction techniques
- simple behaviour modification (using score sheets and diaries)
- structured problem solving—encourage writing down concerns, prioritizing issues; help to break down a problem into manageable parts; discussing possible options or different approaches to address the problem
- cognitive techniques—distraction, reframing, challenging distortions
- complementary therapies—e.g. massage, music, art, journal
- Numerous forms of psychotherapy (e.g. meaning-centred psychotherapy,[4] dignity therapy[5]) and OT-specialized techniques (e.g. hypnotherapy) may be available, and can be accessed by referral to specialist providers.
- Practical psychosocial interventions such as assistance with finances, housing, and end-of-life care arrangements are often a source of significant worry and concern, as are wills, funeral plans, and 'tidying up one's affairs'. Professional assistance in these matters can provide a greater sense of security and help to restore some sense of control and order.

Pharmacological treatment of anxiety

Choice of agent and dosing will depend on patient factors such as diagnosis, prognosis, functional status (active, independent vs frail, dependent), route of administration (oral, PEG, subcutaneous, IV, rectal, sublingual), and drug-drug interactions, in addition to availability/access to preparations and local prescribing guidelines. See Box 22.1.

Benzodiazepines

Benzodiazepines (BZs) are used for short-term intervention, although in some cases more prolonged treatment is required. Ideally, they should be used in conjunction with one or more non-pharmacological interventions. However, in severe anxiety it is often very difficult to engage in non-pharmacological strategies until anxiety has been reduced to more moderate levels.

Box 22.1 Drugs used for anxiety/anxiety disorders

Benzodiazepines

- Options available for clinical use within the benzodiazepine class vary, with duration of action (half-life) being a key difference between preparations.
- long-acting (t1/2 = 30hours+): clonazepam, diazepam
  - may accumulate and cause unwanted sedation
  - diazepam is frequently the benzodiazepine of choice in substance withdrawal states
- short-acting (t1/2 = 12–14 hours): lorazepam
- very short-acting (t1/2<10 hours): temazepam, oxazepam, midazolam

SSRIs (selective serotonin reuptake inhibitors)

- citalopram, escitalopram, sertraline, paroxetine, fluoxetine

SNRIs (serotonin/norepinephrine reuptake inhibitors)

- venlafaxine, duloxetine

Atypical antidepressants

- mirtazapine (often used in mixed anxiety/depression)
- other
  - pregabalin,[1] gabapentin
  - quetiapine, olanzapine[2]
  - trazodone

1 A treatment for generalized anxiety disorder in the UK according to the NICE guideline.

2 Use of these antipsychotics for anxiety is off-label; low-dose, short-term use may be required in some instances; specialist referral is recommended.

Administration requires monitoring for effectiveness of symptom reduction and the emergence of adverse effects (e.g. over-sedation, falls, cognitive impairment). The potential for overuse and misuse—either inadvertent or intentional—also needs to be considered and closely monitored.

SSRIs and SNRIs

Selective serotonin reuptake inhibitors (SSRIs) and serotonin/noradrenaline reuptake inhibitors (SNRIs) are antidepressants which have been shown to have clinical benefits in the treatment of specific sub-types of anxiety disorders such as generalized anxiety disorder, panic disorder, agoraphobia, and social phobia.

If treatment is initiated with these agents, close monitoring to gauge response to treatment and development of side effects is essential. Symptom reduction may be delayed but review of the pharmacological agent and dosing should be undertaken if there is no clinical improvement after 2 weeks, or sooner if there are unacceptable side effects or deterioration.[6]

Early referral to mental health specialist assessment and management in order to receive expert opinion and advice regarding appropriate intervention is strongly recommended for co-morbid mental health disorders.

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Depression

Introduction

Estimates of the prevalence of depression in patients vary greatly depending on setting and patient cohort, but in palliative care settings, prevalence of all types of mood disorder may occur in 30–40% of patients.[1] The presence of depression impacts on an individual's perception of quality of life, adds to their sense of suffering, and may significantly influence their treatment choices and preferences regarding end-of-life care. It is also a source of potential distress for caregivers, who may struggle with the emotional, behavioural (e.g. withdrawal), and cognitive sequelae that can arise in the patient as a result of a depressive disorder, and may add to caregiver burden and burnout. Hence, accurate diagnosis and management of depression is an important part of holistic care.

Diagnostic criteria

The DSM-5 diagnostic criteria for major depressive disorder[2] require the presence of a persistent low mood or loss of interest or pleasure and at least four of the following symptoms, which are present most of the day for the preceding 2 weeks:

- diminished interest or pleasure in all or almost all activities
- psychomotor retardation or agitation
- feelings of worthlessness or excessive and inappropriate guilt
- diminished ability to concentrate and think or indecisiveness
- recurrent thoughts of death (not just fear of dying) and suicide
- fatigue and loss of energy
- significant weight loss or gain
- insomnia or hypersomnia

The inclusion of physical symptoms can cause diagnostic uncertainty, particularly in patients with advanced cancer/late stage disease; however, the presence of feelings of hopelessness and helplessness, persistent negative thoughts or ruminations, decreased motivation, procrastination, and persistent or heightened pain perceptions may also be present and should also be explored. Other variations in presentation may include irritability, agitation/anxiety symptoms, pronounced behavioural changes (e.g. intense anger, risk-taking), somatic preoccupation, or psychotic features (delusions, paranoid ideation).

Collateral history from carers or family members is valuable in clarifying changes in the patient's mood, interests, and social interactions, and in identifying alterations in usual patterns, such as appetite and sleep.

Thorough assessment should include medical and mental health/psychiatric history, substance use, and medication history.

Possible organic causes of depression—such as thyroid disorders, hyperparathyroidism, diabetes, vitamin B12/folate deficiency, hepatic disease, hypercalcaemia, brain surgery, CNS irradiation, and use of corticosteroids—need to be considered as potential contributing factors to the clinical picture.

Screening for depression

Screening tools and rating scales to measure depression are used in many settings, but their validity in a palliative care setting has yet to be systematically evaluated.[3] The benefits of screening, however, help to focus attention on the evaluation of mood states and assist in the identification of those patients who require more comprehensive evaluation or closer follow-up.

Previous research has suggested that a scale developed for use in the postnatal period, the Edinburgh Depression Scale, may be useful for screening in palliative care. It does not include somatic symptoms, but does include symptoms such as sadness, feelings of helplessness, and thoughts of self-harm, which may be particularly discriminatory in the palliative care population. Each item is scored from 0–3—the most negative response scoring highest. A six-item Brief Edinburgh Depression Scale (BEDS) with a score of 6 out of 18 gave a sensitivity of 72% and specificity of 83% (see Table 22.1).[4]

It has been suggested that the single-item question 'Are you depressed?' may have high validity in identifying depression in patients with terminal illness.[5] However, cross-cultural differences exist with respect to specificity

Table 22.1 Brief Edinburgh Depression Scale

Name:

Please UNDERLINE the answer which comes closest to how you have felt IN THE PAST 7 DAYS, not just how you feel today

I have blamed myself unnecessarily when things went wrong	**I have been so unhappy that I have had difficulty sleeping**
Yes, most of the time	Yes, most of the time
Yes, some of the time	Yes, quite often
Not very often	Not very often
No, never	No, not at all
I get a sort of frightened feeling as if something awful is about to happen	**I have felt sad or miserable**
Very definitely and quite badly	Yes, most of the time
Yes, but not too badly	Yes, quite often
A little, but it doesn't worry me	Not very often
Not at all	No, not at all
Things have been getting on top of me	**The thought of harming myself has occurred to me**
Most of the time and I haven't been able to cope at all	Yes, quite often
Yes, sometimes I haven't been coping as well as usual	Sometimes
No, most of the time I have coped quite well	Hardly ever
No, I have been coping as well as ever	Never

Reprinted from Lloyd-Williams M., Shiels C., Dowvick C. (2007). Journal of Affective Disorders, 99(1–3): 259–64. The development of the Brief Edinburgh Depression Scale (BEDS) to screen for depression in patients with advanced cancer, p. 6, with permission from Elsevier.

and sensitivity. Hence the gold standard for assessment is a careful diagnostic interview, which helps to distinguish pervasive mood disorders from transient variations in mood, adjustment disorders, and demoralization,[6] as well as from substance- and medication-induced mood disorders.

Management strategies

Symptoms of depression are often inappropriately dismissed as 'understandable' reactions to life-limiting illness, and may result in little or no treatment. However, if one of the stated goals of palliative care is to enhance quality of life, then it is incumbent upon clinicians to address the issue of depression with their patients in a timely and proactive manner. Asking patients to describe their mood opens the door to dialogue about feelings and encourages self-reporting of mood state.

The role of good communication, active listening, and thorough understanding of the patient's personal life circumstances, coupled with empathy and compassion, is the basis of therapeutic engagement and a collaborative working relationship. It is from this basis that the impact of illness, lifestyle changes, and often multiple losses that are encountered by patients can be fully appreciated.

Formulating a treatment plan requires knowledge of the primary disease process and prognosis. Ensuring that any underlying medical factor which is potentially contributing to the clinical picture is adequately addressed is also an important preliminary step.

In considering the treatment plan, severity of the depression will in part determine the most suitable choice of therapy. Additional factors to consider are patient preference, prognosis/time frame, competing demands of other treatments (e.g. chemotherapy, radiotherapy), clinician expertise, and specialist provider availability.

The challenge of all interventions in the palliative care setting is to tailor a selection of options best matched to patient need and preference that can deliver therapeutic benefit in the time frames available.

Non-pharmacological interventions for depression

Numerous psychotherapeutic and psychosocial interventions have demonstrated benefits in the treatment of depression. These include supportive psychotherapy, cognitive-behavioural psychotherapy, interpersonal psychotherapy, life review, meaning-centred psychotherapy, and dignity therapy. It is important to consider factors other than life-limiting illness that may be contributing to depression, and hence couple therapy, family therapy, and problem-solving may be useful strategies to consider. Other forms of expressive therapy other than 'talking' therapies may also provide benefits (e.g. art, music, journalling). Mindfulness meditation may also have a role to play in the therapeutic armamentarium.[7]

Pharmacological management

There is little high-quality evidence regarding the effectiveness of antidepressant medication in terminally ill patients.[8] There is, however, a body of evidence showing that under-treatment is common, with patients being prescribed antidepressants within the final weeks of life, allowing little time for therapeutic benefit.

Drug selection is based on consideration of the following: previous response to treatment (if there is a positive past history of depression), underlying disease, prognosis, hepatic and renal status, cardiac status, drug interactions, anti-cholinergic load, target symptoms, side-effect profiles, availability, and route and mode of administration.

Classes of antidepressants

- selective serotonin reuptake inhibitors (SSRIs)
- serotonin-noradrenaline reuptake inhibitors (SNRIs)
- tricyclic antidepressants (TCAs)
- atypicals (e.g. mirtazapine, agomelatine)
- ketamine
- psychostimulants

Selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs, e.g. citalopram, escitalopram, sertraline, paroxetine, fluoxetine) are less sedative than tricyclic antidepressants; they have few antimuscarinic effects and low cardiotoxicity. SSRIs may cause nausea, vomiting, and headaches, and extrapyramidal reactions can occur occasionally. Gastrointestinal side effects are dose-related. There is little to choose between the SSRIs, but fluoxetine has a long half-life and may cause more agitation than other SSRIs: it is therefore not recommended as first-line, particularly in patients who are agitated.

- SSRIs may increase the risk of GI bleeding, especially in patients taking NSAIDs.
- A combination of serotonin-related medications may result in serotonin syndrome; early symptoms include agitation and confusion, and should be taken seriously.
- Increased serotonergic effects are seen with St John's wort, which should be avoided.
- Fluoxetine and fluvoxamine both increase the blood levels of carbamazepine and phenytoin (risk of toxicity).
- Paroxetine is a potent inhibitor of CYP2D6 and has many drug-drug interactions; short half-life gives rise to significant discontinuation effects.

Antidepressant discontinuation syndromes occur with both TCAs and SSRIs. SSRI discontinuation symptoms include dizziness, light-headedness, insomnia, fatigue, anxiety/agitation, nausea, headache, and sensory disturbance. SSRIs should be withdrawn gradually when possible, using alternate-day dosing if needed.

Symptoms of withdrawal are more common with paroxetine (short half-life), and least common with fluoxetine (half-life of weeks).

Serotonin-norepinephrine reuptake inhibitors

Venlafaxine, desvenlafaxine (not UK), and duloxetine are serotonin-norepinephrine reuptake inhibitors (SNRIs). Of this class, duloxetine has also been shown to be effective in the management of neuropathic pain. Venlafaxine has significant association with discontinuation syndrome.

Tricyclic antidepressants

Tricyclic antidepressants (TCAs, e.g. amitriptyline, clomipramine, nortriptyline, doxepin) may take several weeks to provide full therapeutic

benefit, particularly as dosing is usually commenced at low levels. They all have antimuscarinic properties to a greater or lesser degree, and therefore may be associated with symptoms such as hypotension, blurred vision, dry mouth, constipation, and difficulty in micturition. Amitriptyline is often used in palliative care at low doses (10–50mg) as an adjunct to opioid analgesics for neuropathic pain or sialorrhoea; however, this dose range is not generally considered to be a suitable antidepressant dose range (150mg).

Atypicals

Mirtazapine is a noradrenergic and specific serotonergic antidepressant (NaSSA). It is generally well tolerated, although it may cause bad dreams and nightmares in some patients. However, it is very useful in the management of insomnia, and at lower doses the antihistaminic effect is predominant, thereby producing sedation. Improvement in appetite and weight gain, as a side effect, is often considered to be of positive benefit by patients in the palliative care setting.

Agomelatine is a novel antidepressant which acts on the melatonin receptors. Its use in palliative care is frequently limited by impaired hepatic function that is often a feature of advanced-stage or metastatic cancer.

Ketamine

There has been focus in recent years on the identification of agents that have rapid onset of action for the treatment of depression, both in the general population and in the palliative care sector. Off-label prescribing and clinical research have occurred in various centres around the world to review the clinical response to the dissociative anaesthetic and analgesic drug ketamine in cases of depression. Ketamine is thought to act by blocking NMDA receptors in the brain, although an alternative mechanism of action for its antidepressant effect has been suggested.

In the USA, ketamine use as a therapeutic agent in treatment-resistant depression is increasing, and has led to the development of a consensus statement to guide clinical use.[9] Its potential benefit is considered to be its rapid onset of action (within hours) and duration of effect (up to 1 week). If administered by infusion, patients must be closely monitored for spiking in blood pressure and dissociative or psychotic reactions. Other routes of administration include oral, intranasal, intramuscular, and sublingual routes.

Ketamine remains a controversial treatment within the context of palliative care.

Psychostimulants

Psychostimulants in palliative care have been used in the management of the following:

- fatigue
- depression
- opioid-induced sedation
- hypersomnia
- cognitive dysfunction

Methylphenidate appears to have been used more widely, but dexamfetamine is equally effective. Modafinil is also within this class of drugs.

Psychostimulants have been shown to be effective in depression in medically ill patients. They are useful because of their rapid onset of action.

Effects are usually seen within several hours of administration; they include mood elevation, feelings of well-being, energizing effect, improved cognitive performance, and appetite stimulation.

Side effects of psychostimulant drugs, including agitation, dysphoria, insomnia, nightmares, and hypomania have been reported.

As monotherapy for depression, methylphenidate and dexamfetamine are best limited to patients with short prognosis (i.e. weeks to live).

Augmentation of standard antidepressant treatment has been reported, but it is not a widely adopted practice.

Psychostimulants have been used as adjuvants to reduce opioid-induced sedation and potentiate analgesia. It is not known whether this is due to a reduction in opioid-induced sedation—thus allowing dose escalation of the opioid—or as a direct potentiation of opioid analgesia.

Initiation of treatment should begin at low dose (e.g. methylphenidate 2.5mg b.d.) with progressive titration until therapeutic benefit has been achieved.

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Suicidal ideation and suicide risk

Serious illnesses such as cancer and chronic physical problems are frequently associated with the development of depressive disorders. Consequently, in cancer patients and patients diagnosed with life-limiting illness who also have a co-morbid diagnosis of depression, subjects such as hopelessness and suicidal ideation should be explored.

Suicidal ideation occurs in up to 45% of terminally ill patients; however, these thoughts are often transitory or episodic in nature, and are associated with feelings of loss of control and anxiety about the future.[1] It is important to clinically assess the patient's feelings, attitudes, and beliefs in relation to self-harm, and whether thoughts of suicide are persistent or intrusive in nature. The extent to which an individual has made plans and the ability and means to carry this plan out is a necessary part of risk assessment. Other factors to consider in relation to suicide risk are previous attempts, co-morbid substance abuse or dependence disorders, social isolation/poor supports, uncontrolled pain, exhaustion and fatigue, increasing dependency or a profound sense of burden to others, recent bereavement, and family history of suicide.

If a patient has been assessed as moderate-to-high risk, steps should be taken to ensure the patient's safety, and arrangements made for timely, comprehensive assessment and appropriate intervention. Patients may require initial close supervision on a one-to-one basis. Alleviation of acute distress may require pharmacological intervention, and careful attention should be paid to ensuring patient comfort. Specialist mental health and psychiatric consultation is strongly advised.

Wish to hasten death

Patients expressing suicidal ideation should be distinguished from patients who request death to be hastened—these latter patients may also be depressed, but may have other underlying fears, e.g. of a painful or undignified death (➔ see also Chapter 1, Ethical issues and the person in the patient), or have the view that life no longer holds any meaning or purpose. The desire or wish to hasten death (WTHD) experienced by some patients with advanced illness is a complex phenomenon, and may arise in response to physical symptoms, psychological distress, existential suffering, or social issues. A recent international consensus definition has identified WTHD as a reaction to suffering, in the context of a life-threatening condition, from which the patient can see no way out other than to accelerate his or her death. This wish may be expressed spontaneously or after being asked about it, but it must be distinguished from the acceptance of impending death or from a wish to die naturally, although preferably soon.[2]

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Hallucinations

Within the context of palliative care, the presence of hallucinations is not uncommon. This may manifest as part of a delirium (➔ see p. 653) or be associated with other organic psychoses secondary to underlying neurological disorders or medical conditions, drug-induced states, or substance-withdrawal states.

Patients may not directly report hallucinations—they may refer to 'bad dreams'. Consequently, it is important to ask patients about any unusual or frightening experiences they may be having as part of routine assessment and review, and obtain a detailed description of their symptoms.

It is important to identify the type of hallucination a patient may be experiencing—visual, auditory, tactile, gustatory (taste), or olfactory, as the type of hallucination may provide some diagnostic clues as to possible aetiology. Auditory hallucinations in particular require detailed review, as command hallucinations or taunting and abusive voices can be particularly distressing to patients and can lead to major behavioural consequences, with safety implications for the patient and staff.

Development of hallucinations should trigger a thorough review of the patient's medical history, including potential for complications of cancer-related diagnoses (e.g. metastases), complications of treatments for cancer (neurotoxicity effects of chemotherapy or radiotherapy), adverse effects of medications (e.g. corticosteroids, opioids, anticholinergics), drug interaction effects, or co-morbid medical conditions (e.g. hypothyroidism). Of equal importance is the need to consider medications or substances which may have been abruptly stopped or significantly reduced. In addition, it is important to consider psychiatric disorders which may have gone undiagnosed or poorly managed, or have arisen as a consequence of illness (e.g. major depression with psychotic features).

If there is no obvious precipitant or identifiable pathology to explain the onset of hallucinations, expert advice/psychiatric opinion should be sought. Early consultation is strongly recommended in order to obtain a comprehensive biopsychosociocultural evaluation and guidance as to the most appropriate management.

Neurocognitive disorders

Cognitive dysfunction is common in the palliative care population. For patients with advanced disease, this may be attributable to a number of factors, such as age, medications, primary disease process, impacts of treatment regimens (e.g. neurosurgery, radiotherapy), and co-morbid conditions (e.g. dementia, delirium, depression).

Whilst terms such as 'confused', 'muddled', 'vague', and 'disorganized' are frequently used clinically, it is important for clinicians to be aware of various cognitive domains. These include executive functions, such as planning, abstract thinking, and judgement; attention and concentration; learning and memory; language (expressive and receptive); visuospatial awareness; and social cognition. Impaired cognition may present as subtle changes, significant alterations, or gross deficiencies in one or more domains, whilst specific impairments may be attributable to localized disease or pathology.

Clinical assessment is assisted by bedside testing and the use of screening tools such as the Mini-Mental State Examination (MMSE), Clockface Drawing Test, Frontal Assessment Battery (FAB), Nursing Delirium Screening Scale (NuDESC), and the Confusion Assessment Method (CAM).

Familiarity and proficiency at administering and interpreting results in one or more of these bedside tests should be part of a clinician's 'toolkit'.

Cognitive impairment impacts on quality of life[1] and may impair recreational pursuits and pastimes, social interactions, and decision-making capabilities.[2] Whilst many situations may not be readily reversible, it is important that clinicians are aware of problems and take the necessary steps to identify any difficulties, complications, or sequelae associated with cognitive compromise. Explanation and education for the patient and carer/family members may provide reassurance and help to modify expectations in relation to patient behaviour and interactions. Referral for more comprehensive testing and assistance with specific support need to be considered.

It is also important that clinicians are aware of the potential impact of cognitive impairment on issues such as competency, consent, legal matters such as wills, and a patient's ability to manage their financial and personal affairs.

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Delirium

Delirium is defined as a disturbance in attention and awareness (disorientation) which may develop over hours to days and fluctuates in severity. It is often associated with poor short-term memory, word-finding difficulty, and perceptual disturbances.

The DSM-5 criteria require evidence from history, examination, or laboratory findings that the disturbance is not a direct consequence of another medical condition, substance intoxication, or withdrawal (including medications), exposure to a toxin, or multiple aetiologies.[1]

The diagnosis may be obvious with a rapid onset of altered behaviour and incoherent rambling speech. However, often the patient can be withdrawn and relatively uncommunicative, which is sometimes mistakenly diagnosed as depression. These variations in presentation are referred to as *hyperactive* and *hypoactive* delirium. However, the features of presentation may fluctuate, and a mixed picture may emerge. Severe delirium can be associated with marked psychotic features such as hallucinations and delusions.

The prevalence of delirium may be as high as 85% for hospitalized terminally ill patients and is particularly common in elderly patients moved from a familiar environment. It may be exacerbated by deafness and impaired visual acuity.

While delirium is often a reversible process, this may not be the case within the context of palliative care, particularly in the terminal phase. Issues to consider in formulating a management plan include the goals of care, illness prognosis, availability of diagnostic and therapeutic interventions, and time frames. Investigations may be considered unnecessarily burdensome and not consistent with maintaining patient comfort.

Possible reversible causes of delirium include the following:

- hypercalcaemia
- hypoglycaemia
- hyponatraemia
- renal failure
- liver failure
- drug-related causes
  - opioids
  - anticholinergic toxicity
  - corticosteroids *and* withdrawal
  - alcohol and withdrawal
  - benzodiazepine *and* withdrawal
  - SSRI withdrawal
  - nicotine withdrawal
  - digoxin
  - lithium
- CVA or transient ischaemic attack (TIA)
- infection
- hypoxia
- dehydration
- thiamine (vitamin B_1) deficiency

The cause is often multifactorial, and symptoms such as pain or those associated with constipation or urinary retention may aggravate confusion.

Management of delirium

Management considerations include the following:

- thorough patient assessment and examination
- investigation and treatment of reversible causes (where appropriate)
- alleviating patient distress

Non-pharmacological

Non-pharmacological strategies include assistance with comfort, warmth, or cooling; limiting excessive noise or overstimulation; ensuring the patient is able to see and hear adequately; ensuring some exposure to sunlight; and attending to bodily requirements such as constipation and urinary retention, thirst, hunger, and sleep deprivation, which may all help to modify aggravating factors. Use of oxygen in hypoxic states and alleviating pain should also be considered.

Information and education for both patient and carer/family is important to alleviate concerns and address any fears. Assistance with orientation both day and night is also an important management technique. Family can assist in this process and are able to provide familiarity and reassurance.

Patient medication charts should be thoroughly reviewed, and potential toxicities or withdrawal/discontinuation states should be identified and amended. Nicotine withdrawal may be managed with replacement therapies. Benzodiazepines are the drugs of choice in managing alcohol withdrawal symptoms and preventing agitation and seizures.

Pharmacological

Pharmacological interventions may be necessary, particularly in those patients who are agitated, hyperaroused, and in danger of hurting or harming themselves. Harm may occur as a result of falls in an agitated and restless patient or as a result of acting on disturbing hallucinations, delusions, or paranoid ideation. In these situations, safety concerns for the patient, carers, and staff are of paramount importance and must be evaluated and appropriately addressed. Unit/service policy or guidelines will dictate appropriate courses of actions, and national guidelines vary in relation to drug recommendations. However, sedation may be necessary if the patient is very distressed and not amenable to reassurance or is a high safety risk.

Antipsychotics are considered to be the drugs of choice for delirium, and low-dose haloperidol is commonly used. Other options include olanzapine, quetiapine, and risperidone. Doses should be adjusted according to age and general condition, level of disturbance, and likely tolerance. The NICE guideline recommends short term (usually one week or less) of haloperidol or olanzapine starting at the lowest clinically appropriate dose and titrating according to symptoms.[2]

Antipsychotics

- *typicals*: haloperidol, levomepromazine (methotrimeprazine), promazine
- *atypicals*: risperidone, olanzapine, quetiapine
  - Atypicals may be better tolerated than other antipsychotics and have a lower propensity than haloperidol for causing drug-induced movement disorders. They should be used with caution with cardiovascular disease, a history of epilepsy, and in the elderly.

Equivalent doses of antipsychotic and benzodiazepine medication

Occasionally patients are taking antipsychotic drugs or benzodiazepines on a long-term basis. The approximate equivalent doses are outlined in Table 22.2, although, as ever, doses should be based on an overall assessment of the patient's individual needs. Switching antipsychotics or benzodiazepines, while not recommended, is sometimes required in the palliative care setting, especially if the previous oral route is no longer available.

Table 22.2 Equivalent doses of antipsychotic and benzodiazepine medication

Antipsychotic drug	Approximate equivalent daily dose
Chlorpromazine	100mg
Haloperidol	2–3mg
Levomepromazine	25–50mg
Olanzapine	2.5–5mg
Pimozide	2mg
Quetiapine	25–150mg
Risperidone	0.5–1mg
Trifluoperazine	5mg

	Equivalent dose anxiolytic/sedative	Approximate duration of action	Approximate subcutaneous dose over 24h
Diazepam	5mg p.o. or p.r.	3h to 4 days	N/A
Clonazepam	**0.25mg** p.o.	6–24h	1mg
Midazolam	**2.5mg** s.c.	15mins to 4h	10mg
Lorazepam	**0.5mg** p.o.	7–8h (mean)	N/A
Temazepam	10mg p.o.	7–8h	N/A

These doses are approximate only. Cautious dosing advised in elderly/debilitated.

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Chapter 23

Spiritual care

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Introduction

Spirituality is a construct, a way of thinking about human experience that can be helpful, but only up to the point at which one begins to believe it exists.

The word 'spirit' is widely used in our culture. Politicians speak about the 'spirit' of their party; veterans talk about the wartime 'spirit'; and religious people discuss the 'spirit' as that part of the human being that survives death, whereas humanists might regard the human 'spirit' as an individual's essential, but non-religious, life force. Related words are equally common and diverse: footballers describe their team as a spiritual home; spiritual music and spiritual art are fashionable; and there are spiritual healers, spiritual life coaches, spiritual directors, and even spiritually revitalizing beauty products.

'Spirit', 'spiritual', and 'spirituality' are established terms among healthcare professionals. But these complex words need to be used with care and understanding. Their origins are essentially religious and/or philosophical, and as such their primary meanings denote technical theological and philosophical ideas. However, they have also developed more commonly used secondary or derived meanings, and it is these that connote some of the more popular understandings.

Beneficial effects of religion and spirituality

A number of studies report reduced mortality rates among religious and spiritual people. One US study found those attending religious services weekly were:

- 53% less likely to die from coronary disease than those who did not
- 53% less likely to die from suicide
- 74% less likely to die from cirrhosis

The religious community seems to be protected from the effects of social isolation. Religion provides and strengthens family and social networks, gives a sense of belonging and self-esteem, and offers spiritual support in times of adversity. A study by Bernardi and colleagues showed that rosary prayer and yoga mantra had an effect on autonomic cardiovascular rhythms.[1] Recitation of the rosary, and also of yoga mantras, slowed respiration to 6/min and enhanced heart rate variability and baroreflex sensitivity. Reduced heart rate variability and baroreflex sensitivity are powerful and independent predictors of poor prognosis in heart disease. Spirituality helps to induce calm, improve concentration, and create a sense of well-being by reducing adrenaline and cortisone levels and increasing endorphins.

Definitions

The root of 'spirit' is breath (Latin *spiritus*), and it is easy to imagine how it became associated with the idea of life essence: when an ancient died, their breath (*spiritus*) departed them.

Western theological/philosophical traditions

In the West, spirit is one of three components of the human being, alongside body and soul. (With Descartes, 'soul' becomes 'mind'.)

> May God himself, the God of peace, sanctify you through and through. May your whole spirit [*pneuma*], soul [*psyché*] and body [*sōma*] be kept blameless at the coming of our Lord Jesus Christ.
>
> The New Testament, 1 Thessalonians 5:23

- 'spirit', or breath, is that which gives life to the body
- soul—or mind (psyche)—is conceived in terms of 'the essential immaterial part of a human, temporarily united with its body'[2]
- historically, Western thought has been more interested in soul than spirit

Eastern theological/philosophical traditions

Eastern spiritual teachers shared similar interests, although their emphasis on consciousness led to their tendency to speak about 'the self', *atman*:

- early Vedic texts link the *atman* with the life breath (*prana*)
- in the later Upanishads, *atman* becomes consciousness, the essence of the human being that transcends the body and its experiences
- Buddhist 'non-self' highlights the inter-being of all states of awareness

Separation of spirituality and secular medicine

The separation of spirituality from modern, secular medicine is rooted in Enlightenment debates about the nature of science and religion. The dominance of scientific method has left little place for the non-material soul.

Freud's hostility towards religion and mystical experience is taken as further support for rejecting language of the soul as anachronistic. However, in coining the name 'psychoanalysis', Freud made conscious reference to the myth of Eros and Psyche (the soul).

> It was Freud's emphasis on the soul that made his analysis different from others. What we think and feel about man's soul—our own soul—is all important in Freud's view.[3]
>
> B. Bettelheim

Healthcare professionals need to be clear about the concepts they are using. However, an effective definition that makes sense of the theological-philosophical roots of these ideas remains an aspiration.

A humanistic-phenomenological definition

A non-religious, humanistic-phenomenological definition of spirituality has been proposed by Elkins and colleagues. This may be helpful insofar as it regards spirituality in very broad terms as 'a way of being':

> Spirituality … is a way of being and experiencing that comes through awareness of a transcendent dimension and that is characterized by certain identifiable values in regard to self, others, nature, life, and whatever one considers to be the Ultimate.[4]
>
> D.N. Elkins et al. (1988, p. 10)

In these terms, spirituality, as 'a way of being', is characterized across a range of relationships:

- with one's self
- with others
- with nature
- with life
- with that which one considers to be Ultimate (which could be God, Spirit, the transcendent Self, Nature/the Universe)

Such a humanistic-phenomenological definition makes possible a much closer association of areas of thought and practice, which have for too long been kept separate and discrete. For this reason, psychotherapists and spiritual carers are beginning to speak of 'psychospiritual care'—a care for the spirit that unites traditional pastoral care, the 'cure of souls', with aspects of psychotherapy, which 'attends to the soul'.[5]

> If I were to choose a phrase that encapsulates the way I currently see myself working, it would be *soul attender* which … is a literal translation of the word psychotherapist.[6]
>
> W. West (2004, p. 128)

Most importantly, a humanistic–phenomenological definition of spirituality allows healthcare professionals, who may not be in any way religious, to be much clearer about spiritual care and their involvement in it.

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Spirituality and religion

In contemporary speech, 'spirituality' is increasingly used as a contrast to 'religion'—usually in its institutional forms, and often with the implication that that which is spiritual is more authentic than that which is religious.

The two orders are intimately related, but while it is possible to be authentically spiritual without being religious, it is difficult to be authentically religious without being spiritual. For this reason, religion can be viewed as one way in which people express their spirituality; but it is by no means the only way. It is important to keep in mind that 'spirituality' is a Western construct and not a term used within Eastern thought, where religion is pervasive in all aspects of life.

The effect of culture on individual spirituality

An individual's spirituality is shaped by the culture in which he/she lives. So, where the language, foods, dress, social structures, and customs are shaped by religious beliefs and practices—say, in Roman Catholic, Hindu, or Muslim countries—spirituality will most likely be expressed through those cultural forms, and effective spiritual care will aim to support the expression of those cultural/religious forms.

When Rajendra was admitted to the hospice it was clear that his prognosis was very limited. His district nurse had asked that he be admitted to a side room because his family, who were devoutly Hindu, wanted to be able to fulfil their familial and spiritual responsibilities to him without upsetting other patients. The family was extremely attentive to his personal physical care and also to his religious requests.

Through the reading of the Hindu scriptures and the burning of incense, Rajendra seemed to derive great comfort.

The hospice was a Christian foundation, with strong links to the local churches and an active chaplaincy department, which visited Rajendra regularly at his request.

Several members of staff found the overt Hindu practices very distressing as they were concerned about demonic influences. A decision was taken that such members of staff would be assigned to different patients.

Several weeks after his death, the family returned to say how much they had valued their last days together with Rajendra in the hospice. They had been nervous when admission had been suggested because they had been aware of the Christian ethos of the hospice.

In secular Western cultures, where beliefs and values are transmitted in the home and/or the faith community, spirituality finds expression in a variety of forms, not necessarily religious. Again, effective spiritual care will understand that spiritual needs are none the less pressing for being non-religious.

The effect of personal journey on individual spirituality

Spirituality is also shaped by the individual's life journey, the experiences they have, and their encounters with others. In particular, being faced with one's own mortality has a profound spiritual impact, which can

fundamentally disturb long-held beliefs and values. This may not in itself be a bad thing, and patients may come to value the kind of freedom a changed perspective brings. However, the distress provoked by re-evaluating beliefs can be upsetting for carers, professionals, and family alike, and a person experiencing the doubt, conflict, and confusion that goes with the disintegration of existing belief may need sensitive support in order to find a place of reintegration.

Equally, a life-threatening illness may reawaken dormant beliefs in those who have no particular affiliations with any faith group. But this reawakening may be sustaining or threatening depending on how the individual perceives it.

> I have learned much from disease which life could have never taught me anywhere else.
>
> Goethe (1749–1832)

Research on belief and the 'good death'

The assumption underpinning much literature on spirituality—i.e. that a terminal illness intensifies patients' search for meaning—lacks empirical support. However, there is some research supporting anecdotal evidence that in a terminal illness, what matters is not so much *what* a patient believes but the *strength* of their beliefs.

- McClain-Jacobson et al. found that belief in an afterlife was associated with lower levels of end-of-life despair (desire for death, hopelessness, suicidal ideation), but was not associated with levels of depression or anxiety, and concluded that spirituality has a much more powerful effect on psychological functioning than afterlife beliefs.[1]
- Smith et al. noticed a significant curvilinear relationship between a patient's perspective about death and their actual fear of death, 'suggesting that [actual] beliefs are a less critical determinant of death fear than is the certainty with which these beliefs are held'.[2]

> The findings indicate the majority did not seek religious comfort or conversion as a response to the challenge of terminal illness, even when this was seen as desirable. Although participants were not actively inspired to be religious as a result of their illness, they did hold a number of spiritual perspectives that were actively at play.[3]

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Faith practices

It is *always* unhelpful to make assumptions about how a patient may value their faith and its practices.

It is important to remember that in most cultures of the world, spirituality has a practical, social, and material impact on people's daily lives—it is the attitudes of Western culture that have been exceptional.

Spirituality plays a vital role in the well-being of large numbers of British residents, and in a pluralistic culture, many will value being able to express their spirituality through their religious and cultural traditions.

The complexion of British multicultural society is increasingly diverse, and it is very difficult for non-specialists to understand the nuances of faith traditions. Chaplains or spiritual care specialists are an important resource for addressing patients' religious and cultural requirements, but the real experts will be the patients themselves, their families, and their faith community leaders/spiritual advisers.

Healthcare professionals should always consult the patient directly, or, if this is impossible, the patient's family, about their religious and cultural requirements. However, caution will be needed, because, while some patients may identify as belonging to a particular faith group, they may wish to deviate from what their family consider 'orthodox' practices.

A woman born Roman Catholic and who later converted to Islam married a Muslim man with whom she raised an Islamic family. Against the wishes of her son and now-divorced husband, she wanted to have a Roman Catholic funeral and be cremated. Her nurse referred her to the chaplain!

Spiritual care team

Members of the spiritual care team are likely to be able to address the religious and cultural requirements (sacraments, etc.) of the majority of patients, and to act as a resource to the multidisciplinary team for advice on dietary and ethical issues.[1]

- If a patient is from a minority faith tradition, the spiritual care team will be able to seek advice from their spiritual advisers/faith community leaders.
- The spiritual care team will also be skilled in conducting, arranging, or even creating 'bespoke' services that address the pastoral needs of individual patients:
  - informal bedside prayers or meditations
  - ad hoc prayers for impromptu family gatherings
  - reaffirmation of marriage vows
  - *in extremis* wedding services
  - baby memorials
  - spiritual healing services, etc.
- The spiritual care team is likely to have religious artefacts (prayer mats, beads, icons, etc.) and texts that patients may want to use to aid their spiritual practices.

Supporting patients' religious practice

It is important to remember that a patient's frustrations with low energy levels during illness are likely to impact on their ability to follow the routine practices of their faith, which may in turn impact on their spiritual well-being. Religious disciplines are normally relaxed during ill health—for example, the fast during the Muslim holy month of Ramadan or the Roman Catholic fast before taking Holy Communion.

> Faith practices can be particularly helpful in times of stress and change. In the context of illness and the inevitable medicalization inherent in modern treatment pathways, faith practices can help to maintain a person's sense of individual identity distinct from that of being a 'patient'.

Around the period of death, faith practices can have particular value, underscoring the transition from life to death. These practices may help patients and relatives with the following:

- make sense of their loss
- be supported through the pain of transition and loss
- provide a framework for dealing with the process of letting go

Reference

1. For general information, see http://www.diet.com/g/religion-and-dietary-practices

Spiritual pain

Because spiritual pain causes patients to suffer, and because palliative care is concerned with relieving suffering, spiritual pain is often taken as something that healthcare professionals must strive to relieve. However, spiritual pain can be a difficult concept for healthcare professionals to understand.

> The realization that life is likely to end soon may well … give rise to feelings of … the unfairness of what is happening, and at much of what has gone before, and above all a desolate feeling of meaninglessness. Here lies, I believe, the essence of spiritual pain.[1]
>
> C. Saunders

Saunders's closely identified spirituality with the human search for meaning and her approach to 'spiritual pain' is reflected in NICE Guidance:

> The diagnosis of life-threatening disease has a profound effect on people who are ill.… Questions relate to identity and self-worth as patients seek to find an ultimate meaning to their lives.
>
> NICE Guidance on Cancer Services[2]

White cites Saunders directly when she asserts the 'link between human spirituality and existential questions about meaning and purpose seems to be at the heart of [discussions about spirituality]'.[3] McSherry takes the point a stage further:

> It is the healthcare professionals' role to assist individuals to make sense and find meaning in times of crisis such as the acceptance of a terminal diagnosis.[4]
>
> W. McSherry

Current discussion in palliative care suggests that spiritual pain arises variously from the patient's inability to accept the dying process, the realization that it is too late to change a life that has not been what they hoped, and the loneliness of dying. Burton describes spiritual pain as

> manifest in a wide variety of symptoms such as constant and chronic pain; withdrawal or isolation from spiritual support systems; conflict with family members and friends; anxiety, fear or mistrust; anger; self-loathing; hopelessness; feelings of failure … unforgiveness; despair; and fear or dread.[5]
>
> R. Burton (p. 4)

Holloway and Moss suggest three sources of spiritual pain: (a) alienation, dissonance, or deep conflict in the inner self; (b) the 'dark night' or 'groanings' of the soul, which they link with spiritual/religious crisis; and

(c) loss of faith, which, they observe, may be overlooked by healthcare professionals who have not themselves had some sort of association with a faith community.[6]

McSherry also references 'the dark night of the soul'.[4] This is the idea of spiritual search and confusion, originally explored by the sixteenth-century Spanish mystic St John of the Cross. However, it is important to note that St John does not see the 'dark night' as a pathology but as a spiritual crisis and an opportunity for growth. In this case, spiritual pain may achieve the following:

- draw out compassion, or even rekindle love between estranged friends/relatives/partners
- prompt in the patient a reappraisal or re-evaluation of their life
- lead to the recovery of values, beliefs, talents, ways of being long since lost or forgotten
- be a transition point along the patient's journey towards greater self-understanding

'I was angry, very angry—angry at the world—and that's not me. I'm not like that. I'm usually very calm. That's not the way I want to be. I think that's a quite natural reaction; but I don't want to be angry, I don't want to die angry. But actually, I feel as if I'm moving on from that now. I feel as if I'm moving into trying to making sense of what is ahead'.

This is not the old theological idea that humans are sinful and that, therefore, suffering is necessary and good; rather, it develops Saunders's idea that 'the last part of life may have an importance out of all proportion to its length'.

- The patient may have important things yet to do, which in the short term may cause distress, but which may ultimately be healing.
- The desire always to relieve spiritual pain, even when it is a feature of spiritual growth, may conflict with the patient's need to do 'life-work'. In which case, the desire to intervene prematurely in spiritual pain may say more about how healthcare professionals deal with pain in others and about how Western culture currently views death and dying.

Spiritual pain can be thought of as the pain of growth associated with the patient's struggle to respond to the question, 'How shall I *be*—with my self, with others, in the world, nature, and towards the Ultimate—when I am facing my own death?'.

However many dying people I've known, this person is dying for the first time and I don't know what they need: everyone has different needs. You must hold your previous experience of dying patterns very lightly.… Death reveals that life's about change, so how can we hold to our fixed ideas?

Buddhist staff member of a US hospice

If this is the case, the spiritual pain of a patient poses a profound question to the healthcare professional:

'How will I respond to the patient in front of me? Will I be their
- consultant?
- physiotherapist?
- social worker?
- chaplain?
- nurse?

Or will I simply be with them as another human being who has a particular set of knowledge and skills that might be of some help?'

'I couldn't bring rule books about how to be with dying people. When I walked into a room with a person who was dying, there was just the person and me and here we are. And if I'm full of hiding in roles and identities I cut myself off from them and they're left alone, which is the hardest way to die'.

Ram Dass[7]

Finally, religious and cultural interpretations of illness can be a significant source of spiritual pain, especially where a person has internalized a punitive model of God and interprets their suffering as punishment. Research suggests so-called negative religious coping can deleteriously affect health.

Anticipatory grief

Those who care for a dying person also experience spiritual pain. When circumstances force a carer to live incongruously, the experience can be profoundly disturbing.

- Awareness of their own needs—repressed or suppressed by the demands of constant care—may cause them to feel they are betraying or abandoning their partner, parent, or friend.
- They themselves may feel betrayed or abandoned by their loved one, and they may be shocked by the strength of their anger towards the one for whom they care.
- Anticipating what life will be like after the death, or even planning for the funeral, may seem premature and again shocking, and may arouse strong feelings of guilt.

For some time Maureen had been planning a foreign holiday. Caring nonstop for 6 months, she was feeling in real need of her break. However, her first husband had died while she was away and she feared the same would happen again. Nonetheless, she was determined that she had to go.

When her husband had been admitted to the hospice and was expected not to have long to live, Maureen's immediate question had been, 'Will I still be able to get away?'. She felt guilty and embarrassed that her first thoughts had been of herself.

In her carers' group she talked about guilt and responsibility, and about what long-term caring for a dying person does to the carer. Maureen spoke about wanting the best for her husband, but felt she needed an end to her stress. The seemingly endless experience created emotions

within her that made her think and feel in ways that were incongruent with how she would normally have expected to have thought and felt.

Maureen was being squeezed into a spiritually detrimental situation: living inauthentically against herself over an extended period.

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Spiritual assessment

> It cannot be assumed that all patients have spiritual needs at all times, and when they do, that they always want or need to share them with health professionals.[1]
>
> R.A. Farvis

Assessment has been defined as 'the process of gathering, analyzing, and synthesizing salient data into a multidimensional formulation that provides the basis for action decisions'.[2] There are two contrasting approaches to spiritual assessment:

- the use of a formalized 'spiritual assessment tool'
- the intuitive use of interpersonal skills

Formalized spiritual assessment

Formalized assessment tools include sets of both quantitative and qualitative questions aimed at understanding the patient's current spiritual needs. These may be based around the taking of a spiritual history.[3]

FICA

- **F**aith/belief: does the patient consider themselves to be spiritual or religious? Do they have spiritual beliefs that help them cope?
- **I**mportance: what importance do these beliefs have for them?
- **C**ommunity: is the patient part of a believing community?
- **A**ddress in care or action: how would the patient like the healthcare professional to address these issues?

- Advantages of formalized assessment tools
  - provide a frame within which healthcare professionals can open conversations about spiritual issues with a patient
  - promise a means by which any healthcare professional can make a spiritual assessment
- Limitations of formalized assessment tools
  - patients may experience such assessment as intrusive and insensitive to their need to be met at the level of their subjectivity
  - inept use of an assessment tool may dehumanize the patient and hinder the formation of a compassionate therapeutic relationship

Intuitive spiritual assessment

A more intuitive approach to spiritual assessment is the use of interpersonal skills developed through reflective practice on 'being with' patients. This depends entirely on the particular experience, skill, and personality of the spiritual assessor, and is rooted in the quality of the relationship between healthcare professional and patient.

- Challenge of intuitive assessment
  - demands high levels of self-awareness and empathy on the part of the healthcare professional

- requires the healthcare professional to demonstrate 'a personal awareness of the "spiritual" dimension, [be] themselves searching for meaning, have experienced a life crisis, recognize "spiritual" care as part of their role and [be] particularly sensitive and perceptive people'.[4]

The intuitive approach to spiritual assessment relies on careful listening to the stories patients tell about themselves and the particularities of the language they use.

The language of spiritual pain

Loss: As a child, I had a place in my mind where I would go until things became safe again. I need it now, but I've lost it … I can't find it.

Helplessness: Ah well, nothing to be done, nothing to be done … nothing to be done.

Isolation: There's no way really to know that what you're going through is normal.

Fear (of losing control): If I could only get control of my emotions, then everything would be fine.

Pointlessness: This shouldn't be happening.… We used to do this differently. Years ago, they would've just upped the morphine.

While it is the case that all members of the multidisciplinary team contribute to spiritual care, it is debatable whether all are qualified to undertake spiritual assessment. It is questionable whether healthcare professionals who are unfamiliar with their own spirituality or religious practice should be expected to attempt to deliver spiritual care.

Possible questions for initiating a conversation about spiritual assessment:

- What is important to you at the moment?
- How is all this affecting you?
- How's it going?
- Where is your source of hope today?

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Skills needed in spiritual care

Spiritual care is less about imparting specialist knowledge, be that of theology, philosophy, or ritual practice, than it is about the ability to *be* genuinely present to another person during an episode of spiritual pain. Consequently, spiritual care is not the sole prerogative of paid specialists; any multidisciplinary team member *can* offer spiritual care. However, only those capable of what has been called 'watch-with-me vulnerability' actually *do* provide real spiritual care.

The 'cure of souls' ('traditional' spiritual care) and 'soul attending' (psychotherapy) are closely associated, and the skills of psychospiritual care are similar to those of counselling and psychotherapy:

- self-awareness—understanding how one is affected by others; understanding one's limits and triggers
- unconditional positive regard—'prizing' the other; love
- empathy—intuitively sensing the patient's world 'as if' it were one's own, but without ever losing the 'as if' quality
- active listening
- sense of humour
- spiritual integrity—balancing one's personal spirituality with what at times can be the challenging beliefs of others

> When the client's world is this clear to the therapist, and he [*sic*] moves about in it freely, then he can both communicate his understanding of what is clearly known to the client and can also voice meanings in the client's experience of which the client is scarcely aware.

Spiritual companion: *Anam Cara*

Spiritual care, particularly of those facing their own death, demands the response of a wise and compassionate 'spiritual friend' (Celtic *Anam Cara*). Not every member of the multidisciplinary team will want to or be equipped to offer this level of spiritual care. But each can contribute to enabling a patient to find a 'way of being' that will help them to go through the experience of dying in the way appropriate to them.

> The old acceptance of destiny has gone, and a new sense of outrage that modern advances cannot finally halt the inevitable makes care of the dying and their families demanding and often difficult, but perhaps all the more rewarding.
>
> Dame Cicely Saunders

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Chapter 24

The contribution to palliative care of allied health professions

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Introduction

Palliative care has been very successful at taking ideas, values, and techniques from other disciplines in healthcare. Such borrowing of ideas has nearly always included considerable adaptation from the parent discipline. However, the notion of cross-boundary, interdisciplinary working is now highly developed in palliative care. Some disciplines such as medicine and nursing have become core parts of the specialist team, whereas others have been accessed on an as-required basis. Increasingly, individual allied health professions have seen the need to evolve the palliative care specialism within the generic discipline. Allied health professionals (AHPs) include occupational therapists, physiotherapists, nutritional experts, speech and language therapists, clinical psychologists, social workers, chaplains, pharmacists, and art and music therapists.

Rehabilitation

Palliative rehabilitation aims to improve the quality of survival. The emphasis of palliative rehabilitation is to attempt to restore quality of life by a maintenance, compensatory, and empowering approach even if a 'normal' functional level is not possible.

The length of survival for most patients with cancer and other life-limiting illness continues to increase, but this can be associated with the challenge of living with increasing physical dependence due to progressive weakness, fatigue, deconditioning, and the burden of other symptoms such as dyspnoea and pain.

Most patients are fearful of being dependent on others. Through the use of rehabilitation techniques, they can be helped to be as independent as possible, improve self-esteem, and live a fulfilled life within the constraints of their illness. This not only helps the patient but can also reduce carer burden.

Patients within the palliative care setting will experience fluctuating functional status. Rehabilitative techniques need to be individually tailored to adapt to the different needs of the patient. Realistic and achievable goal-setting, in conjunction with patients' and carers' wishes, is essential. These goals must be continually reassessed, in parallel with the exacerbations and remissions of disease and symptoms. In the later stages of the disease trajectory, the goals may have to be reassessed on a daily or even hourly basis. These goals will undoubtedly differ depending on the stage of illness. For a patient with a prognosis of weeks/months, a goal may be to get away on holiday, attend an important family event, or restart playing sport, whereas in the last few weeks of life it might be to sit out of bed to eat a meal or find the support and carers to manage a home death with confidence.

A rehabilitative approach is now becoming embedded in the way patients with life-limiting illness are supported and empowered, and a new term, 'rehabilitative palliative care', has been introduced. This approach integrates rehabilitation, enablement, and self-care, and supports people to live fully until they die. It is person-centred and acknowledges the need to involve all members of the team working collaboratively with the patient and carers to achieve personal goals and priorities.

Palliative rehabilitation

- adopts a person-centred and empowering approach
- helps people gain opportunity, autonomy, independence, and dignity
- responds quickly to help people adapt to changing functional status
- takes a realistic approach to goal-setting
- takes the pace from the individual
- adds life to patients' days, not days to their lives[1]
- is everybody's business

Considerations when adopting a rehabilitative approach

Biological/medical status

Careful assessment of the underlying disease and other disease pathologies needs to be undertaken in order to maximize symptom control and inform realistic goal-setting in relation to potential prognosis.

Psychological status

Patients experience many losses as their illness progresses. These include loss of role within the family, loss of mobility, and loss of self-esteem, as well as loss of future expectations and plans for their lives. These factors, together with potential loss of control over their lives, may intensify feelings of anger, apathy, depression, and hopelessness, which will affect the approach and impact of a rehabilitative approach.

Cognitive status

Decreased cognitive function will impact on the approach to goal-setting and rehabilitation. However, goals can still be set and met, especially with the knowledge of any advanced care plan and through consultation with family and carers.

Social and environmental factors

Family and social support, financial and environment constraints, and emotional state can all impact on goal-setting and the ability to work towards achieving these goals.

Successful palliative rehabilitation depends on the following:

- adopting a holistic inter-professional approach
- responding quickly as a team
- adapting constantly to changing circumstances
- setting realistic goals
- supporting patients and carers through change

Rehabilitation team

- the patient, family, and carers
- chaplain
- complementary therapist
- dietician
- doctors
- lymphoedema therapist
- nurses
- occupational therapist
- physiotherapist
- psychologist
- social worker
- speech and language therapist
- welfare benefits adviser
- other specialists according to need

Members of the rehabilitation team will have specific expertise and skill to optimize the benefit of rehabilitation, but it is important to understand that there will be some overlap of treatment and roles.

The rehabilitative palliative care approach is holistic, taking place at any stage of a person's disease trajectory and in any location (the inpatient unit, day service unit, person's home).

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Occupational therapy

Occupational therapy enables people to achieve health, well-being, and life satisfaction through participation in occupation.[1] In working with people who are terminally ill, occupational therapists value an individual's remaining life, help a client live in the present, recognize an individual's right to self-determination, and acknowledge and prepare for the approaching death. The occupational therapist (OT) uses an activity-based, symptom-led approach to treatment, rather than a disease- or diagnosis-led approach. The OT assesses various factors prior to advising on an appropriate intervention strategy.

Occupational history

A profile of the patient is built up based on family history, past self-care abilities, work experience, and leisure and recreational patterns. A functional assessment is then made which includes the following:

- self-maintenance: looking after oneself
- productivity: productive to life, either in the form of domestic activities or earning a living
- leisure

Self-esteem

A degree of social equilibrium and homeostasis is needed for a peaceful life, in harmony with all that life brings. When patients are diagnosed with a life-threatening illness and are changing from being totally independent to fluctuating or increasing levels of dependency, chaotic feelings can emerge. The natural protective reactions to this assault on self-esteem include anger, loss, resentment, bitterness, and hostility.

These feelings are energy-wasting, serve no useful purpose, and can lead to withdrawal, apathy, and depression—behaviours that can significantly impact on an individual's quality of life. Furthermore, carers are inevitably entrenched in this vicious circle of trying to cope not only with their own feelings but also those of the patient, who may be continuing to verbalize that their present life is unacceptable. This extra burden and stress can trigger feelings of helplessness, hopelessness, and uselessness in both patients and carers.

People are only able to feel self-worth if they are in a position to contribute, as a result of which they can engender respect in others. The role of the OT is to help identify and analyse the cause of these feelings and reactions and to provide the patient with coping strategies to facilitate empowerment and a sense of control. This may be through the interview process, relaxation, and anxiety management, or through the selective use of a more specific psychological approach such as cognitive behavioural therapy (CBT).

Physical systems

An analysis of the patient's physical capabilities will depend on the diagnosis and the course of the illness. The OT will need to have an understanding of the likely symptoms and prognosis in order to advise realistically, sensitively,

and appropriately, while recognizing palliative patients' dual states of both living and dying.

The OT assesses physical dysfunction as it relates to muscle strength and endurance, assessing the degree to which disuse may have affected this and to what extent some rehabilitative potential might exist. The OT will need to be aware of muscle spasms and other pain, and what factors trigger them. They will also assess ambulation and balance. The impact of cognitive and perceptual abilities will also be relevant, and techniques will be found to compensate for these.

Quality of life

Quality of life is defined by the individual. As professionals, we can see potential and give advice that we believe might improve satisfaction (subjectively) in the patient and carer, and from which achievement can be measured (objectively). However, it is ultimately the choice of the individual, which must be valued and respected, to take or reject advice.

A patient may, for example, feel that they gain more by not fighting physically or mentally to retain any vestige of their independence.

Goals

With the patient's full cooperation, the OT can help to set realistic goals. The goals must be feasible and structured. If a patient has always been very independent and is 'internally motivated', it may be very difficult for them to accept having to adapt to different methods of performance and what they perceive as unacceptably low goals yet still maintain their pride and dignity.

Carers may find pursuing goals a burden. For instance, they may worry about hurting the patient or themselves. They should not be asked or required to do more than they are physically or emotionally capable of doing. Carers are often reassured by being told that they will be taught what to do. They need support from health professionals and other support groups, as well as advice for the often unspoken, unrecognized, and unrewarded burden of care. Occupational therapy also has a role in educating both patient and carers about energy conservation, lifestyle changes, leisure activities, and alternative means of carrying out activities of daily living.

Treatment planning

Patients and families are vulnerable and often fearful of the uncertain future. They may vacillate chaotically between objective, logical thought and subjective, emotional despair. The aim is to work alongside these feelings and to raise the level of functioning by helping independence.

A problem-solving, compensatory approach is usually required to achieve this. Both patients and carers can regain a semblance of order, structure, purpose, and control. Sometimes, however, change or deterioration can happen quickly or unexpectedly, and OTs will need to be able to react to that. Continuous review is essential to ensure that the therapist is still

working towards the priorities of the individual, and that priorities are still realistic and achievable.

Examples of occupational therapy interventions

- carrying out home assessments and modifications to enable independence
- retraining in personal activities, including toileting, feeding, bathing, and dressing, using either a change of technique or appropriate equipment
- retraining in domestic activities with the use of appropriate equipment, e.g. kitchen activities
- ensuring a safe environment, e.g. devising and implementing complex manual handling plans using adaptive equipment
- liaising with appropriate organizations in the community for packages of care
- encouraging increasing engagement in purposeful activity; teaching time management and the usefulness of daily routines; redeveloping a sense of purpose and accomplishment to increase self-esteem
- facilitating lifestyle management with continued engagement in hobbies and leisure pursuits; promoting therapeutic activity programmes, such as involvement in creative activities and socialization, while encouraging the achievement of individual treatment goals
- providing relaxation training and anxiety management; training in energy conservation and work simplification techniques to cope with fatigue and breathlessness either as individual sessions or group work
- supporting and educating carers
- facilitating psychological adjustment to loss of function, e.g. through the use of CBT; retraining in cognitive and perceptual dysfunction, e.g. learning compensatory techniques to improve procedural memory during domestic tasks
- assessing for and prescribing wheelchairs, pressure-relief posture management, and seating; assessing muscle flexibility and positioning; where necessary, having splints made and aiding transfers as well as incorporating both indoor and outdoor needs

Occupational therapists define a clear, structured, graded plan of action with the patient and carers to provide strength of purpose and dignity. Life is a delicate balance: a matter of coping and adapting to a situation in which being productive and feeling valued are paramount. The OT is critical to facilitating a person's sense of mastery and competence and for re-instilling substance and control into the quality of living.

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Dietetics and nutrition

Laughter is brightest where food is best.

Nutrition is not solely concerned with refuelling the body, but has profound emotional and cultural significance. Food preparation symbolizes tangible care and affection and, as far as possible, should continue to be part of daily social interaction. For carers, a good intake by the patient is often thought of as a hopeful sign, whereas a decreasing intake, particularly as the patient deteriorates, often causes much conflict and distress. The patient may feel guilty for not eating and often forces themself to eat in order to please the family.

You must eat up if you want to get better.

My Gran

A good assessment of factors affecting nutritional status is important. Nutritional intervention focuses on ensuring that symptoms of disease and side effects of treatment are managed well, and on initiating appropriate dietary advice and strategies to prevent further morbidity. The aims of nutritional support in palliative care will change as the disease progresses.

Aggressive nutritional intervention is needed during the earlier stages of illness, allowing the patient to cope with the following:

- metabolic demands of illness and treatment
- repair of tissue and prevention of infection
- maintenance of well-being and quality of life

Palliative nutritional care, on the other hand, concentrates on symptom control and targeted nutritional intervention later in the disease process, in order to enhance quality of life.

The incidence of malnutrition in patients with cancer is high, and nutritional screening is required for all patients.

Anorexia

Anorexia is the absence or loss of appetite despite obvious nutritional needs. Reversible causes of anorexia must be addressed.

Cachexia

Cachexia is the metabolic inability to use nutrients effectively, resulting in weight loss, lipolysis, loss of muscle and visceral protein, anorexia, chronic nausea, and weakness.

Role of the dietitian in palliative care

State-registered dietitians are experts in nutrition, and are therefore able to translate scientific theory into practical advice for patients, carers, and other health professionals depending on the patient's needs. They can be accessed within the hospital or the community setting, and work closely with other members of the multidisciplinary team. Their role is to enhance quality of life.

Tasks for the professional advising on nutrition:

- Assess a patient's nutritional status.
- Elicit the patient's goals regarding nutrition.
- Provide specialized nutritional advice at diagnosis, during treatment, and in the palliative phase.
- Advise on food preparation/fortification/supplementation as appropriate.
- Relax dietary restrictions if possible, e.g. for patients with diabetes and hypercholesterol states.
- Recommend and calculate feeding regimens to suit an individual patient's requirements, using enteral or parenteral access.
- Provide psychological and emotional support.
- Listen to patients' fears.

Dietitians don't just give out nice little boxes of milky supplements!

Dietary management of common symptoms affecting nutritional status

The common symptoms experienced require a multidisciplinary team approach.

Loss of appetite

- Eat small frequent meals and add a nutritious snack between meals.
- Eat slowly and relax after meals.
- Appetite may be variable; make the most of the times when it is at its best.
- Cooking smells can reduce appetite; cold foods may be better tolerated, or consider 'take-aways' and pre-cooked, delivered meals.
- Keep plenty of snacks to hand, e.g. cheese and crackers, biscuits, dried fruit, nuts, flapjacks, cakes, creamy yoghurts.
- Take simple exercise or a glass of alcohol, if permitted: these can be useful stimulants.
- Have your drinks between meals rather than with your meals.
- Have a nourishing drink if unable to manage a meal—milk-based drinks are ideal, e.g. hot chocolate, malt drink, milky coffee; use fortified milk* to enhance the nutrition content without affecting volume.

**Fortified milk*

Fortified milk can give you extra nourishment and can be used as you would use ordinary milk, e.g. as a drink or added to cereal.

Milk powder can be found easily in most supermarkets. Make fortified milk by adding 2–4 tablespoons of milk powder to a pint of full-fat milk.

Sore mouth

- Choose foods with plenty of sauce or gravy, e.g. casseroles, fish in parsley sauce; cut food into small pieces.
- Moisten food with milk, butter, cream.
- Choose soft foods, e.g. pasta dishes with sauces, creamy soups, egg dishes, milk puddings, and mousses.
- Blend and moisten foods that are dry or solid; mix them in with soups or sauces, gravies, and casseroles.
- Avoid irritants such as citrus fruits (or juice), spicy or salty foods, and rough, coarse, dry foods such as raw vegetables, toast, crackers.

- Sip fluids rather than gulping: sipping is more refreshing than gulping—using a straw may help.
- Alcohol, caffeine, and tobacco may irritate the mouth.
- Choose lukewarm or cold foods that are soothing; very hot foods can cause discomfort; try freezing fruits, and suck on ice lollies or ice chips.
- Keep the mouth clean—brush teeth, gums, and tongue at least three times a day with a soft toothbrush.
- Use mouthwashes regularly but avoid using mouthwashes that contain alcohol (which will cause burning).
- Suck ice before being treated with 5- fluouracil, other than in head and neck cancer, as it helps to prevent mucositis.

Nausea and vomiting

- Cold foods may be more acceptable than hot.
- Eat small amounts slowly and avoid long periods without eating.
- For sickness in the morning, eat prior to getting out of bed, e.g. plain biscuits, dry toast, or cracker.
- Keep meals dry; do not add gravy or sauces.
- Sip fluids after meals.
- Keep upright whilst eating and for 2h afterwards.
- Sipping cold fizzy drinks between meals may help, but you may find these easier if left to go flat; drinking ginger ale and soda water may help ease nausea.
- Use a fan to direct away odours, especially in hospital.
- Grill foods: fatty foods may make nausea worse.
- Check for other reversible causes, such as opioid medication, constipation, patient anxiety.

Taste changes

- Try chicken, fish, milk, cheese, beans, or nuts if the patient finds red meat tastes unpleasant; these foods are bland in taste and may be more acceptable.
- Marinate meat in lemon juice or vinegar to improve flavour.
- Use herbs and spices to mask the taste of meat.
- Freshen the mouth with oranges, grapefruit, pineapple, and lemon fruits or juices.
- Consider cold food: these may taste better than hot food; it may suit the patient to have frequent cold snacks throughout the day rather than a more traditional three-meal pattern.
- Avoid food and drink which contains saccharin or other artificial sweeteners since they may give food a bitter taste.
- It is important to keep the mouth clean, brush teeth three times a day, and use a recommended mouthwash.
- Use plastic utensils if the patient experiences a metallic taste.

Diarrhoea

- Discourage a high-fibre intake, i.e. reduce bran, fruit, vegetables, pulses.
- Avoid strong tea and coffee, which are gut stimulants.
- Avoid spicy foods.
- Reduce greasy, fatty foods: certain fats may make diarrhoea worse.

- Check inappropriate laxative use.
- Consider malabsorption.

The foregoing includes only some of the advice available and is a guideline only to the merits of a formal dietetic assessment.

Nutritional supplements

Oral supplementation is available to assist rather than replace food, but it will not increase weight or prolong the life of patients with cancer. Benefits include increasing calorie and nitrogen intake and stimulating the appetite.

Many products are available on the market which range in nutritional support and can be expensive. Ideally, they should be recommended after the patient has been assessed by a registered dietitian, who will then select the most appropriate product for that individual, according to their preferred taste and perceived need. The challenge for dietitians working with patients in the palliative care setting is to use their expertise to cater to the particular needs of the individual patient whose requirements and goals may change rapidly.

Oral nutritional supplements can be divided into the following categories:

Oral sip feeds

- Some are nutritionally complete and provide a full range of vitamins and minerals.
- Milk, juice, or yoghurt options are available.
- Good source of protein and energy.

Fortified puddings

- Provide protein and calories in small volumes.
- Useful for dysphagic patients.

Modular supplements

- A concentrated source of carbohydrate/protein/fat.
- Beneficial only if used in conjunction with a diet plan to ensure that a range of nutrients is provided.
- Carbohydrate drinks are unsuitable for diabetics without supervision.
- In powder form, they can be incorporated into foods without increasing volumes.
- Need to be calculated to patient requirements to maximize use and reduce risk of volume overload.

Alternative feeding

Tube feeding

Tube feeding is generally nasogastric or gastric through a percutaneous endoscopic gastrostomy (PEG) or radiologically inserted gastrostomy (RIG), but rarely may be duodenal or jejunal. The aim of feeding may be to replace normal food intake or to supplement it.

There is some evidence that artificial feeding prior to definitive oncological treatment, including surgery, may assist in stabilizing weight, improving quality of life, and contributing to better treatment results. However, there is no evidence that artificial feeding prolongs life in those patients with advanced cancer.

The decision to feed artificially requires clinical judgement within the multidisciplinary team and good understanding of the patient's needs and feelings. If used appropriately (e.g. for some patients with neurological conditions when proper counselling and discussion have taken place, and occasionally in patients with head and neck cancer), it can be useful and take the pressure off patients and carers when eating has become a burden and food can no longer be tolerated or enjoyed.

Total parenteral nutrition (TPN)

The use of PN (parenteral nutrition) in a patient with advanced cancer is infrequent but certainly not unheard of. It can be used particularly in patients presenting with malignant bowel obstruction. If all other routes of feeding are not tolerated, PN may be considered.

Ethical issues

Healthcare professionals working within the palliative care setting are faced with ethical dilemmas daily. Decisions should be made with the support of the team and consideration of the patient and carers. In order to make a justifiable, considered decision, the following questions should be considered prior to commencing artificial feeding:

- What are the patient's wishes? In the event the patient is no longer able to communicate their wishes, is there an advance directive in place regarding nutrition?
- What benefit will it bring to the patient?
- How much discomfort is caused by eating and drinking normally?
- How keen or able is the patient to continue eating and drinking?
- What are the risks and discomforts associated with artificial feeding?

It is important to repeat the questions at regular intervals in the patient's journey, and document clearly the rationale and aim of the nutrition intervention that has been agreed. Equally, however, it is important to record those instances where intervention is refused (by the patient) or is deemed inappropriate.

Documents are available to offer guidance on nutrition and hydration to health professionals, and some are listed here.

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Physiotherapy

Physiotherapy helps restore movement and function when someone is affected by injury, illness, or disability. A physiotherapist will use evidence-based physical interventions in the promotion, maintenance, and restoration of an individual's physical, psychological, and social well-being, taking account of variations in health states.

In palliative care, the role of the physiotherapist is to reduce the degree to which disabilities, caused by the disease or treatment, interfere with everyday life. The aim is to support patients to function at a minimum level of dependency and optimize their quality of life, regardless of life expectancy. This is particularly pertinent for those patients whose disease trajectory may be short and are deteriorating rapidly. A physiotherapist's core skills can help people adapt to their changing condition.

The physiotherapist, with a knowledge of the underlying pathological condition, adopts a problem-solving approach in which goals of treatment are planned jointly with the patient. This gives the patient a measure of control at a time of multiple losses. These goals must be realistic and achievable for the phase of illness, and must be continually reviewed. Goals may be simple (to be able to sit out of bed for a meal) or more complex (to attend and enjoy a wedding). This is known as 'active readaptation'.

A physiotherapist has a detailed knowledge of functional anatomy and ergonomics, and is able to analyse movement and posture in its relationship to the environment. For instance, weakness and immobility may lead to poor posture, which places a strain on muscles and ligaments and can cause pain, particularly around joints. These stresses may be relieved by strategic physical positioning.

The physiotherapist may be the first professional to be alerted to the signs and symptoms of spinal cord compression due to malignant disease. Alongside immediate medical treatment, the initial aim will be an attempt to minimize loss of function. Should a more complete picture of motor, sensory, and autonomic impairment develop, the physiotherapist will be instrumental in helping the patient cope with adapting to a drastic reduction in functional ability by helping the patient to develop a strategy for the future. This may involve balance training, development of upper body strength, instruction in transfers, and the use of a wheelchair. Relatives and other carers will also require instruction in passive movements, the positioning of paralyzed limbs, the use of wheelchairs, and in moving and handling techniques.

Physiotherapists have much to offer patients through their pragmatic approach with a focus on empowerment, enablement, and self-management.

Core skills and attributes

- holistic approach
- knowledge of disease trajectories and potential prognoses
- robust clinical assessment and decision-making
- broad physiotherapy skill base

- ability to plan interventions based on the patient's lived experience
- advanced communication skills
- resilience

Physiotherapy interventions

Optimizing mobility

As diseases progress, mobility becomes more challenging. Initially, a stick or crutches may be necessary to support independence, but later the provision of a walking frame or working towards independent mobility in a wheelchair may be more appropriate. Facilitating independence of transfers by strategically positioned furniture or the use of a sliding board may allow patients to remain independent within a smaller environment.

Pain management

Bone pain and neuropathic pain due to cancer are notoriously difficult to manage. Relief may be obtained by the use of transcutaneous electrical nerve stimulation (TENS) or acupuncture. Local application of heat, in the form of heat pads or wheat bags, is also used for pain relief. Progressive disease often leads to a more sedentary life, causing pain due to stiffness and poor posture.

Maintenance of joint range and muscle power

Massage and exercise therapy are the core skills of all physiotherapists. Maintenance of joint range by the use of active or passive exercises along with therapeutic massage will be beneficial. Therapeutic massage using stroking and gentle kneading may be used to reduce muscle spasm, stimulate circulation, relieve pain, and aid relaxation.

Maintenance of joint range is also important in the management of neurodegenerative diseases. Passive and active assisted exercises should be built into the patient's daily routine and taught to relatives and other carers.

Physiotherapists can also supply and fit collars and splints, and advise on various other adaptations which will support joints, correct posture, and facilitate functional ability.

Exercise groups

Exercise groups have been shown to be an effective tool in improving physical functioning and psychological well-being. They can be graduated from short chair-based groups to longer circuit-based groups, and should allow for some individualized adaptation, depending on the functioning of those attending the group.

Breathlessness management

All physiotherapists are trained in respiratory care and can teach patients and their carers techniques to reduce the work of breathing, to encourage relaxation, to aid the expectoration of secretions, and to advise on coping strategies in order to improve breathing control.

Breathlessness groups are an effective way of supporting patients and carers experiencing breathlessness, offering advice on non-pharmacological management of breathlessness, and providing valuable peer support. The

physiotherapist is a key member of the multiprofessional team involved in running these groups.

Many physiotherapists will also incorporate acupuncture, acupressure, reflexology, and aromatherapy into their practice when supporting breathless patients.

Physiotherapists often help in the management of patients in the use of non-invasive ventilation and cough-assist machines for respiratory failure, e.g. secondary to neuromuscular disability such as in motor neurone disease.

Fatigue management

Although fatigue management is mainly the domain of the occupational therapist, physiotherapists need to embed fatigue management into all interventions, as the pacing of activities is key to optimal functioning.

Psychological support

The physiotherapist often works on a one-to-one basis with patients. Patients may discuss their hopes and fears with a sensitive listener. They feel safe to ask searching questions in these situations and, therefore, the physiotherapist needs to be adequately prepared and informed to deal with these issues. Advanced communication skills are a necessary requirement of all physiotherapists supporting palliative care patients, as they are often required to communicate life-changing news, e.g. that the patient will not walk again.

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Speech and language therapy

Speech and language therapy (SLT) is necessary in palliative care since patients often have difficulties with communication and swallowing. Some palliative care teams have their own SLT service; others access SLT from local hospital or community services. The abilities to both communicate effectively and swallow safely are integral to being autonomous social creatures and maintaining life, in sickness as well as in health. Therefore, any problem with communication is an adverse symptom and reduces the patient's independence, quality of life, and informed decision-making. Similarly, swallowing problems reduce quality of life and give rise to risks of reduced intake, choking, and aspiration. The speech and language therapist plays an important role in the multidisciplinary team at all stages of disease management—at diagnosis, and in symptom control, palliative rehabilitation, and terminal care.

Aims and principles of SLT intervention

SLT assessment contributes to diagnosis, monitoring of disease progression, and prognosis, and provides accurate identification of the type, severity, and causes of the communication or swallowing problem. This allows appropriate and relevant intervention. The aim of SLT input in this context is the maintenance and facilitation of remaining function within the limits of the disease, and compensation for deficits, rather than the restoration of original abilities. SLT is helpful in contributing to an assessment of competence, and also at times when the patient needs to communicate their wishes or symptoms or to discuss prognosis, but communication is difficult, e.g. due to fear, fatigue, pain, or to a specific problem with speech, language, reading, or writing.

SLT helps patients make informed, realistic, and timely choices, and to set appropriate personal goals for communication and swallowing by means of the following:

- early involvement: to build understanding and trust, monitor progression, and anticipate future problems
- patient-led, whole-person approach: to enable relevant, appropriate, and timely management for the individual
- accurate identification of problems and causes: e.g. differentiating dysphasia from dysarthria, due to cortical vs bilateral brain lesions or brainstem disease
- immediate strategy formation to maximize function, manage symptoms, and reduce risk; e.g. swallow techniques to reduce choking and the risk of aspiration
- patient, relative, carer, and team support, information, and education: to increase understanding and improve appropriateness and effectiveness of management
- anticipation of future problems; preparation and planning

Communication difficulties

The ability to communicate is always important, but particularly so, as happens in palliative care, when an individual has to understand unfamiliar or frightening information, ask difficult questions, and express emotionally complex ideas. Even apparently mild problems with communication give

rise to heavy physical, cognitive, emotional, and psychological burdens, as well as time burdens on the patient and also on their relatives, friends, and healthcare staff. They can result in the patient withdrawing and others avoiding contact. A significant number of palliative care patients have been shown to have previously unidentified communication problems and have also reported concern about their communication, feeling it is impaired.

Dysphasia

Dysphasia is a difficulty with verbal language and the processing of words. It includes problems with word-finding, syntax, writing, and spelling (i.e. *expressive* dysphasia) and with understanding spoken words and reading (i.e. *receptive* dysphasia). The type and severity of the expressive and receptive problems vary between patients, but there is almost always an element of comprehension deficit, even though this may not be obvious. For a variety of reasons, patients, relatives, and even healthcare staff tend to underestimate the degree of comprehension, but it is also important not to underestimate the underlying competence of the patient. Usually, dysphasia is caused by damage to the cortex of the dominant left hemisphere of the brain. It is frequently present in palliative care as a result of stroke or primary or metastatic cerebral disease.

Examples of strategies that may help patients with dysphasia include the following:

- allow additional time, not being rushed, and ensure a reduction in background noise and distractions
- establish a reliable yes/no response
- word-finding—encourage the patient to talk around the target word or describe the object (circumlocution), substitute another word, focus on the initial sound, or use pointing or gestures
- auditory comprehension—speaker slows own speech down; simplifies what is being said; shortens sentences and 'chunks' information; uses pauses, repeats, and reiterations
- alternative augmentative communication (AAC) can support or replace verbal communication, e.g. picture/alphabet chart, computer-based system; there is no best type of AAC system—will depend on personal preferences, abilities, and needs; it will also need to change as illnesses progress

Dysarthria

This is a motor (movement) problem of speech. There is a reduction in the range, speed, or coordination of facial and oral movements, affecting articulation and resulting in slow or slurred speech and reduced intelligibility. The specific type of dysarthria depends on which motor pathway has been affected and where. Dysarthria can be caused by stroke and cerebral tumours, and occurs in almost all the progressive neurological conditions, such as motor neurone disease (MND), Parkinson's disease (PD), progressive supranuclear palsy (PSP), cerebellar atrophy, multiple system atrophy (MSA), and multiple sclerosis (MS), dependent on the disease progression. Sometimes cognitive problems complicate diagnosis and management. Ill health, general weakness, and breathing difficulties may also give rise to dysarthria.

In addition, articulation difficulties are almost always a problem for those patients with head and neck cancers, owing to structural changes as a result of the disease, surgery, or oncological treatment (see Chapter 14, Palliation of head and neck cancer).

Examples of strategies that may help patients with dysarthria:

- allow additional time and ensure a reduction in background noise and distractions
- encourage sitting up straight and breathing slowly and deeply
- encourage slowing down speech, shortening phrases, breathing between phrases, and over-articulating
- alternative augmentative communication (AAC) to support or replace verbal communication (see earlier)

Dysphonia

Dysphonia is a problem with the voice: it may be quiet or hoarse or it may disappear intermittently or completely. The causes in palliative care are numerous. There may be reduced breath support to make the vocal cords vibrate, due to lung disease or general weakness. There may be a vocal cord palsy due to a lesion of the recurrent laryngeal nerve, as can happen in the spread of lung tumours and disease in the neck. Dysphonia can also be caused by cerebrovascular disease; it occurs in progressive neurological diseases such as MND, PD, and MS.

Patients with head and neck cancers frequently have voice problems caused by structural changes due to the tumour or treatments. In those patients with laryngeal cancer treated by radiotherapy, with or without chemotherapy, there are long-term structural changes to the vocal cords which affect how they vibrate and, therefore, the sound they produce. When laryngeal cancer is treated by laryngectomy, the larynx, including the vocal cords, is removed and the patient no longer has the anatomy to make normal voice sounds. (see Chapter 14, Palliation of head and neck cancer.)

Examples of strategies that may help patients with dysphonia:

- reduce background noise
- ensure good vocal hygiene— see following explanation
- encourage adequate breath support, frequent top-ups of breath, and not speaking on residual air
- encourage patients to open their mouths wide to let the sound out and project the voice but not strain it
- use an amplifier

Vocal hygiene

'Hygiene' is used in the sense of 'good care' or 'cleanliness'. So vocal hygiene means doing things that are good for the voice/vocal cords/larynx and not doing things that are harmful. Speech and language therapists and ear, nose, and throat specialists give standard vocal hygiene advice to almost everyone they see with a voice problem, with good explanation and support. Bearing in mind that patients with palliative care needs may have a short time to live and that the emphasis is on quality of life, advice will need to be adapted to the individual patient's circumstances.

Vocal hygiene includes the following:

- increasing fluid intake
- avoiding carbonated, caffeine-containing, or diet drinks
- managing reflux (with medication as necessary)
- humidifying the environment if possible
- avoiding smoky environments and other known irritants, such as car fumes and some cleaning fluids
- trying not to talk against background noise
- not shouting
- stopping habitual throat-clearing and coughing
- stopping throat lozenges, pastilles, and sweets
- trying steam inhalations
- trying to build voice 'rest periods' into the patient's timetable
- stopping smoking
- avoiding alcohol, especially spirits

Swallowing difficulties

Dysphagia (or swallowing difficulties) occurs when there are structural, malignant, or neurological changes to the lips, tongue, cheeks, upper and lower jaw, teeth, palate, pharynx, larynx, and oesophagus. It can also occur when the level of responsiveness is reduced or there are cognitive problems, or as a secondary effect of disease elsewhere. Dysphagia leads to reduced intake and may result in choking and putting the patient at risk of aspiration. Dysphagia is caused by head and neck, brain, and other cancers and their treatments. It is also caused by stroke, and is seen in almost all progressive neurological diseases, such as MND, PD, and MS. Dysphagia and reduced eating and drinking are also part of the terminal stage of disease and the dying process.

The type and severity of dysphagia depend on which structures are affected, how and why they are affected, and how severely. Therefore, an SLT assessment establishes the type and severity of dysphagia (including symptoms requiring palliation), risks, and prognosis. The SLT can then suggest strategies to make swallowing easier, more efficient, and safer. The SLT works closely with all members of the multidisciplinary team in the management of dysphagia, including the dietitian, physiotherapist, and occupational therapist. In circumstances where there is a long-term high risk of repeated choking and aspiration and inadequate intake (such as in MND and some head and neck cancers), it is appropriate to consider stopping or supplementing oral intake using tube feeding via a PEG or RIG. Some patients will have made an informed choice to continue to eat and drink despite experiencing difficulty and risks. The SLT's role is to support them, their family, and the professionals involved in their care with this risk feeding decision.

Examples of strategies that may help patients with dysphagia:

- ensuring thorough, frequent mouth care
- advising on an upright sitting posture with head in the midline
- limiting the amount eaten and drunk at one time—little and often
- modifying the consistency of foods and drinks may help to overcome a delayed swallow and make swallowing safer, e.g. soft, wet, mashable

foods rather than hard foods; and syrup-thick drinks (pre-thickened or hand-thickened) rather than thin fluids
- modifying head position and using various swallow manoeuvres may compensate for a weak or ineffective swallow and poor airway protection, e.g. head turned to the affected side, supraglottic swallow

The SLT should be consulted whenever a patient is having difficulties, as described earlier, in order to explain which strategies are appropriate.

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Clinical and other applied psychology in palliative care

Psychologists are registered professionals who provide psychological support to patients, their families, and other clinical staff. Within the palliative care setting, psychologists undertake expert psychological assessments and interventions which promote well-being.

Psychologists are increasingly being employed within the palliative sector to work with individuals with complex psychological issues.

Although growing in number, an alternative to expert psychological input is to access existing services within community mental health teams and primary care. If considering referring to these services, it is necessary to bear the following in mind:

- Patients may have difficulty with the perceived stigma of being referred to mental health services.
- Some mental healthcare professionals have little training in the needs of palliative care patients. However, mental health clinicians can often adapt their skills to meet the needs of the patient. Therapies such as solution-focused therapy and the compassion and mindfulness therapies lend themselves to working with palliative care patients.

Much of the work of psychologists in palliative care is directed towards supporting or working in collaboration with other staff: this can only be achieved by becoming an integral member of the palliative care team.

Roles for the applied psychologist in palliative care

Psychologists can provide expert counselling to patients experiencing end-of-life issues:

- loss of control
- feeling a burden on others
- the need to resolve 'unfinished business'
- the need to find meaning

People who are near their end of life frequently have to make complex decisions. Families are often part of the decision-making process. Psychologists can assist in decision-making by exploring the patient's and family's options. These options may be spiritual, legal, existential, or medical in nature.

Psychologists can also provide expert care to family and caregivers around anticipatory mourning. This care may reduce the risk of a complicated grief by promoting healthy anticipatory mourning.

The activities of applied psychologists can be considered under five main headings: treatment, assessment, teaching and training, consultancy, research and audit.

1 Treatment

Often the primary reason for including a psychologist in the palliative care team is to provide additional treatment. Because of a broadening of the definition of 'palliative care' and improvements in treatments, more people receiving palliative care have a lifespan that enables psychological interventions to be effective. Changed circumstances lead to changed perspectives, priorities, and duties for the palliative care patient. Psychological intervention can

facilitate adjustment, resilience, and restitution of an essentially normal life. Commonly occurring problems include the following:

- difficulties adjusting to change
- loss of hope
- lack of purpose and direction
- passivity and dependency induced by being cared for
- fear of the future
- communication difficulties in the family and with health professionals
- the need for increased coping strategies

The body of psychological research in cancer and chronic pain has been especially productive in devising intervention strategies to facilitate the following:

- constructive acceptance and adjustment to disability and shortened lifespan
- beneficial emotional expression and regulation
- skilful coping and personal control despite disease progression
- purposeful living and improved motivation
- effective communication with carers
- enhancement of self-esteem despite appearance changes and loss of roles
- facilitating self-acceptance and self-compassion

Mental health problems of anxiety, depression, and anger are often reasons for referral to the psychologist, whilst pain management referrals are also appropriate where prolonged experience of chronic pain exists.

Cognitive behavioural therapy (CBT) encourages people to modify their unhelpful thoughts and behaviours, thereby constructively changing situational outcomes (e.g. resolving a dilemma), emotional responses (e.g. raising low mood), and physical reactions (e.g. reducing muscle tension). The attraction of this therapeutic approach is partly because of its brief pragmatic interventions focused on current problems, and partly because of the substantial research evidence base on which this approach is developing. However, a characteristic that often distinguishes psychologists from counsellors is a reluctance to be closely allied to any one particular treatment model. Evidence-based techniques often determine psychologist interventions rather than therapeutic models. Thus psychologists, may, for example, use a mix of CBT methods with others selected from the psychodynamic ways of working (exploring the effects of early life experiences) and a systemic approach (examining interactions and roles, particularly within the family).

2 Assessment

The psychologist's basic history and information gathering is identical to any good in-depth initial interviewing conducted by other healthcare professionals, but it may also include some less common features such as the use of questionnaires and between-session record-keeping.

Tools measuring psychological adjustment and psychopathology are used to assess distress and changes in a patient's mental state, and to screen the need for psychological interventions. The psychologist's role is to make professional interpretation and comparison of results with these assessment

instruments, especially those that have been less rigorously evaluated. Other psychometric tools—including measures of cognitive functioning, intellectual ability, attainments, personality, and aptitudes—rarely form part of the palliative care psychologist's role.

Since devising new rating scales and questionnaires is a skill for which psychologists receive training, they can assist others who are developing assessment tools.

3 Teaching and training

Many psychological skills are transferable to other professionals.[1] Applied psychologists expect to keep updating their fellow team members in relevant psychological knowledge and skill developments.[2] The NICE guidance[3] places particular emphasis on this role and that of supervision for staff working at lower levels in their model of psychological assessment and support.

Psychologists frequently use an educational approach ('psychoeducation') to groups of patients in preference to a therapy group as an effective means of enhancing insight and coping skills.

4 Consultancy

Giving advice and support to fellow team members is often more appropriate than seeing the patient personally. This is particularly true towards the end of a patient's life, when time may be of the essence and meeting new professionals should be minimized. The psychologist can offer advice (and sometimes techniques) to staff that enables them to proceed in providing skilful assistance with more self-assurance; team meetings and case reviews can be strengthened by this means as well.

5 Research and audit

Some psychologists are involved in aspects of healthcare primarily from a research perspective. A culture of undertaking research is integral to psychologists' training, so most psychologists seek to develop or support local research and audit projects.

Types of applied psychologist employed in healthcare

- *Assistant* psychologists are psychology graduates without additional training. They carry out research and clinical support tasks under the supervision of a vocationally trained psychologist, and are not normally employed in other roles.
- *Research* psychologists who have an academic background and no vocational training similarly limit their role to supervised or non-clinical activities as agreed within local clinical governance arrangements. (Research and audit role as described earlier.)
- *Health* psychologists have postgraduate training focused around the psychological aspects of illness, healthy and unhealthy behaviours, health-related attitudes, and health promotion and communication, as well as research into psychological aspects of healthcare delivery. Although health psychologists are few in number and are a new group of qualified and experienced applied psychologists, their skills are relevant in palliative care, particularly with reference to communication skills, information needs, and service provision research. (See roles 2–5 earlier.)

- *Counselling* psychologists are also a relatively new breed of applied psychologist and are present in many psychology services. Training tends to be focused around a thorough knowledge of therapeutic models; therefore they are especially well equipped to provide specific therapy services for patients and carers. (See roles 1–5 earlier.)
- *Clinical* psychologists remain the most common of all the applied psychologists offering clinical care. Breadth of psychological knowledge is often greater than that of the health or counselling psychologist, but is perhaps achieved by limiting depth during training. The all-rounder quality of training makes the clinical psychologist a good choice in the development of palliative care psychological services. (See roles 1–5 earlier.)

All applied psychologists need to receive supervision of their work from more experienced applied psychologists. In the first instance, new or small palliative care services should employ psychologists with at least 5 years' practice or arrange contracts with larger local psychology services.

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Social work

Social workers are an integral component of the palliative care team, and address many non-physical issues crucial to the holistic care of patients and their families. It is relatively easy to recognize physical problems such as shortness of breath, but healthcare professionals often assume that health concerns are the most important issues in the patient's mind, whereas family relationships and problems of everyday living may be just as, or more, important. When someone suffers from a life-threatening illness, it affects all family members and changes the dynamics, roles, and relationships within the family. The social worker's focus is on the effects of the illness on the family and other social and community networks important to the patient. Social workers, therefore, are often in the best position to enable patients to express and deal with emotional, psychological, and social issues in their lives, helping them to reduce fear and anguish, and enabling them to feel reconnected with friends, family, and community.

Social work has three main roles:

- Role 1: to strengthen people in managing and dealing with emotional, psychological, and social consequences of what is happening to them
- Role 2: to enable people to make the best possible use of welfare services and family, social network, and community resources that will help them
- Role 3: to develop community organizations and groups to provide mutual help and support for people in dealing with the problems in their lives

It is not always possible to treat physical symptoms until the patient's emotional, psychological, social, and spiritual distress is understood and addressed, and until difficulties in accessing and using practical help and welfare services are resolved. All members of the multidisciplinary team attend to some of these needs, but patients may not want to talk about their emotions to the professionals who are giving them physical care. Also, they may be inhibited from raising family and welfare issues with team members whose focus is mainly healthcare. Social workers usually approach clinical problems from a different angle, being guided first by the patient and their family, empowering them to identify and express what they feel are their most important needs.

Families

Families come in many different shapes and sizes; they are the set of relationships within which a patient experiences kinship, child-parent, and caring and support relationships (e.g. a gay or lesbian relationship may be more important for caring and support than the patient's parents, siblings, or children). As well as the patient, friends, family members, and partners need help to cope with their fear and anger at the situation. They need to feel involved in care and decision-making, which is essential in order to avoid additional grief in their bereavement. Patients, families, partners, and friends can be helped to say their goodbyes, to be given the opportunity to heal rifts, and to complete unfinished business. Working together to enable a person to die at peace with themself is a fundamental goal for all members

of the multidisciplinary team, but the social worker's skills specifically equip them to empower patients and those close to them to say, 'I love you', 'Thank you', 'Sorry', and 'Goodbye'—perhaps the most important messages people need to give to each other at the end of life.

Families and individuals who are particularly vulnerable and at risk will be identified following a full social work assessment and offered appropriate interventions and support. A full assessment is often aided by constructing the family genogram, finding out who is important to the patient and highlighting relationship issues.

Among the issues to think about when preparing and talking about a genogram to a patient or family member are the following:

- the stage of life each family member is at
- their special responsibilities in the family (e.g. caring for a family member with learning disabilities)
- important memories (e.g. previous deaths) and expectations (e.g. to be cared for in old age)
- strengths and resources of each member
- the availability of support or likely demands from the extended family, the patient's social networks, or community connections
- moving into 'gaps' (e.g. children 'replacing' a dead person)
- Who cares for whom? Who cares for carers?
- What changes, separations, illnesses, and losses have children and others experienced?
- Who was involved in or absent from family crises, deaths, funerals?
- Who confides in whom?
- Who is in conflict with whom? Who gets left out?

The social network may include ethnic and cultural issues that need to be understood to facilitate family communication. A genogram may be adapted to show wider social networks. Strong, unfamiliar, and often conflicting feelings can be a barrier to open communication. Rifts within families and social networks may emerge and will, therefore, need managing sensitively, often allowing the reconciliation and rebonding of relationships. However, barriers to communication can also occur when families want to protect each other from the pain of bad news and the limited future.

Children

Families may need help so that they feel more confident about knowing how to tell and involve their children. They may try to protect children (and other dependents, such as family members with learning disabilities) by trying to keep up an unrealistic front about the illness or prognosis. Telling children and young people about someone in the family suffering from a serious illness early is helpful because it prevents problems arising and reduces difficulties later. Children are helped by feeling included and valued, and they need to be prepared for possible eventualities in much the same way as adults. Children affected by the illness of a close relative include daughters and sons, grandchildren, and nephews and nieces. It is natural for adults to want to soften the pain and shock of bad news, but it is important for children to be told when something is wrong. Sometimes adults want to delay telling children bad news because they hope the next test results or treatment will enable the telling to be less painful. However, there is probably

never a 'right' time, and putting things off usually makes the difficulties greater. A good time may never arrive, and it may become increasingly difficult to explain why such important information was not given earlier.

Sometimes adults think that by not saying anything about someone's illness their children will somehow not be affected. However, the reality is that, even if adults try to hide from their children what is happening, children notice when something is wrong and may blame themselves (e.g. 'I made my mum's illness worse because I behaved badly') unless things are properly explained to them. Children who are not included in being helped to understand such profound changes in their family situation may later feel angry at having been excluded.

Social workers can help parents and other close family members think about making memory boxes or writing letters for their children. A memory box is a collection of significant items, including writings, drawings, recordings of favourite music, and pictures that will remind a bereaved child or adult of important shared experiences. Usually, a memory box will contain photographs, details of special family events, and information about the person who is dying, as well as particular items that help a person to understand more about the dying family member later on. A memory box helps a person to understand their own life story by giving information about the past, and so helps the person to feel more confident about themselves, their identity, and their roots.

Dignity

Maintaining dignity for patients approaching death is a core principle of palliative care. However, translating that principle into methods of guiding care at the end of life can be a complicated and daunting task. Social workers may use dignity therapy, a psychological intervention developed by Dr Harvey Max Chochinov, designed specifically to address many of the psychological, existential, and spiritual challenges that patients and their families face as they grapple with the reality of life drawing to a close. Dignity therapy offers a way to preserve meaning and hope for patients approaching death. It can change the end-of-life experience for those about to die and for those who will grieve their death.

Social work may also help to address spiritual pain by helping to relieve isolation and giving comfort, knowing that concerns, even if unanswered, are taken seriously and recognized as being important and valid. Difficulties such as body image, sexuality, and intimacy may need discussion with a social worker. Patients rarely volunteer these problems and may need prompting to see whether they want to talk about them. Appropriate guidance is needed to help patients and families cope with the changing circumstances.

Practical help involves enabling patients to make decisions and to exercise choice, both for practical reasons and also to promote a sense of worth and dignity. They may need basic assistance in obtaining grants to help with the extra costs incurred as a result of their changed circumstances, to help paying bills, or to execute more complicated tasks such as preparing a will and thinking about the future of dependants. It is important to ensure that patients receive benefits to which they are entitled. The patient and family may want to know about the law and other social institutions, family and mental health legislation, and community services according to

their particular situation. Social workers, along with other palliative care professional workers, have a duty to ensure that vulnerable people who are unable to make their own decisions are empowered and protected by the relevant statutory framework.

Ensuring that patients receive packages of care to enable them to stay in their own home may also be part of the social work role. Some people may need support making decisions about an alternative placement, such as a residential aged care facility. Funding private nursing care is often a source of real anxiety, and the social worker can advise and make referral to appropriate services if the patient is eligible. Continuing care is a complex and sensitive area of healthcare provision and can affect people at a very vulnerable stage in their lives. Social workers can advise people about the different types of healthcare funding, including the principles of eligibility and the assessment process, which will differ from country to country.

In some countries, carers may be entitled to a carers' allowance. Many carers benefit from support at such a distressing time, and by having their own needs assessed they can receive appropriate help and relief. Caring for someone who is terminally ill can place huge personal, financial, emotional, and practical demands on family members and close friends. Carers' groups are often established and facilitated by social workers to give support to people in similar circumstances.

Social workers seek to enable patients and families retain or regain control, to promote empowerment and choice, and to help people find inner strength and confidence. Families and carers can feel powerless in these situations, but social workers can help them set realistic goals and make plans to enable them to make the most of the important time that is left.

After death, bereavement support is fundamental to the role of palliative care social workers, who may work with bereavement support workers and counsellors within the team. Families may be offered individual, family, or group counselling. Social workers may also organize and offer special bereavement sessions for children, teenagers, and younger bereaved spouses.

Further reading

Books

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Chaplaincy

Chaplaincy addresses the spiritual, religious, pastoral, and cultural needs of patients, relatives, and staff in a healthcare context that is increasingly dynamic and pluralistic.

- Cultural needs include the need to be in an environment that reinforces the familiar—this takes in language, food, dress, family and social structures, customs, etc.
- Religious needs include the need for support to practise sacred rituals and hold certain beliefs, and will require provision for prayers, sacraments, holy books, and religious artefacts (e.g. prayer mats, rosary beads).
- Pastoral needs include the need for support at critical moments in the life cycle—relationship formation, illness, death, etc.—typically addressed with reference to particular beliefs or values, religious or otherwise.
- Spiritual needs include the need for a sense of 'well-being', which is often nurtured by being well related to one's self, others, and one's source of ultimate meaning; some chaplains refer to this as 'psychospiritual need' (see Chapter 23).

All members of the multidisciplinary team contribute to spiritual care, but because of their specialist training and by virtue of the fact that chaplains set high value on their own spiritual development—usually formed within the spiritual disciplines of a faith tradition—they are uniquely qualified as specialists in this area. Although most chaplains have a religious affiliation, it is against their codes of professional practice to proselytize: chaplains only address spiritual needs; they never seek to create them.

Religious needs

Many chaplains work generically, offering spiritual care to anyone in need; some are faith-specific. The appointment of chaplains often reflects the proportionality of religious affiliation among the patient group.

Networking with local faith communities

Chaplains routinely network among those religious groups not represented on the chaplaincy staff, and are able to provide local information to help address the usual needs of minority religions. Respect for the religious beliefs and practices of patients, relatives, and staff is fundamental to the ethos of chaplaincy.

Dedicated sacred space/chapel/quiet room

As far as possible, provision must be made for a dedicated space for quiet reflection and prayer. This sanctuary/chapel/prayer room will respect the sensibilities and needs of all and be available for religious services.

Pastoral needs

Marriage

The sanctuary/chapel/prayer room may be used for marriages. In extremis, registrars normally attend a patient at very short notice; however, divorced people must ensure they present all necessary documents to the

registrar. Religious restrictions may set limits on the involvement of some ministers and priests, e.g. the marriage of divorcees by Church of England clergy. Advice must be sought in advance of any proposed ceremony.

Funerals

Chaplains are an important resource to families with technical questions about funerals, access to services, and beliefs.

Many chaplains receive requests to take funerals, either because they have developed a special relationship with a patient or because they were particularly helpful to the patient's relatives. However, the practice of individual chaplains varies:

- Some want to continue an established pastoral relationship, in order to personalize the funeral, or to encourage a more open attitude to the funeral liturgy.
- Others prefer to encourage the community-based provision of bereavement and pastoral aftercare.

Bereavement and remembrance services

Where chaplains are not centrally involved in providing bereavement support, they are likely to work closely with the bereavement service to organize remembrance events. Most hospices hold remembrance services, either regularly or as an annual event, typically around Christmas time.

Spiritual needs

Chaplains offer themselves to patients and their carers as 'soul friends' and, according to their training, they provide a broad range of support:

- listening/counsel
- prayer/sacrament
- life-review/reminiscence

Sharing the patient's journey—to the extent to which they are invited—chaplains will contain anxiety, absorb hostility (directed at their representative role), challenge and stand by patients and families. Chaplains will be non-judgemental.

Healing

See also Spirituality and healing, pp. 661–2.

Healing can be understood as physical cure, be that medically or miraculously. But it is also applied to a range of therapeutic activities. Most religious traditions include prayers and rituals for healing, and many chaplains have experience or training in healing prayer. A ministry of healing is normative in many Christian churches, and ranges from informal prayers to short, formalized liturgical services; either may include 'the laying on of hands'.

Trained spiritual healers, with no particular allegiance to an established faith tradition, are an emerging feature within spiritual care. Independent healers—ones who are not themselves chaplains or part of the chaplaincy team—should belong to a healing organization regulated by UK Healer, e.g. the National Federation of Spiritual Healers or the Complementary and Natural Healthcare Council.[1]

Chaplains as professional colleagues

Multidisciplinary working

Chaplains bring a particular perspective to the multidisciplinary team, and expect to participate fully in team meetings. Because chaplains work with the highest regard for confidentiality, there should be an easy flow of communication between chaplains and multidisciplinary colleagues.

Training levels

In the UK there is currently no universally required qualification for healthcare chaplains. Traditionally, chaplains have been recruited from within the faith traditions and will normally have a religious formation. However, the professionalization of healthcare chaplaincy is aiming to establish graduate entry, and postgraduate programmes are available through several universities. Professional chaplaincy bodies, collaborating under the multifaith umbrella UK Board of Healthcare Chaplains (UKBHC), expect ongoing, in-service training as well as continuing professional development. UKBHC sets standards and maintains a register of UK chaplains.

Assessment

A number of assessment models are available, but it is often inappropriate to attempt a formal assessment of spiritual need.

Chaplains consider a patient's spiritual, religious, and pastoral needs, as well as their cultural needs, and welcome insights from colleagues on the multidisciplinary team. Chaplains continually assess patients' spiritual needs, which they will document in patient notes as appropriate.

Availability

Chaplaincy provision is a requirement of specialist palliative care, but staffing levels depend upon the resources of the individual unit. The chaplaincy time with patients will vary. Most units have 24-hour cover from chaplains, sometimes with support (voluntary or paid) from local clergy; some units have teams of chaplaincy volunteers.

Staff support

Chaplains typically support staff in one-to-one counselling support and clinical supervision of individuals and groups, supporting the organization spiritually, and in creating memorials or ceremonies to mark important moments in the life of the institution.

Education and research

Chaplains have a key role in teaching spiritual care; depending on their experience and expertise, some also undertake research for publication in peer-reviewed journals, including the professional chaplaincy journals *Health & Social Care Chaplaincy* and *Journal of Health Care Chaplaincy* (USA).

Awareness of religious diversity

All religions contain a wide variation of approaches to their faith, from orthodox practitioners, for whom correct procedures are vitally important, to liberal groups, who are likely to be quite relaxed about their practices. Religious obligations frequently relate to the following:

- alcohol
- carers of a different sex or gender
- food
- religious objects
- privacy
- washing
- touching/preparing the body after death

All religions have a concern with death, and provide rituals and customs associated with the processes of dying. Some faiths require religious ministers to carry out particular rituals, while others will accept suitably experienced lay people to officiate.

Avoiding assumptions in caring for religious needs

Even when patients identify with a religious group, it should be kept clearly in mind that people are individuals and that their belonging will always be particular to them. It is not unusual for the beliefs and the behaviours of a healthy individual to change, sometimes dramatically, when they become terminally ill: a religious label noted on a hospital form is a poor indicator of an individual patient's past or current beliefs, practices, or preferences.

To sensitively and effectively care for a dying patient, it is necessary to understand their philosophy of life, their religious beliefs, and their expectations about what might happen after death. Chaplains are skilled in gaining this kind of information by a sensitive mix of observation, careful active listening, and tactful questioning of the patient and family.

The following guidelines can only indicate very general points around 'Care for the dying' and 'Procedure at death' for patients from faiths most commonly encountered in the UK.

Two helpful principles

- Always check with the patient (and/or family) concerning beliefs and practices, even if these are many years past.
- When in doubt, follow the more orthodox procedures.

Buddhists

Care of the dying

- A basic Buddhist belief is that a person's state of mind at the moment of death influences the character of their rebirth.
- Some patients may want help to find quiet for meditation; some may welcome Buddhist chanting to influence their state of mind.
- Some may wish to avoid palliative treatments that lessen conscious capacity or awareness as they approach the moment of death.
- Buddhists may require vegetarian food.

Procedure at death

- It may be necessary to contact a Buddhist priest after a death.
- Buddhists normally prefer cremation to burial.

Christians

Care of the dying

- Many Christians will want access to a Bible; some may welcome a prayer book or hymn book.
- Even where the chaplain shares their faith, practising Christians may want their own religious minister to pray with or for them.
- Pentecostal Christians may want to pray for physical healing, even if the patient is close to death. The patient may welcome this and staff should be clear about the patient's desires and respond appropriately.
- Roman Catholic/Orthodox Christians will likely want a priest to hear their confession, bring Holy Communion, and offer the Sacrament of the Sick.

Procedure at death

- There are no special requirements; Christians may be buried or cremated.

Hindus

Care of the dying

- For Hindus, there is religious significance in dying at home, and Hindu patients may welcome support to die in their home setting.
- Inpatients may welcome the priest (*pandit*) to read holy texts and perform holy rites.

Procedure at death

- Non-Hindus should not touch or wash the dead body—family members will want to wash and prepare their dead relative.
- In the absence of family members, healthcare staff should
  - use disposable gloves to straighten the limbs and close the eyes;
  - leave jewellery, sacred threads, and religious objects on the body;
  - wrap the body in a plain sheet.
- Hindus normally request cremation.

Jews

Care of the dying

- Orthodox Jews will want Jewish (kosher) food, which their relatives may want to provide; the family or a rabbi should be consulted for advice and they may need help to meet this requirement.
- There are no 'last rites', although a Jewish patient may want a rabbi to visit; staff should try to find the appropriate rabbi for the patient, i.e. orthodox for orthodox, liberal for liberal.
- The Jewish emphasis on the present life may mean that patients or families question treatments that could be seen to weaken the fight for life.

Procedure at death

- If possible, the body should not be touched by non-Jews. However, if this causes difficulties, even the strictest Jews will permit healthcare staff to do the following:
  - bind the lower jaw;
  - straighten the arms and lay the hands at the side of the body;
  - wrap the body in a plain sheet.

- Ideally, the dead body should not be left alone, and some Jews have watchers to stay and recite Psalms.
- The family—or, in their absence, a Jewish undertaker—should be informed immediately and (except during the Sabbath [Friday dusk to Saturday dusk] or festivals), a funeral should be held as soon as practicable, preferably within 24 hours.
- Post-mortem examinations are forbidden unless ordered by the coroner, in which case they must be carried out as soon as possible.

Muslims

Care of the dying

- Fasting during the Holy month of Ramadan is a requirement of all Muslims; however, sick patients are exempt.
- The majority of Muslims will want Islamic (*halal*) food; some will not accept medicines if they contain alcohol.
- Muslims will need facilities for washing as an essential prerequisite to performing their daily prayers.

Procedure at death

- People of the opposite sex should only touch the body if absolutely necessary and should wear disposable gloves; family members will want to prepare their dead relative for burial.
- In the absence of family members, healthcare staff should
  - avoid washing the body;
  - wrap the body in a plain sheet.
- Because Islam teaches the resurrection of the body, Muslims will normally request burial, which should be arranged as soon as possible.
- Post-mortem examinations are forbidden unless ordered by the coroner, in which case they should be carried out as soon as possible.

Sikhs

Care of the dying

- As an act of faith, Sikhs wear five symbols (known as the Five Ks): uncut hair (*Kesh*); small comb in the hair (*Kangha*); steel wrist band (*Kara*); dagger (*Kirpan*); white shorts (*Kaccha*)—these symbols must be respected at all times.
- Sikhs may get strength from reciting hymns from their holy book, the *Guru Granth Sahib*; any practising Sikh may help with this.

Procedure at death

- Family members will want to wash and prepare the body, but there are no restrictions on non-Sikhs attending a dead Sikh.
- In the absence of family members, healthcare staff should:
  - pay special regard to the Five Ks;
  - refrain from cutting or trimming the hair or beard;
  - straighten the limbs and wrap the body in a plain sheet.
- Sikhs normally request cremation.

Further reading

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Nolan S. (2009) In defence of the indefensible: an alternative to John Paley's reductionist, atheistic, psychological alternative to spirituality, *Nursing Philosophy* **10**(3), 203–13.

Useful websites

Chaplaincy websites

www.ahpcc.org.uk Association of Hospice and Palliative Care Chaplains
www.healthcarechaplains.org College of Health Care Chaplains
www.sach.org.uk Scottish Association of Healthcare Chaplains
www.nihca.co.uk Northern Ireland Healthcare Chaplains Association
www.hcfbg.org.uk Healthcare Chaplaincy Faith and Belief Group

Religion/culture websites

www.bbc.co.uk/religion BBC Religion & Ethics
www.corab.org.uk Commission on Religion and Belief in British Public Life
www.interfaith.org.uk Interfaith Network for the UK
www.shapworkingparty.org.uk The Shap Working Party on World Religions in Education

Pharmacy

Within recent years, recognition of the knowledge and skills that a pharmacist can contribute within palliative care has led to an increasing number of hospitals and hospices appointing a specialist palliative care pharmacist to work as an integral member of the multiprofessional palliative care team.

The palliative care pharmacist is responsible for specialist medicines and pharmaceutical-related issues in the care of palliative patients. Palliative care patients are often prescribed multiple medicines to manage the symptoms or side effects created by their treatment or medication, and the specialist palliative care pharmacist can assist the patient to achieve concordance with optimal medications.

The role of the specialist palliative care pharmacist will vary according to local practice, but should include most of the following aspects.

Provision of a clinical service to palliative patients

Specialist palliative care pharmacists working within a hospital or hospice have a clinical responsibility to the patients, and their duties may include the following:

- responsibility for specialist advice on the use of medicines in palliative care, especially as many medicines are unlicensed or are used off-licence
- confirming patients' previous medication history and making recommendations for rationalizing patients' medication on admission to the hospital or hospice
- monitoring inpatient prescribing for appropriate dose, formulation, interactions, and compliance with guidelines and policies
- coordinating with other healthcare professionals to resolve any medication-related issues
- assisting with the procurement of specialist palliative medicines and management of medication stock
- participating in consultant-led ward rounds and multiprofessional team meetings to provide specialized advice
- disseminating drug alerts, ensuring that they are appropriately actioned
- practising as a supplementary or independent non-medical prescriber to assist in timely alterations to the inpatient prescription in response to change in a patient's symptoms
- promoting antimicrobial stewardship to ensure appropriate prescribing

Helping patients to accept and understand their medication

As patients' symptoms change, their medication regimens will change, and the pharmacist will be in a position to counsel and reassure patients and their carers by the following means:

- explaining why their medicines have been prescribed or changed, and how the medicines work to alleviate their symptoms
- ensuring that medication is in an acceptable form to take, whether as solid dose, liquid, buccal, rectal, transdermal, or parenteral preparations, and advising on alternatives as the patient's condition or symptoms progress
- ensuring that the patient knows when and how to take their medicines to achieve optimum relief of their symptoms with minimal side effects

Liaison with community pharmacy services and nursing homes on discharge from hospital or hospice

Palliative patients are frequently weak and debilitated, and anxious about their medication; they should have access to a prompt and efficient community pharmacy service. The specialist palliative care pharmacist is ideally situated to do the following:

- communicate with the community pharmacist to ensure consistent standards of care with a continued supply of specialist medication on the patient's discharge from hospital or hospice
- provide individualized advice to nursing homes on the use of medicines to manage a patient's symptoms
- provide written information on the specialist use of medicines for the patient and carer, community pharmacist, GP, and other healthcare professionals when necessary
- inform the patient's GP and community nurse about any specific monitoring requirements for medicines when patients are transferred from the specialist setting back into the community
- provide aids to assist the patient and their carers in coping with medication at home

Teaching and training other healthcare professionals in palliative care pharmacy-related issues

The principles of palliative care enshrine the principles of good practice for all healthcare professions. A specialist palliative care pharmacist may be expected to do the following:

- contribute to the provision of training on medicine use in symptom control for pharmacy students, medical students, nurses, and other healthcare professionals
- review journals to ensure that current practice reflects the latest research and evidence
- assist nurse specialists in the provision of syringe driver training for nursing staff
- assist in training on prescribing for syringe drivers to medical and pharmacy staff

Participation in service development, research, and audit

Palliative care is a relatively new specialty within pharmacy, and there is an expanding knowledge base on the use of medicines to manage symptoms in palliative care. A specialist palliative care pharmacist is in a position to do the following:

- contribute to the development of local, regional, or national guidelines and protocols in light of a growing evidence base
- audit local prescribing practice for compliance with guidelines and protocols to ensure safe, maximal patient care
- develop the service within their own locality to provide safe, legal, timely, and convenient access to medicines for the optimum benefit of patients and their carers

Art therapy

Art therapy is a form of psychotherapy that uses art media to produce images as its primary mode of communication. Images may be 2D or 3D. Patients need no previous experience or skill in art. The overall aim is to enable a patient to effect change and growth on a personal level through the use of art materials in a safe and facilitating environment.

The relationship between the therapist and the patient is of central importance. Art therapy differs from other psychological therapies in that it is a three-way process between the patient, the therapist, and the image. It offers the opportunity for expression and communication, and can be particularly helpful when people find it hard to express their thoughts and feelings. Issues may emerge very quickly when working on an image, enabling the patient to explore and resolve them through the art-making.

Art therapists have considerable understanding of art processes, underpinned by a sound knowledge of therapeutic practice. They work with both individuals and groups in a variety of palliative care settings. The process—what happens in a session—is confidential between the patient and therapist, and a degree of privacy is essential. Art therapists have become adept at securing this privacy even when working at the bedside in a busy ward or in the client's home as part of the community team.

Many facilities now have a designated art therapy space with good lighting, an accessible work area, and secure storage for images. The art therapist is a key professional in the provision of psychosocial support, working within the interdisciplinary team, attending team meetings, and providing assessments and feedback. Art therapists can also provide staff support and team reflection where there has been a particularly difficult or complex death. Bereavement programmes for children and families, partners, and parents often have a significant art therapy component.

Art therapists work psychodynamically with complex and challenging issues, which call for skill and sensitivity in working with this particularly vulnerable client group. The training, which combines theoretical and experiential work, is generally an advanced diploma, degree, master's or postgraduate diploma.

Art therapists maintain high standards of professional care and are registered in many countries. To protect both the patient and therapist, members should undertake professional clinical supervision (usually one session for every 20 client hours) with an ongoing programme of continuing professional development. Art therapists should also abide by a code of conduct and ethics.

Further reading

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Music therapy

> And lull'd with sound of sweetest melody?
>
> Shakespeare, *2 Henry IV*, III. i. 14

References to the therapeutic use of music across many cultures date back to ancient Egypt. In the twentieth century, a growth in interest in the therapeutic properties of music from musicians, psychologists, and doctors culminated in the formation of professional groups in the UK such as the Association of Professional Music Therapists, and, more recently, state registration with the Health Professions Council, alongside other arts therapies and allied health professions. Early work in special needs education laid the foundations for music therapy in a wide range of fields, including mental health, neurology, care of the elderly, and palliative care. Postgraduate training courses, leading to qualifications at diploma and master's level, equip therapists with an understanding of child development, psychology, psychodynamic theory, and the physical and emotional effects of music. As with art therapy, clinicians are qualified to work at levels 3 and 4 in the recommended model of psychological support in NICE guidance.[1]

Music therapists may use techniques which involve the use of prerecorded music to meet specific clinical goals, such as relaxation and pain control. However, more often they will create music with patients in joint musical improvisation or song writing, where the nature and scope of the work is multidimensional. Such interactive techniques may provide the vehicles for individuals to express their inner feelings relating to suffering and loss, or help them gain a sense of meaning and control over their lives. Whilst no musical skill is required to participate in therapy, the experience of co-producing improvised music and songs with therapists may open up new avenues of creativity as well as providing a sense of accomplishment for patients. Music therapy may take place in designated therapy rooms (ideally soundproofed), hospital wards, day hospices, or the patients' homes.

Palliative care providers are increasingly incorporating music therapy posts as part of their psychosocial provisions for patients, the bereaved, and carers; the discipline's holistic approach provides a natural fit with palliative care philosophy.

This expansion has provided the impetus for a wide range of studies, ranging from those exploring patient and staff experiences of music therapy, to the more empirical investigations providing evidence for pain reduction, improved mood, decreased fatigue, and increased spirituality.[2-4]

Music has been described as the most social of all art forms. This is well illustrated by the ability of music therapists to collaborate with a wide variety of other disciplines—e.g. joint physiotherapy/music and movement work, and music reminiscence projects, and with spiritual care professionals in planning remembrance services. Sensitively performed live music may also enhance healthcare environments, providing a humanizing influence on clinical settings such as hospital wards. However, professionals untrained in music therapy wishing to utilize the benefits of music should seek guidance from registered clinicians, as patients may be defenceless against the emotional impact of this powerful medium.

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Further reading

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O'Callaghan C. (2004) The contribution of music therapy to palliative medicine. In *Oxford Textbook of Palliative Medicine* (3rd edn) (ed. D. Doyle et al., pp. 1041–6). Oxford: Oxford University Press.

Websites

Association of Professional Music Therapists and British Society For Music Therapy http://www.apmt.org/

Towersey Foundation (music therapy in palliative care) http://www.towerseyfoundation.org.uk/

Chapter 25

Complementary and alternative medicines

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Group 1: Alternative medical systems *721*
Group 2: Mind–body therapies *725*
Group 3: Biologically based practices *732*
Group 4: Manipulative and body-based therapies *736*

Introduction

Complementary and alternative medicines (CAM) comprise a diverse array of treatment modalities that are not presently considered part of conventional/mainstream medicine. CAM emphasize a holistic approach towards healthcare, i.e. they are based on the belief that mind, body, and spirit are interconnected, and that health depends on wholeness and balance between them.

Definitions

- *alternative* treatments aim to replace conventional treatments
- *complementary* treatments are used alongside the conventional treatments
- *integrated* (or US integrative) treatments aim to combine best conventional treatments with best complementary treatments

Types of therapy

In palliative and supportive care, CAM is primarily used to increase the client's well-being and even improve quality of life, such as alleviating pain and other symptoms of the disease, improving sleep, decreasing stress and anxiety, and reducing the adverse effects of conventional treatments. They are often used as an addition to conventional treatments. Some CAM modalities claim a direct effect in the prevention or treatment of cancer. Widely practised treatments are acupuncture, aromatherapy, herbalism, homeopathy, hypnotherapy, reflexology, relaxation, and energy therapies.

The individual therapies described in this chapter will be considered under four headings: alternative medical systems; mind–body therapies, biologically based practices, and Manipulative and body-based therapies.

Principles of CAM

A central tenet of CAM is the strong belief in the uniqueness and wholeness of the individual and the ability of the body to heal itself.

Patients who consult complementary practitioners often have chronic conditions that are difficult to manage, such as chronic pain, rheumatological conditions, and cancer. The interest in CAM in the palliative care setting is perhaps not surprising given the inherent need for the terminally ill to feel supported with respect to physical, psychosocial, and emotional domains in achieving an acceptable quality of life.

Prevalence

Precisely what constitutes complementary medicine differs considerably between countries. Different historical developments and traditions mean that therapies such as herbal medicine and massage are firmly established in mainstream medicine in many European countries, while they are often classified as complementary, even alternative, outside Europe. Regardless of these national differences and inconsistencies in many surveys, there is evidence that CAM is used by a sizeable proportion of both adult and paediatric populations (see Table 25.1).

Prevalence studies in patients with life-threatening or chronic illnesses from Europe and the USA report an average CAM use in cancer patients of

Table 25.1 One-year prevalence of CAM in general population samples

Country	Year	Sample (*n*)	Prevalence (%)
UK	2001	669*	28
USA	2004	31,044*	**36**(excl. prayer)
Germany	2004	1750*	62.3
Japan	2002	1000**	76

*Representative **random.

35–40%. Another survey reports CAM use in cancer patients at 7–54%. Small surveys in the UK have reported similar results.

An increasing number of departments of oncology employ at least one type of CAM practitioner in the palliative care setting, with most hospices now offering a range of complementary therapies for their patients. Initially, therapists were largely volunteers, but units increasingly recognize CAM as part of basic and expected care.

Reasons for seeking CAM

One important and consistent finding is that the majority of CAM use does not occur instead of conventional medical care, but in addition to it. A number of explanations for patients seeking CAM have been proposed. Perhaps the most obvious reason for trying CAM is that more health professionals are recommending to their patients to access it, as there is more evidence to support its use. Other reasons include being persuaded by the media, a recommendation from someone else who has tried something, or by personal experience. Many consumers are convinced that CAM is effective and improves psychosocial functioning. CAM is often also wrongly perceived as the *only* medicine that addresses the cause of an illness rather than the symptoms. There are many websites that are very informative about things to consider when seeking the use of CAM. Some of these are listed at the end of the chapter.

Certain fundamental premises of most forms of CAM contribute to its persuasive appeal. One of these is the perceived association of CAM with nature. It is linked with certain terminology such as 'natural' rather than 'artificial', 'pure' as opposed to 'organic'. 'Natural' is also often somewhat naively equated with 'safe'. Another fundamental component of CAM is 'vitalism'. The enhancement or balancing of life forces, which is central to many forms of CAM, has an intuitive appeal to patients because of the non-invasive notion of healing from within. Many therapies have long intellectual traditions and sophisticated philosophies contributing to their credibility and authority. Spirituality, which bridges the gap between the domains of medical science and (religious) belief, is a further element in the appeal of CAM. CAM's approach tends to be person-centred; the language is one of unity and holism in contrast to the often distant, reductionist terminology of normative science.

The main reasons why people use CAM can be categorized in 'push' and 'pull' factors.

Possible factors contributing to CAM use

Push factors

- dissatisfaction with orthodox medicine
  - ineffective
  - adverse effects
  - poor communication with doctor
  - waiting lists
  - cost
- rejection of orthodox medicine
  - anti-science or anti-establishment attitude
- desperation

Pull factors

- philosophical congruence
  - emphasis on holism
  - active role of patient
  - explanation intuitively acceptable
  - natural treatments
- personal control over treatment
- good relationship with therapist:
  - on equal terms
  - time for discussion
  - allows for emotional factors
- accessibility

Evaluation

Negative attitudes towards research in the palliative care setting, which encompass ethical and methodological issues, particularly when patients are reaching their last few weeks of life, are pertinent. In addition, there are those who argue that scientific evaluation of CAM in the palliative care setting is not needed since patients feel better after therapy. However, these attitudes, and the relative lack of research evidence, have long been a barrier to collaboration between conventional and complementary practitioners. The provision of CAM in mainstream care can, however, only be based on solid evidence, and research efforts have been demonstrably increased over the last decade. The evidence for or against CAM treatments in palliative care that have been tested in controlled clinical trials is discussed in the following therapies sections.

Safety

A common reason for using CAM is that it is erroneously considered safe—certainly safer than conventional medicines. Even when a particular therapy's effectiveness is in doubt, it is often still taken because of the belief that 'It may not work but it won't do any harm'. Although some CAM treatments are associated with only mild and rare risks, others are harmful in a number of ways. Herbal medicines have been associated with toxicity, herb-drug interactions, and contamination. Acupuncture and chiropractic have been associated with serious adverse events such as pneumothorax and stroke; hypnosis may be associated with negative physiological and psychological effects.

There are also more general safety issues associated with CAM as a whole. CAM can be dangerous when it causes the patient either to be misdiagnosed or if it delays access to life-saving treatments. CAM is potentially dangerous when patients self-medicate. Often, patients do not tell their doctors about their CAM use, and doctors often fail to ask patients about it.

The notion that CAM is safe can be dangerously misleading. The situation is not helped by a serious level of under-reporting of adverse events. To date, no effective system is in place for recording and analysing the occurrence of adverse events.

Practitioner accountability

Legislation and statutory regulation that restricts the practice of CAM varies between countries. There is no legislation that restricts the practice of CAM in the UK or Australia. Osteopathy and chiropractic are the only two complementary professions that, so far, have achieved statutory regulation in the UK. In Australia, Chinese medicine, chiropractic, and osteopathy have statutory regulation.

Many other CAM have a recognized body or association where practitioners are encouraged to be members. Such associations provide guidelines that support practitioners with their professional practice. As they are not regulated, membership is not compulsory.

It is important that patients consult a CAM practitioner who is fully qualified and a member of a recognized body or association and holds professional liability insurance cover, and also that the recognized body has a code of ethics and conduct, as well as a complaints and disciplinary procedure.

Useful resources of how to find a practitioner can be found on the internet. Most modalities have associations, organizations, or councils with a list of appropriately qualified practitioners.

Conclusions

The use of CAM alongside conventional medicine in palliative care is increasing and is perceived as contributing to improvements in symptom control, well-being, and satisfaction. It is seen as an important component of best practice in cancer care. It is, however, important to use treatment modalities backed up by research evidence and not to deceive patients.

Further reading

Books

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Websites

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- https://nccih.nih.gov/health/integrative-health
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- https://www.cancer.org.au/content/about_cancer/treatment/Understanding_complementary_therapies_booklet_April_2018.pdf
- https://www.tga.gov.au/sites/default/files/australian-regulatory-guidelines-complementary-medicines-argcm.pdf
- http://www.csh.umn.edu/education/online-learning-modules-resources/online-learning-modules

Group 1: Alternative medical systems

Alternative medical systems are complete systems of theory and practice. Examples of alternative medical systems developed in Western cultures are homeopathy and naturopathy. Others have evolved apart from and earlier than the conventional medical approach used in the West, e.g. traditional Chinese medicine and Ayurveda.

Acupuncture

Background and theory

The history of acupuncture dates back more than 2000 years. It is an integral part of traditional Chinese medicine (TCM) and based on its principles. *Acupuncture* involves the stimulation of certain points on the body by inserting fine needles, whereas *acupressure* involves firm manual pressure on these points.

The workings of the human body are thought to be controlled by a vital force or energy called 'qi' (pronounced *chee*) which circulates between organs along channels called meridians. The twelve main meridians are thought to correspond loosely to twelve major functions or organs of the body. On these meridians, more than 350 acupuncture points have been defined, and it is believed that qi energy must flow through each of the meridians and organs for health to be maintained. The acupuncture points are situated along the meridians and through these the flow of qi can be altered. Traditional acupuncture theory is based on the concept of yin and yang, which should be in balance: any imbalance (particularly blockage or deficiency) in the continuous flow of energy causes illness. Acupuncture point stimulation redresses this balance, allowing the healthy unimpeded flow of qi.

There are many different schools of acupuncture. Western medical acupuncturists relate acupuncture points to various physiological and anatomical features such as peripheral nerve junctions. The concept of 'trigger points' has also been recognized, whereby areas of increased sensitivity within a muscle cause referred pain in relation to a segment of the body.

There is no evidence to confirm the physical existence of qi or the meridians. However, attempts have been made to explain the effects of acupuncture within a conventional physiological framework. It is known that acupuncture stimulates A delta nerve fibres which enter the dorsal horn of the spinal cord and mediate segmental inhibition of pain impulses carried in the slower unmyelinated C fibres. Through their connections with the midbrain, descending inhibition of C-fibre pain impulses is also enhanced at other levels of the spinal cord. It is also known that acupuncture stimulates the release of endogenous opioids and other neurotransmitters such as serotonin, which are involved in the modulation of pain.

Uses

Acupuncture is used in the management of pain, anxiety, fatigue, and digestive disorders, among other uses.

Practical application

Acupuncture may be delivered in a number of ways. Between four and ten needlepoints are typically selected. These points are often located in areas

where they represent the relevant local, regional, and distant meridians. Needlepoints may also be centred around the area of pain.

In the UK, the practice is to use sterile disposable needles which are usually inserted to a depth of about 5 millimetres (or more deeply into muscle). Needles are left in situ for approximately 15 minutes. Needle sizes differ, but typically measure up to about 30mm long and 0.25mm in diameter. It is possible that the sensation of 'de qi' (pronounced *dechee*), which causes feelings of soreness or numbness at the point of needling, is necessary both to indicate that the anatomically correct site has been needled and that the treatment will work well. However, the treatment is also often considered successful in the absence of de qi or any sensation at the point of skin puncture.

Stimulation of the acupuncture point can be increased by gentle turning or manipulation of the needles, or using a small electric current, laser beams, or ultrasound. Acupuncture studs remain in situ and may be pressed by the patient as necessary to give more sustained stimulation. In *moxibustion*, the needles are heated by smouldering a substance called moxa over the points.

Evidence of effectiveness

Good evidence exists to support acupoint stimulation in treating the nausea and vomiting induced by chemotherapy: adjunct stimulation with needles and electroacupuncture has been shown to reduce the incidence of acute vomiting but not nausea, while acupressure reduced nausea but not vomiting.

For relieving cancer pain, some encouraging short-term results have been reported, but there is not enough evidence available to make any firm conclusions. Similarly, insufficient evidence is available for the relief of cancer-related fatigue, chronic obstructive pulmonary disease, dyspnoea, Alzheimer's disease, Parkinson's disease, multiple sclerosis, and pain associated with cystic fibrosis and chronic heart failure. Hence, acupuncture is unlikely to be beneficial for neuropathic pain associated with AIDS/HIV.

Safety

Acupuncture is generally considered to be a relatively safe form of treatment with a low incidence of serious side effects if practised by a skilled practitioner. Some events, such as nausea and syncope, can be mild and transient. While there is no official mechanism for reporting adverse events, there have, however, been accounts of pneumothorax, septicaemia, spinal injuries, and hepatitis B/C transmission. The use of acupuncture studs in the ear may result in perichondritis of the underlying cartilage.

Acupuncture should be used with care in any patient in whom there is a risk of infection or bleeding. It should be avoided in patients with valvular heart disease. Acupuncture to spinal muscles should be safe unless there is an unstable spine, in which case it is contraindicated. Extra care should be exercised in those patients receiving their first acupuncture treatment as they may react strongly, with dizziness and drowsiness. The initial treatment should be given supine, and patients should be advised not to drive or to operate machinery for a few hours.

Homeopathy

Background and theory

Homeopathy was founded by the German physician Samuel Hahnemann (1755–1843). This method often uses highly diluted preparations of a variety of different substances. Homeopathy is based on two key principles. The first is that 'like cures like'. Patients are given preparations whose effects, when administered to healthy subjects, correspond to the manifestations of the disorder (symptoms, clinical signs, and pathological states) in the unwell patient. For instance, hayfever, which presents with lacrimation, stinging, and irritation around the eyes and nose, might be treated with the remedy *Allium cepa*, derived from the common onion. According to the second principle, remedies are prepared by a process of serial dilution and succussion (vigorous shaking). The greater the number of times this process of dilution and succussion is performed, the greater the potency of the remedy. Homeopathic medicines are diluted so much that they are unlikely to contain even a single molecule of the original substance.

Prescribing strategies vary considerably. In 'classical' homeopathy, practitioners aim to identify a single medicine that is needed to treat a patient, taking into account current illness, medical history, personality, and behaviour. 'Complex' homeopathy involves the prescription of combinations of medicines.

Common homeopathic medicines include those made from plants (e.g. belladonna, arnica, and chamomile), minerals (e.g. mercury and sulphur), animal products (e.g. sepia, or squid ink, and lachesis, or snake venom), and, more rarely, biochemical substances (e.g. histamine or human growth factor).

Uses

Many different—often chronic and recurring—conditions are treated with homeopathic medication. Self-prescription for various conditions such as the common cold, bruising, hayfever, and joint sprains is common.

Practical application

A very detailed history is taken in order to find the optimally matching drug ('similimum'). Information is also gathered about mood and behaviour, likes and dislikes, responses to stress, personality, and food reactions. A 'symptom picture' is thus built up and matched to a 'drug picture' described in the homeopathic *Materia Medica*. One or more homeopathic medicines are then prescribed, usually in pill form, either as one or two doses or on a more regular basis.

A patient's initial symptom picture commonly matches more than one drug picture. Follow-up allows the practitioner to define the best medication for a particular patient.

Evidence of effectiveness

Controlled clinical results report encouraging but not fully convincing results for homeopathic treatment of chemotherapy-induced stomatitis and radiodermatitis. No convincing effects of homeopathy have been reported for general radiotherapy-related side effects, menopausal symptoms in breast cancer survivors, and oestrogen withdrawal in breast cancer patients.

Overall, there is no convincing evidence of the effectiveness of any homeopathic remedy for any condition.

Safety

Serious adverse effects of homeopathic medicines are rare. However, symptoms may become acutely and transiently worse (aggravation reactions) after starting treatment, and patients should be warned of this possibility. The occurrence of an aggravation reaction is interpreted by homeopaths as a sign that the treatment will be beneficial.

The more serious issue is the view of some practitioners who adamantly believe that conventional medication reduces the efficacy of homeopathic remedies. Serious adverse effects have occurred when patients have failed to comply with conventional medication.

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Books

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Group 2: Mind–body therapies

Mind–body medicine uses a variety of techniques designed to enhance the mind's capacity to affect bodily function and symptoms.

Relaxation therapy

Background and theory

Relaxation therapy uses a range of techniques for eliciting the 'relaxation response' of the autonomic nervous system. This results in decreases in oxygen consumption, heart rate, respiration, and skeletal muscle activity, and in the normalizing of blood supply to the muscles. One of the most common techniques is progressive muscle relaxation, which consists of progressive clenching followed by the conscious relaxation of all the muscles in the body in parallel with concentration on breathing control. Other relaxation techniques involve passive muscle relaxation, refocusing, or imagery. In imagery-based relaxation, the idea is to visualize oneself in a place or situation associated with relaxation and comfort.

Uses

Relaxation therapies are commonly used for the relief of anxiety, stress disorders, musculoskeletal pain, and headaches.

Practical application

Relaxation is usually taught in groups or by listening to recordings. With progressive muscle relaxation, the muscle groups are systematically contracted, then relaxed in a predetermined order while the patients are sitting comfortably in a chair or lying on their back. In the early stages, an entire session may be devoted to a single muscle group. With practice, it becomes possible to combine muscle groups and then eventually relax the entire body all at once. Regular practice is often needed in order to be able to evoke the relaxation response within seconds.

Evidence of effectiveness

In cancer palliation, relaxation has been shown to be a useful adjunct for preventing nausea and vomiting associated with chemotherapy and other treatment-related symptoms in patients undergoing, for example, radiotherapy, bone marrow transplantation, or hyperthermia. It has also proved to have a significant effect on decreasing anxiety. Encouraging effects have been reported for the reduction of tension and amelioration of the overall mood, but not enough data are available.

Similarly, data from rigorous trials into the benefits of relaxation therapy are too scarce to make any recommendations for its use in cancer-related fatigue, hot flushes in breast cancer patients, dyspnoea associated with chronic obstructive pulmonary disease, and chronic heart failure.

Safety

Relaxation techniques are not associated with any serious safety concerns. They are, however, contraindicated in schizophrenic or actively psychotic patients. Those techniques requiring inward focusing may intensify a depressed mood.

Further reading

Articles

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Tipton J.M., et al. (2007) Putting evidence into practice: evidence-based interventions to prevent, manage, and treat chemotherapy-induced nausea and vomiting. *Clinical Journal of Oncology Nursing*, **11**(1): 69–78.

Website

Examples of relaxation therapies

https://www.beyondblue.org.au/docs/default-source/senseability/relaxation-techniques.pdf?sfvrsn=2

On some aspects of alternative medicine we are fighting an almost medieval belief in magic but debunking such beliefs is like telling people that the tooth fairy is sniffing glue.

John Diamond

Hypnotherapy

Background and theory

Hypnotherapy involves the induction of deep physical and mental relaxation, resulting in an altered state of consciousness which leads to a greatly increased susceptibility to suggestion. Once patients are guided into a hypnotic trance, they may recall memories not easily accessed by their conscious minds. The dissociation between the conscious and the unconscious mind can be used to give therapeutic suggestions, thereby encouraging changes in behaviour and the relief of symptoms. The goal of hypnotherapy is to gain self-control over behaviour, emotions, or physiological processes. A fundamental principle of hypnotic phenomena is that the hypnotized individual is under their own control and not that of the hypnotist.

Uses

Hypnotherapy is more commonly used for anxiety, for disorders with a strong psychological component (such as asthma and irritable bowel syndrome), and for conditions that are modulated by levels of arousal, such as pain.

Practical application

The initial visit involves gathering a history and discussion about hypnosis, suggestion, and the client's expectations of the therapy; various tests for hypnotic suggestibility may also be conducted. The hypnotic state is achieved by first relaxing the body, then shifting attention away from the external environment towards a narrow range of objects or ideas suggested by the therapist. Sometimes hypnotherapy is carried out in group settings.

Evidence of effectiveness

In children with cancer, hypnosis has potential as a clinically valuable intervention for procedure-related pain and distress. It has also been shown to be helpful for anticipatory and post-chemotherapy nausea, again particularly in children. More data are required for its usefulness in the relief of pain, anxiety, and fatigue, as well as hot flushes in patients with breast cancer.

Safety

Hypnosis is generally safe when it is practised by a clinically trained professional. It can, however, sometimes exacerbate psychological problems, and is contraindicated in psychosis and personality disorders.

Further reading

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Guided imagery and visualization

Background and theory

Guided imagery is a visualization technique based on the notion that the mind can affect the body. It uses imagination and mental images to encourage physical healing, promote relaxation, and bring about a change in attitude or behaviour. Stimulating the brain through visualization may have direct effects on the endocrine and nervous systems, and may lead to changes in immune and other functions.

Uses

Imagery is commonly used by those patients undergoing conventional cancer treatment or surgery, for stress and anxiety, and for chronic pain conditions.

Practical application

Imagery is generally taught in small classes. Patients will either sit in a chair or lie on a treatment table or a floor mat. Sessions usually begin with general relaxation exercises and then move on to more specific visualization techniques, introduced by the practitioner. Patients will be led to build a detailed image in their mind. Patients with cancer, for example, may be asked by their practitioner to picture their cancer being attacked by their immune system, their tumours shrinking, or their body freeing itself of cancer. Once experienced and confident, a patient may be able to undertake guided visualization by themselves.

Evidence of effectiveness

In cancer patients, guided imagery seems to be psychosupportive, decreasing anxiety and depression and increasing comfort. Although some encouraging effects on cancer-related pain have been reported, the available data are insufficient to make any firm recommendations. Guided imagery may increase oxygen saturation in patients with chronic obstructive pulmonary disease, but further data are required to make any firm recommendations.

Safety

Although guided imagery and visualization are generally safe, they are contraindicated in those with severe mental illness, latent psychosis, and personality disorders.

Further reading

Book

Hall E., et al. (2006) Guided Imagery: Creative Interventions in Counseling and Psychotherapy. Thousand Oaks, CA: Sage Publications.

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Meditation

Background and theory

Meditation refers to a range of practices aimed at focusing and controlling attention to suspend thinking and relax the body and mind. It is believed to result in a state of greater physical relaxation, mental calmness, and psychological balance. Meditation comprises a very diverse array of practices, most of which are rooted in Eastern religious or spiritual traditions (e.g. transcendental meditation, Sahaja yoga/meditation, mindfulness meditation, and meditative prayer). They are based on listening to breathing, repeating a mantra, detaching from the thought process, or self-directed mental practices. Meditation is aimed at inducing physiological changes, e.g. altering the fight-or-flight response. It is believed to reduce activity in the sympathetic nervous system and increase activity in the parasympathetic nervous system. The specific mechanisms remain, however, unknown.

Uses

Meditation is often used for the relief of anxiety, asthma, stress, drug and alcohol addiction, epilepsy, heart disease, and hypertension.

Practical application

Two common approaches to meditation are mindfulness meditation and transcendental meditation. In mindfulness meditation, the meditator learns to concentrate on the sensation of the flow of the breath in and out of the body and focus on what is being experienced, without reacting to or judging that experience. Eventually the meditator should learn to experience thoughts and emotions in normal daily life with greater balance and acceptance. Transcendental meditation uses a mantra (a word, sound, or phrase)

repeated silently in order to prevent distracting thoughts from entering the mind. Eventually this should allow the mind to come to a quieter state and the body into a state of deep rest.

Meditators are initially instructed by a teacher in several sessions and then are encouraged to practise regularly. Continuous regular practice is expected to increase the effects.

Evidence of effectiveness

Positive results in patients at the end of life have been reported for mood disturbance, anxiety, depression, anger/hostility, emotional suppression, psychological distress, stress, intrusive images, confusion, and coping mechanisms. For other symptoms and signs—including nausea and vomiting, quality of life, sleep disturbance, and fatigue—there are not enough data available.

Safety

Although meditation is generally safe, patients suffering from psychiatric problems who wish to take up meditation should be supervised by a qualified psychiatrist or psychotherapist experienced in the use of such techniques in a therapeutic context. People with epilepsy or those at risk of developing epilepsy should consider the theoretical risk of precipitating attacks before proceeding.

Further reading

Articles

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Energy therapies

Background

Energy therapies is a general term for many different types. They are all similar, with their own specific differences. The practitioner and a patient interact with the intention of generating improvement. Practitioners believe they channel 'energy' (e.g. of cosmic or divine origin) into patients, which helps to restore balance. The concept is not supported by scientific plausibility.

Uses

Energy therapies are used to alleviate symptoms in a variety of clinical situations, including anxiety and pain, and to promote calmness and general well-being.

Practical application

Energy therapies are generally given in two ways: laying-on of hands or distant healing. In the former, practitioners hold their hands near to but not touching (or only lightly touching) the body, identifying areas of concern

and transmitting 'energy' into the patient's body, which promotes relaxation and allegedly enhances the self-healing potential of the body. In the latter, practitioners send signals mentally as meditation, prayer, or healing wishes from a location that can be many miles away from the patient.

Many varieties of energy therapies exist. These include, but are not limited to, therapeutic touch, healing touch, spiritual healing, and Reiki.

Evidence of effectiveness

There is not enough evidence available to support energy therapies as a treatment for any condition. Although encouraging results for healing touch on cancer-related pain are available, the data are not sufficient to make any firm recommendations. Energy therapies have shown encouraging results in reducing anxiety levels and increasing well-being, but studies are methodologically weak.

Safety

Energy therapies are generally a safe treatment and there are no known serious side effects, although it is contraindicated in those patients with psychiatric illnesses.

Further reading

Book

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Professional organization

National Federation of Spiritual Healers http://www.thehealingtrust.org.uk
Therapeutic Touch International Association http://therapeutic-touch.org

Creative therapies

see Art therapy, p. 712, and Music therapy, p. 713.

Background and theory

In creative therapies, art, music, prose, and poetry are used as alternative forms of expression and communication. These therapies may release suppressed deep fears and feelings and evoke memories that, with careful and sensitive guiding by the therapist, may be used in trying to help the patient work through them constructively and positively. Receptive music therapy uses the analgesic and anxiolytic properties of music, which can lead to a lowering of stress levels and stress hormone production similar to the relaxation response.

Uses

Art and music therapies are popular in palliative care, helping with the patients' feelings of loss, fear, anger, guilt, anxiety, and depression.

Practical application

Both art and music therapists work in a wide range of settings, using art or music to achieve therapeutic goals. Art therapy combines traditional psychotherapeutic theories and techniques with an understanding of the psychological aspects of the creative process, especially the affective properties

of the different art materials. In music therapy, the most basic distinction is between *receptive* music therapy (listening to music played by the therapist or recorded music) for relaxation and pain relief, and *active* music therapy (the patient is involved in music-making) as a form of expression.

Evidence of effectiveness

Only preliminary data exist for the evaluation of art therapy. They relate to improving coping resources in women with primary breast cancer undergoing radiotherapy, and increasing positive and collaborative behaviour in children during painful procedures.

Music therapy has been shown to be beneficial for procedure-related anxiety. In a range of conditions, music therapy has shown encouraging effects, but there are not enough data available to draw any firm conclusions. Clinical music therapy might improve quality of life in patients with terminal cancer; preliminary data are positive for psychological problems in cancer palliation. Music therapy may have some effect in relieving nausea and vomiting associated with chemotherapy. Similar encouraging, yet only preliminary, results have been reported for recorded music as an adjunct during routine chest physiotherapy for cystic fibrosis; for reducing agitation and aggressive behaviour in Alzheimer patients; for strengthening of respiratory muscles through the coordination of breath and speech in multiple sclerosis; and for motor, affective, and behavioural functions in Parkinson's patients. The data are methodologically too limited in patients with dementia.

Safety

There are no known safety concerns associated with art or music therapy.

Further reading

Book

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Group 3: Biologically based practices

Herbal medicine

Background and theory

Plants have been used for medicinal purposes since the dawn of humanity. They form the origin of many modern medicines, e.g. digoxin from *Digitalis purpurea* (foxglove) or salicin from *Salix* spp. (willow). Herbal extracts contain plant material with pharmacologically active constituents. The active principle(s) of the extract, which is in many cases unknown, may exert its effects at the molecular level and may have, for instance, enzyme-inhibiting effects (e.g. escin). A single main constituent may be active, or a complex mixture of compounds may produce a combined effect. Known active constituents or marker substances may be used to standardize preparations.

Modern Western herbalism—or phytomedicine as practised in many European countries such as Germany—is integrated into conventional medicine with compulsory education and training for physicians and pharmacists. It follows the diagnostic and therapeutic principles of conventional medicine.

Other more traditional systems include Chinese herbal medicine, which is based on the concepts of yin and yang and qi energy. In China, ill health is seen as a pattern of disharmony or imbalance, and Chinese herbal medicines are believed to harmonize these energies and ultimately restore health. In Japan, this system of traditional herbal medicine has evolved into *kampo*. Ayurveda, the traditional Indian medical system, frequently uses herbal mixtures. Characteristic of these systems is a high degree of individualization of treatments. In contrast to modern phytomedicine, all traditional herbal medicine systems predominantly use complex mixtures of different herbs.

Uses

Herbal medicine is generally used for a wide range of conditions. In palliative care, it is used for anxiety, depression, pain, radiation-induced dermatitis, chemotherapy-induced nausea, vomiting, hot flushes, and quality of life, as well as for the prevention and treatment of cancer.

Practical application

During an initial treatment session, the practitioner will usually take the patient's medical history. Information may also be sought on the patient's personality and background, which may influence the selection of herbs. Individualized combinations of herbs may be prescribed. Follow-up appointments may be arranged and the herbal preparations and regimen reviewed. The regimen depends largely on the nature and severity of the condition, but consists generally of either one or two appointments per week for a treatment period ranging from one to several weeks. Medication is usually administered orally in the form of tablets, capsules, tinctures, or teas. Topical applications, e.g. ointments and compresses, are also used.

Evidence of effectiveness

No convincing evidence exists for any herbal medicine in the treatment of cancer. The effectiveness of a range of herbal medicines in cancer palliation is unclear owing to insufficient data being available. The herbal medicines for which there is insufficient evidence include the following: cannabinoids

for pain control, appetite, and quality of life; ginkgo (*Ginkgo biloba*) for lymphoedema; ginseng (*Panax ginseng*) for fatigue and quality of life; marigold (*Calendula officinalis*) for radiation-induced dermatitis in breast cancer; and the Chinese herbal remedy *huangqi* for nausea and vomiting induced by chemotherapy. *Aloe vera* showed no convincing effects on radiation-induced skin irritation or oral mucositis. The results regarding black cohosh (*Actaea racemosa*) on hot flushes are contradictory, and it has been associated with liver damage. Cranberry (*Vaccinium macrocarpon*) and phytoestrogens showed no efficacy in the treatment of prostate cancer symptoms or hot flushes, respectively.

In patients with AIDS, the effectiveness of boxwood (*Buxus sempervirens*) as well as tea tree oil (*Melaleuca alternifolia*) for oral candidiasis is unknown. Many different preparations of Chinese herbal mixture exist, but the data are not encouraging for use in patients with AIDS. No evidence of effectiveness is available for St John's wort (*Hypericum perforatum*) on antiviral activity or for topical application of capsaicin to reduce pain.

Ginkgo (*Ginkgo biloba*) improves cognition and function in Alzheimer's disease. The Kampo medicine choto-san might lead to a general improvement. Not enough data are available for *Huperzia serrata*, lemon balm (*Melissa officinalis*), and sage (*Salvia officinalis*). Ginseng (*Panax ginseng*) is likely to be ineffective for improving somatic symptoms, depression, and anxiety.

In chronic obstructive pulmonary disease, the effects of Chinese herbal mixtures, ginseng (*Panax ginseng*) on lung function, and ivy (*Hedera helix*) leaf extract for dyspnoea are not clear. Studies of pomegranate (*Punica granatum*) juice were negative.

In chronic heart failure, extracts from the leaf and flower of the hawthorn (*Crataegus* spp.) may improve cardiac function, while milk vetch (*Astragalus* spp.) has been shown to improve left ventricular ejection fraction. The evidence for shengmai—a combination product including *Panax ginseng, Ophiopogon japonicus*, and *Schisandra chinensis*—is inconclusive owing to the low quality of the studies. Not enough data are available to make any firm recommendations for Ayurvedic medicines, Chinese medicines, Ginseng (*Panax ginseng*), and Kanlijian.

St John's wort (*Hypericum perforatum*) has been shown to be effective in the treatment of mild-to-moderate depression.

The results so far from studies of cannabis (*Cannabis sativa*) for multiple sclerosis are somewhat contradictory, but some data suggest there is an improvement in mobility, pain, and sleep. It might also reduce the number of incontinence episodes, but not enough data are yet available. It is unlikely to be beneficial in reducing tremor. Some preliminary data for ginkgo (*Ginkgo biloba*) suggest it may improve fatigue, symptom severity, and functionality, but not cognitive function.

In Parkinson's disease, preliminary data are encouraging for the use of *Mucuna pruriens*, a traditional Ayurvedic herbal medicine, which is a natural source of levodopa Cannabis (*Cannabis sativa*) is unlikely to reduce tremor.

Safety

Because plant extracts have pharmacological effects, their potential for adverse effects and interactions needs to be considered. They vary for each individual herb and should be evaluated individually. St John's wort (*Hypericum perforatum*), for example, interacts with warfarin and the

contraceptive pill, while kava (*Piper methysticum*) has been associated with liver damage. In general, those patients taking herbal medication on a regular basis should receive regular follow-up and appropriate biochemical monitoring. Patients should always be asked about self-prescription use of herbal medicine. In the UK, the MHRA Yellow Card Scheme can be used to report adverse effects from herbal or homeopathic products https://yellowcard.mhra.gov.uk/

Other safety issues associated with herbal medicines are toxicity, contamination (in particular traditional Chinese medicines), adulteration, and misidentification or quality issues.

Further reading

Books

Basch E.M., Ulbricht C.E. (eds) (2005) *Herb and Supplement Handbook: The Clinical Bottom Line*. St Louis, MO: Elsevier Mosby.

Braun L., Cohen M. (2005) *Herbs and Natural Supplements: An Evidence-based Guide*. Sydney: Elsevier Mosby.

Article

Linde K., et al. (2005) St John's Wort for depression. *Cochrane Database of Systematic Reviews*, **2**: CD000448.

Databases

Natural Medicines https://naturalmedicines.therapeuticresearch.com

The Natural Medicines Comprehensive Database http://www.naturaldatabase.com/

Therapeutic Goods Act: Complementary Medicine Regulation, Australia (2016) https://www.tga.gov.au/sites/default/files/australian-regulatory-guidelines-complementary-medicines-argcm.pdf

Professional organizations

The British Herbal Medicine Association http://www.bhma.info/

National Herbalists Association of Australia http://www.nhaa.org.au

Aromatherapy

Background and theory

Aromatic plants, and the infusions prepared from them, have been employed in medicines and cosmetics for thousands of years. Aromatherapy uses oils extracted from plants, which are usually referred to as 'essential oils'. These are the pure, concentrated hydrophobic liquids containing the volatile essences of plants: flowers (e.g. rose), leaves (e.g. peppermint), barks (e.g. cinnamon), fruits (e.g. lemon), seeds (e.g. fennel), grasses (e.g. lemongrass), bulbs (e.g. garlic), and other plant substances. Fresh plant material usually yields 1–2% by weight of essential oil on distillation. A typical essential oil contains a complex mixture of over 100 different chemical compounds, which give the oil its smell, therapeutic properties, and, in some cases, its toxicity.

! Essential oils are highly toxic if ingested undiluted.

Essential oils are considered to act not only on the body, by stimulating physiological processes, but also on the emotions and the mind. Odour stimulates the olfactory senses and these relay to the limbic system, which is central to the emotions and memory. In turn, the limbic system is associated with the hypophyseal–pituitary axis, which regulates the endocrine system, affecting a person's reactions to fear, anger, metabolism, and sexual stimuli.

Practical application

Usually, diluted essential oils are applied to the skin through gentle massage. The individual choice of oil, lotion, or cream is determined by the experience of the therapist. Essential oils are also used in diffusers, baths, and spritzers.

Evidence of effectiveness

Aromatherapy in combination with massage has positive short-term effects on psychological well-being in cancer patients, with the effect on anxiety supported by limited evidence. The effects on physical symptoms such as nausea and vomiting are thought to be useful; however, they are not supported by sufficient evidence. Evidence is mixed as to whether aromatherapy enhances the effects of massage.

Encouraging results have been reported for reducing agitation and neuropsychiatric symptoms in dementia patients and symptom control and well-being in patients with Alzheimer's disease, but there are insufficient data to make any firm recommendations. Aromatherapy failed to show benefits in terms of symptom control in cancer patients; pain control, anxiety, or quality of life in hospice patients; or on psychological outcomes during radiation therapy.

Safety

Essential oils should not be taken orally or used undiluted on the skin. Some oils cause photosensitivity. Allergic reactions are possible with all oils. Some oils have carcinogenic potential, and certain oils should be avoided in cancer patients.

Patients with cancer are often highly sensitive to the sense of smell, which may have altered owing to chemotherapy. Certain smells can be very nauseating, and this should be assessed with the patient before therapy.

Further reading

Books

Buckle J. (2015) *Clinical Aromatherapy: Essential Oils in Healthcare* (3rd edn). London: Churchill Livingstone.

Kerkhof-Knapp Hayes M. (2015) *Complementary Nursing in End of Life Care—Integrative Care in Palliative Care*. Wernhout, Netherlands: Knowledge Institute for Complementary Nursing.

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Articles

Graham P.H., et al. (2003) Inhalation aromatherapy during radiotherapy: results of a placebo-controlled double-blind randomized trial. *Journal of Clinical Oncology*, **21**: 2372–6.

Soden K. (2004) A randomised controlled trial of aromatherapy massage in a hospice setting. *Palliative Medicine*, **18**: 87–92.

Wilkinson S.M., et al. (2007) Effectiveness of aromatherapy massage in the management of anxiety and depression in patients with cancer: a multicenter randomized controlled trial. *Journal of Clinical Oncology*, **25**: 532–9.

Professional organizations

The Aromatherapy Council http://www.aromatherapycouncil.co.uk/

International Aromatherapy and Aromatic Medicine Association http://www.iaama.org.au

Group 4: Manipulative and body-based therapies

These therapies in CAM are based on manipulation and/or movement of one or more parts of the body. Some examples are chiropractic or osteopathic manipulation, massage, and reflexology. For many patients, these body-based therapies are very nurturing, especially as physical touch is often lacking for many palliative care patients.

Massage

Background and theory

Massage is one of the oldest healthcare practices in existence. It was documented in Chinese texts more than 4000 years ago and has been used in Western healthcare since Hippocrates in the fourth century BC. Massage therapy is the manipulation of the soft tissues of the body for therapeutic purposes. It consists of manual techniques that include applying pressure and traction. The friction of the hands as well as the mechanical pressure exerted on cutaneous and subcutaneous structures affect all body systems, in particular the musculoskeletal, circulatory, lymphatic, and nervous systems.

Uses

Massage is widely used in the treatment of a variety of conditions, including lymphoedema, stress, anxiety, back and other pain, and insomnia. Through the relaxation of muscle tension and the relief of anxiety, massage therapy may reduce blood pressure and heart rate. Massage may also enhance the immune system. Abdominal massage may be useful for constipation.

Practical application

Either the whole body or relevant specific parts may be treated. The practitioner may play background music depending on the patient's preference. Patients may be encouraged to breathe steadily and to communicate with the therapist. Oils, including aromatherapy oils, may also be used, depending on the individual patient and the aims of treatment.

Evidence of effectiveness

Both massage and/or aromatherapy have been shown to have positive effects on the well-being of cancer patients in general, and on anxiety in particular.

Encouraging results exist for the effect of massage in chemotherapy-related nausea, as well as anxiety and depression in multiple sclerosis, but further data are required. The relaxing effects of massage may have some, albeit non-specific, influence on the well-being of most patients.

Safety

Massage is comparatively safe and adverse effects are extremely rare. There is no evidence that it encourages the spread of cancer, although it is contraindicated where it might damage tumour or frail normal tissue, particularly in treatment-related areas.

It is generally contraindicated in patients who have advanced heart disease, phlebitis, thrombosis and embolism, kidney failure, infectious diseases,

contagious skin conditions, acute inflammation, infected injuries, unhealed fractures, conditions prone to haemorrhage, and psychosis. It is also contraindicated in the acute flare-up of rheumatoid arthritis, eczema, goitre, and open skin lesions.

➔ For aromatherapy massage, see the Aromatherapy section, pp. 734–5.

Further reading

Book

Rich G.J. (2002) *Massage Therapy: The Evidence for Practice*. Edinburgh: Mosby.

Articles

Corbin L. (2005) Safety and efficacy of massage therapy for patients with cancer. *Cancer Control*, **12**: 158–64.

Fellowes D., Barness K., Wilkinson S. Aromatherapy and massage for symptom relief in patients with cancer. *Cochrane Database of Systematic Reviews* 2004, Issue 3, Art. No. CD002287. doi:10.1002/14651858.CD002287.pub2. http://www.mrw.interscience.wiley.com/cochrane/clsysrev/articles/CD002287/frame.html

Professional organizations

Massage Therapy UK ℞ http://massagetherapy.co.uk

Australian Traditional-Medicine Society ℞ http://www.atms.com.au

Reflexology

Background and theory

The therapeutic use of hand and foot pressure for the treatment of pain and various illnesses existed in China and India over 5000 years ago.

It is suggested that there are ten longitudinal, bilateral reflexes or zones running along the body, which terminate in the hands and feet. All systems and organs are reflected onto the skin surface, particularly that of the palms and soles. By applying gentle pressure to these areas, it is possible to relieve blockages or imbalances of energy along the zone. It is believed that specific organs as well as the interrelationship between organs and bodily systems can be influenced to regain and maintain emotional, physical, and spiritual homeostasis, resulting in the relief of symptoms and facilitating the prevention of illness and the promotion of healing. As well as the hands and feet, ear and facial reflexology are starting to be used as well.

Uses

Reflexology is used for a variety of clinical problems. Of particular relevance to palliative care are control of pain and anxiety, induction of deep relaxation, and improvement in sleep.

Practical application

Although there are different schools of teaching in the application of reflexology, the underlying principles are consistent. Gentle pressure is applied to the foot (or hand) along each zone systematically until the dorsum, sides, and sole (or palm) have been covered. The practitioner then repeats the treatment on the other foot or hand. Initially, gentle massage and stroking movements are used, followed by deep thumb and finger pressure. The reflex areas on the foot or hand may feel tender or painful if 'blocked', but are relieved as the treatment works and the 'blockage' is removed.

Evidence of effectiveness

There is no convincing evidence of the effectiveness of reflexology from controlled clinical trials to support its use for any indication, including symptom control in chronic obstructive pulmonary disease, agitation in dementia, and motor sensory and urinary symptoms in multiple sclerosis. It is unlikely to be beneficial in improving quality of life in patients with cancer.

Safety

Contraindications to reflexology include its use in the first trimester of pregnancy. Care should be taken in patients with depressive and manic states, epilepsy, and acute conditions.

Patients receiving reflexology may notice an increase in urination and body discharges, leading to fears that medicinal drugs such as chemotherapy agents might be eliminated more quickly from the body and thus be less effective. However, there is no evidence for this.

Further reading

Books

Barraclough J. (ed.) (2007) *Enhancing Cancer Care: Complementary Therapy and Support*. Oxford: Oxford University Press.

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Tiran D. (2010) *Clinical Reflexology: A Guide for Integrated Practice* (2nd edn). London: Churchill Livingstone.

Article

Devlin B. (2006) The art of healing and knowing in cancer and palliative care. *International Journal of Palliative Nursing*, **12**(1): 16–19.

Professional organization

Reflexology Association of Australia http://www.reflexology.org.au/RAoA/

Chapter 26

Population-based end-of-life care

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The changing face of end-of-life care

From inability to let well alone; from too much zeal for the new and for contempt for what is old; from putting knowledge before wisdom, science before art, and cleverness before common sense, from treating patients as cases, and from making the cure of the disease more grievous than the endurance of the same, Good Lord deliver us.

Sir Robert Hutchison (1871–1960)

From *Modern Care British Medical Journal* 1: 671 (1953) with permission from BMJ Publishing

Building on the major advances in palliative or end-of-life care across the world over recent decades, there now seems to be radical groundswell of change in this area, as we face the major challenge of meeting the needs of the ageing population. This challenge, most noted in the developed nations, now places specific and seemingly overwhelming unprecedented demands on all our health and social care services. Some would argue that a new approach is needed, building on lessons learnt, to care for the rising numbers of people nearing the last stage of life within our population—in other words, a *population* approach to end-of-life care.

The new demographic challenges throw into stark relief the answers we thought we knew, and make us question how we can provide care for all in need within the wider population.

We have reached one summit in palliative care, only to find there are several other higher mountains still to climb.

Key changes related to demographic challenges

- increased longevity—more people living longer with increasing advances in medicine
- death rate increasing—related to post-war baby boomers reaching old age
- increased complexity—more people with serious long-term conditions and multi-morbidity
- fewer people with single diseases such as cancer, and more cancer patients dying from other causes—cancer becoming just one of a number of long-term conditions
- the number of 'old old' or 'super-aged' is increasing, i.e. those over 85, notably in countries like Japan
- over-reliance on institutionalized or hospital care
- reducing health resources in most developed countries
- reductions in countries like the UK in investment in social care and increases in privatization of some areas, e.g. care homes
- heightened expectations of baby boomers—demanding extended quantity and quality of life
- limited number of palliative care 'experts' in symptom management to meet these demands, and the need for widespread enabling of

generalists and non-professional carers who provide the vast majority of support for people approaching the end of life
- need for an earlier, more proactive approach—identifying people who might be approaching the end of life earlier and introducing more active supportive care for more people

There is an imperative to reframe thinking around our service models to provide 'good enough' care for all and to make best use of our scarce resources. The palliative care movement has proved what is possible to achieve for a few—the challenge now remains for the others. An adequate response requires an expansive approach; how can we ensure equity of care for all whilst not reducing standards and gains already made—i.e. not just a 'Rolls Royce service for a few but a bicycle for everyone'. A twenty-first century population-based approach is required for the increasing numbers of people in the last stage of life to meet the needs of everyone in the ageing population.

Some key UK statistics
- 70% of all deaths in the UK occur in over-75-year-olds
- 30% of people live alone
- use of care homes in the final days and weeks of life is increasing, with more residents admitted from hospital for shorter times—it is not always their place of residence
- 80% of care homes are privately owned: four large companies ~ 15% of beds; 20 other companies ~ 15% of beds; ~ 50% owned by small providers
- 12% of care homes are owned by the voluntary sector
- the remaining 8% are owned by local authorities

The broader population-based approach can challenge assumptions on the significance and impact of roles of specialist experts by emphasizing the vitally important contribution of generalists (GPs, care home staff, ward staff, etc.), family, carers, and the community.

Terminology

There is much debate on the definitions used in the UK and other countries in relation to palliative care. Here, the term 'end-of-life care' follows the broader GMC definition of end-of-life care used in other UK National Policy documents, meaning 'care for people who might be in their last year of life', rather than just their final *days* of life. Specific care of the dying is more commonly now referred to as 'care in the final days' or 'care of the dying'.

The GMC definition of end of life

People are approaching the end of life when they are likely to die within the next 12 months. This includes people whose death is imminent (expected within a few hours or days) and those with the following:
- advanced, progressive, incurable conditions
- general frailty and co-existing conditions that mean they are expected to die within 12 months
- existing conditions if they are at risk of dying from a sudden acute crisis in their condition
- life-threatening acute conditions caused by sudden catastrophic events

Care in the final days has been in particular focus over recent years, since the ending of the Liverpool Care Pathway,[1] with updates in policy and NICE Guidance on care for the dying adult.[2] The term 'palliative care' as defined by the WHO[3] indicates a holistic approach to care for people nearing the end of their lives which is applicable to both specialists and generalists. However, for some countries where the palliative care specialty is further developed and formally recognized within medical structures, such as the UK, referring to 'palliative care' can mainly indicate referral to a specialist palliative care service, so this term can also be confusing.

End-of-life care is everyone's business

There will never be enough palliative medicine specialists to care for everyone who is dying—and perhaps some argue there never should be. Enabling everyone to play their role is key to meeting the needs of the ageing population.

Specialist palliative care is increasingly reaching beyond cancer.

In many developing countries, communicable diseases such as AIDS, TB, and malaria are still the main causes of death. There can be an intrinsic assumption that all dying people need specialist palliative care help, which of course is untrue and impossible to achieve, and can undermine the importance and value of the care provided by generalists in this area.

Can we frame the challenge to recognize the invaluable contribution from many and build a stronger base from which to meet the needs of the increasing numbers in the last chapter of their lives?

We start with the fact of our mortality—we all die. For most people whose death is predictable, there can be a time of preparation for dying. For some this is less possible, e.g. those with short illnesses such as stroke, myocardial infarction, or overwhelming infections. But if people could be identified earlier and a degree of planning put in place, then additional 'supportive' care can be introduced to prevent crises later, allowing families and clinical staff to begin to get ready sooner. This includes the wider communities (as in the Compassionate Communities movement),[4] health and social care professionals, both generalist and specialist, spiritual leaders, social workers, lawyers, and many others. So in this context and taking this approach, end-of-life care includes all care for people as they approach the end of their lives—every person, every condition, every setting, and everyone else involved.

With a public health perspective, therefore, with about 1% of the population dying each year, it is the responsibility of all governments and health and social care providers to care for people nearing the end of their lives. The challenge is how best to do this.

Much of palliative care has been based on the predictable trajectory of illness of the cancer journey (Fig 26.1). Despite the inherent difficulties of poor prediction and prognostication, there can be an inherent inequity or 'diagnostic apartheid' in provision of care for cancer patients that is not available for non-cancer patients. But with more people dying from non-cancer causes, the changed paradigm becomes even more important. Beginning with the fact that people die, these people have a variety of needs that can be met; support can be given to them and their families to help them live well before they die, and to die well in the place and manner of

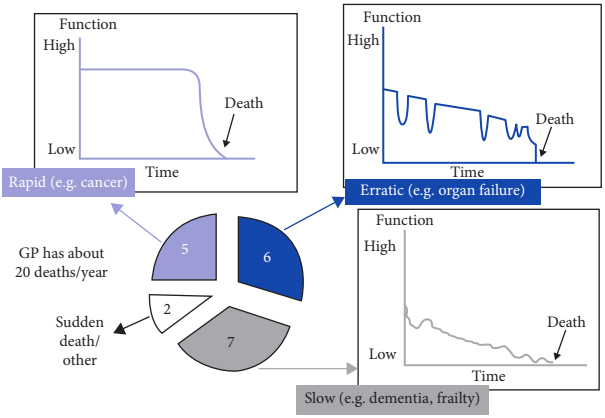


Fig 26.1 Variations in trajectories of illness. Adapted from Lunney J.R, Lynn J., and Hogan C. (2002) Profiles of older medicare decedents J Am Geriatr Soc. 50(6): 1108–12 with permission from Wiley.

their choosing. Some of this support can come, if they are available, from palliative care specialists: dedicated and renowned experts in the complexities of care for dying patients, especially in pain relief and symptom management of those with cancer. But for most people, the majority of care will be provided by people who are not specialized in palliative care—the generalist front-line staff in hospitals, the community, care homes, prisons, and other settings, as well as the wider community of families, carers, volunteers, church/faith groups, and other support workers.

Tinetti and Fried point out in their seminal paper that we are now facing 'the end of the disease era', and that person-centred outcomes not related to specific conditions are the aspiration.[5] In the disease-orientated model, clinical decision-making is focused on disease and its pathology; clinical outcomes are determined by measuring the disease progress of specific markers; survival is the main goal. In the integrated, individually tailored model, clinical decision-making is patient-focused, examining a complex interplay of factors, treating symptoms and impairments; clinical outcomes are determined by the patient; survival is not the only goal (see Table 26.1).

However, for those in developing countries, where most of the world's deaths occur, communicable diseases, accidents, and childbirth still outnumber first-world non-communicable diseases such as frailty and dementia; trajectories are often shorter, with less time to prepare before death. A population-based approach here—meeting needs of those nearing the end of life with the available resources and support—can mean a very different response, with less reliance on concentrations of knowledge by a few specialists, and greater reliance on a broader generalist upskilling approach for the many (see Table 26.2).

Table 26.1 Changing goals of care—the end of the disease era

Disease-orientated model	Integrated, individually tailored model
Clinical decision-making is **disease** focused	Clinical decision-making is **patient**-focused
Cause—discrete **pathology**	Cause—**complex interplay** of factors
Treatment is targeted at the **disease** pathology	Treatment is targeted at the **patient's** modifiable factors
Primary focus of treatment—**causative** disease	Primary focus of treatment—**symptoms and impairments**
Clinical outcomes are determined by the **disease**	**Clinical outcomes** are determined by individual patient preference
Survival is the main goal	Survival is **not** the only goal

Reproduced from Tinetti M and Fried E (2004) The end of the disease era Am J Med 1:116(3):179–85 with permission from Elsevier

Table 26.2 Comparison of UK and Africa causes of death

UK	Africa
Life expectancy—79–83y	Life expectancy—59–63y
1. Non-communicable disease (NCD) • Dementia/frailty • Heart disease • COPD • Cancer • Liver disease • Renal failure	1. Communicable disease (CD) • HIV • Malaria • Diarrhoea • TB
2. CD	2. NCD • Heart disease • Stroke • Cancer
3. Trauma	3. Trauma

Meeting these needs requires significant investment, and yet most health services in the Western world are struggling to meet the demands of an ageing population with increasingly limited economic resources. So not only is there a significant impact of poor end-of-life care on people's individual stories, but there is also an important and sometimes overlooked impact on health economics. With about a third of our health expenditure used in care for people in the last year of life (estimations vary), good end-of-life care is therefore needed for our buckling and overwhelmed health systems. With excessive reliance on hospitals, and without the counterbalance of the possible futility of some interventions in the light of people's preferences,

a new era of potential over-medicalization is dawning,[6] balanced by medical regulation that aspires to provide care tailored to individual patients.[7] In short, we now face the imbalance of overuse by some and underuse of resources by others. 'Just because we can doesn't mean we should' becomes the mantra—provided we allow ourselves time to reflect and enable a space to reflect before pursuing repeated medical processes, especially for the elderly.

There are different providers of care for those nearing the end of life; see Fig 26.2.

End-of-life care is everybody's business

End-of-life care is everybody's business: we are all involved; we all have a contribution to make. The key is to releasing the talents and affirming the confidence of all, including non-clinical staff and those closest to the bedside.

There are many ideas for possible solutions—some suggested here—to maintain appropriate health systems and reconfigure care in line with a population-based approach to meet twenty-first-century demands. See Table 26.3.

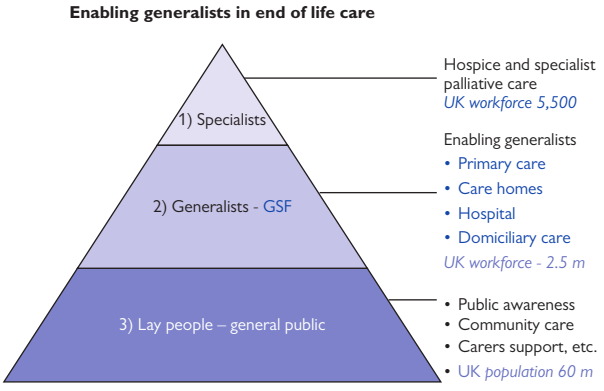


Fig 26.2 Enabling generalists in end-of-life care.

Table 26.3 Population-based end-of-life care to meet the challenges of an ageing population

Why do we need this?	What can we do?	How can we do this?
The world is changing	**Reframe—new focus**	**Develop collective vision**

• Demographic changes
  • Ageing population, increasing numbers dying, frailty, and multi-morbidity is the future.
• Current inequity:
  • 'diagnostic apartheid', many have poor final year of life and poor death, over-medicalization
• Doing nothing is not an option
  • Increasing demands on services, over-reliance on hospitals, current system is buckling under demands
	• Greater awareness by the public, policy leads, politicians, clinicians, strategic planners, etc.
	• Reframe—think differently
	  • Strategic, integrated, values-based, cross-boundary care for all populations of people in the last years of life
	• Culture change
	  • For all in a population and workforce, enabled, motivated, transformational
	'EOLC is everybody's business'
		• Population-based strategic planning with integrated whole-system thinking
		• Value-based healthcare
		• Inclusive
		  • Everyone is involved
		  • Training, enabling all, up-skill and mobilize workforce, release talents
		• Be proactive
		  • Plan ahead, early identification
		• Person-centred
		  • Tailored to individual needs
		• Measurement: population-based outcomes measures, consistency, reliability
		• Aspire
		  • Build national momentum of best practice

Reproduced from Gray J.A.M (2013) How to practise population medicine. Oxford: Offox Press with permission.

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Principles of population-based medicine

(With acknowledgement to Professor Sir Muir Gray.)

The time is right to begin to apply a population-based approach to end-of-life care, to meet the challenges of the ageing population.

According to Muir Gray, a renowned public health consultant, now is the time to be thinking of population-based healthcare to meet the demands of the twenty-first century.

> For the last four decades the paradigm of healthcare has focused on effectiveness, quality, and safety, primarily involving clinicians and institutions but a new paradigm is emerging … with a primary focus now of value for populations and individuals.
>
> Muir Gray, senior public health physician

Population healthcare focuses primarily on populations defined by a common need, which may be a symptom such as breathlessness, a condition such as arthritis, or a common characteristic such as frailty or end-of-life care. It does not focus on institutions, specialties, or technologies. Its aim is to maximize value for those populations and the individuals within them; clinicians practising population medicine can and must play a leading part in its creation.

Population medicine is a style of clinical practice or a way of working. It does not replace other paradigms such as evidence-based medicine or patient-centred care; instead it complements and supplements them.

> Clinicians in the twenty-first century are expected to act as the stewards of the allocated resources, and to become conscious not only of the people who could benefit, but also of the 'benefit foregone' by the whole population … not just to the patients who happen to have made contact with their services but also for all the people whose needs could have been met, directly or indirectly by their service.
>
> Institute of Health Economics, Alberta, Canada

Skills

See Box 26.1.

Population-based care

- See Fig 26.3.

Box 26.1 The skills for population medicine

- maximizing value
- reducing waste and increasing sustainability
- mitigating inequity
- promoting health and preventing disease
- creating systems
- building networks
- clarifying pathways
- developing budgets
- managing knowledge
- engaging the population and patients
- changing the culture

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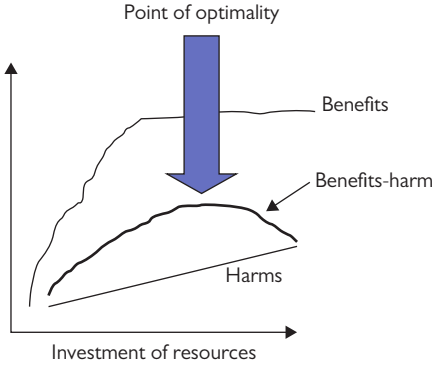


Fig 26.3 Population-based care. Courtesy of Gray, J.A.M.

Population-based end-of-life care—key factors

This public-health, population-based medicine approach to end-of-life care would include considering the total population of people in a country or region who might die in the coming year or years, and instigating methods to identify them early, prevent crises, and plan care to meet their varying needs. One such example of using this approach in practice in the UK is the National Gold Standards Framework (GSF).

Within developed areas of the world, a rough rule of thumb for estimating numbers of the population requiring end-of-life care is as follows (see Fig 26.4):

- **1% of the general population**—the rough proportion who die each year in the UK
- **30% of the patients in hospital**—based on the Clark study[1]
- **80% of residents of care homes**—with most in nursing homes living under a year now in the UK but more living longer in residential homes, which outnumber nursing homes in the UK

Key factors in developing a population-based approach to end-of-life care

- population-based strategic planning with integrated whole-system thinking
- value-based healthcare
- inclusive—everyone is involved with training, enabling all, and upskilling the mobilized workforce
- proactive planning with early identification
- person-centred—tailored to individual needs
- measure—population-based outcomes measures ensuring consistency and reliability
- aspire—building a national momentum of best practice

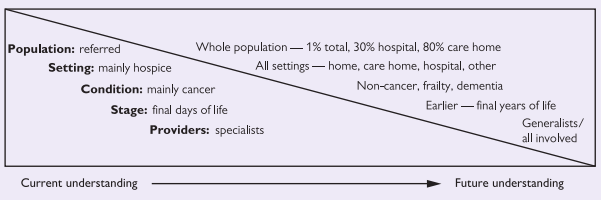


Fig 26.4 Population-based approach to end-of-life care. Reprinted from Thomas K. and Gray M. (2018) Population-based, person-centred end-of-life care: time for a rethink. Br J Gen Pract 2018; 68(668): 116–17. © 2018 British Journal of General Practice, reproduced with permission.

Population-based strategic planning with integrated whole-system thinking

Across any given geographical patch or relevant locality, population-based strategic planning involves the development of whole systems and integrated cross-boundary care. Within this geographical community, a patient may be moved across a number of institutions or services: e.g. receiving care from one GP, followed by a hospital admission, community hospital step-down care and outpatients, transition to a care home for rehabilitation, back to their home, where they may receive community care including district nurse support, domiciliary care, GP out-of-hours care or hospice-at-home services, plus other services from social care. For many, the challenge is to develop joined-up care across these sectors using a common vocabulary and shared information transfer vehicles such as the emerging information-sharing vehicles in the UK, EPaCCS (Electronic Palliative Care Coordination Systems).

The interdependence of each 'microsystem' means that change will only be possible with whole-systems thinking.

Delayed discharges from acute hospitals due to lack of local authority social care funding[2] leads to fewer beds available in hospitals for admissions from the community and a lack of appropriate medical interventions for those that need them.

Some of the GSF integrated cross-boundary care sites are working to use GSF as a common vocabulary to support more integrated care, encouraging earlier identification of patients, advance-care planning, and other proactive systems to improve information transfer and reduce crisis admission to hospital.

Value-based healthcare

There is increasing awareness of the need for transformation and 'triple value healthcare' to maintain health services globally and continue improving population health.[3] Triple value healthcare includes the following:

- **allocative value**—allocate resources to different groups equitably and in a way that maximizes value for the whole population
- **technical value**—improve the quality and safety of healthcare to increase the value derived from resources allocated to particular services
- **personalized value**—base decisions on the best current evidence, careful assessment of an individual's clinical condition, and an individual's values

Inclusive—everyone is involved with training, enabling all, and upskilling the mobilized workforce

As has been discussed, caring for people nearing the end of life has to be everybody's business. Enabling the generalist workforce is therefore key to improving end-of-life care in a population.

Be proactive, plan ahead—early identification

The early identification of patients considered to be in their final year of life is the beginning of the process of providing care tailored to patients' needs. The GSF Prognostic Indicator Guidance (PIG) is one of a number

of tools, widely used internationally, that can prompt earlier recognition of such patients. There is increasing evidence that it is possible to identify the population in the community, hospital, and care homes who would benefit from end-of-life care using guidance tools such as the GSF PIG.[4]

In some GSF areas, once patients are identified, they are known as 'gold patients', with specified benefits, including access to benefits advice from social care, spiritual care assessment, free car parking, open visiting, and, in Airedale Yorkshire, a gold line 24-hour helpline support. This has been shown to help reduce emergency admissions and enable more to die at home.[5]

In addition to identification of patients, families and carers can be assessed separately and given additional support.

Person-centred—tailored to individual needs

People live differently and die differently—no two people want exactly the same things as they are nearing death, yet there are some common themes relating to patient choice.

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Factors related to patients' choice at end of life

People

Repeated surveys suggest that people approaching the end of their life want to be surrounded by those they love, and for their families and others close to them to be supported and cared for to ensure minimum distress.

Place

Place of care is not always the top priority for people, despite it being a tangible and measurable factor, and one favoured by policy and political leaders. Most people express a preference to die at home if asked, perhaps because home feels more than a geographical location but a place they can be fully themselves. It is often more realistic to discuss a range of options with patients depending on changing circumstances. (With just under half the population still dying in hospital, it is estimated that about half of these could have died at home if there was more proactive and comprehensive community support.)

Pain and other symptoms managed—being comfortable

Appropriate symptom control, including pain relief, is of crucial importance, as a fear of dying in pain is commonly voiced. For those with non-cancer conditions, other key symptoms are more apparent, such as lack of energy, breathlessness, immobility, agitation, and confusion. Emotional and spiritual pain also add to feelings of agitation, and spiritual distress is well recognized. Symptom control and pain relief in particular are key factors for many, and are contributors in the 'trade-offs' discussions surrounding the most suitable place of care.

Planning ahead, avoiding crises, and being in control

As disease progresses, being able to retain some control over some aspects of life becomes particularly important to many—clinical management decisions, control over visitors and solitude, not needing to repeat their personal information, or the number of hours they have to wait for secondary care.

Crises, whether escalating pain or emergency admissions, create a sense of lack of control, panic, and fear. Therefore, reducing crises and anticipating appropriate responses to a change of conditions helps reduce anxiety, e.g. clarifying instructions as to which drug to use for pain relief before calling the emergency doctor service.

Peacefulness, being normal, and focusing on quality of life

As people come to terms with the reframing of their lives, moving from a person who thinks little about mortality to someone who knows life is limited, a gradual sense of tranquillity, peacefulness, and growing acceptance can develop. Meanwhile, people like to 'live normal lives' with maximum focus on quality of life, fulfilling a 'bucket list' of wishes, enable healing of relationships and the resolution of barriers towards the final letting-go. Such progress, especially in the final days of life, require a calm and nurturing atmosphere in which life-closure discussions can be continued for the benefit of both family and patient.

Offering advance care planning (ACP) discussions is one of the important means of remaining person-focused at all times, creating a space in which a person's underlying views can be heard, clarified, and enacted. There is some debate about terminology, but in essence ACP discussions involve good listening.

Advance care planning is defined as a process of planning for future health and personal care, whereby the person's values and preferences are made known so that they can guide decision-making at a future time when the person cannot make or communicate their decisions. In order to deliver care in line with preferences, this element of advance care planning discussion can be critical.

Further reading

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Population-based outcome measures, ensuring consistency and reliability

The value of measurement is to measure for progress (formative) as well as measure for attainment above standards (summative). In the area of end-of-life care, it is important to be clear which level we are measuring—see Box 26.2. A variety of measures are increasingly available, including assessment of symptoms and identification rates, numbers of ACPs being offered, etc, but few as yet describe the population-based, area-wide measures that might support better commissioning.

Raising standards of care—building the national momentum of best practice

Examples of teams excelling can be an inspiration and encouragement to others. Describing what is possible to achieve can grow to become recognized standard practice and become 'a national momentum of best practice'.

National momentum

GSF-trained and GSF-accredited care homes demonstrating major reductions in hospital admissions have become showcased examples of excellence for others to follow. Likewise, the steady decline in hospital death rates in the UK is testament to what is possible to achieve through engaged, nationally supported, whole-system thinking.

Box 26.2 Different points at which end-of-life care measures need to be applied

1. Individual—person
   - patient
   - family
   - member of staff
2. Organization—team
   - practices
   - care home
   - ward
3. Community—locality
   - population area
   - footprint
4. National—policy
   - regulation
   - quality standards

Enabling generalists

The term 'generalist' in the UK was defined in the NHS End of Life Care Strategy 2008[1] as those who care for patients with many conditions, including those who are in their last year of life, whereas specialists exclusively care for patients in their last years of life. Generalists include GPs, district nurses, care home staff, hospital staff, including specialists in other areas, domiciliary care workers, healthcare assistants, social workers, chaplains, and others.

In countries where the specialty of palliative care provides added expertise, patients with conditions that are complex and severe or causing significant distress should be referred to palliative care specialists. Different countries have different triggers for palliative care referral, but with growing awareness of the benefits of specialist care, many are focusing more on appropriate referrals to this service. Within the total population—where 75% die of non-cancer conditions—GPs, community nurses, care home staff, and geriatricians provide the majority of clinical supervision, meaning that they are the greatest professional providers for hands-on end-of-life care in the UK.

Examples of generalist competencies in palliative or end-of-life care

Overall goal

To be aware of the continuum of care for people living with long-term, life-limiting illnesses, including frailty and dementia, recognizing the contribution that everyone can make as a part of usual care (see Fig 26.5).

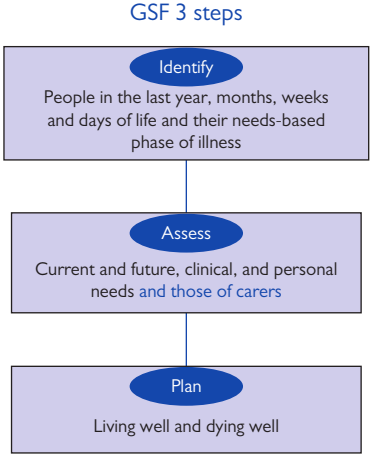


Fig 26.5 The Gold Standard Framework: three steps to formalizing best practice in end-of-life care.

Identifying patients early

- recognize the signs of decline, including use of updated GSF Proactive Identification Guidance http://www.goldstandardsframework.org.uk/pig
- identify people potentially in their last year of life—use the 'surprise question'
- be aware of general indicators of decline
- be aware of specific clinical indicators for particular diseases

The surprise question

'Would I be surprised if this person were to die in the next 12 months?' This simple question is accurate seven times out of ten.

Assess clinical and personal needs and those of carers

- clinical needs—holistic assessment; appropriate clinical, referral, and provision of first-line symptom management for basic issues
- personal needs, wishes, and preferences—offer advance care planning discussions
- assess family's and carers' needs and provide appropriate support

Plan living well and dying well

- support people nearing the end of life to live as well as possible in their preferred place; reduce crises and emergency hospital admissions; spiritual care and psycho-social care is included here
- recognize, support, and care for patients in the final days of life, managing common symptoms (in England, Five Priorities of care, in line with NICE Guidance); offer continued communication and bereavement support to families

Reference

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Examples in practice—experience from the GSF Centre

GSF is a systematic, evidence-based approach to optimizing care for all patients approaching the end of life, delivered by generalist front-line care providers. GSF runs training programmes that help to support all people approaching their last years of life in any setting.

> Developed from the bedside, refined by clinicians, rooted in practice in each setting to ensure programmes are transferable, effective and sustainable in practice. GSF programmes are now widely used in the UK in all settings—primary care, care homes, hospitals, domiciliary care, hospices and others.
>
> GSF

GSF was originally developed in 2000 as a grassroots initiative to improve primary palliative care. First piloted in primary care, it was developed for care homes in 2004, with the acute hospital training beginning in 2008. See Fig 26.6.

The GSF Centre provides nationally recognized training and accreditation programmes, tools, measures, and support, enabling transformation and culture change that lead to 'gold standard' care for people nearing the end of life.

It uses the broadened definition of end-of-life care to include all in the final years, months, weeks, and days of life and enables earlier recognition

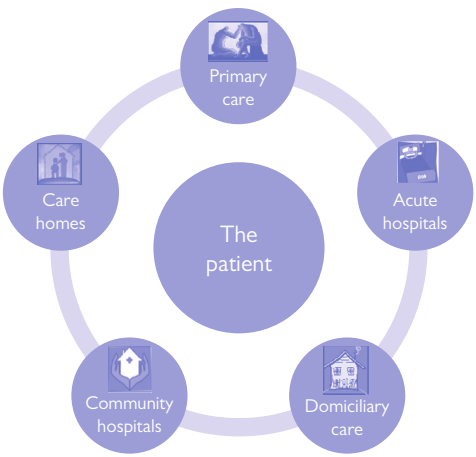


Fig 26.6 GSF patient-centred care.

of decline and identification using needs-based coding, better listening to people's needs, wishes, and preferences through advance care planning discussions and better proactive planning to ensure more of these wishes are met and people live well and die well in the place and manner of their choosing.

GSF is about a practical process providing consistent person-centred care—right person, right care, right place, right time, every time.

What difference does GSF make?

See http://www.goldstandardsframework.org.uk/evidence

GSF used in different settings has been found to improve the following:

- quality of care—better quality and experience of care
- coordination and communication
- patient outcomes
- more living and dying where they choose; reduced hospital deaths, enabling more to die at home; increasing cost-effectiveness and best use of scarce resources
- more recorded advance care planning discussions and preferences met

Culture change, existential, and spiritual issues

Culture change

Amidst the measurable changes made to patient care, there can be other tangible but less measurable impacts—a 'culture change' that can be sensed in a changing organization that is trying to reach beyond itself. Such cultural changes may include the following:

- a facing of mortality
- an acknowledgement that death is not a failure, but a bad death is
- an openness when discussing death and dying
- a hunger to learn from each mistake or less-than-perfect outcome for the patient
- a strong sense of teamwork, and valuing the contribution of all
- a clear focus on values and shared decision-making, with better listening to the person most affected and their family or carers

> GSF has given us the framework to engage with relatives and put things in place to ensure the outcome they want for their relative.... I think the biggest change has been the culture change. GSF is the framework that allows us to make that happen. The best bit is making sure that patients receive the care they want, where they want it, when and how they want it, and the satisfaction they and we get from that.
>
> Consultant geriatrician

Holistic care

Compassionate healthcare doesn't happen automatically, as events and reports into poor-quality care show. Such enquiries have also demonstrated that even good people sometimes do bad things. To encourage compassion we need to pay attention to the inner resources which produce compassionate care as their outcome. GSF frames this work as being about head, hands, and heart (see Fig 26.7):

- 'head' is about the medical knowledge that is needed to give good end-of-life care
- 'hands' is about the way that care is organized
- 'heart' is about the way we give that care

> How we make people feel will be remembered long after our words and our actions have been forgotten.

Spiritual care

Definitions

- spirituality is a personal search for meaning and hope
- religion is an organized system of beliefs and practices; religion is about accountability and connection
- spiritual care—caring for all that helps human beings flourish and be resilient in the face of life's uncertainties; see http://www.goldstandardsframework.org.uk/spiritualcare

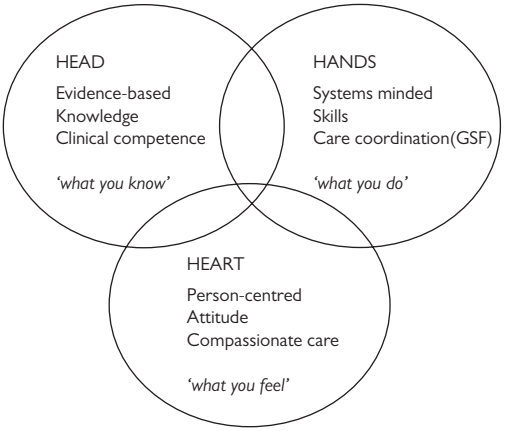


Fig 26.7 Improving holistic end-of-life care: head, hands, and heart.

Effective spiritual care

Effective spiritual care is more about sharing our humanity than our medical knowledge. For example, many of those at the end of their lives will be facing loss in different forms—loss of physical and mental capacity, of home, spouse, and other relationships. As health and social care professionals, it is our experience of loss in our own lives that we can bring to connecting our care to others.

Presence

In making spiritual assessment of those in our care, mnemonics such as HOPE and FICA have been used (see Table 26.4).

Table 26.4 Spiritual assessment tools

HOPE	
H	What are your sources of hope?
O	Is organized religion important to you?
P	What is your personal spirituality?
E	What is the effect of healthcare on you?
FICA	
F	Do you have a faith, and if so, what is it?
I	How important to you is it?
C	Do you belong to a faith community, and how important is that?
A	How are we going to address the questions that this discussion has raised?

The most important quality we bring to spiritual assessment is that of our presence (see Fig 26.8). Whatever the pressures we have come from or are going to, we need to be able to be fully present with the person in front of us. The quality of the time we give is more important than the quantity. Spiritual assessment entails the following:

- our capacity to listen both to what is said and what is unsaid
- our sensitivity to visual clues and body language
- our willingness not to fill silences
- the power of touch where appropriate
- our capacity to be 100% present with the person in front of us, our minds still and undistracted, effectively allows us to discern sources of hope and resilience, and draw out what they most need to communicate; health and social care practitioners are increasingly finding that some sort of daily *mindfulness* practice is an effective way of preparing the necessary stillness of body and mind for such care encounters

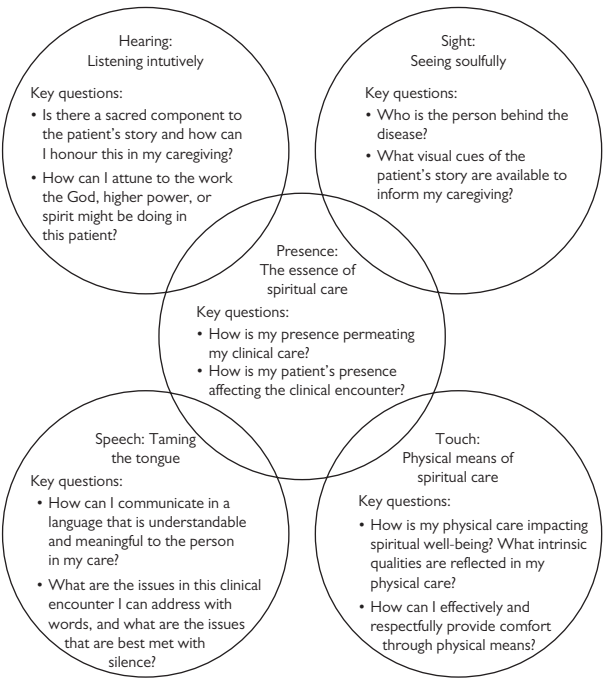


Fig 26.8 The five senses of spiritual care. Reproduced from Sinclair et al (2012) Spiritual Care: how to do it. BMJ Supportive and Palliative Care 2;319–27 with permission from the BMJ Publishing Group.

Intelligent kindness

In *Intelligent Kindness*, John Ballatt and Penelope Campling argue that we must be more fully aware of that which encourages compassionate care within the NHS and other health and social care environments, and more aware of that which discourages it. Everyone involved in health and social care needs to ask themselves both what encourages their own intelligent kindness and what discourages it.

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Chapter 27

Hospital liaison palliative care

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Introduction

It has been suggested that between one-third and two-thirds of people in developed world countries will die in hospital.[1] The hospital, probably more than any other healthcare setting, is a challenging environment in which to support the human dimension in patient care. The focus is on investigation, treatment, and cure; priorities, such as quality-of-life issues, can get overshadowed.

Many hospitals in the UK have some form of palliative care[1] hospital liaison support, varying from a single nurse to consultant-led multidisciplinary teams. Models exist for inpatient hospital beds where the palliative care specialist provides clinical leadership, but the majority of teams work in an advisory capacity and are known as hospital specialist palliative care teams (HSPCTs). Many teams have direct relationships with the local specialist palliative care providers, through joint working contracts.

Reference

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The need for a hospital palliative care liaison service

- Up to 90% of patients receive some form of hospital care in their last year of life; approximately 22% of hospital bed-days are taken up by people in their last year of life.[1, 2]
- Some 5–23% of hospital inpatients have been estimated to have palliative care needs at any one time.[3]
- The large majority of patients die in hospitals, despite the research clearly showing that the majority of people would want to die at home.[4]
- Just under 50% of cancer deaths in the UK occur in hospital, and this percentage is much higher for those with a non-cancer diagnosis. Although some of the factors involved in preventing this need to be addressed within the community, there are also many challenges for hospital services.
- Studies show that the experience of dying in hospitals is often poor: high prevalence of symptoms which are poorly assessed and managed; poor communication and patient involvement in decision-making; poor recognition of dying; lack of privacy; and lack of emotional support.[5, 6]
- These unmet needs are even greater in those patients with a non-cancer diagnosis,[7] who, until recently, have not had ready access to specialist palliative care (SPC) support. Although this is changing, the large majority of patients under SPC teams still have a cancer diagnosis. Given the high proportion of patients with non-cancer diagnoses dying in acute hospitals, this is a particular challenge for hospital teams.
- The ready availability of intensive treatments can skew the balance of patient-centred care and lead to the over-treatment of some patients. Many elderly patients at the end of life prefer a treatment plan focused on comfort.[8]
- The majority of complaints received by hospital involve communication problems. The highly emotive situation of end-of-life care compounds this.
- Despite these identified needs, HSPCTs have been shown to be underutilized.[9]

Challenges to enable more patients to be discharged to die at home

- Early recognition of dying, in order to stop investigations and treatments that are not going to impact on outcome and to allow the change in focus which can enable a safe and timely discharge
- Recognition of the potential for dying, in order to facilitate discussions around future care preferences
- Improving communication skills to support discussions around end-of-life care
- Good multidisciplinary team (MDT) structures to support timely assessments and planning for discharge to die at home
- Recognition by the MDT that dying at home is possible

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The challenges in an acute hospital setting

- **busy, stretched staff**: in one study, ward nurses had an average of 3 minutes per patient per shift for psychological care[1]
- **lack of consistency in treating teams**: e.g. shift working, multiple ward moves, weekly team changeover of junior medical staff, changing consultant team of the week, and frequent staff turnover
- **variability in models of communication amongst the MDT**: there are some good models of MDT working, but this is not consistent
- **difficulty accessing clinical information**: particularly important on admission to hospital and when a patient comes to A&E. Good communication between community/hospital teams and hospital/hospital teams is invaluable. The use of electronic records, where available, should facilitate communication. In the absence of this, there is no substitute for consulting widely. Inadequate information leads to inadequate care!
- **environment**: there is frequently lack of privacy; lack of quiet rooms in which to talk; lack of attention, lack of dignity; difficulty accessing outside green spaces; difficulty for loved ones to stay overnight; lack of free and/or convenient parking for visitors
- **attitudes and skills**: variability in knowledge and acceptance of a palliative care approach; generalists may see palliative care professionals as 'giving up' on patients; there is fear in prescribing drugs used for symptom control, e.g. morphine
- **bureaucracy as a limit** to creativity and empowering patient-centred choices: strict visiting times; lack of flexibility in food choices
- **hospital-acquired infections**: with the vulnerable being most at risk
- **providing support out of hours**: given the small size of many hospital teams and lack of funding, out-of-hours provision is often inadequate

Reference

1. McDonnell M. et al. (2002) Palliative care in district general hospitals: the nurse's perspective. International Journal of Palliative Nursing, 8(4): 169–75.

Aims and evaluation of a hospital specialist palliative care team

Aims

- integrate hospice values and practice into the acute care setting
- be a visible and practical support and resource within the hospital
- by working in an advisory capacity, support the needs of both patients and their families
- be dedicated specialists, with the time and focus to truly influence the patient experience
- develop models of MDT working and communication; foster trusted relationships with consultant colleagues and other specialists involved in caring for those patients with advanced progressive illnesses, e.g. clinical nurse specialists working with neurodisabilities such as Parkinson's or motor neurone disease
- help identify and be present at junctures in the patient's experience to ensure review and resetting of treatment plans in the light of (changing) patient preferences, e.g. working closely with oncology colleagues by attendance at cancer site-specific MDTs and outpatient clinics; presence at ward rounds or outpatient clinics for, for example, heart failure and end-stage renal disease
- optimize collaborative working with the local community and hospice services; different models exist which range from joint appointments of staff working across multiple settings, to community team attendance at hospital MDT meetings or outpatient clinics, to fully integrated community/hospital palliative care teams
- develop MDT education programmes to raise standards throughout the hospital, covering all aspects of holistic care, e.g. physical, emotional, social, spiritual, and ethical elements; provide informal and formal teaching covering a wide variety of staff, including those at the periphery of patient care who may still be affected and interact with patients, e.g. porters and ward clerks
- provide and/or develop patient information in an accessible form
- promote clear ethical decision-making through joint working with clinicians and education/participation in hospital clinical ethical committees
- promote audit and research to evaluate service and ensure best care
- influence policy development and raise the profile of palliative care within the hospital, through involvement at all levels; it is crucial to engage with management in order to change culture
- represent and participate in hospital and regional groups, e.g. cancer locality groups, cancer or other disease networks
- be a role model and mentor; empower and enthuse professional colleagues and encourage the next generation of palliative care specialists

Evaluation

There are inherent difficulties in evaluating hospital palliative care teams. The evidence base showing a benefit for HSPCTs is limited,[1] reasons for which include the difficulty in evaluating advisory teams, attrition rate of patients and bias, and the clinical complexity of patients with whom palliative care teams are involved, e.g. those who have intractable pain or difficult psychosocial problems. However, there are a few established tools, such as the Palliative Care Assessment Tool (PACA) and Palliative Care Outcome Score (POS) which have shown benefit from HSPCT involvement in a variety of areas, such as pain, symptom control, and patient and carer insight.

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Things to think about when considering a referral to the hospital palliative care team

- What are your team's plans for ongoing care?
- What treatment options are available?
- What are the patient's wishes for care or place of care?
- If there are symptoms, what do you think is the underlying cause, and what steps have already been taken to address them?
- If the referral is for terminal care, has your team reached a consensus that this is the aim of care? Is this reflected in the care which is being provided?
- Have you thought through and identified the specialist palliative care needs of your patient, e.g. difficulties with pain and symptom management, psychological and social needs and issues surrounding the anticipated dying process?
- Have you made sure the patient is aware of and in agreement with any referral? This will usually imply a level of understanding of their illness and prognosis.

Of course, difficulties in the foregoing areas may be the exact reason why you want to refer to the HSPCT. By thinking these issues through before contacting the HSPCT, you will pre-empt their questions!

Urgent discharge of a dying patient who wants to die at home

Sometimes, following sudden realization of a rapid decline, patients may decide that they want to go home to die. In these changing circumstances, time can be short and clinicians need to be flexible for this to be possible. Based on an NHS Cancer Network example of a discharge plan process, steps to aid clinicians' facilitation of safe discharge include the following:

Communication

Remember to enhance understanding through consideration of first language, learning disability, and literacy skills. Use of interpreters or advocates may be needed.

Patient

- Ensure it is the patient's wish to die at home.
- Explain the level of care available and ensure they are aware of limitations in support and the impact of the discharge on carers.
- Re-check that the patient still wants to go home to die.

Family/carer, where possible with patient

- Is the family/carer in agreement with the patient's wishes?
- Are they aware of the aims of care and the short prognosis?
- Does the family understand the medications?
- Ensure the family knows which community agencies will be involved and what their roles and level of commitment are.
- Give the family contact numbers for in-hours and out-of-hours GP, community nursing, community palliative care, and other involved agencies.
- Advise the family on what to do when a patient dies at home.

Ward nurse

- Make verbal referral supported by an electronic update to community nurse.
- Nursing letter should include details of the patient's diagnosis, their nursing needs, medication, poor prognosis, understanding, and wishes. Indicate other referrals made.
- Consider local supports that may be available, including night nurses and volunteer agencies.
- Provide a letter/form to go with the patient, for the in-hours/out-of-hours community nursing service.
- Make verbal referral supported by an electronic update to the community specialist palliative care team (CSPCT).
- If patient is oxygen-dependent, check adequate oxygen availability at home. If not, ensure arrangements are made for home oxygen through local policies.
- Ensure regular liaison with MDT members involved in the patient's discharge from hospital, e.g. coordinators, occupational therapists.
- Book ambulance: ensure the ambulance service is aware that the patient is not for resuscitation, and that a written DNAR order is with the patient (e.g. in the form of a letter, or a copy of the hospital DNAR order—local policies will apply).
- Liaise with the HSPCT for advice and support.

Doctor

- Make verbal update supported by electronic communication to the GP ± out-of-hours GP service. Emphasize the patient's wish to die at home. List the medications. Ensure an early review by the GP who may also need to undertake death certification.
- Complete and fax out-of-hours handover forms, where available, to local GP out-of-hours service and, where agreements exist, the local ambulance service.
- Ensure DNAR form is signed and current.

Medication

Doctor

- Prescribe at least 1 week of *oral* medication. Include p.r.n. analgesia and anti-emetics.
- Even if the patient can swallow on discharge, they are likely to become unable to swallow in the near future, so subcutaneous medication *must* also be prescribed.
- Prescribe regular medication needs for delivery via syringe driver, plus p.r.n. medication needs for possible distressing symptoms (➔ see Chapter 30, The terminal phase). Remember also to prescribe water for injection or normal saline for the syringe driver diluent.
- Doctors must write a prescription chart for the syringe driver and p.r.n. SC medications to go home with the patient, so that district nurses can administer medications. This can be in the form of a letter or utilization of local charts, as available.

Nurse

- Provide a written medication chart to go home with the patient. Include information about the reason for the medication, dosage, and frequency.
- Explain to the patient and family and ensure understanding.

Equipment

Ward nurse's responsibility for equipment needed for discharge

- For patients with a syringe driver, *either*
  - supply a clearly labelled syringe driver for early return by district nurse, or other explicit arrangement; *or*
  - give stat medications prior to transfer to cover the known symptoms and arrange for the district nurse to set up the syringe driver shortly after the patient's arrival at home.
- When sending the patient home with a hospital syringe driver, remember to include the following:
  - a spare battery
  - a range of Luer-lock syringes: 2mL, 10mL, 20mL, 30mL (× 4)
  - needles: orange, blue, and green (× 4)
  - syringe driver lines (× 4)
  - occlusive dressing (× 4)
  - labels for barrel of syringe
  - water for injection
  - sharps box (× 1)

- For patients with additional needs, discuss with the occupational therapist the need for:
  - hospital bed
  - commode
  - urinal
  - any other equipment

It may not be possible to provide all the equipment, but don't let this stop you from fulfilling the patient's wishes. Where items are not available, discuss possible solutions with the community nurse/patient/family. Communication is key to a successful discharge.

- At any stage, liaise with the HSPCT for advice and support.

Case

A 95-year-old widower was admitted to hospital with pneumonia. He had had previous strokes, which significantly affected his mobility. He lived alone and had no children or close family. Early in the admission, he said that he didn't want any more treatment and wanted to be allowed to die.

His infection caused intermittent confusion, and the treating team were concerned that he did not have capacity to refuse treatment. They felt he could benefit from treatment and so continued to offer antibiotics. He then became increasingly distressed and mistrustful of staff and started to refuse all treatment, including symptomatic measures such as pain control. He was referred to the HSPCT for symptom control and support in the knowledge that, despite their efforts, he was probably dying.

On meeting him, the HSPCT were able to talk through his understanding of his condition and his wishes for care. He had nursed his wife through a long illness and saw her death as a blessing. He had also lost close friends recently. He felt he had a poor quality of life owing to his strokes and did not want to prolong his life any more. He had agreed to come in to the hospital so he could die in a place of safety, but he had not anticipated the battle to keep him alive. He understood there would be friends who would be upset by his dying, but said he had spoken to them and said his goodbyes. He was, at that moment, competent in his refusal of life-sustaining treatment. He also had many other symptoms that had either not been addressed (nausea, shortness of breath associated with his anxiety, constipation) or had been inadequately managed (regular analgesia had been prescribed, but he had refused). The HSPCT were able to talk through his drug chart and rationalize medication for comfort only, and spoke with staff so they would explain clearly what was being given.

By meeting with the treating team, the team were able to clarify aims of care and to ensure consistency of care. This reassured him. He did not want a single room, as he liked the activity of the open ward. He deteriorated steadily. A syringe driver and p.r.n. medications were advised and he died comfortably a few hours later.

Dying in the intensive care unit (ICU)

A large number of patients who die in hospital spend some time on the ICU during their last admission.[1] However, the experience of dying on an ICU is reported as variable, with a high prevalence of symptoms and poor communication around the end-of-life preferences. In such an aggressive treatment environment focused on saving life, ensuring a peaceful death may get lost as a central goal of clinical care.

In the American SUPPORT study (the Study to Understand Prognosis and Preferences or Outcomes and Risks of Treatments), from the perspective of bereaved relatives, 60% of patients would have preferred comfort care. Poor communication around end-of-life issues may, therefore, influence admissions to ICU and lead to invasive treatment which does not always follow patients' wishes.

A study that looked at the quality of dying in an ICU from the perspective of bereaved relatives showed that 24% of patients were never aware of dying and that 34% were only aware in their last week of life.

The most important aspects of the perceived quality of dying were good pain control, being prepared for death, having control over events, feeling at peace, and maintaining dignity and self-respect.

More than 70% of deaths on an ICU can be predicted, e.g. by withdrawal of treatment that has failed. In some circumstances, withdrawal of treatment can precipitate a very rapid death, within minutes to hours. Some patients will be stable enough to be transferred to other areas.

HSPCTs clearly have a role in supporting end-of-life care in an ICU, and the challenge is to develop relationships with ICU colleagues to allow this. Opportunities include developing joint education programmes to raise the profile of a palliative care approach so it is seen as a core goal of care, not a failure of care; ensuring clear criteria for referral to HSPCTs; looking at models of MDT working; adapting approaches to the dying phase in the light of the often fast clinical deterioration; and highlighting variations in routes and types of medications needed.

The National Liverpool Care Pathway (LCP) Centre has developed an ICU version of the LCP which is currently being evaluated. The HSPCT can actively support the transition of dying patients who are transferred from ICU to other settings. Throughout the hospital, the team has a role in promoting the need for early communication around end-of-life preferences with patients, enhancing their control over events and supporting the staff in the communication skills needed in these difficult situations.

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Chapter 28

Palliative and end-of-life care for people with learning disabilities

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Support in the bereavement period *783*

Background

> People with learning disabilities are a part of us rather than being apart from us.
>
> S Todd[1]

Concerns exist around choice and the quality of end-of-life care that people with learning disabilities may be offered.[1] A number of different terms have evolved over the years for 'learning disability'. Currently this term is used in the UK, but in Europe and in other parts of the world, the term 'intellectual disability' is used. Internationally there is a consensus that a learning disability can be identified when the following criteria are present: intellectual impairment (known as reduced IQ), social or adaptive dysfunction combined with reduced IQ, and early onset.[2] It is thought that around 2.5% of the population in the UK have a learning disability, but it has also been predicted that this may increase by 1% per year over the next number of years. The increase has implications for service provision, as this population are living longer and will have an increased risk of advanced progressive disease requiring palliative and end-of-life care. However, it is known that in contrast to the general population, people with learning disabilities have the following:

- a longer than previously thought, but still lower, life expectancy than the general population
- a higher number of healthcare needs which are also more complex
- a higher level of unmet healthcare needs
- a different pattern of healthcare needs and leading causes of death[3]

The leading cause of death in people with learning disabilities is respiratory disease,[4] mainly due to pneumonia and aspiration. This is normally associated with gastro-oesophageal reflux disorder (thought to be caused by community living contributing to a high rate of *Helicobacter pylori* infection), and problems with swallowing, feeding, and posture. The second cause of death in people with learning disabilities is reported to be cardiovascular disease, normally associated with that which is congenital.[5] It has been found that there are lower rates of lung, prostate, and urinary tract malignancies, but increased incidence and risk of oesophageal, gastric, and gall bladder malignancies.[6, 7] Higher rates of dementia than in the general population are present with people with learning disabilities, and in particular people with Down's syndrome have a higher incidence of Alzheimer's disease.[8, 9] The link between Down's syndrome and dementia is thought to be due to the presence of the third chromosome 21, which is associated with the production of the beta-amyloid protein, and has been found in the brains of people with Alzheimer's dementia.[10] The place of death for people with learning disabilities is difficult to determine, as deaths are recorded as disease-specific, and it is often not noted that the person had a learning disability.[11]

1 Todd S (2006) A troubled past and present—a history of death and disability. In S. Read (ed.) *Palliative Care Learning Disability* (pp. 13–25). London: Quay.

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Key issues in caring for people with learning disabilities at end of life

There are a number of key issues or challenges in caring for someone with a learning disability at the end of their life. These broadly fall into the following sections:

- holistic assessment and care planning
- communication
- consent
- support in the bereavement period

Holistic assessment and care planning

People with learning disabilities tend to have a late diagnosis of advanced progressive disease, owing in part to lack of screening opportunities. The diagnosis of an advanced incurable disease can be equally distressing to this population as it is to anyone else. A person with a learning disability has the same needs at end of life as the general population, but often has additional needs which require addressing. This can make assessment and care planning challenging to services.

There is evidence that partnership working between learning disability and palliative care services, with the person with a learning disability and their carers at the centre, can enable end-of-life assessment, care planning, and delivery to be more effectively carried out.[1]

- Work closely with people and services familiar to and with the person with a learning disability, and with their methods of communicating.
- Be sensitive to the expertise and long-term caring role of family members.

People with learning disabilities should have equal access to a holistic assessment and multidisciplinary care at end of life. The concept of 'total pain' and multidimensional suffering can still be applicable. Those with a mild learning disability are often able to locate their pain on a body chart or photograph.

Identifying distress is only the beginning of assessment in people with more severe learning disabilities. Distress may be due to pain, but it can also be caused by anxiety or other symptoms. People known to the person will be able to identify and interpret their sounds, mannerisms, facial expressions, and changes in behaviour where they are unable to self-report what they are experiencing. The Disability Distress Assessment Tool (DisDAT) can be used to assess and identify distress cues in people who are cognitively impaired.[2]

Careful assessment and monitoring are required where the person with a learning disability has gastrointestinal cancer owing to the risk of intestinal obstruction and the need for early detection.

Communication

- Remember, all people with learning disabilities can communicate in some way, but this may not always be apparent, and it may not be with verbal methods of communication.
- Try to establish how the person with a learning disability normally communicates. This could be through using alternative communication

(a system alternative to speech) or augmentative communication to support speech (signs, symbols, photographs, or pictures).

- It may be necessary for professionals to facilitate receptive and expressive communication with the person with a learning disability and also to adapt how they normally communicate. This can mean using straightforward language, using accessible information tailored for the person, and providing time for them to process information. Accessible information can be found in the Useful Websites and Resources section at the end of this chapter.
- Breaking bad news guidelines, which are adaptable to individual ability and understanding, have recently been developed for use with people with learning disabilities.[3] For a person with a learning disability, breaking bad news is a process rather than an event. This may not happen in a clinic, but rather in the person's own setting with familiar people around; information may be given in chunks over a period of time. It is noteworthy that people with learning disability may not understand 'warning shots' used in traditional breaking bad news models, or the need to ask questions to get information.
- Where possible, people with learning disabilities should be included in and facilitated to take part in advance care planning.
- Skill and sensitivity may be required to maintain the autonomy of a person with a learning disability, where there may be immense pressure from family members or carers to withhold information about diagnosis and prognosis.

Consent

For a person with a learning disability, it is very important that assumptions are not made about their lack of capacity to give or withhold consent, or lack of capacity to be a partner in decision-making about their care and treatment. Central to this is the right for people with learning disabilities to have choice and to be treated equally to other adults in being considered capable to provide consent unless this is demonstrated otherwise.

Health and social care professionals should always seek advice from local disability discrimination and capacity/incapacity legislation and guidelines for examination, treatment, and care, which should be followed.

People with learning disabilities can often make some decisions, and it is necessary to find out what decisions they can make. With each decision the person's ability must be considered. The only way to establish that the person with a learning disability cannot give valid consent is to seek to establish it.

It is vital to remember that 'reasonable adjustments' may need to be made to information given and in facilitating the person to take part in decision-making. If necessary, an assessment by a speech and language therapist can be helpful in determining the person's capacity to make decisions and ways to communicate with them.

If an adult with a learning disability cannot give consent, no one can consent on their behalf. Instead, a careful and clearly documented process of 'best interests' decision-making should take place. Central to this is being able to show that any decision-making was primarily in the best interests of the person with a learning disability.

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Support in the bereavement period

A person with a learning disability can experience multiple losses, particularly if their main carer dies and they are required to live in alternative accommodation, which may mean loss of much which is familiar to them. A person with a learning disability may express grief in different ways, or their grief may be delayed. Often the person's grief may not be recognized or validated by well-meaning friends or family, who do not enter into discussions about death with the person or involve them in death rituals such as attendance at the funeral.

Assessment

A Bereavement Assessment Tool for use with people with learning disabilities has been developed.[1] This tool encourages the use of three main questions about the person with learning disability who has been bereaved:

- Has the person's ability to communicate with others been affected by this loss?
- What impact has the death had on the person's familial network?
- Does the person recognize their emotions and can they express them?

Support

The following are thought to be important in supporting someone with a learning disability in bereavement:

- Ensure the active involvement of the person with a learning disability in death rituals if that is what they desire. This may be by visiting the grave or attending the funeral. Explanation is important, as this may be the person's first time taking part in death rituals.
- Maintain consistency in being open and honest.
- Provide information about bereavement in an accessible format which the person can understand.
- Memory books and life story books may be helpful.
- Bereavement counsellors may use a variety of other approaches with this population, such as art work, family trees, pictures, and photographs.[2]

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Useful websites and resources

Easy Health Website—provides accessible information about health issues for people with learning disabilities: www.easyhealth.org.uk

Guidelines for breaking bad news to people with learning disabilities: www.breakingbadnews.org
Palliative Care for People with Learning Disability Network: www.pcpld.org

Further reading

Books

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Chapter 29

Emergencies in palliative care

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Introduction

In most medical specialties, emergencies are those situations which, if left untreated, will immediately threaten life. In palliative care, where death is an expected outcome, emergencies are those conditions which, if left untreated, will seriously threaten the *quality* of remaining life.

While this chapter focuses on the common oncological emergencies in palliative practice, emergencies may include a wider range of issues, such as the following:

- emergency discharge so a patient's wish to die at home can be met
- emotional emergencies, with high levels of expressed anxiety
- spiritual/existential/social emergencies with pressure to 'sort things out' before it is too late (➔ see Chapter 23)
- pain crisis or other unrelieved symptoms

It is important to have a clear understanding of emergencies in palliative care, as their timely management is critical. A crisis situation filled with anxiety may be transformed to an atmosphere of comfort and well-being by pre-decided standardized team responses that demonstrate clarity and decisiveness to the patient and their family.

Faced with an emergent, acute problem in the palliative care setting, clinicians would do well to first establish answers to the following simple questions:

- Where can we place this patient on their disease trajectory?
- What is causing this particular problem at this particular time?
- What understanding, concerns, and expectations do the patient and family have?
- How will improvement of the acute problem impact the patient's overall condition?
- Would active intervention maintain or improve this patient's biological prospects and quality of life?

There are several emergency situations, which can occur during the palliative care time frame, requiring urgent and prompt diagnosis and management. Maintaining calmness and patient comfort is vital during the decision-making process and during interventions. Anticipating events and having clearly defined protocols for managing them can reduce the dissonance among staff, team members, and other patients. It is equally important that all staff appreciate the nature of these emergencies and the appropriateness of an urgent and competent response.

Sepsis in the neutropenic patient

All clinical staff should be acutely aware of the serious risk and precarious condition of patients who have become neutropenic and febrile following oncological treatments. If not managed rapidly and effectively, these patients will die from overwhelming infection.

Fever during chemotherapy-induced neutropenia may be the only indication of a severe underlying infection, because typically, signs and symptoms of inflammation are attenuated. Physicians must be keenly aware of the infection risks, diagnostic methods, and antimicrobial therapies required in managing febrile neutropenic patients.

Risk assessment

In practice, all patients with a neutrophil count of $<0.5 \times 10^9$/L should be monitored closely. At the first suspicion of fever, or the patient becoming less well, investigations and treatment for neutropenic sepsis should start urgently.

Nutropenic sepsis is defined as a fever higher than 38°C, or symptoms and/or signs of sepsis in a person with a neutrophil count of 0.5×10^9/L or lower.

Management of sepsis in neutropenia

General approach

Management for patients with neutropenia is mostly supportive and based on the aetiology, severity, and duration of the neutropenia. Fever and infections occurring as complications of neutropenia require specific treatment. Surgical care is not usually indicated.

General preventive measures to be taken include the following:

- Use careful oral hygiene to prevent infections of the oral mucosa and teeth; control pain due to oral and gingival lesions with local anaesthetic gels and gargles. For those with ongoing mucositis, include oral rinses 4–6 times/day with sterile water, normal saline, or sodium bicarbonate solutions. Patients should brush their teeth >2 times/day with a soft regular toothbrush.
- Avoid rectal temperature measurements and examinations.
- Skin care during neutropenia should include daily inspection of skin sites likely to be portals of infection (e.g. the perineum and intravascular access sites).
- Regular observation and care for wounds and abrasions.
- Administer stool softeners for constipation. Avoid enema.

Antibiotic therapy

Treat suspected neutropenic sepsis as an acute medical emergency and offer empiric antibiotic therapy immediately. The regimen should be started with advice from the local bacteriologist since antibiotic regimens will vary.

Agents from other antimicrobial classes (e.g. aminoglycosides, fluoroquinolones, vancomycin) may be added for management of complications such as hypotension and pneumonia, or when there is antimicrobial resistance.

Role of antifungal therapy

If the neutropenic patient's fever does not respond within 4–5 days or if the fever recurs with the administration of broad-spectrum antibiotics after an initial afebrile interval, consider re-investigation and adding empiric antifungal coverage with amphotericin B (preferably lipid formulation), a broad-spectrum azole (e.g. voriconazole), or an echinocandin (e.g. caspofungin).

Empiric antifungal therapy

Patients already on antifungal prophylaxis should be switched to a different class if fever persists. Continue therapy for 2 weeks if patient has stabilized and no infectious nidus has been identified.

Role of antiviral therapy

Antiviral treatment for HSV or varicella-zoster virus (VZV) infection is only indicated if there is clinical or laboratory evidence of active viral disease. Influenza virus infection should be treated with neuraminidase inhibitors if the infecting strain is susceptible.

Discharge plan for patients having neutropenic sepsis

Offer discharge to patients having empiric antibiotic therapy for neutropenic sepsis only after the following:

- patient's risk of developing septic complications has been reassessed as low
- taking account of the patient's social and clinical circumstances and discussing the symptoms to look out for and the need to return to hospital promptly if a problem develops

Superior vena cava obstruction

Superior vena cava obstruction (SVCO) may be due to external compression, thrombus formation inside, or direct invasion of the SVG by malignancy. It is caused most commonly by carcinoma of the bronchus (75%), particularly small or squamous cell and lymphomas (15%). Cancers of the breast, colon, oesophagus, and testis account for the remaining 10%.

Symptoms and signs

SVCO usually presents insidiously. When acute, the resulting symptoms are very distressing.

Symptoms

- predominantly those of venous hypertension
- breathlessness
- visual changes
- dizziness
- headache—worse on stooping
- swelling of face, neck, and arms

Signs

- conjunctival and peri-orbital oedema
- dilated neck veins—non-pulsatile
- dilated collateral veins—arms and anterior chest wall
- oedema of hands and arms
- increased respiratory rate
- stridor, cyanosis, and papilloedema are late signs

Management

Confirmation of diagnosis may be done by CT scan, although in the palliative care setting, the nature of the tumour is usually known. The patient should be referred to the oncology centre for urgent management.

General measures

- Dexamethasone 8–16mg p.o. or IV (with proton pump inhibitor cover). There is no good evidence for the efficacy of steroids, but they have been found clinically helpful for associated stridor by reducing airway oedema, or as an anti-tumour agent for lymphoma.
- Immediate relief of distress due to dyspnoea and anxiety through pharmacological and non-pharmacological methods is necessary. Opioids and possibly benzodiazepines are indicated. Supplemental oxygen may be indicated where breathlessness is associated with hypoxia.
- Diuretics like furosemide may be useful by reducing the volume of venous return, decreasing preload to the heart which relieves the increased pressure in the superior vena cava. Dose must be individualized. Depending on response, administer at increments of 20–40mg, no sooner than 6–8h after previous dose, until desired diuresis occurs.

- SVCO with a risk of thrombo-embolism may be treated with streptokinase, urokinase, or recombinant tissue-type plasminogen activator or anticoagulants such as heparin or oral anticoagulants. These agents are most effective when patients are treated within 5 days after the onset of symptoms.
- Patients with SVCO are at risk of seizure, but evidence is very limited in the use of antiseizure prophylaxis.
- Analgesia using the principles of the WHO 3-step analgesic ladder may be useful for the relief of headache.

Definitive treatment

Based on the available expertise, consider standard oncology treatment for the particular underlying cancer, e.g. chemotherapy for small-cell lung cancer (SCLC) and lymphoma, or radiotherapy for non-small-cell carcinoma of the bronchus. An intraluminal stent can be inserted, and is the treatment of choice for patients with severe symptoms. Thrombolysis may be considered prior to stenting.

Prognosis

Without treatment, SVCO can deteriorate over several days, leading to death. Prognosis is poor in a patient presenting with advanced SVCO unless the primary cancer is responsive to radiotherapy or chemotherapy.

Haemorrhage

Haemorrhage may be directly related to the underlying tumour, or caused by treatments, e.g. gastric/duodenal erosion due to treatment with steroids or non-steroidal anti-inflammatory drugs (NSAIDs). A generalized clotting deficiency, seen in thrombocytopenia, hepatic insufficiency, or anti-coagulation therapy may also contribute.

Non-acute haemorrhage

Treatments for non-acute haemorrhage include oncological, systemic, and local measures. Palliative radiotherapy is very useful for treating bleeding from superficial tumours and those of the bronchus and genitourinary tract. If radiotherapy is not appropriate, coagulation should be enhanced with drugs like tranexamic acid.

Intravenous/oral tranexamic acid can be given in the dose of 1.5g as a starting dose, followed by 1g t.d.s./q.d.s. for a week after cessation of bleeding. For oral bleed, tranexamic acid can be used as a 5% mouthwash 10mL q.d.s. Dilute contents of a standard 10% (500mg/5mL) ampoule for injection with 5mL of water, or use a locally prepared solution. These antifibrinolytics can also be applied topically, rectally, or by intrapleural instillation. The adverse effects are dose-dependent and occur in 25% of cases, usually seen as nausea, vomiting, and diarrhoea. Caution is necessary with haematuria, as clot formation may result in further problems such as urinary retention. Local measures for superficial tumours, such as topical tranexamic acid or adrenaline (1:1000) soaks, may be useful. Adding sucralfate as a local astringent to a proton pump inhibitor such as omeprazole or lansoprazole can be beneficial to mitigate mucosal bleeding of the stomach.

Acute haemorrhage

Erosion of a major artery can cause catastrophic haemorrhage, as a terminal event.

Identification of patients at risk of haemorrhage

An attempt should be made to identify patients at high risk for bleeding so that preventive measures may be taken before a crisis occurs. Clinicians may recognize an episodic 'sentinel' or 'herald' bleed, of trivial amount; e.g. mild haemoptysis may occur 24–48 hours before a major bronchial arterial bleed. Caregivers of those patients at risk for major bleeds ought to be informed and prepared mentally and emotionally for such an eventuality. This is to be done with a very high level of sensitivity so as not to cause undue anxiety. In most cases, true catastrophic terminal haemorrhagic events do not occur, even in high-risk patients. Hence, when preparing patients and families of the possibility of a terminal haemorrhage, it is important to temper the information by communicating the rarity of the event.

It is also a time when decisions about transitions in goals of care are made for patients as an advance healthcare directive. It is ideal for families and healthcare providers to know the patient's wishes ahead of time and to talk with the patient openly about end-of-life plans. It may be appropriate to discuss what should be done in the event of a cardiac arrest, and clearly document the details of the discussion in the patient's notes. Depending on where the patient is, a decision should be made regarding the most

appropriate place of care for the patient. Facilities for highly specialized interventions (e.g. specialist surgery, radiotherapy, or interventional radiology) may or may not be available. It may not be appropriate for patients at the end of life to be subjected to transfer to another healthcare centre for interventions that may not confer survival benefit or add to their quality of life.

If the patient chooses to be looked after at home, communicate to the family and staff (and the patient) regarding the need for sedation during the event. It is very important to clarify that the sedation is not intended to hasten the death of the patient. Hospice team assistance at home usually takes charge of the situation, but in certain regions of the world, where there is a dearth of home hospice care, the family member who is briefed and educated on the eventuality may be required to administer the pre-loaded sedative medications themselves.

The planned management is documented and communicated clearly to all staff involved in the patient's treatment. See Box 29.1.

Management of acute severe bleeding

Non-pharmacological management

If the patient has a massive haemorrhage and is clearly dying, support and non-pharmacological interventions are more important; the patient will usually lose consciousness rapidly and may be frightened, especially if left alone.

- Maintain calm. Call for help. Be with the patient and reassure and comfort them. If appropriate, position the patient so as to minimize the possibility of choking.
- Utilize dark blankets or thick red towels to soakup the blood and reduce the visual impact.
- Consider protecting the family members and children from the emotional trauma such that they are not in direct visual view of the catastrophic bleed.

Box 29.1 Anticipatory planning for acute severe bleeding

- Identify 'at-risk' patients: those with a herald bleed, head and neck cancers, haematological cancers, or tumours encasing major vessels.
- Formulate a plan of action, which includes what to expect, whom to contact, and clear documentation of the care plan, including out-of-hours services.
- Communicate the care plan with the patient, caregivers, and healthcare providers.
- Discuss and document resuscitation status.
- Ensure caregivers at home have an emergency contact number.
- Prepare a 'crisis pack' containing sedatives and analgesics: pre-drawn and at bedside for rapid palliation of dyspnoea or pain.
- Ensure supply of dark blankets or thick red towels to soak up the blood.
- Ensure equipment like gloves, aprons, plastic sheet, and clinical waste bags for the disposal of waste and bloodstained materials.
- Suction device—beneficial when patients are choking or aspirating on blood.
- Warm blankets—patients are likely to be cold from ensuing hypotension.

Sedative medication in massive terminal haemorrhage

Control symptoms when possible using 'crisis' medications. A rapidly acting benzodiazepine is indicated for the anxious, distressed patient. The available route of administration guides the choice of drug:

- IV midazolam 5–10mg
- IM injection: midazolam 10mg can be given into a large muscle such as deltoid or gluteal
- rectal route or via a stoma: diazepam rectal solution 10mg
- sublingual: midazolam 5–10mg can be given using a parenteral preparation or the buccal liquid

Note: if the patient is already on benzodiazepines, incrementally higher doses may be needed.

After the event

Caregivers and family members who witness such an event will need a great deal of support.

- Be available to the family to clarify their perceptions.
- Death of a patient due to acute bleeding is a very traumatic event, even for the staff members who engage in the management of the situation. Offer detailed discussions and venting opportunities to the team.
- Provide ongoing support as necessary for relatives and staff members.

Spinal cord compression

Spinal cord compression occurs in 3–5% of patients with cancer. Some 10% of patients with spinal metastases develop cord compression, the frequency being highest in multiple myeloma and cancers of the prostate, breast, and bronchus.

Causes of spinal cord compression

- intramedullary metastases
- intradural metastases
- extradural compression (80%)
  - vertebral body metastasis
  - vertebral collapse
  - tumour spread
  - interruption of vascular supply

Metastatic spinal cord compression as a palliative care emergency

- Potentially preventable cause of severe and irreversible disability, e.g. quadriplegia/paraplegia, loss of bowel and bladder function.
- Patient may die sooner as a consequence of complications due to their disability rather than disease progression.
- Often presents as a neurological emergency (patient may develop irreversible neurological damage within hours/days).
- Rapid assessment, referral, investigation, and treatment are key to prevention of irreversible neurological damage.

Every comprehensive cancer programme should have a clear care pathway for the diagnosis, treatment, rehabilitation, and ongoing care of patients with metastatic spinal cord compression (MSCC).

Symptoms and signs

Spinal cord compression is an emergency, and two questions need to be answered urgently:

- Does this patient have a reasonable likelihood of having spinal cord compression?
- Would this patient benefit from instituting emergency investigation and treatment?

Clinical suspicion is the key to early diagnosis of spinal cord compression.

Sites of spinal cord compression

- thoracic 70%
- lumbosacral 20%
- cervical 10%

Pain

Back pain is the most common symptom, occurring in about 90% of patients, and pain often predates neurological changes by some considerable time. Spinal cord compression must be considered in all cancer patients with back pain. Compression can occur without pain in some 4–17% of patients. The back pain may present as follows:

- new, progressively severe back pain, particularly around the thoracic region
- band-like pain encircling the body and commonly made worse by coughing or straining
- burning or shooting pain radiating down anterior or posterior thigh, as seen in sciatica
- associated difficulty in walking or climbing stairs; reduced power due to progressive motor weakness
- associated sensory impairment or altered sensation in limbs
- bowel or bladder disturbance and loss of sphincter control is a late sign with a poor prognosis

Cauda equina syndrome

Compression of lumbosacral nerve roots below the level of the cord itself results in a different clinical picture:

- new, severe root pain affecting low back, buttocks, perineum, thighs, legs
- loss of sensation, often with tingling or numbness in the saddle area
- leg weakness, often asymmetrical
- bladder, bowel, and sexual dysfunction; occur earlier than in cord compression
- loss of anal reflex

The keys to diagnosing spinal cord compression include the following:

- Having a high index of suspicion in patients with spinal metastases, particularly in patients with breast, lung, and prostate cancer and with pain and tenderness on palpation or percussion of the vertebra at the level of the suspected lesion.
- Giving due attention to patients' complaints about back pain, odd sensations in the legs, and difficulties in passing urine.

Signs

- Multiple sites of compression may produce different and confusing neurological signs (Table 29.1).

Management

The treatment for metastatic spinal disease and metastatic spinal cord compression may be considered in two broad groups. Both levels of treatment are relevant and would improve symptoms, quality of life, and survival:

- treatments primarily to relieve pain and/or prevent vertebral collapse and spinal cord compression
- definitive treatment of bony instability and/or neurological disability

Deciding whether the particular course of treatment is appropriate for a particular patient involves an overall assessment.

Table 29.1 Neurological signs of upper and lower motor neuron lesions

	Upper motor neuron lesion: lesions above L1	Lower motor neuron lesion: lesions below L1
Power	Reduced/absent	Reduced/absent
Tone	Increased	Reduced
Sensation	Sensory loss	Sensory loss
Reflexes (plantars)	Increased (up-going)	Absent/reduced (down-going)

Key questions in deciding on emergency investigations and management:
- Is the patient still walking?
- Is the patient suffering from severe back pain?
- Does the patient already have established cord compression?
- Does the patient have a short prognosis (e.g. week-by-week deterioration)?
- What does the patient want?

Where suspicion of spinal cord compression is high, it is quickest to telephone the oncology team in the cancer centre where the patient has been managed, who can then initiate and coordinate the necessary investigations and appropriate emergency treatment.

The following inputs may be considered immediately after assessment:
- Start on high-dose corticosteroids (e.g. dexamethasone 16mg daily). Steroids are usually begun at high doses, and then tailed off gradually and completely discontinued after some time (4–6 weeks), or to the lowest dose that maintains stability. Radiation-induced oedema may exacerbate symptoms, and the dose of steroids may need to be increased temporarily during radiation treatment.
- Consider gastroprotection with proton pump inhibitors and thromboprophylaxis with low molecular weight heparin.
- Patient should be nursed lying flat if possible.
- If radiotherapy is appropriate, consider transferring the patient to a specialized unit where an MRI scan can be carried out and treatment decisions may be made. If there is complete paraplegia and loss of sphincter control, radiotherapy may improve pain control but is unlikely to restore function.
- If radiotherapy is not relevant or not possible, a detailed communication session is done with the family to discuss and collaboratively decide on the appropriate care setting.

Definitive treatment with radiotherapy and surgical decompression are to be considered urgently. See Table 29.2.

Continued palliative care multidisciplinary team support through optimal symptom control, nursing care, physiotherapy, occupational therapy, and psychosocial support add value to the treatment outcomes and rehabilitation.

Analgesia

To patients with painful spinal metastases, offer conventional analgesia, including NSAIDs and non-opioid and opioid medication, as required, in

Table 29.2 Definitive treatment of spinal cord compression

Indications for surgical decompression	Indications for radiotherapy
• Uncertain cause—to confirm by histology	• Radiosensitive tumour
• Radiotherapy has not been effective or symptoms persist despite maximum radiotherapy	• Multiple levels of compression
• Radio-resistant tumour, e.g. melanoma, sarcoma	• Unfit for major surgery
• Unstable spine	• Patient choice
• Major structural compression	
• Cervical cord lesion	
• Solitary vertebral metastasis	

escalating doses as described by the WHO three-step pain relief ladder. Consider referral for interventional procedures such as epidural or intrathecal analgesia and vertebroplasty, and neurosurgical interventions for patients with intractable pain from spinal metastases.

Vertebroplasty and kyphoplasty

Vertebroplasty or kyphoplasty are indicated when patients develop vertebral metastases with no evidence of cord compression or spinal instability, but have persistent mechanical pain resistant to conventional analgesia.

Institute the following nursing and rehabilitation measures to reduce morbidity:

- mobility management (risk of venous thrombosis)
- skin management in a patient confined to bed (risk of pressure sores)
- bowel management
- urinary system care

There is no consensus on the optimum time to start mobilizing patients diagnosed with cord compression. In general, if the spine is stable and the pain is relatively well controlled, it would seem wise to introduce physiotherapy as soon as possible to maintain muscle tone and motor function. Occupational therapy benefits outcomes through goal-setting and rehabilitative support that improves function.

Ensure that communication with patients and families with known or suspected spinal cord compression is clear and consistent. Patients, families, and caregivers should be informed of the reason for the symptoms, helped to nurture realistic expectations, and involved in the decision-making process.

Prognosis

Function will be retained in 70% of patients who were ambulant prior to treatment. Functional improvement is also seen in 5% of those who were paraplegic at the outset. Return of motor function is better in those with incomplete spinal compression, and particularly so with partial lesions of the cauda equina. Loss of sphincter function indicates poor prognosis.

Overall, 30% of patients survive for one year. A patient who is ambulant after treatment may survive for 8–9 months, but the life expectancy for a patient who remains paraplegic is generally a few weeks.

Hypercalcaemia

see Chapter 15, Endocrine and metabolic complications of advanced cancer.

Malignancy-associated hypercalcaemia is a potentially life-threatening condition estimated to occur in 20% of patients with cancer during the course of their disease. This condition requires attentive management in patients who are otherwise functioning well.

The most common type of hypercalcaemia associated with cancer is humoral hypercalcaemia of malignancy (HHM), seen in 80% of cases. It can occur in the absence of bone metastases in patients with squamous carcinomas; renal, bladder, and ovarian carcinoma; and HTLV-1 lymphomas. Owing to local osteolysis, it often develops in patients with skeletal metastases, associated with metastatic breast cancer, and multiple myeloma. In both situations, tumour-derived parathyroid hormone-related peptide (PTHrP) is thought to play a major causative role by promoting osteoclastic bone resorption and tubular reabsorption of calcium filtered by the kidney. The other rare causes of hypercalcaemia are secretion of active vitamin D by some lymphomas and ectopic parathyroid hormone (PTH) secretion. The development of hypercalcaemia usually indicates limited life expectancy (weeks to months), except in multiple myeloma and breast cancer.

The plasma level of calcium is closely regulated. It is useful to measure the ionized calcium level, especially when the serum albumin is not within normal ranges, or when a calcium disorder is suspected despite a normal total calcium level.

Corrected calcium

See Table 29.3

Signs and symptoms

The severity of symptoms relates not only to the absolute calcium level but also to how fast it takes for the rise in serum calcium. Total serum calcium levels higher than 3.5mmol/L (14mg/dL) can be life-threatening, and must be treated aggressively. See Tables 29.4 and 29.5.

Mild prolonged hypercalcaemia may produce mild or no symptoms, or recurring problems such as constipation or kidney stones. Sudden-onset and severe hypercalcaemia may cause dramatic symptoms, usually including confusion and lethargy, possibly leading quickly to death if left untreated.

Table 29.3 Corrected calcium level and normal ranges

Corrected calcium = measured calcium + [(40-serum albumin g/L) x 0.02] See pp. 463–5	Total calcium (mg/dL) + 0.8 (4.0 albumin (g/dL))
Normal range	
Total calcium	2.2–2.6 mmol/L

Data sourced from Payne R.B. et al (1979) Interpretation of serum total calcium: effects of adjustment for albumin concentration on frequency of abnormal values on detection of change in the individual. J. Clin. Path 32:56–60

Table 29.4 Hypercalcaemia definitions (check local laboratory)

Corrected serum calcium >2.60mmol/ L **or** ionized calcium >1.25mmol/L	
Mild	2.6–3mmol/L
Moderate	3–3.5mmol/L
Severe/Life-threatening	>3.5mmol/L

Table 29.5 Symptoms and signs of hypercalcaemia

Central nervous system	• Lethargy • Weakness • Confusion • Coma
Renal	• Polyuria • Nocturia • Dehydration • Renal stones • Renal failure
Gastrointestinal	• Constipation • Nausea • Anorexia • Pancreatitis • Gastric ulcer
Cardiac	• Syncope from arrhythmias

Management

The decision to treat hypercalcaemia must take into consideration the patient's position in the disease trajectory, and the potential benefits and burdens of undergoing investigations and administering parenteral fluids and medications, as well as the patient's preference and overall goals of care. The urgency of treatment depends on the severity of hypercalcaemia and associated symptoms. A patient who is already extremely debilitated by the effects of advanced cancer is less likely to experience benefit from treatment of hypercalcaemia. It may be altogether unnecessary if the patient is very near to death.

General measures

Normal diet may be continued. The absorption of calcium from the gut is generally reduced, so patients may eat what they wish regardless of the calcium content of food. Mobilization of the patients should be encouraged when appropriate.

Hydration and diuresis

Patients are usually dehydrated and need adequate fluid replacement. Oral intake of fluid should be increased appropriate for the clinical condition. In patients with severe hypercalcaemia, intravenous rehydration is recommended. Normal saline should be used to achieve a urine output of 200mL per hour. A loop diuretic may be used in low dosages (e.g. furosemide 10–20mg) to lower the serum calcium level further if necessary, after the intravascular volume has been restored.

Specific management

While anti-hypercalcaemic therapy can be used temporarily to resolve hypercalcaemic symptoms, treatment for humoral hypercalcaemia of malignancy (HHM) ultimately requires long-term surgical, radiotherapeutic, or chemotherapeutic treatment targeted at the PTHrP-producing tumour.

Bisphosphonates

In malignancy-associated hypercalcaemia, bisphosphonates are the mainstay of treatment. This group of drugs inhibits osteoclastic bone resorption. Bisphosphonates are appropriate to administer when corrected serum calcium is ≥ 3.0mmol/L, or when a serum calcium of < 3.0mmol/L is accompanied by symptoms. The plasma calcium levels start to decline in 48 hours after the commencement of treatment and fall progressively for the next 6 days. Consider monitoring serum calcium weekly; treatment may need to be repeated when hypercalcaemia recurs.

Renal failure is the most serious potential adverse effect. Therefore, adequate hydration should be maintained and serum creatinine checked, especially if treatment with bisphosphonates is being considered. Caution is required in patients receiving other drugs that may affect renal function (e.g. NSAIDs, ACE inhibitors, aminoglycosides).

The available agents for treatment of hypercalcaemia are pamidronate, zoledronic acid, ibandronic acid, and sodium clodronate (not UK). No agent has been proven to be clearly superior to the others in terms of efficacy.

The parenteral route is preferred to the oral route owing to the poor oral bioavailability of bisphosphonates and the high frequency of gastrointestinal intolerance.

If the IV route is inaccessible, bisphosphonates can be administered by CSCI, together with SC hydration.

- pamidronate disodium 90mg in 1L 0.9% saline over 12–24h
- zoledronic acid 4mg IV over 15 minutes
- sodium clodronate (not UK) 1,500mg in 50–250mL 0.9% saline or 5% glucose over 2–3h

Denosumab

The US Food and Drug Administration (FDA) approves denosumab (Xgeva), a monoclonal antibody that specifically targets RANKL (receptor activator of nuclear factor kappa-B ligand) for treatment of hypercalcaemia of malignancy refractory to bisphosphonate therapy.

Calcitonin

In severe hypercalcaemia refractory to saline diuresis, calcitonin can be given every 6 hours. This treatment has a rapid onset but short duration of effect, and patients develop tolerance to the calcium-lowering effect.

Glucocorticoids

In hypercalcaemia mediated by vitamin D and in haematological malignancies (e.g. myeloma, lymphoma), glucocorticoids are the first line of therapy after fluids.

Other antiresorptive agents that are used occasionally (not UK) include plicamycin (Mithracin) and gallium nitrate (Ganite).

Dialysis

In cases of resistant, life-threatening hypercalcaemia, haemodialysis against a low-calcium dialysate is more effective than peritoneal dialysis in lowering serum calcium levels. Therapy for the underlying condition should be instituted as soon as possible.

Surgery

Surgical interventions come into play when the hypercalcaemic crisis resulting from primary hyperparathyroidism or skeletal conditions are amenable to surgical correction.

Prognosis

Some 80% of cancer patients with hypercalcaemia survive less than one year.

Further reading

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Chapter 30

The terminal phase

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Introduction

> Death is not extinguishing the light; it is putting out the lamp because the dawn has come.
>
> Rabindranath Tagore

The terminal phase is the period of inexorable and irreversible decline in functional status prior to death.

It is the period when there is day-to-day deterioration, particularly of strength, appetite, and awareness. This may unfold gradually over days or weeks, or occur precipitously following an unexpected event, e.g. stroke. These challenges may present as sudden changes in the clinical status needing urgent attention. More often they are predictable, and reflect a final common pathway of many progressive illnesses. See Box 30.1.

Despite the several guidelines made available over the past few years on managing end-of-life care, knowledge and confidence among healthcare professionals for looking after those in the last few days, weeks, months, or even years of their lives is still far from ideal.[1]

If we are able to foresee these and take proactive steps, then it can result in better quality of life for the patient as well as the family.

Principles of a good death

- to know when death is coming, and to understand what can be expected
- to be able to retain control of what happens
- to be afforded dignity and privacy
- to have control over pain relief and other symptom control
- to have choice and control over where death occurs
- to have access to information and expertise
- to have access to any spiritual or emotional support required
- to have access to hospice care in any setting—hospital, home, or in the community
- to have control over who is present
- to be able to issue advance directives and ensure wishes are respected
- to have time to say goodbye, and utilize the precious moments, per individual yearnings
- to be able to leave when it is time to go, and not to have life prolonged pointlessly[2]

Box 30.1 The challenging aspects of managing the terminal phase

- complex symptoms
- overwhelming spiritual concerns
- psychosocial distress
- functional decline
- communication challenges
- difficult decisions
- increasing need for clinical vigilance and care

Discussing prognosis

Patients frequently ask, 'How long have I got?'.

It is notoriously difficult to predict when death will occur, particularly so for a patient with a long-term chronic illness. It is wise to avoid the trap of making a prediction for 'how long' or venture a guess. If pushed to do so, it should be made clear that any predictions are only a guide. It is best to talk in terms of 'days', 'weeks', or 'months', as appropriate.

> When we see someone deteriorating from week to week, it is better to predict in terms of weeks; when there is deterioration from day to day, then we are usually talking in terms of days, and yet … everyone is different.

It is crucial to enquire into the feelings and the real questions behind the patient's words. When a patient asks, 'Doctor, how long?', the implicit question usually is, 'Doctor, now that I have very little time left, what can I expect? How can you help me?'. This approach can provide opportunity to surface the anxieties and fears that the person may be harbouring, which may be further addressed through effective communication and counselling.

Signs and symptoms of approaching death

Patients may have expressed wishes regarding the manner and place of their death. A key factor to facilitating these wishes is for the healthcare professional to know when the patient is dying. It can be difficult to estimate when a patient is approaching the end of life, and one should allow for a range of possibilities when planning care.

The starting point is careful consideration of the patient's overall clinical prospects. An affirmative answer to the self-addressed question, 'Would I be surprised if this person were to die in the next few days?', can be helpful in reorienting the clinical attention.

The clearest signs of approaching death are picked up by the day-by-day assessment of deterioration (Table 30.1).[3]

Table 30.1 Signs and symptoms of approaching death

Profound tiredness and weakness	Reduced interest in getting out of bed Needing assistance with all care Less interest in things happening around them
Diminished intake of food and fluids	
Drowsy or reduced cognition	May be disorientated in time and place Difficulty concentrating Scarcely able to cooperate and converse with carers
Gaunt appearance	
Difficulty in swallowing medicine	

Should such symptoms develop over a matter of days instead of the usual weeks, it is important to exclude reversible causes for the deterioration, such as infection, hypercalcaemia, or adverse effects of changes in medications.

Goals for the last few days

- Ensure the patient's comfort physically, emotionally, and spiritually.
- Make the end of life peaceful and dignified.
- By the care and support given to the dying patient and their carers, make the memory of the dying process as positive as possible for the family.

The process of dying is a very personal experience. Helping to explore the patient's wishes about death and dying should ideally take place when the disease becomes unresponsive to available treatment options, much before final days of life are reached. However, important discussions can still take place even at this late phase, and professional teams should encourage this dialogue. It is important to seek the patient's views and feelings on care plans and interventions while they remain conscious, even when the weakness makes communication difficult. Some of the questions may include preferred place of death, burial/cremation, or issues related to financial or 'unfinished' business.

As the patient becomes unable to participate in the discussions, the role of the family becomes more important, although their wishes need to be balanced with the team's understanding of the patient's best interest. Relatives need to be given time to have their questions and concerns clarified as clearly as possible. Each family has their own unique dynamics of interaction, decision-making, and communication. Honest and caring dialogue, even about bad news and poor prognosis, can reduce feelings of guilt, depression, and hopelessness. Once the family has clarity on matters that are important to their loved ones, they gain great moments together.

Where possible, families and carers should be offered the opportunity to participate in the physical care of patients. Carers should be invited to stay, if they want to, while nursing and medical procedures are carried out. Occasionally, relatives would like to participate in carrying out the last offices after death, and this can be a very important part of their last 'duty' on behalf of their dead loved one. Sensitive responses to ongoing events and fostering an atmosphere of competence and compassion can greatly influence the grieving process of those left behind. Providing the environment to say the last goodbyes to close family members, children, and dependents, and time to forgive and express love, can be therapeutic and enables normal bereavement.

In countries where end of life happens mostly at home, active involvement and empowerment of the family in every aspect, with ongoing support from the hospice team, becomes the main channel for delivering the necessary care.

Approach to care in the terminal phase

The majority of expected deaths continue to occur in hospital settings, which are often not the best setting for end-of-life care.[4] Providing culturally sensitive end-of-life care is perceived as challenging by most healthcare professionals owing to lack of sufficient training and a dearth of evidence-based medical practices and guidelines. It can be difficult to express sufficient sensitivity and warmth when challenged with the complexities of the symptoms and the uncertainties of the terminal phase.

Collaborative multidisciplinary approach

Effective terminal care needs a team approach. No single member of the palliative care team, no matter how committed or gifted, can meet all the palliative care needs of a patient and their family.

Effective multidisciplinary working depends on

- recognizing the centrality of patient and family needs
- clear understanding of the role of other professionals and the value of their inputs
- good communication amongst the team members
- early integration of specialist palliative services

Referral to specialist palliative care services is most appropriate when

- one or more distressing symptoms prove difficult to control
- there is severe emotional distress associated with the patient's condition
- there are dependent children and/or elderly vulnerable relatives

Assessment of patients' needs

The focus of assessment in the last few days of life is to determine what, apart from dying itself, the patient is most concerned about and which concerns may be effectively addressed. Patients may under-report their symptoms. Although families may be very helpful in understanding non-verbal cues, they may also misinterpret and exaggerate the patient's symptoms in their own distress. Thorough systematic evaluation of the patient's comfort and palliative care needs—including need for pain relief; control of breathlessness, agitation, or other distressing physical or psychological symptoms; and keeping their nutrition and hydration status under review—are important components of competent care.

Talking about death and dying

As a taboo subject, few people feel comfortable about discussing death and dying, even though it is natural, certain, and is happening all around us all the time.

Opening up discussion can be very liberating to patients who can feel they have not been given permission to talk about dying before, as this would be admitting defeat.

Sometimes the direct question, 'Are you worried about dying?', is most appropriate.

Often a patient's biggest fears are groundless, and reassurances can be given. Where reassurance cannot be given, it is helpful to break the fear down into constituent parts and try to deal with the aspects of the fear that can be dealt with (➔ see Chapter 2, Communication in palliative care).

Language and cultural barriers compound the challenges when making critical decisions. Different religions and cultures have divergent approaches to the dying process. It is important to be sensitive to the patient's set of beliefs. If in doubt, ask a family member. Offence is more likely to be caused by not asking than by asking (➔ see Chapter 23, Spiritual care).

Principles of symptom management during the terminal phase

- maintain an analytical approach to symptom control
- avoid unnecessary interventions
- review drugs—the need for each and the route of administration
- maintain excellent nursing care
- maintain effective communication, update the family and carers about the situation, and assist in their coping
- assure regular medical review for overall comfort
- assure availability

Physical needs

Common problems that need to be addressed are nausea, pain, oral concerns, sleep disturbance, weakness, confusion (sometimes hallucinations), and pressure sores. All ongoing medications are reviewed, and only those that treat symptoms and add to comfort are continued. Skilled nursing care is crucial to ensure patients' comfort. Examples include back care, using a pressure-relieving mattress to reduce the risk of pressure sores and the need for frequent turning, offering the patient a urinary catheter if they are too weak to get out of bed, and ensuring that the mouth is kept clean and moist when fluid intake is poor. Patients rarely worry about nutritional and fluid intake, but this may be a major concern for the family, and needs to be dealt with due sensitivity and patience.

Psychological needs

The key to psychological care is regular communications with the patient, in a gentle and sensitive manner. How the patient interprets their disease and its symptoms may be a cause of suffering itself. Assessing how the patient feels about their situation can shed light on their needs and distress (Table 30.2). However, deep probing at this stage may be inappropriate, as the goal is psychological comfort and peace, now. Anxiety and agitation may require medication.

Table 30.2 Patients' fears

Fears associated with symptoms	**E.g.** 'The pain will escalate to agony', 'Breathing will stop if I fall asleep'
Other emotional distress	Perceptions on dependence on the family, e.g. 'I am a burden and it would be better if I was out of the way'
Past experience	Contact with and memories of patients who died in unpleasant circumstances and with unresolved issues
Preferences about treatment or about withholding treatment	**E.g.** 'What if nobody listens to me? 'What if no one takes my wishes seriously?'
Fears about morphine	**E.g.** 'If I use morphine now, it will not work when I really need it'
Death and dying	Patients frequently adapt to the fact that they will die, but are fearful of the process leading up to death

Dignity

Sense of dignity is the very personal appraisal of the situation. Maintenance of dignity in a manner conducive to the particular patient's comfort is an important goal of palliative care. 'What do I need to know about you as a person to give you the best care possible?' is a well-researched approach that ignites warm conversations and helps to personalize the care plan.[5]

Spiritual needs

Spiritual disquiet or spiritual pain may be relieved by allowing the expression of feelings and thoughts, particularly of fear and loss of control. Patients often harbour deep concerns about the close family at this stage. There may be a need to address issues of unresolved conflict or guilt.

Families often want to know that the patient is comfortable and not suffering. If appropriate, it may be helpful for them to be aware of the experiences of people who have had near-death experiences, which are often described as tranquil and peaceful. The team can also assist the family and the patient in accomplishing specific religious tasks, e.g. absolution, confession, or other forms of religious preparation.

Physical examination

Examination is kept to the minimum to avoid distress. Examine the following:

- any site of potential pain; patients may be comfortable at rest but in pain on being turned, which they may not readily admit
- any relevant area of the body as suggested by the patient's history or non-verbal signs that might be causing discomfort
- mouth and back, including back of the head and ears
- sites of insertion of IV/SC lines

Investigations

There is little need for investigations in the terminal stages. Any investigation at the end of life should have a clear and justifiable purpose, such as excluding reversible conditions where treatment is available and would make the patient more comfortable.

Review of medication

At this stage comfort is the priority. Unnecessary medication should be stopped, but analgesics, anti-emetics, anxiolytics/antipsychotics, and drugs being used for symptom control, including anticonvulsants, will need to be continued. If the patient is unable to swallow their essential medicines, an alternative route of administration can be considered. These changes are explained to relatives, who may become anxious if the tablets which the patient has had to take for many years have now been suddenly discontinued.

Routes for medicine delivery in the terminal phase

- The intramuscular route for injections should be avoided as it is too painful.
- If buccal medicines are given, it is important that the mouth is kept moist.
- The rectal route can be very useful for certain patients, although it is more or less accepted in different cultures.
- Topical fentanyl or buprenorphine patches should be avoided for pain in the terminal stages unless they have been used and stabilized before this time, since titration to the right dose at this stage is difficult.
- In many instances a syringe driver is used so that finer adjustments can be made in accord with the patient's changing requirements.

Even when patients are dying, it is often possible to communicate with them and to get their consent for, for example, subcutaneous medication.

- Potential sedative side effects of analgesia may need to be explained.
- The treatment plan should define clearly what should be done in the event of a symptom breakthrough.

As the patient becomes less aware, however, it is the family and the nursing staff who become the patient's advocate. At this point a plan of 'goals of care' needs to be understood and agreed between the doctors, nurses, family members, and other carers through regular, honest, and clear communications.

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Common problems in the last 48 hours

> How people die remains in the memory of those who live on.
>
> Dame Cicely Saunders

Four common end-of-life care domains considered important to both patients and their families: (1) effective communication and shared decision-making, (2) expert care, (3) respectful and compassionate care, and (4) trust and confidence in the care team.[1] In addition to efforts at extending life, being free of pain and other symptoms and dying at home are important considerations for persons at the end of life.

Common problems in the terminal phase

- respiratory tract secretions
- restlessness/anguish
- pain
- breathlessness
- nausea/vomiting
- myoclonic twitching

Respiratory tract secretions

Weakness in the last few days of life can result in an inability to clear respiratory secretions, leading to noisy, moist breathing (death rattle). It occurs in 50% of dying patients and is caused by fluid pooling in the hypopharynx. This is often very distressing to family members; it should be treated prophylactically, as it is easier to prevent secretions forming than removing those that have gathered in the upper airways or oropharynx.

Management

General measures

General measures include repositioning the patient to allow draining of oral fluids. Explain to the family that the noise is due to the collected secretions. It is important to reassure the relatives that the noise does not indicate suffocation, choking, or distress. Suctioning is not recommended unless secretions are easily accessible in the hypopharynx. If the patient is deeply unconscious, gentle suction can be used.

Specific measures

Prophylactic use of hyoscine butylbromide 60mg/24h has been shown to significantly reduce the incidence of 'death rattle'. Late administration produces limited results.

- alternatives to hyoscine butylbromide:
  - glycopyrronium bromide 200mcg stat or CSCI 0.6–1.2mg/24h (glycopyrronium does not cause sedation or confusion. It is useful for the patient who is still conscious and wishes to remain as alert as possible)
  - hyoscine hydrobromide 200–400micrograms stat or CSCI 1.2–2.4mg/h (more sedating than hyoscine butylbromide)

- if the respiratory rate is >20 breaths/min, the noise may be reduced by slowing the respiratory rate: e.g. inj. morphine 2–5mg SC (or one-sixth of the 24h dose if already on CSCI) and repeat after 30min if the respiratory rate still >20/min
- sedative drugs such as midazolam may be used if necessary to ensure that the patient is not distressed

Restlessness/anguish

All potentially reversible causes of agitation (see the 'Think list' in Box 30.2) in the terminal phase should be excluded. A diagnosis of terminal agitation can only be made if reversible conditions are excluded or are failing to respond to treatment.

Restlessness, agitation, paranoia, and combativeness are also associated with delirium that occurs in around 80% patients in the final days. If the patient is clearly distressed, some degree of sedation is warranted. This decision should be discussed with the patient, if at all possible, and the family.

Management

Examination and explanation

Treat the treatable causes. Once any treatable causes of agitation have been excluded, it is important to inform the family in attendance of the clinical findings, and of the management options, emphasizing clearly that the goals of treatment in this situation are primarily comfort and dignity. The combination of haloperidol with a benzodiazepine (midazolam) is effective. The subcutaneous route is preferred, usually as CSCI. Intermittent SC doses are equally effective in circumstances where an infusion facility is not available.

Medication

- Midazolam 2.5–10mg SC stat and 15–30mg/24h given by CSCI or intermittent SC doses of 2.5mg q.4h. If sublingual route is tolerated, lorazepam 0.5mg q.4h is a good alternative. Clonazepam (1–4mg CSCI/24h) is sometimes used instead of midazolam, particularly if the patient has neuropathic pain and can no longer take medications by mouth. If the patient remains distressed, other medications (e.g. levomepromazine) could be added.

Box 30.2 'Think list' for some common reversible causes of terminal agitation

- pain
- urinary retention
- full rectum
- nausea
- cerebral irritability
- anxiety and fear
- side effects of medication
- poor positioning

- Levomepromazine is another option. It is given as 10–25mg SC stat followed by 25–100mg/24h by CSCI. It is unusual for patients to require larger doses, but, if necessary, up to 200mg/24h can be given. This drug can lower the seizure threshold.
- Haloperidol 1.5–5mg SC stat followed by 1.5–5mg/24h CSCI may be used, very rarely going above 10mg/24h. Extrapyramidal symptoms can occur, particularly at higher doses. Haloperidol is less sedating than levomepromazine.
- Phenobarbital 100mg IM/IV stat and 300–600mg/24h by CSCI should be effective, but higher doses may be needed. As phenobarbital is incompatible with most other drugs, a second syringe driver is needed. An intermittent IV/IM dose of phenobarbital is 50–100mg q.8h and this may be adjusted based on clinical response. Avoid multiple sc doses since it can cause local necrosis. If stat doses are required, they may be given using IV/IM if available and then followed by CSCI.
- If a syringe driver is unavailable, alternative phenothiazines or benzodiazepines may be given sublingually or rectally, e.g. chlorpromazine is given as 25mg per rectum 4–6 hourly, which is escalated gradually (up to 100–200mg 4h), based on the response. Diazepam may be used rectally as 10mg p.r.n. and clonazepam sublingually as 0.5mg and this may be titrated upwards.
- Propofol, an anaesthetic agent, has been used intravenously under specialist supervision to treat intractable cases.

Cerebral oedema

In the terminal stages of patients with cerebral tumours, intracranial pressure due to cerebral oedema can cause a rapid and severe escalation of headache (which can be made worse by opioids) and terminal agitation. Generous doses of opioids, however, may be effective in addition to an NSAID and midazolam. In a dying unconscious or semiconscious patient, it is unnecessary to replace oral steroids with subcutaneous steroids. The oedema by this stage is usually not controlled by steroids. At best, it may only serve to prolong the dying phase. Emphasis is placed on adequate pain control and sedation.

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Standards of care for the dying patient

The Liverpool Care Pathway

The Liverpool Care Pathway (LCP) was a unique document developed in England in the late 1990s by the Marie Curie Palliative Care Institute in Liverpool and the Royal Liverpool University Hospital to enable systematic care of terminally ill patients.

It was recognized that patients in acute care settings do not have the same comfort, care, and dignity at the end of life as in hospices. The LCP delineated a care pathway based on the standards of care of the dying in the hospice setting. The aim was to transfer the ethos of appropriate end-of-life care to all healthcare settings and provide clinical teams with a guide to review the need for investigations and interventions at the end of life. To support hospital staff, it also offered general guidance regarding anticipatory prescribing for symptoms that occur during the terminal phase.[1]

What were the issues?

The LCP was used extensively in many regions of the UK for over a decade and is still used in other parts of the world. From around 2009 onwards, adverse publicity regarding its inappropriate use in several patients started to appear in the media. They highlighted situations where there was misuse of the LCP, and poor communication regarding its use. There were examples of food and fluids being inappropriately denied to dying patients, and hospitals being paid incentives to use the LCP.

All this adverse publicity prompted the Department of Health in the UK to launch an independent review of the LCP in 2012, chaired by Baroness Julia Neuberger. Entitled 'More Care, Less Pathway', it was published in July 2013.[2] The review highlighted major contributors to the issues with the LCP in managing the end-of-life phase, such as difficulties with diagnosing dying, ineffective communication, and lack of sustained training for generic staff. It recommended that the LCP be phased out and be replaced with an individualized end-of-life care plan. It also stated that the care decisions should rest with a senior clinician responsible for the patient. A new system-wide approach to improving the quality of care for the dying was recommended. The use of the LCP was phased out by the end of July 2014 and is no longer being used in the UK.

The five priorities for end-of-life care

Following the LCP review and its withdrawal, the Leadership Alliance for the Care of Dying People (LACDP) published a report called 'One Chance to Get It Right' in June 2014, with five priorities for care.[3] These highlight important principles of care at the end of life for each individual and provide practical guidance for each theme of care.

Many hospital trusts in the UK have moved away from using protocols and specific documents since then, and are using these guiding principles with individualized care plans for each patient. There is also emphasis on consistent and ongoing training for healthcare staff involved in managing patients at the end of life.

Pathways based on the LCP continue to be used and evaluated in several other countries for patients in the terminal phase of life, with varying levels of impact.[4]

The five priorities for caring for people at the end of life are as follows:

1 Identification

The possibility that a person is dying and may be in the final days and hours of life should be recognized so that the person's needs and wishes are respected and honoured. Potentially reversible causes of clinical deterioration need to be excluded as the diagnosis of dying can be quite difficult to confirm at times. It is therefore advised that senior clinicians responsible for the patient should be involved in this assessment.

2 Communication

Sensitive and clear communication should occur between the patient, staff, and those who are important to the person. Issues such as hearing loss, visual loss, language difficulties, and learning difficulties should all be considered. The recommendation is to ensure that important information is clearly documented for continuity of the same care plan in all settings and amongst all staff involved.

3 Treatment decisions

Decisions about treatment and care should be discussed appropriately with the dying person and those important to them. Ceilings of care need to be considered, e.g. the appropriateness of using antibiotics if an infection develops. The preferred place of care for the dying person should also be established and clearly documented so that the patient's wishes are respected and honoured as much as possible.[2]

4 Family and carers

The needs of the family and carers should be assessed, respected, and supported during the last days with their loved ones and into their own bereavement. As this can be a very emotional and exhausting time for families, compassion and consideration are central in the interactions during this time. A few examples are flexibility in visiting hours, provision for close family to stay overnight, help and advice regarding transport, and assistance in resolving other matters, e.g. finance-related concerns. Communication with the primary healthcare team is important at this stage. When families are bereaved, it is vital that follow-up and counselling are offered and arranged with the bereavement services, especially if the dying process has been particularly traumatic or complex.

5 Care plan

An individual care plan should include guidance regarding feeding, hydration, and symptom management. If the patient is still able to swallow and wishes to continue eating and drinking, then this should be facilitated appropriately. Any medication that may be needed for distressing symptoms at the end of life should be prescribed in anticipation to ensure they are readily available when needed without delay. The spiritual, psychological, and social care needs of the person should also be assessed and delivered in a holistic manner with the help of experienced and trained staff.

An overview of the current situation

Various UK national organizations, such as the Care Quality Commission, General Medical Council, Nursing and Midwifery Council, Royal College of Nursing, and Royal College of General Practitioners, have committed to

improve end-of-life care by acting on the recommendations in the report 'One Chance to Get It Right'. This has been carried out using a systems-wide approach, including inspections, working groups, workshops, issuing new guidance, online training, and incorporating end-of-life care into undergraduate curricula. This overview of progress was published in another report entitled 'One Chance to Get It Right: One Year On Report' in July 2015.[4] In addition, the National Institute of Health and Care Excellence (NICE) published new guidance on the management of care for dying adults in December 2015.[5] Overall, these organizations have jointly increased awareness amongst healthcare staff regarding the importance of competent assessment of persons at the end of life, in order to provide the best care for them and their family.

In many countries of the world, the concept of terminal care and dignified dying are still to take root. In a few of them, e.g. India, end-of-life care guidelines based on the International Collaborative for Best Care for the Dying Person suitable to the clinical and cultural practices of the region are being evaluated. Although the accreditation boards of hospitals in most countries expect an active end-of-life care policy at healthcare institutions, the systems to make them functional and effective are far from ideal owing to poor training and awareness in this realm of care. Much effort is required globally to incorporate dignity and quality of life as valued parameters during decision-making in healthcare. As awareness improves, processes for instituting the most appropriate care for a patient in advanced intractable multisystem failure would naturally follow.

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Chapter 31

Bereavement

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Introduction

> Grief is itself a medicine.
>
> William Cowper (1666–1709), anatomist and surgeon

Grief and mourning are generally adaptive responses following a bereavement or other major loss. Their manifestations will vary from person to person, but will often include physical, cognitive, behavioural, and emotional elements. For a close personal bereavement, grief is likely to continue for a long time and may recur in a modified form, stimulated by anniversaries, further losses, or other reminders. Most cultures provide accounts of what happens after death (such as religious accounts of an afterlife) and provide guidance about how the bereaved should feel and behave, but in an increasingly secular society these may now have less influence. Although people are likely to be changed by the experience of loss, most, in time, find they are able to function well and enjoy life again. A compassionate approach surrounding the death can positively impact on adjustment in bereavement.

Normal manifestations of grief

Physical manifestations

Symptoms experienced by a bereaved person may include a hollow or churning feeling in the stomach, tightness in the chest or throat, oversensitivity to noise, shortness of breath, muscle weakness, unexpected bouts of tears (particularly distressing in public), lack of energy, and dry mouth. People may misinterpret these symptoms as indications of a serious illness and require reassurance. However, in light of increased morbidity following caregiving and bereavement, completing a thorough assessment of physical health is good practice and relieves concerns for both the bereaved and those supporting them.

Emotional manifestations

For many, a sense of shock and numbness is the initial emotional response to bereavement. Feelings of anger (directed at family, friends, medical staff, God, the deceased, or no one in particular) and feelings of guilt (relating to real or imagined failings) are common, as is a yearning or desire for the return of the deceased. Anxiety and a sense of helplessness and disorganization are also normal responses. Sadness is the most commonly recognized manifestation of grief, but the greatest depth of sadness, something akin to depression, is often not reached until many months after the death. For some, feelings of relief and freedom may also be present, although people may then feel guilty for having these feelings.

Cognitive manifestations

Disbelief and a sense of unreality are frequently present early in a bereavement. The bereaved may be preoccupied with thoughts about the deceased and ruminate about the lost person. It is also common for the bereaved to have a sense (visual, auditory, etc.) of the presence of the deceased. Short-term memory, the ability to concentrate, and sense of purpose are frequently detrimentally affected for some time.

Behavioural manifestations

Appetite and sleep may be disturbed, and dreams that involve the deceased can occur and may be comforting or disturbing for the bereaved. The bereaved person may withdraw socially, avoid reminders of the deceased, or act in an absent-minded way. They may also engage in restless overactivity, behaviour which suggests that they are at some level either avoiding the pain of loss or searching for the deceased. A desire to revisit places or carrying objects that remind them of the deceased is common. Some people contemplate rapid and radical changes in their lifestyle (e.g. new relationship or move of house), which may represent a way of avoiding the pain of bereavement. Such rapid changes soon after a bereavement are not normally advisable. At times, the bereaved may question their lack of tears and interpret this as a failure on their behalf. Mourners who experience this require validation of their emotional responses.

Theories of grief

Psychological/psychiatric models

Grief and bereavement have been analysed over many years, and it is generally agreed that there is no single 'correct' or 'true' theory that fully explains the experience of loss or accounts for the emotions, experiences, and cultural practices which characterize grief and mourning. Within broad cultural constraints, individuals manage bereavement in different ways, reflecting the diverse range of human responses and cultures. In the UK, for example, there are a number of accepted ways to behave, but most are characterized by stoicism and emotional restraint, especially in public. Bereavement support services can facilitate emotional expression where appropriate, and help to normalize the experiences of grief.

Psychological models

Psychological models are based on developmental notions of change and growth. It is assumed that bereavement is a process in which there is an outcome of increasingly redirecting energy from the past into the future. Individuals progress through nonlinear phases or stages and achieve certain tasks in the adjustment process. The theories are based on the assumption that people have some control over their feelings and thoughts. These theories hold that individuals need to accept the reality of the loss so that the emotional energy can be released and redirected.

The effortful, mental process of withdrawing energy from the lost person is referred to as 'grief work'. It is regarded as essential to alter the relationship with the deceased, and to allow reinvestment of emotional energy.

The most influential and earliest theories emerged from psychoanalysts such as Freud, who also described normal and pathological grief.[1] Bowlby proposed a complex theory of close human relationships in which separation triggers intense distress and subsequent behavioural responses.[2] Parkes proposed that people progress through phases in coming to terms with their loss and that they have to adapt to changes in relationships, social status, and economic circumstances.[3] Kübler-Ross also proposed a nonlinear model of the emotional expression of loss, described in terms of shock/denial, anger, bargaining, depression, and ultimately acceptance.[4] Worden based his therapeutic model on phases of grief and tasks of mourning. He suggests that grief is a process, not a state, and that people need to work through their reactions to loss to achieve a complete adjustment.[5] Worden's model is outlined in Table 31.1.

Each of these theories have been modified and developed by their authors and remain popular ways to explain bereavement adjustment and grief experiences. For some bereaved people, these concepts are helpful in understanding their experience. Various techniques are used to support and encourage people to move forward and to begin engaging in life again.

Stress and coping model

Stress and coping models are based on an assumption that if certain things, called 'stressors', are present in sufficient amounts, a physical and psychological stress response is triggered. People are able to adapt to most things, but things that challenge the adaptation process are considered to

Table 31.1 Worden's therapeutic model

Task 1	To accept the reality of the loss
Task 2	To experience the pain of grief
Task 3	To adjust to an environment in which the deceased is missing
Task 4	To find an enduring connection with the deceased while embarking on a new life

Data sourced from Worden J.W. (2009) Grief Counselling and Grief Therapy (4th edn). London: Routledge.

be stressful. Lazarus and Folkman's transactional model of stress and coping proposed that any event may be seen as threatening.[6] Cognitive appraisal is undertaken to estimate the degree of threat and mobilize the internal and external resources to cope with it. Coping may focus on dealing with the threat directly (problem-focused), or may emphasize the emotional response (emotion-focused). Stroebe and Schut further developed this idea with their dual processing model.[7, 8] They propose that after death, people oscillate between restoration-focused coping (dealing with everyday life) and grief-focused coping (e.g. expressing their distress) as a dynamic and fluctuating experience. For adaptation to occur, people move between the two states and become more restoration-focused with time.

Social and relationship-focused models

Social and relationship-focused models are based on an assumption that people wish to maintain feelings of continuity and that, even though physical relationships may end at the time of death, relationships can be transformed and remain important within the memory of the bereaved individual. Walters in the UK and Klass et al.[9] in the USA developed the concept of continuing relationships (emotional bonds) and emphasize the benefit for the living to integrate the memory of the dead into their ongoing lives through recognizing and drawing on the enduring positive influences of the deceased.[10, 11]

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Bereavement support

> Give sorrow words. The grief that does not speak whispers the o'er-fraught heart, and bids it break.
>
> Shakespeare, *Macbeth*, 4.3.209–10

In practice, bereavement support, whether through GPs or professional accredited counsellors, provides a chance to reflect on loss experiences and adjustment. GPs may become involved in grief counselling, but their main role is to screen for people who may be most at risk from a complicated bereavement. Most bereaved people manage well with their own resources, family support, and the help of community groups. Specialist services such as Cruse (UK), Doughy Centre (USA), and Skylight (NZ) are available if needed.

Specialist palliative care and bereavement

The philosophy of the hospice movement encompasses the care of patients and their families. The provision of bereavement support is regarded as integral to their services. Bereavement support is offered as an acknowledgement that death is a stressful life event and that a minority of people will experience substantial disruption to their physical, psychological, and social functioning. A multidisciplinary team (MDT) including social workers, nurses, chaplains, counsellors, and doctors is usually involved. Occasionally clients present with such difficult and complex problems that psychiatrists, clinical psychologists, or other specialist healthcare workers may be required.

In the UK, national standards are now in place for bereavement support, building on NICE recommendations that three levels of support should be available, depending upon the complexity of the needs of the bereaved person:[1, 2]

- Component 1: all bereaved people should be offered information about grief and how to access support services
- Component 2: about one-third may require additional support to help them deal with the emotional and psychological impact of loss by death
- Component 3: specialist interventions are required by a small proportion (7–10%), which will involve referral to a range of services including mental health services, psychological support services, and specialist counselling services.

Emerging evidence recommends a targeted approach to offering specialist bereavement interventions to improve effectiveness of therapy for problems in adjustment. However, provision of specific bereavement information and generalist support also remains a critical element of early intervention. Bereavement support may include a broad range of activities, such as social evenings, befriending, one-to-one counselling, and support groups (see Table 31.2). Mindfulness and body work practices, such as gentle yoga and exercise, also facilitate coping.

Table 31.2 Types of hospice and palliative care bereavement support for adults

Social activities	Supportive activities	Therapeutic activities
Condolence cards	Drop-in centre/ coffee mornings	One-to-one counselling with professional or trained volunteer
Anniversary (of death) cards	Self-help groups	Therapeutic support groups
Bereavement information leaflets	Information support groups	Drama, music, or art therapy
Bereavement information resources (videos/books)	Volunteer visiting or befriending	Relaxation classes
Staff attending the funeral		Complementary therapies
Social evenings	Psychotherapy	
Memorial service or other rituals		

Reproduced from M. Lloyd-Williams (ed) (2008) *Psychosocial Issues in Palliative Care*. Oxford: Oxford University Press. p. 215 with permission from Oxford University Press.

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Complicated grief

Complicated grief is also termed prolonged grief or persistent complex grief.

Normal and abnormal responses to bereavement cover a continuum in which intensity of reaction, presence of a range of related grief behaviours, and time course (>6 months) betray the presence of an abnormal grief response.

> Complicated grief involves the presentation of certain grief-related symptoms at a time beyond that which is considered adaptive. We hypothesize that the presence of these symptoms after approximately 6 months puts the bereaved individual at heightened risk for enduring social, psychological and medical impairment.
>
> Prigerson et al., 1995[1]

> Complicated mourning means that, given the amount of time since the death, there is some compromise, distortion or failure of one or more of the … processes of mourning. The deceased is held on to as though alive. Symptoms do not resolve spontaneously and need active intervention.
>
> Rando, 1993[2]

> [Complicated grief] is more related to the intensity of a reaction or the duration of a reaction rather than the presence or absence of a specific behavior.
>
> Worden, 1982[3]

Risk factors for developing complicated grief

Personal

- markedly angry, ambivalent, or dependent relationship with the deceased
- history of multiple losses and/or concurrent losses
- mental health problems
- perceived lack of social support

Circumstantial

- sudden, unexpected death, especially when violent, mutilating, or random
- death from an overly lengthy illness such as dementia
- loss of a child
- mourner's perception of loss as preventable

Historical

- previous experience with complicated grief
- insecurity in childhood attachments

Personality
- inability to tolerate extremes of emotional distress
- inability to tolerate feelings of dependency
- self-concept that values 'being strong'

Social
- socially unspeakable loss (e.g. suicide)
- socially negated loss (e.g. loss of ex-spouse)
- absence of social support network
- absence of a body on which to conduct funeral rites (e.g. lost at sea)

Symptoms

Complicated grief includes the following symptoms in abnormal intensity or duration (Table 31.3):
- symptoms of depression and/or anxiety
- grief-specific symptoms of extraordinary intensity and duration that include:
  - preoccupation with thoughts of the deceased
  - disbelief
  - feelings of being stunned
- lack of acceptance of the death
- searching for the deceased

Common psychiatric disorders related to grief:
- clinical depression
- anxiety disorders, alcohol abuse, or other substance abuse and dependence
- psychotic disorders
- post-traumatic stress disorder (PTSD)

Table 31.3 Clinical presentations of complicated grief

Category	Features
Inhibited or delayed grief	Avoidance: postpones expression
Chronic grief	Perpetuation of mourning long-term
Traumatic grief	Unexpected and shocking form of death
Depressive disorders	Both major and minor depressions
Anxiety disorders	Insecurity and relational problems
Alcohol and substance abuse/ dependence	Excessive use of substances impairs adaptive coping
Post-traumatic stress disorder	Persistent, intrusive images with cues
Psychotic disorders	Manic, severe depressive states, and schizophrenia

Reproduced from N Cherny. et al. (eds). (2015) *Oxford Textbook of Palliative Medicine* Doyle DH et al. (2004) *Oxford Textbook of Palliative Medicine*. (3rd edn), p. 1140. Oxford: OUP with permission from Oxford University Press.

While frank psychiatric disorders following bereavement are reasonably straightforward to diagnose, it is more difficult to pick up complicated grief, in which the pathological nature of the grief response is only distinguishable from normal grief by its character. Recognition of complicated bereavement calls for experienced clinical judgement that does not 'rationalize' the distress as understandable. Symptoms may appear early and require monitoring.

Warning signs of complicated grief

- long-term functional impairment
- exaggerated, prolonged, and intense grief reactions
- significant neglect of self-care
- substance overuse or abuse
- frequent themes of loss in conversation, activity, behaviour
- idealization of the deceased
- impulsive decision-making
- mental disorders following loss
- PTSD-like symptoms

Ways of helping a bereaved person during the first months

- 'being there' for them
- non-judgemental listening
- encouraging them to talk about the deceased
- giving permission for the expression of feelings
- offering reassurance about the normality of feelings and experiences
- promoting coping with everyday life and self-care (e.g. adequate food intake)
- screening for damaging behaviours (e.g. increased alcohol use, smoking, etc.)
- providing information, when requested, about the illness and death of their loved ones—also about the range of grief responses
- educating others (family members and other support networks) about how best to help the bereaved person
- becoming familiar with your own feelings about loss and grief
- offering information about local bereavement support services, e.g. hospice services, Cruse, Solace, and specialist therapists if required

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Bereavement involving children

One feature of the grief of most children is that they do not sustain grief over continuing periods of time, but tend rather to dip in and out of grief—jumping in and out of puddles, rather than wading through the river of grief.

Adults should be aware that children will learn what is 'acceptable grief' from the adults around them.

Childhood bereavement services seek to support children with their loss experience and to help parents deal with a bereaved child.

Reproduced from Payne S., Rolls L. (2008) Support for bereaved family carers. In Family Carers in Palliative Care (ed. P. Hudson, S. Payne). Oxford: Oxford University Press with permission from Oxford University Press.

Children's grief

Children may be bereaved of family members (e.g. siblings, parents, or grandparents) and this will precipitate a cascade of changes and loss. They will become a child of bereaved parents who may need help in dealing with their own loss and also help in how to parent a bereaved child. Children will be helped by knowing that the expression of feelings of distress is acceptable. Children may express their emotions and grief in many ways, e.g. through play, artwork, music, drama, etc.

Children's understanding, responses, and needs will be affected by many factors, including their previous experiences of loss and how these were handled. It is also important to consider the age and the developmental level of the child, although any attempt to consider responses according to age will require flexibility as there is considerable crossover between different children. See Fig 31.1.

Age and grief

Children under the age of 2–3 years

Children under the age of 2 or 3 may have little concept of death, but will be aware of separation, and may protest against this by detachment or regressive behaviour. Children of this age need a consistent caregiver, familiar routines, and the meeting of their physical and emotional needs.

Children aged between 3 and 5 years

Children of age 3–5 do not see death as irreversible. Rather, their concerns will relate to separation, abandonment, and the physical aspects of death and dying. Their response may include aggressive and rejecting behaviour. They may also become withdrawn or demonstrate an increase in clinging or demanding behaviour. There may also be regression to infant needs. Routine, comfort, reassurance, and a simple answering of their questions will help a child of this age. They should be allowed to participate in family rituals and to keep mementos of the deceased. Adults should be aware of the words they use since they can be misinterpreted (e.g. do not associate death with sleep or a long journey).

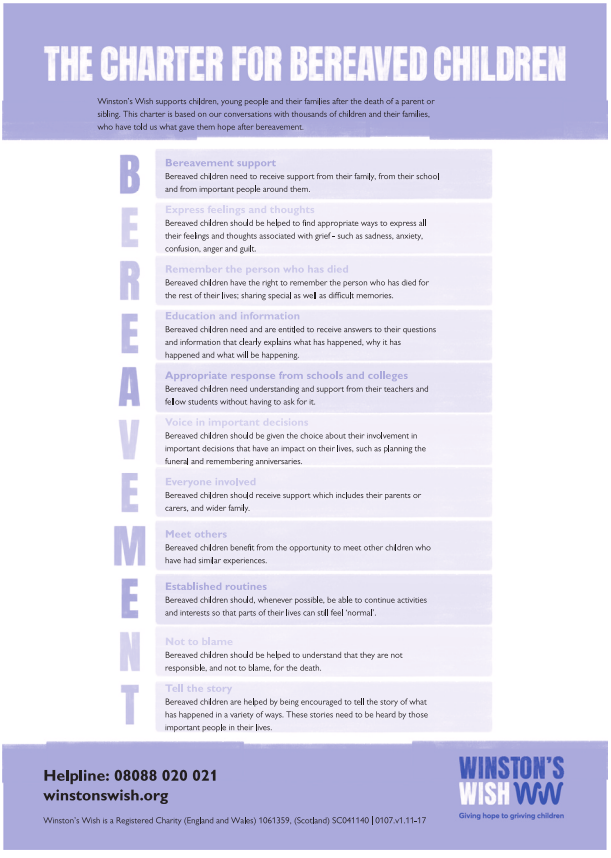


Fig 31.1 A charter for bereaved children. © Winston's Wish 2018. Charity registration number 1061359.www.winstonswish.org.uk, reproduced with permission.

Children aged between 6 and 8 years

Children aged 6–8 seek causal explanations. A whole range of behaviours may be evidence of their response to grief—withdrawal, sadness, loneliness, depression, acting-out behaviour, or becoming a 'perfect' child. Short, honest, concrete explanations will help a child of this age, as will maintaining contact with friends and normal activities. Short-term regression may be allowed, and they should be reassured that they will always be cared for. Involvement in the family's grief-related rituals will also help.

Pre-teenage children

Pre-teens appear to have a calmer and more accepting attitude to death. They often have a good factual understanding of what has happened. The child should be encouraged to talk about the deceased and be provided with clear and truthful answers to their questions. The feelings of adults do not need to be hidden, allowing the child to provide mutual help and reassurance.

Teenage children

Teenagers are engaged in a search for meaning and purpose in life and for their identity. They feel that they have deep and powerful emotions that no one else has experienced. Teenagers may exhibit withdrawal, sadness, loneliness, and depression, or else they may act out in an angry, hostile, and rejecting way. They may seek to cover up fears with joking and sarcasm. Young people of this age need as much comfort as possible, involvement, boundaries, a sense that their feelings are being taken seriously, and reassurance that their feelings are normal. Continuing contact with their peers should be encouraged. Young people will often identify for themselves someone with whom they feel comfortable to talk.

Specialist services exist to assist children, teens, and their families, such as Canteen (Australia, cancer-specific), Doughy Centre (USA), Skylight (NZ), and Winston's Wish (UK).

Risk factors for complicated grief in bereaved children

Risk factors may be divided into three groups:

Features of the loss

- traumatic
- unexpected
- protracted

Features of the child

- history of psychiatric disorder
- multiple losses
- child under 5 years old
- adolescent

Features of the relationship

- ambivalent/conflicted
- unsupportive family
- death of a father (adolescent males)
- death of a mother (very young children and adolescent females)
- mental illness in surviving parent
- child of a single parent who has died

Bereavement due to death of a child

The death of a child is a devastating loss, particularly in times when most childhood illness can be prevented or cured. It profoundly affects all those involved—parents, siblings, grandparents, extended family, friends, and others involved in caring for the child. As a community, we rarely experience

the death of a child, which makes it all the more difficult when we do. There is a sense that the natural order of things has been upset, with grief about the loss being felt throughout the remainder of the parents' life.

Principles for working with bereaved parents

- Make early contact and assess the bereaved parents.
- Provide assurance that they can survive their loss, but acknowledge the uniqueness of their pain.
- Allow adequate time to grieve.
- Facilitate the identification and expression of feelings, including negative feelings such as anger and guilt.
- Encourage recall of memories of the deceased child.
- Maintain a professional and realistic perspective—not all pain can be 'fixed'.
- Allow for individual differences in response relating to gender, age, culture, personality, religion, and the characteristics of the death.
- Assist in finding a source of continuing support.
- Promote confidence in their parenting of their surviving children.
- Identify complicated grief reactions and refer to the appropriate services.

Interpret resolution of grief to parents, explaining that it is not a betrayal of their deceased child. Health professionals need to recognize the significance they may have in a family's life. Many children are treated over long periods, and the hospital/hospice may become something of a second home. Health professionals also care for families during the intense highs and lows of serious illness, and may even be present at the time the child dies. The significance of this cannot be overstated. These relationships cannot be abruptly ended, and many (but not all) families will want ongoing contact with those people they feel truly understand what they have experienced. A follow-up appointment with the child's paediatrician should always be offered to discuss the child's illness and treatment, the results of any outstanding investigations, including post-mortem examinations, and how the family is coping.

Sibling grief

Siblings almost universally experience distress, but many feel unable to share this for fear of burdening their already-fragile parents. One of the many factors which influence sibling grief is developmental level and the impact this has on the child's understanding of illness and death. As children develop and experience life, their concept of death becomes more mature. Most children learn to recognize when something is dead before they reach 3 years of age. However, at this early age, death, separation, and sleep are almost synonymous in the child's mind. Table 31.4 shows the six sub-concepts acquired during this process (average age of attainment in parentheses).

Supporting bereaved children

Adjusting to the loss of a loved person does not necessarily require 'letting go' of the relationship. Indeed, bereaved children (and adults) often maintain a connection to the dead person. The relationship is reconstructed over time and maintained by remembering the person, keeping their belongings, and sometimes talking to them. Children spend most of their time

Table 31.4 Six sub-concepts of children's understanding of death

Separation (age 5)	Dead people do not coexist with the living
Causality (age 6)	Death is caused by something, be it trauma, disease, or old age
Irreversibility (age 6)	A dead person cannot 'come alive' again
Cessation of bodily functions (age 6)	The dead person does not need to eat or breathe
Universality (age 7)	All living things will die
Insensitivity (age 8)	The dead cannot feel fear or pain

in the care of their parents. It is therefore important to empower parents to support siblings by equipping them with knowledge and ideas. Staff can encourage the family to do the following:

- provide information in simple, developmentally appropriate language
- be alert to misunderstandings which may arise as a consequence of an incomplete death concept
- set aside special time for the child/young person
- openly express emotion
- recruit family, friends, and teachers to help
- allow the child to play with friends and reassure them that it is OK to have fun
- help the child create memories, e.g. stories, photos, drawings, memory books
- maintain normal routines and discipline as much as possible
- allow the child/young person opportunities to feel in control
- resist any temptation to 'fix their grief'
- encourage them to do what feels right for them whilst remaining safe
- be there—to provide love, reassurance, and routine
- allow the child time alone—private space is important
- talk about the death as appropriate
- answer questions, no matter how explicit
- do not be surprised if children use symbolic play, stories, and art to make sense of their experience
- invite children to take part in rituals that promote sharing about the deceased, without demanding their involvement

School grief

After the family, the school community may contain the people most affected by the death of a child—friends, fellow students, teachers, administrative staff. Parents form part of a wider school community. Close attachments are formed between children and their teachers, so that the death of a child may be a personal as well as a professional loss.[1]

In a school, there will be a range of grief responses. It is anticipated that both staff and students will be vulnerable to stress and may express themselves differently. For the student, the closer they were to the child who died, the more profound will be the consequences. Teachers may notice a

change in the other students' behaviour, thought processes, concentration, and academic performance. A greater level of support, monitoring, and care may be warranted, even for those students who may not be expressing their grief in an obvious way.

People who may be at increased risk

- those who have already experienced significant loss in their lives
- those who have had a close relationship with the child who has died or the child's siblings
- those who have similar health problems themselves or in their family

The school is in an ideal position to provide opportunities for students to be supported as well as to identify those who may be experiencing difficulty. The child's parents should always be consulted before any information is released so that their privacy and the best interests of any siblings are considered and respected.

Ways in which the school can help

- Inform staff and students of the child's death as a priority. Anxiety and misinformation are fuelled by uncertainty and delay.
- Senior staff need to acknowledge the sadness of what has happened, perhaps by way of assemblies, class announcements, and letters home.
- Staff and children need the opportunity to talk about what has happened, to ask questions, and to express their feelings. This is best done in familiar small groups, though it may also be appropriate to set aside a time when people can come and talk together. Students can also be given opportunities to write farewell letters or tributes, and to create artwork as an expression of their thoughts and feelings.
- A sense of routine provides reassurance to staff and students who have experienced trauma. It is, therefore, important that the school continues to function as a supportive and stable part of the staff and students' environment.
- Staff need their own support. Staff meetings provide an opportunity to provide information, monitor the reactions of the children, and discuss feelings. In some cases, it may be helpful to hold a special meeting facilitated by someone with expertise in this area. Senior staff are usually required to manage the immediate crisis and may experience a delayed reaction.
- The school can maintain contact with the family in a number of ways. This may be through friends or formal rituals. Some families welcome the participation of the school in the funeral, for example, and may wish to be involved in school memorial services. The child may also have expressed wishes regarding the involvement of their school friends.

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Assessment of bereavement risk

The assessment of bereavement risk presupposes that some individuals will display a grief reaction that does not fit a 'normal' or expected pattern or level of intensity. The factors that influence complicated bereavement are:

- stage of the life cycle, particularly when
  - the bereaved parent is an adolescent and family support is perceived as inadequate
  - the surviving parent of a deceased child is a single mother/father as a result of divorce or being widowed
- history of previous losses, particularly if unresolved
  - loss of a pregnancy
  - loss of a job
  - divorce
- concurrent or additional stressors
  - family tension
  - compromised financial status
  - dissatisfaction with caregiving
  - reliance on alcohol or other psychotropic medications pre-bereavement
- physical and mental illness, particularly
  - current/past history of mental health problems that have required psychiatric/psychological support
  - family history of psychiatric disorders
- high pre-death distress
- inability or restriction in use of coping strategies
  - maintenance of physical self-care
  - identification of prominent themes of grief
  - differentiation between letting-go of grief and forgetting the bereaved
  - accessing available support
- isolated, alienated individuals
- low levels of internal control beliefs, such as
  - feeling as if they have no control over life
- availability of social support, particularly if
  - people in the immediate environment are, or are perceived to be, unsupportive
  - support from family and friends immediately prior to death was good and following death it subsided
- the bereaved lacks a confidant with whom to share feelings, concerns, doubts, dreams, and nightmares
- the bereaved is dissatisfied with the help available during their child's illness

Monitoring adjustment following bereavement requires awareness of indicators of both sound adjustment and warning signs. Adequate time to adapt is necessary without leaving individuals in states of unremitting distress. Following identification of adjustment difficulties, clarity and confidence in provision of next steps are essential. Services such as local hospices are often helpful in providing guidance and information.

Further reading

Books

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Chapter 32

Self-care for health professionals

Impact of caring for dying people *836*
Supportive environments *837*
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Warning signs of prolonged stress *840*
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Impact of caring for dying people

In aircraft safety demonstrations, we are repeatedly advised to put on our own oxygen mask before looking to help others. For those working with the dying, maintaining our own physical, emotional, and spiritual health is a crucial component of sustaining quality care.

Background

Sources of stress are multiple, may be accumulative, and are linked to all areas of an individual's life. Working with dying people may be stressful, particularly if staff experience personal bereavement and loss. Such work can put staff in touch with personal anxiety about loss and death.[1, 2] Palliative care staff also find it very stressful to deal with patients who experience intractable pain, those who have young children, and those patients who are afraid to die. Symptoms that leave nurses feeling helpless, useless, and impotent are the most stressful to deal with, as is dealing with distressed relatives.

Overall, however, stress and burnout in palliative care have been found to be less than in other specialties. Some research have shown that this is an area where there is a very high degree of job satisfaction; staff feel they are privileged to be in the position to provide this care. Working with dying people has also been found to influence the attitude of staff towards death and dying. In death anxiety scoring, people who coped well in this field of work scored higher on inner-directedness, self-actualizing value, existentiality, spontaneity, self-regard, self-acceptance, acceptance of aggression, and capacity for intimate contact. They were also more likely to live in the present, rather than the past or future. It is suggested that the reason for lower stress and burnout within hospice palliative care units is due to the recognition that stress may be inherent to the field of death, dying, and bereavement, and consequently more robust support mechanisms have been built into those organizations that provide palliative care.

Hospice and hospital palliative care teams differ considerably, and it has been found that palliative care physicians based in hospitals experience more stress than their hospice colleagues. However, a comparison of 401 specialist registrars' experience of occupational stress in palliative medicine, medical oncology, and clinical oncology showed there was no significant difference between the specialties. One in four of the specialist registrars (SpRs) experienced stress, and more than one in ten showed clinically important levels of depression.[3] The most common suggestions for reducing stress were improved relationships with colleagues and having 'supportive seniors'. The importance of coping strategies received far more emphasis from the group of palliative medicine trainees than those SpRs in clinical or medical oncology.

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Supportive environments

The Health and Safety Executive, UK, recommend that all organizations have a stress policy that outlines the responsibilities of managers and staff to identify stress in the workplace, and provide strategies that may be used to manage this stress and support the staff within the organization. Of note, they recommend the provision of specialist advice and awareness training. A supportive environment and supportive working relationships are essential ingredients in managing the potential stress of working with dying and bereaved people; in addition, it has been found that satisfaction with support in training is protective against stress.

Of importance are the following:

- regular team meetings, where time is provided to evaluate and reflect on difficult situations encountered by the team
- promoting shared decision-making in the management of patient care as the norm
- respecting each other's expertise

Provision of protected time for clinical supervision and/or reflective practice sessions that support clinical learning and development within a supportive framework are essential, as is a need to support staff in developing realistic expectations of clinical interventions in order to minimize any sense of failure and helplessness.

It is also important that managers provide effective education opportunities for staff who care for dying and bereaved people, such as the development of advanced communication skills and 'professional competence', i.e. knowledge, technical skills, relationship insight, and the appropriate attitudes. Interventions to improve resilience and develop positive coping can also help protect against the impact of stress and adverse events. Another means by which this can be achieved is through education in ethics: specifically, virtue ethics or philosophy of care. This is an important component of education in fields of care which involve intense human interactions, as is the case in palliative care.

Sources of stress

Personal life

- personal relationships—spouse/partner, children, caregiver responsibilities, no close relationships/loneliness
- illness—in self or one close to self
- recent bereavement
- minority-related stress—victim of racism, sexism, ageism, disability prejudice, etc.
- gender-related stress—pressure to do everything/pressure to provide

Patients/clients

- inability to create relationships
- negative attitudes—hostility, open dislike, anger
- potential/actual physical violence
- emotional pressures
- problems of emotional involvement
- guilt feelings—feeling responsible
- dependent clients

Colleagues

- inability to create relationships
- lack of support
- 'each doing their own thing'—no teamwork
- open conflict—practice undermined
- bullying
- negative/pessimistic attitudes to work
- bringing problems at home to work
- own anxieties about work
- resentful of others' positions—professional jealousy

Managers

- lack of support—no supervision, etc.
- no attention paid to personal development
- 'routines' before 'people'
- little positive feedback
- discriminatory behaviour
- bullying
- given inappropriate client group, caseload, etc.
- practice skills not recognized
- overwork, heavy demands
- faced with crises
- lack of involvement in decision-making

Organizational issues

- lack of resources
- 'routines' before 'people'—bureaucracy
- impersonal links with 'hierarchy'
- poor pay/poor conditions of service
- lack of clarity in roles

- little professional 'expertise'
- administrative procedures/paperwork
- functions limited by resources
- lack of clarity of work expectations—low status
- poor staffing ratios
- staff shortages/vacancies not filled

Warning signs of prolonged stress

Physical

- palpitations
- chest pains
- recurrent headaches
- heartburn
- stomach cramps
- stomach full of gas

Intellectual

- memory problems
- poor concentration
- anxiety
- errors in judgement
- feeling 'woolly-headed'
- inability to make decisions

Emotional

- frequent feelings of anger, irritation, and frustration
- feeling dull and low
- feelings of helplessness and insecurity
- inability to love and care
- feeling tearful
- sleep disturbance

Strategies for coping with stress

Organizational

- developing a supportive culture within the organization
- opportunities to express work-related feelings and discuss problems in the workplace
- regular team meetings
- mandatory clinical supervision
- provision of a counselling service for staff
- support in developing competencies for working in palliative care
- robust education programmes for staff that include developing insight into individual/personal potential areas of difficulty, avoiding excessive involvement with particular clients, handling emotions, advanced communication skills, etc.

Personal coping strategies

- having a sense of competence, control, and satisfaction in working in palliative care
- having control over workload
- taking time off
- having non-job-related outside activities
- engaging in physical activities and diversions
- ensuring adequate sleep and nutrition
- using relaxation techniques, e.g. physical activity, yoga, meditation, complementary therapies
- developing a personal philosophy regarding death that may or may not relate to individual religious or spiritual beliefs

Further reading

Gillman L., et al. (2015) Strategies to promote coping and resilience in oncology and palliative care nurses caring for adult patients with malignancy: a comprehensive systematic review. *JBI Database of Systematic Reviews and Implementation Reports*, **13**(5):131–205.

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Chapter 33

Access to palliative care: international perspectives

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Introduction

For over a century, the majority of healthcare delivery systems globally have been modelled for the efficient management of acute, episodic care needs of patients with an emphasis on curative treatments. Palliative care emerged in the late twentieth century to respond to the needs of patients falling outside the curative spectrum. Beginning with compassionate and competent management of symptoms for patients in advanced stages of cancer, the humanitarian considerations that shaped the early growth of the field instilled the component of 'quality of life' into the healthcare thought processes.

Since its modern inception, palliative care practitioners have established themselves as experts in evaluating and managing symptoms, utilizing scientific knowledge and innovative practices to relieve suffering and improve the well-being of those living with incurable illness. We now have a robust body of evidence-based practices for nurturing the physical, psychosocial, and spiritual well-being of persons with chronic medical conditions, applicable within different clinical care settings, including home-based care.

Increasingly, chronic progressive conditions predominate, and the complex symptomatology, multiple co-morbidities, psychosocial concerns, and persistent care needs associated with chronic diseases challenge the limits of healthcare systems globally. The avenues available for managing such patients remain unsatisfactory, fragmented, and geared towards inpatient and emergency care; they contribute to increasing healthcare costs without a comparable increase in quality of care. The aggressive, invasive interventions commonly employed during the end-of-life phase are undignified, distressful, and often futile. In low- and middle-income countries in particular, extremely high costs for such futile interventions without consideration for what is beneficial for the person often entail large out-of-pocket payments, which have contributed significantly to poverty.[1] Even countries with well-established, funded healthcare systems are incorporating the palliative care approach owing to the significantly positive influence on care outcomes the improvement in the individual's quality of life entails.

In this context, there has been a major resurgence of interest in the field of palliative care with recognition of its relevance, beneficence, and value. Care approaches utilizing basic principles of palliative care are enhancing the capacity to care for many debilitating conditions besides cancer, and improving outcomes. For example, a cancer patient who previously suffered from isolation because of persistent pain and foul-smelling wounds may now have access to a supportive team that helps manage these symptoms by providing care and training to the family at home, which in turn builds the patient's capacity to reintegrate back to regular life.

Reference

1. Sixty-Seventh World Health Assembly WHO.19 Agenda Item 15.5 24 May 2014. http://apps.who.int/gb/ebwha/pdf_files/wha67/a67_r19-en.pdf

Inequity in access to palliative care

Despite its relevance and importance, access to palliative care and to pain relief remains abysmal in most parts of the world. The demand for good palliative care services far exceeds its existing availability, with less than 10% of those who need it actually receiving it.[1] In 2014, the WHO and the Worldwide Hospice and Palliative Care Alliance published the Global Atlas of Palliative Care at the End of Life, a resource that sought to quantify the need for, and availability of, palliative care worldwide. Fig 33.1 illustrates each country's level of palliative care development, indicating that approximately 74% of countries worldwide have little or very limited palliative care.

Another indicator of palliative care service availability is the quality of death index that was developed by evaluating and comparing the availability and access to standard palliative care amongst 80 countries. This index utilized 20 quantitative and qualitative indicators across five categories: (1) the palliative and healthcare environment, (2) human resources, (3) affordability of care, (4) quality of care, and (5) level of community engagement. More than 70% of countries surveyed had unsatisfactory indices, reflecting gross global inequities.[2]

References

1. Worldwide Hospice and Palliative Care Alliance, World Health Organization. Global Atlas of Palliative Care at the End of Life. January 2014. Available at: http://www.who.int/nmh/Global_Atlas_of_Palliative_Care.pdf
2. Murray S., Line D. (2015) The 2015 Quality of Death Index: ranking palliative care across the world. A report by the Economist Intelligence Unit. https://eiuperspectives.economist.com/sites/default/files/2015%20EIU%20Quality%20of%20Death%20Index%20Oct%2029%20FINAL.pdf

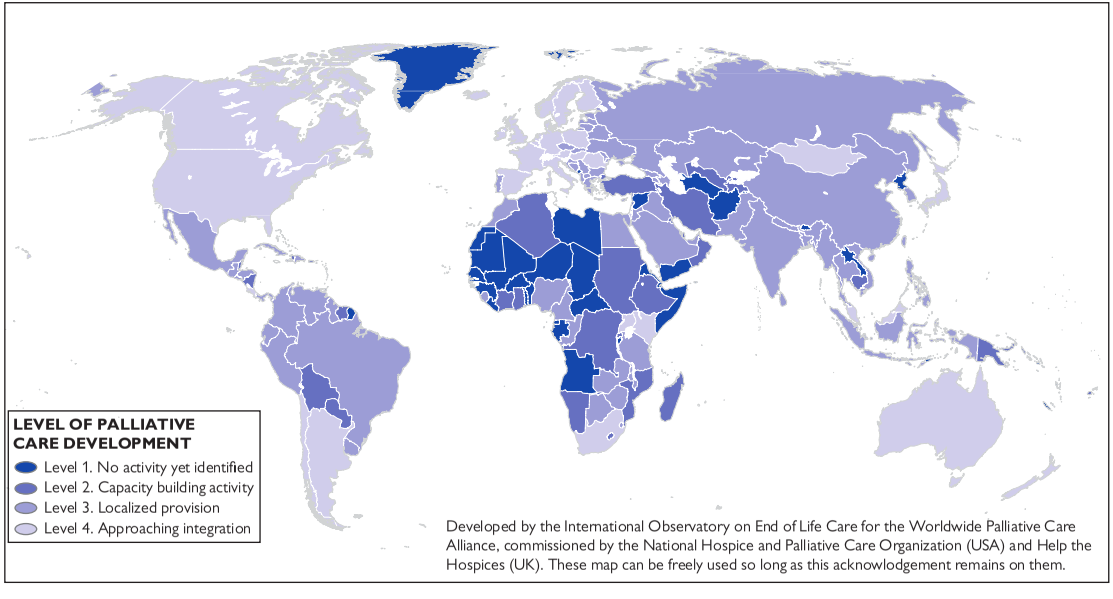


Fig 33.1 Levels of palliative care development. Used with permission from the Worldwide Hospice and Palliative Care Alliance.

Barriers to palliative care availability

There are many factors that contribute to the inadequate availability of palliative care. Current medical training and healthcare services are geared towards curative interventions and often overlook aspects that bring comfort to the person seeking care. Mindsets and protocols for care management are guided by investigatory parameters, which orient healthcare systems and funding towards acute episodic care within hospital settings. Processes to ensure quality of life have not been established within systems of clinical care and research parameters. Communication techniques that facilitate shared decision-making involving patients and their families are unfamiliar to most practitioners. The application of clinical ethics in guiding complex clinical decision-making is neither part of professional training nor used in practice. Lastly, policies for integrating the care of patients with chronic conditions, including palliative care, within public healthcare systems are usually lacking.

A central barrier to the availability of quality palliative care is the lack of access to pain medicines. Relief of pain is the cornerstone of palliative care. Yet managing needless suffering due to persistent pain remains largely unrecognized within the spheres of medical training, practice, and research.

Opioid analgesics are safe, effective, and economical in treating moderate-to-severe pain, and are often the only means to treat patients with advanced disease, where disease-modifying interventions have little role and pain is severe. Indeed, the WHO has designated morphine as an essential medicine since 1977 for the relief of pain and other symptoms, while at the same time morphine and other opioids are internationally controlled substances. Regulatory barriers entrenched within the controlled drug policies have led to poor availability of these essential medicines in medical settings. Generations of professionals have completed their training with no exposure or experience in the medical use of opioids, and this has constrained the response of healthcare professionals around the world to patients in pain. The misconceptions and myths surrounding opioids are widespread; this has also reduced the accessibility of these medicines for patients with severe pain.

> 5.5 billion people (83% of the world's population) live in countries with 'low or non-existent access to controlled medicines for the treatment of moderate to severe pain'.
>
> WHO Executive Board Report 2016

After the 1986 WHO publication of the three-step ladder treatment recommendation for cancer pain, which included opioids in steps 2 and 3, the total global consumption of opioids increased significantly, but the increase mainly occurred in a limited number of industrialized countries.[1] Combining epidemiological factors that influenced regional medical need with the INCB consumption data from 2013, Fig 33.2 depicts access to opioids for medical use across the world.

The disparity in opioid consumption is further illustrated by the extremely unbalanced consumption of morphine globally. In 2013, less than 10% of the morphine consumption was by low- and middle-income countries, which represented more than 80% of the world population (Fig 33.3).

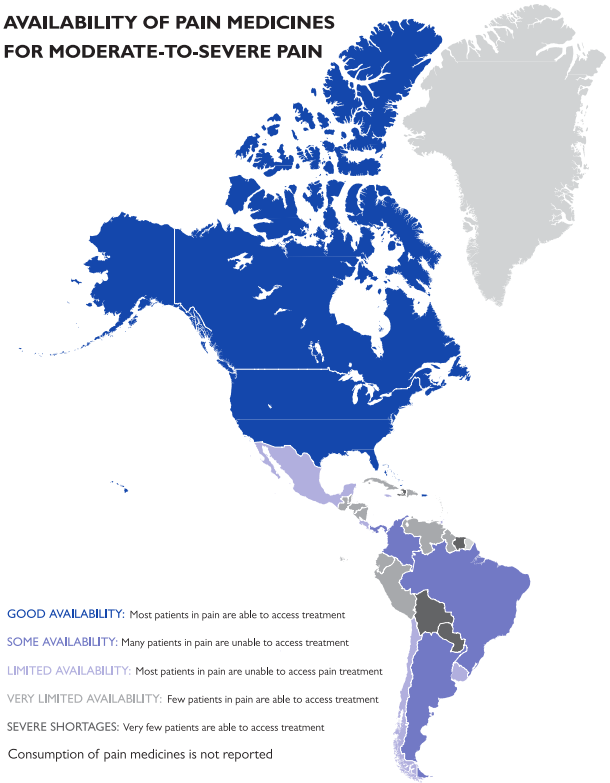


Fig 33.2a Availability of palliative medicine in the Americas.

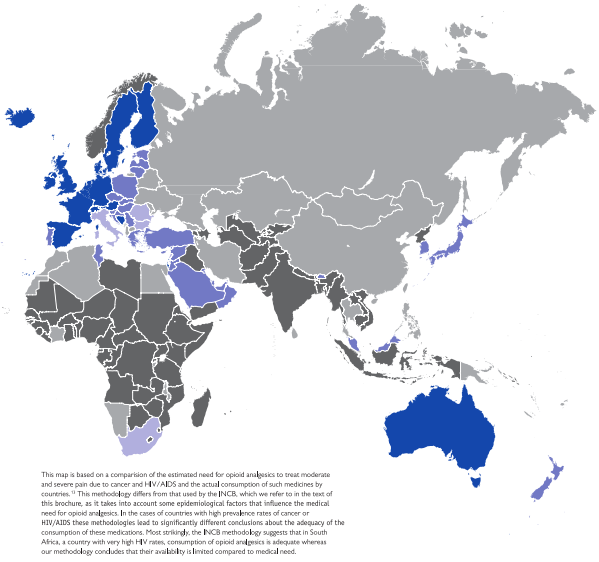


Fig 33.2b 2013 availability of medicines for moderate-to-severe pain. Reproduced from National Drug Control Strategies and access to controlled medicine © 2015 Human Rights Watch, with permission from Human Rights Watch.

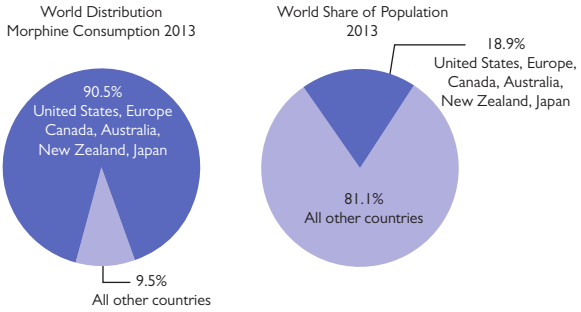


Fig 33.3 2013 global morphine consumption by share of world population. Reproduced from National Drug Control Strategies and access to controlled medicine © 2015 Human Rights Watch, with permission from Human Rights Watch.

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1. World Health Organization (2011) Ensuring balance in national policies on controlled substances: Guidance for availability and accessibility of controlled medicines (2nd and rev. edn). Geneva: WHO. Available at: http://www.who.int/medicines/areas/quality_safety/GLs_Ens_Balance_NOCP_Col_EN_sanend.pdf

Global efforts to improve palliative care

Global health and regulatory authorities have recognized the dire need for improving essential palliative care services, including access to pain relief. The World Health Organization (WHO) has taken measures to educate and empower national governments to develop suitable policies and implementation processes. Beginning with its seminal 1996 publication, *Cancer Pain Relief: With a Guide to Opioid Availability*, the WHO introduced a framework to guide nations for developing palliative care. It recommended orientation of the field with a public health approach which included the following:

- a government policy that integrates palliative care services with the national healthcare system
- an educational programme that supports training of healthcare professionals and improves awareness
- a drug policy that ensures the availability and access of essential medicines for medical use (e.g. opioid analgesics) with effective measures for preventing and managing misuse

The WHO emphasized the importance of addressing all the measures concurrently, with committed leadership from the respective governments and participation from societal stakeholders for effective implementation.

Over the years, the WHO has supported the development of palliative care through a number of initiatives, including guidance on national cancer control programmes, which include palliative care, and various clinical guidelines. Most recently, in 2014, in a move to encourage supportive government policies, the World Health Assembly unanimously passed a resolution that outlined the specific intent and guidelines to strengthen national health systems by incorporating palliative care. The resolution acknowledged palliative care to be an ethical responsibility of health systems; it asserted that healthcare professionals had an ethical duty to alleviate pain and suffering. The resolution welcomed the inclusion of palliative care in the definition of universal health coverage and emphasized the need for health services to provide integrated palliative care in an equitable manner in the context of universal health coverage. It urged member states, where appropriate, to develop, strengthen, and implement palliative care policies to support the comprehensive strengthening of health systems, integrating evidence-based, cost-effective, and equitable palliative care services in the continuum of care across all levels. It emphasized service inclusion within primary, community, and home-based care, and universal coverage schemes; and to ensure adequate domestic funding and allocation of human resources, as appropriate, for palliative care initiatives.

The WHO and the International Narcotics Control Board (INCB) acknowledge that ensuring adequate availability of controlled substances for medical and scientific purposes is one of the core objectives of the international drug control treaties that has yet to be universally achieved. They have called upon countries to examine existing narcotic policies to identify potential barriers and, if necessary, take measures to amend, reorient, or repeal the laws.

To assist governments in this task, the WHO has developed guidelines for "Ensuring Balance in National Policies on Controlled Substances: Guidance for Availability and Accessibility of Controlled Medicines"; updated since its original publication in 2000. This document provides clear guidelines for improving the availability, accessibility, and affordability of controlled medicines from a policy perspective. In addition, in 2012, the WHO and INCB issued guidance to assist countries in maintaining accurate annual estimates of opioid requirements, an essential component in ensuring adequate production and distribution of opioids across the globe. Policy-makers, academics, and other individuals whose area of work or interest is drug control or public health may potentially work with these guidelines in order to ensure that controlled medicines are made accessible and available, and that more patients benefit from the advantages that their rational use can offer.

Another important development for palliative care took place in March 2016 at the 59th Session of the UN Commission on Narcotic Drugs. An outcome document about access to controlled medicines was approved for the UN Special Session of the General Assembly on the world drug problem in April 2016. The document reiterated the strong commitment of member states to improving access to controlled substances for medical and scientific purposes by addressing existing barriers, and recommended specific measures towards achieving this goal.

Recent advances in palliative care development in different regions of the world

The intensive debates on drug policies and the international emphasis on access to palliative care as a human right, especially in the first decade of the twenty-first century, have significantly influenced several countries to review their healthcare systems and reorient their national policies, thus impacting palliative care positively. It is noteworthy that countries with a high index in the quality of death survey[1] have synchronously implemented policy, education, and opioid availability guidelines within their public health practices. The common characteristics within their health systems include the following:

- a strong and effectively implemented national palliative care policy framework
- extensive palliative care training resources for general and specialist healthcare workers
- wide availability of opioid analgesics
- generous subsidies to reduce the financial burden of palliative care on patients
- public awareness of palliative care

The following section describes efforts to develop palliative care programmes in four countries with diverse socio-political milieu and healthcare needs. Although the individual components of the programmes vary, overall processes are in alignment with the suggested WHO three-pronged framework. It may be noted that the development of palliative care in higher income regions (Spain, Uruguay) has received support early from public healthcare systems, whereas the palliative care development efforts in low- and middle-income countries (India, Kenya) have seen more innovative practices and pioneering work by individuals, communities, or institutions.

Country examples

India

With the emergence of cancer, HIV, and non-communicable systemic diseases as major public health issues, the prevalence of patients with palliative care needs in India is estimated to be around six million.[2] Beginning with the first modern hospice care facility at Shanti Avedna Sadan Mumbai in 1985, the non-governmental sector has taken the lead in developing the field of palliative care.

The Pain and Palliative Care Society (PPCS) formed in 1993 in Kerala became the pioneer organization in the field and a WHO demonstration project owing to its association with the WHO Collaborating Centre (WHOCC) at Oxford, its affiliation with a medical school, and the dynamism of its founding members. While offering a robust training programme in the essential principles of palliative care for healthcare professionals, it fostered active involvement and contribution from regional community members that spawned a unique network for palliative care deeply aligned with the socio-cultural milieu.[3] The Institute of Palliative Medicine, created

by the PPCS, was designated a WHOCC for Community Participation in Palliative Care in 2010. In consultation with the WHO and the government of India, the Indian Association of Palliative Care (IAPC) was formed in 1994 as a national forum to connect, support, and motivate individuals and institutions involved in palliative care. The IAPC annual conferences and faculty workshops and its peer-reviewed journal have become the common platform for the palliative care community in the country to get together, to exchange information, and to learn together. Pallium India, dedicated to fostering the capacity and competence of professionals and to advocating for supportive policies, founded Trivandrum Institute of Palliative Sciences, which became a centre of excellence and the WHOCC for Training and Policy on Access to Pain Relief in 2012.

Diligent efforts of the palliative care community with the federal and state governments over the last two decades have led to progressive policy initiatives. The National Program for Palliative Care (NPPC), formulated by the Ministry of Health and Family Welfare in 2012, has defined objectives for expanding quality palliative care services across both governmental and private settings by strengthening capacity for care. One of the central barriers to the accessibility of opioids for palliative care in India was the outdated narcotics regulations, with complex licensing requirements for inter-state transportation. The archaic Narcotic Drugs and Psychotropic Substances Act 1985 was predominantly prohibitory in its scope and did not adequately ensure availability for medical purposes as a core objective. In 2014, the Act was amended, illustrating the joint commitment of the government and palliative care advocates in facilitating access to essential controlled medicines.

The IAPC certificate course in essentials of palliative care, conducted since 2008 through 30 centres across India, has succeeded in expanding awareness amongst thousands of healthcare professionals and in inspiring new members to become part of the field. The Medical Council of India accepted palliative medicine as a specialty in 2010, and the first cohort of students graduated (MD Palliative Medicine) in 2012. Efforts are underway for incorporating basic concepts of palliative care into undergraduate medical and nursing curricula. National palliative care faculties have also developed the minimum standards for quality of palliative care appropriate to the Indian situation.

Currently, more than 200 centres provide palliative care services, and scores of pioneering institutions—both within the government as well as in the non-government sector—provide opportunities for palliative care education. Several service units are expanding the scope of their programmes to include care for HIV, paraplegia, and patients with advanced systemic diseases.

While these successes are significant, it is important to acknowledge that gaps and barriers still remain, limiting access to palliative care to just 1% of the population. The field remains largely unknown in many parts of India, even among healthcare professionals. The progress and limitations are to be evaluated in the context of the following:

- a population of 1.2 billion, with 21% living below the poverty line and a 64.8% literacy rate
- 1.1% of the GDP allocated for healthcare

- absence of either socialized medicine or insurance system, with 70% health expenditure being out of pocket
- dominance of the private healthcare system, constituting 80% of all healthcare facilities
- ill-defined checks and balances to guide healthcare delivery operations

Strong governance, clear implementation processes, public and media advocacy, supportive policies, and continued engagement by the professional community at all levels are essential for achieving the vision of ensured access to palliative care for all those who need it in the country.

Spain

As a society based on traditional Christian values, compassion for the patient and family has been at the forefront of medical care in Spain, which has provided fertile ground upon which palliative care has taken root.

The first palliative care services started in the Canary Islands, Catalonia, and Madrid with mentorship from English hospices, the National Cancer Institute of Milan, and the Royal Victoria in Montreal. Palliative care services spread to other areas with pioneering efforts of individuals and non-governmental institutions such as the Spanish Association Against Cancer and the Catholic Order of St John of God. A decisive public health strategy gave a major boost to the development of the field and led to the expansion of a mere 17 teams in the 1990s to more than 400 active services in the country today. Spanish palliative care service teams have maintained the balance between community, home care, and hospital-based services, with doctors and nurses working in coordination to provide a high quality of care.

The Spanish Society of Palliative Care (SECPAL) is a multidisciplinary professional association, founded in 1992, which has played a unique role in the advocacy and development of the field. It engages with health authorities, provides leadership to the palliative care activities, supports the development of key documents, and provides the platform for scientific discussion, conferences, and knowledge sharing. SECPAL publishes the only Spanish scientific journal, *Medicina Paliativa*, dedicated to studies in the field of palliative care in various Latin American countries. Furthermore, Spain has hosted two European scientific congresses in 1995 (Barcelona) and in 2014 (Lleida). The University of Navarra in Spain has supported successive editions of the European Atlas of Palliative Care.

There is universal access to essential opioid medications, including all necessary formulations. However, the mandatory requirement of double prescriptions (one form for all the medications and another form only for opioids) hinders prescribing and dispensing.

Pioneers in the country have been actively involved in training programmes, sharing their expertise and providing practical guidance within their own centres. About half of the Spanish universities have incorporated generalized basic palliative care education in the undergraduate medical and nursing curricula. Although certified courses offering structured training are available at the universities, palliative medicine has not yet received recognition as a specialty.

The Ministry of Health has prioritized the development of paediatric palliative care, which is lagging behind in most parts of the country. Since 2003,

through legislation in the General Health Law, the government has designated palliative care as a right. The first National Palliative Care Plan (2003) was revised with clear guidelines, operating procedures, and evaluation processes in 2007. This has provided great momentum for the development of the field within individual Spanish regions.

Kenya

The history of modern palliative care in Kenya dates back to the early 1990s with the opening of the Nairobi hospice, supported by not-for-profit organizations. Community initiatives have since supported the growth of the field in Kenya, with most hospices being conceived and led by motivated citizens through mobilization of local community support and resources. Non-governmental organizations provide the required services in an affordable, culturally sensitive manner. They raise funds through charity events with innovative agendas that also serve to educate and increase the awareness of palliative care amongst the population.

In sub-Saharan Africa, an estimated 24.7 million people were living with HIV/AIDS in 2013, accounting for 70% of the global HIV disease burden. The growth pattern of palliative care in Kenya and Africa has been uniquely influenced by the HIV/AIDS pandemic and the associated socioeconomic and public health impact. Given the high prevalence and burden of distressing symptoms in advanced HIV, there is a substantial need for supportive care services, including palliative care.

The Kenya Hospices and Palliative Care Association (KEHPCA) was established in 2007 to foster palliative service development, integrate palliative care into the healthcare system, and improve access to pain medications. The KEHPCA is at the forefront of training in palliative care for both healthcare professionals and volunteers, using a variety of educational methods including e-learning programmes. In 2013, National Palliative Care Guidelines and a National Palliative Care training curriculum were developed, and palliative care is now recognized as both a medical and a nursing specialty in the country. Palliative care is also included within the core curricula for undergraduate medical and nursing training. In addition, short-term (e.g. one week) programmes and degree courses have been made available through the support of organizations such as the International Association for Hospice and Palliative Care and the Worldwide Hospice and Palliative Care Alliance.

In 2010, the Ministry of Health requested KEHPCA to work with 11 government hospitals to integrate palliative care into mainstream healthcare. Based on the recommended WHO public health approach, integration has commenced after a baseline survey to identify the gaps and possible solutions. Palliative care is recognized in the National Cancer Control Strategy (2010–2016) and the national framework for NCDs, and the specialty is now factored within the government health budget.

Private health insurance institutions are assisting government to integrate palliative care as an essential healthcare service with mandated coverage through their policies. In Kenya and throughout Africa, the US President's Emergency Plan for AIDS Relief (PEPFAR) has supported disease-modifying treatment as well as palliative care for patients with HIV/AIDS, while providing education to patients, families, communities, and clinical teams.

Regulatory barriers in the Narcotic Drugs and Psychotropic Substances Control Act 1994 (repealed in 2012) impeded the importation and distribution of appropriate medical use of opioids. An amendment to this Act is necessary so that pharmacists and doctors do not fear handling, prescribing, and dispensing opioids. In recent years, the Kenya Medical Supplies Agency has engaged with hospitals, hospices, and other partners to import morphine and streamline its distribution, with centralized production of oral morphine solution.

While there are 60 centres providing palliative care throughout Kenya, this provides for less than 10% of the population who need this service. As the scope for palliative care expands to cover NCDs and as people with HIV/AIDS live longer, there has been a massive increase in demand for palliative services. A three-pronged approach has been adopted to address the needs of the country: (1) educating policymakers, healthcare professionals, and the community at large regarding palliative care; (2) updating healthcare policies so that the service is provided early in the disease trajectory; and (3) ensuring access to strong analgesics. In another significant development, palliative care has found a place in the Kenya National Patients' Rights Charter, 2013.

Growth and access to palliative care is expected to improve.

Uruguay

Early activities in palliative care began around 1985 in Uruguay, but there has been accelerated development in the field after the establishment of the Palliative Medicine Department in Maciel public hospital in 2004, fostering a unique model of palliative care. It represented an adaptation of the model developed by Prof. Gómez Sancho that emphasized continuity of care across all settings, including the hospital and the home. Through coordinated teamwork and good communication channels connecting physicians, nurses, and counsellors, the 'Maciel model' allows home-based care to be a choice for patients with advanced disease. This department has become the national palliative care referral service for the public healthcare system. It has influenced care approaches and ensured that home-based care is a consistent aspect of palliative care services provided in the country.

In 2013, the Ministry of Health developed a National Palliative Care Plan with input from the Maciel Hospital Palliative Medicine Department which identified palliative care as a strategic objective for 2015–2020. The national plan aims to increase awareness about palliative care, improve professional education, and promote capacity and skills of teams for imparting care. It also supports and delineates guidelines for public-private partnerships.

The Uruguayan Society for Palliative Care (USPC), founded in 2001, has a membership which includes most of the palliative care professionals in the country today. Increasing USPC membership and the collaborative work of palliative care professionals over the years culminated in the successful organization of the first Uruguayan Congress of Palliative Care involving 500 professionals in November 2015.

Palliative care training is not formally included in the curricula for undergraduate students in the schools of medicine and nursing. However, in 2014 the School of Medicine of the University of the Republic (UDELAR) created the Teaching and Care Unit for Palliative Care, which offers palliative care as

an option for medical, nursing, and psychology students. This initiative has proved effective in enabling the wider availability of care and training opportunities. A new project in palliative care at the UDELAR School of Medicine offers a free-of-charge diploma in palliative care. Training is also expected to enhance the availability and access to essential opioids and improve the per capita consumption of opioids.

The Maciel Hospital has utilized the Extension for Community Healthcare Outcomes (ECHO) project in a most effective manner for establishing a nationwide network of palliative care professionals in 20 centres across the country (http://echo.unm.edu). Since early 2015, medical, psychological, social, and nursing aspects of palliative care clinical cases are shared, analysed, and discussed by interdisciplinary teams from each centre every fortnight. This project has succeeded in improving the capacity and confidence of participating professional teams working across the country and has decreased the sense of isolation for many health workers.

The current palliative care services cover about 25% of the patients in need of care, with three more regions left to incorporate palliative care services. Further progress depends on adopting a national palliative care policy, recruiting trained professionals to the field, and improving the use of opioids for pain management. Uruguay is committed to expanding services in palliative care to all those who need it, including paediatric patients and those with non-cancer diagnoses, by improving the number and multidisciplinary composition of palliative care teams.

> Meaningful palliative care requires a combination of socio-economic, cultural, and medical solutions. All three must be addressed. Not purely a medical issue, the cultural and socioeconomic factors determine what kind of death we face. Today's overemphasis on medical approaches can be balanced only by the people taking ownership.
>
> Jan Stjernswärd

International growth in palliative care

The foregoing stories illustrate the influence that pioneering individuals and collective efforts have had on the development of palliative care in different regions. It is noteworthy that once palliative care activity in a country reaches a critical level in terms of awareness regarding its scope and purpose, there is often an organic evolution of societal forces that eventually leads to crucial policy decisions and acceleration of its growth.

It is important to appreciate that palliative care practices in countries or regions of the world are often very different from one another, as palliative care cannot be delivered in a cultural vacuum. For example, in many parts of Asia, communities are cohesive and family ties are strong. This social capital has been effectively moblized in some regions to build a 'community safety net' around patients with long-term care needs. In parts of India, family members of a patient at the terminal phase of life are trained to administer subcutaneous medicine, and this enables continued control of symptoms at the preferred place of care, i.e. the home. Another example involves training family or community members in preventing and managing

bedsores and in providing basic essential nursing care where necessary. Such empowerment of families and carers avoids repeated expensive hospital visits and admissions.

Innovative methods used to strengthen home-based care have thus made palliative care interventions possible, even in regions of the world where public healthcare facilities are suboptimal. Community participatory actions have had demonstrable impact also on encouraging structural changes to government policies connected with palliative care.

A unique educational experiment to kindle empathy in doctors

The experiential learning described below was designed for medical undergraduates at the Patan Academy of Health Science, a newly formed health science university in Nepal, with the vision of graduating socially responsible doctors for rural Nepal. The objective was to orient medical knowledge, skills, and attitudes of doctors with a palliative care approach, when managing patients with chronic conditions. The experiment aimed to develop 12 attributes in students: (1) compassion and empathy, (2) communication skills, (3) commitment to serve the disadvantaged, (4) awareness of socioeconomic and cultural issues, (5) awareness of community health needs and social determinants of health, (6) professionalism, (7) leadership and team spirit, (8) clinical competence, (9) critical thinking, (10) lifelong learning, (11) innovation, and (12) commitment to research.

After introducing communication skills and breaking bad news, as well as ethical issues surrounding end-of-life care early in the curriculum, students are sent to rural areas to experience life with a family in the villages, as a part of a community-based learning and education programme. The objective is to help students understand life in rural Nepal and to develop empathy and humanitarian qualities essential for caring.

First-year students are asked to follow the trajectory of one patient with a chronic illness (e.g. COPD, chronic renal failure) over one year, or engage with a family with a disabled child. During this period, the student visits the patient's homes twice a month and engages with the family to understand their perspectives and concerns. A mentor is available for each student to discuss and clarify their doubts and questions. They are also encouraged to bring up ethical concerns at the discussion forums. The method of reflective learning continues in the second and third years of the training with the study of other patients with chronic progressive conditions. The 'dying patient' is included as an important learning objective within the curriculum. The learning includes management of symptoms at the end of life, palliative care emergencies, and an approach to providing dignified, symptom-free dying.

A semi-structured reflective portfolio on what the student has learned is part of the formative and summative assessment. In the final year, students submit a detailed write-up of a patient who was under their observation. This helps to elucidate the student's understanding of care needs at the physical, emotional, social, and spiritual levels in these complex conditions. A two-day intensive course is conducted during their internship to reinforce the learning.

Qualitative analysis of 25 students' reflective portfolios suggests that students are accessing a much deeper level of experiential learning when they visit patients at home or in hospices. They are also more capable of integrating and applying what they have learned in real-life situations. This is most clearly seen in the students' reflections on the communication of diagnosis and prognosis to terminally ill patients. The use of reflective portfolios seems to increase the depth of students' understanding of the challenges experienced by patients and families, as well as the impact of empathetic and non-empathetic care inputs.[4]

Students also expressed a desire to challenge current medical practices surrounding care of chronic diseases.

In effect, the experiential learning seems to equip the professional with greater empathy to respond effectively to various end-of-life situations. It is hoped that this integration of palliative care learning during the undergraduate training period will help not only to improve care of the dying in Nepal, but also to encourage the maturation of medical students into compassionate, caring physicians.

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Resources for developing palliative care

There are many resources available for those interested in developing or expanding palliative care services in their own regions.

Policy resources

Table 33.1 presents resources to assist with developing government policies that integrate palliative care into the national health system. The resources include examples of existing national laws, regulations, national strategies, national plans, palliative care needs assessments, and standards/protocols for palliative care.

Table 33.1 Policy resources

Laws, regulations and national strategy files	Worldwide Hospice Palliative Care Alliance (WHPCA)	http://www.thewhpca.org/resources/category/laws-regulations-and-national-strategies
Disease-specific plans and guidance files	WHPCA	http://www.thewhpca.org/resources/category/disease-specific-plans-and-guidance
Palliative care country reports and needs assessments	WHPCA	http://www.thewhpca.org/resources/category/country-reports-and-needs-assessments
Standards, clinical guidelines, and protocols	WHPCA	http://www.thewhpca.org/resources/category/standards-clinical-guidelines-and-protocols

Education/training resources

The International Association for Hospice and Palliative Care has extensive resources for those in the process of developing palliative care: http://hospicecare.com/home/. In particular, they maintain an international listing of education and certificate programmes in palliative care at: http://www.hospicecare.com/global-palliative-care/global-directory-ofeducation-programs.

See Table 33.2.

Table 33.2 Examples of graduate programmes in palliative care

Flinders University—Adelaide, South Australia	6 month certificate 1 year diploma 1.5 year Master's
Kings College—Cicely Saunders Institute—London, UK	Doctorate in Palliative Care Research MSc in Palliative Care PG Diploma and PG Certificate
Lancaster University—UK	Doctorate in Palliative Care
University of Cape Town, South Africa School of Public Health and Family Medicine	Diploma in Palliative Medicine Master of Philosophy in Palliative Medicine
University of Cardiff—Wales, UK	Certificate, Diploma, and Master's in Palliative Medicine Master's in Palliative Care
University of Edinburgh—Scotland	Doctorate in Palliative Care Research
Norwegian University of Science and Technology—Trondheim, Norway	
European Palliative Care Research Network	
European Certification in Essential Palliative Care (Princess Alice Hospice, Esher, UK)—10 week distance learning certificate	
Bristol University, UK—MSc in Palliative Medicine	
Indian Association of Palliative Care Certificate Programme—Distance learning http://palliativecare.in/tag/iapc-certificate-course	

Opioid availability resources

See Table 33.3.

Table 33.3 Opioid availability resources

Ensuring Balance in National Policies on Controlled Substances	World Health Organization
Guide on Estimating Requirements for Substances under International Control	Developed by the International Narcotics Control Board and the World Health Organization
Online course: Increasing Patient Access to Pain Medicines Around the World: A Framework to Improve National Policies that Govern Drug Distribution	Pain & Policy Studies Group/ WHOCC for Pain Policy and Palliative Care
Website: Global, Regional, and Country opioid consumption data	Pain & Policy Studies Group/ WHOCC for Pain Policy and Palliative Care
Website: Access to analgesics and other controlled medications	World Health Organization website https://www.who.int/medicines/areas/quality_safety/access_Contr_Med/en/
Report: National Drug Control Strategies and Access to Controlled Medicines	Human Rights Watch

Lastly, the Worldwide Hospice Palliative Care Alliance has numerous resources on its website to support palliative care workers (Table 33.4)

Table 33.4 Resources from the Worldwide Hospice Palliative Care Alliance

Palliative Care Toolkit	Developed to empower health workers in resource-poor settings to integrate palliative care into the work they are doing.
Training Manual for the Palliative Care Toolkit	Produced to accompany the Palliative Care Toolkit. It contains structured teaching modules and resources which can help others use the toolkit.
Advocacy toolkit	Highlights the key advocacy tools for hospice and palliative care organizations to develop their advocacy work.
An introduction to resource mobilization	Provides information about effective fundraising. It was produced by the Resource Alliance for the Worldwide Hospice Palliative Care Alliance membership.

Conclusion

To effect changes it will be critical for all palliative care experts to spend 40% to 50% of their time educating and supporting other health care professionals and community support systems, in addition to providing consultation and direct patient/family care.

Stjernswärd J, Foley KM, Ferris FD. (2007) The public health strategy for palliative care. *Journal of Pain and Symptom Management.* 33(5): 486–93.

This chapter has summarized the foundation, resurgence, and current status of palliative care, as well as global efforts for developing palliative care. Guided by the three WHO recommendations for implementing palliative care with a public health approach, advocates have made significant progress in expanding quality palliative care services, although much more championing is needed to meet the enormous needs around the world. The international mandate to improve palliative care is strong and supportive for those interested in taking action. It is hoped that clinicians who have observed the lack of palliative care would look beyond the limits of their clinical roles, explore the resources, and take initiatives for making the world a more caring place to live and die in.

Chapter 34

Miscellaneous

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Legal and professional standards of care

Medicine frequently poses complex situations that as clinicians can challenge our understanding of the legal and ethical framework we work within. The legal framework is structured to protect patients and doctors, and provide guidance in dealing with what can sometimes be unclear and difficult situations. In addition, doctors, like all other healthcare professionals (HCPs), work in an increasingly litigious and legally regulated environment. Sadly, for both patients and doctors, at times a simple failure by doctors to appreciate the nature and extent of their legal and professional responsibilities can lead to significant medico-legal problems. Thus, it is essential that doctors are aware of the standards set out by the GMC within its professional codes of conduct, and the medico-legal requirements of medical care. This is particularly true in palliative medicine, where doctors are involved at a highly emotional time in patients' and families' lives, when numerous ethical issues are encountered, e.g. deciding best interests or capacity. The Mental Capacity Act 2005 (MCA 2005), by looking at the legality of interventions for adults who lack the capacity to make their own decisions, has helpfully clarified many key medico-legal aspects of healthcare provision within English statute law. This has helped with some of the clinical dilemmas created by the previous uncertainty and legal inconsistency. It is important to acknowledge that England and Wales are covered by this act, whilst Scotland works within the legal framework set out in the Adults with Incapacity (Scotland) Act 2000; Northern Ireland had the Mental Health (Northern Ireland) Order 1986, which has been superseded by the Mental Capacity Act (Northern Ireland) 2016. The overarching themes of all legislation are, however, the same.

Doctors' key legal and professional responsibilities cover the following:

- capacity
- best interests—for children and adults with or without capacity
- advance decisions (previously, advance directives or living wills)
- the right to medical treatment
- appropriate withholding and/or withdrawing of treatment
- clinical negligence
- provision of care for patients with mental health disorders
- dealing with violent or aggressive patients
- caring for victims of mental and/or physical abuse
- informed consent, battery/trespass
- communication with patients and colleagues
- medical records: keeping adequate clinical notes and patient access to records—data protection and patient confidentiality
- witnessing of patients' wills or advance decisions
- prescribing controlled drugs for patients travelling abroad
- medical cause of death certification and notification of the coroner
- DVLA notification of patients' fitness to drive

Mental Capacity Act 2005 (MCA)

Before April 2007, doctors in the UK were expected to make decisions on behalf of patients lacking capacity according to common law and accepted best practice. However, it was feared that without clear legislation inconsistencies could follow and that patients' autonomy could potentially be undermined. There were particular concerns around the lack of any formal legal status for a 'next of kin' and the risk of unfair presumptions of incapacity based only on diagnosis. The increasing numbers of people lacking mental capacity, up to 2 million in England and Wales, also added to the pressure for new legislation (e.g. people with dementia, learning difficulties, mental health problems, stroke, brain injuries, or intoxication). The Mental Capacity Act 2005 (MCA)[1] was enacted to cement the principles from case law and best practice into UK statute law and to reform the existing relevant statute. It received royal assent in April 2005, and came into force in stages between April 2007 and October 2007. The MCA provides England and Wales with a clear legal framework to define and govern the clinical decision-making process for people who lack mental capacity, to protect and promote patients' rights (particularly autonomy), to involve and guide relatives/representatives, and to protect and guide professionals (with a binding code of practice). Greater clarity, legal backing, and the improved options provided within the MCA empower patients' self-determination and improve consistency within decision-making processes after capacity is lost. This has meant that the MCA has been broadly welcomed, despite some inevitable limitations.

The MCA is underpinned by five key principles

- presumption of capacity:
  - capacity is assumed unless established otherwise
- supported decision-making:
  - the right to receive all practical support to enhance capacity and hence to be as self-determining as possible
- acceptability of unwise decisions:
  - the right to make seemingly eccentric or unwise treatment decisions
- the requirement of best interests:
  - any action or decision made for people without capacity must be in their best interests
- least restrictive interventions:
  - any action or decision made for people without capacity should be the least restrictive of their basic rights and freedoms

The MCA clarifies the legal position in the circumstance where decisions need to be made for a person who lacks mental capacity, as it:

- describes who can act on someone else's behalf; when it is appropriate; and how it should be done
- specifies the test to assess capacity and the need to support people to enhance their capacity

- provides a checklist of relevant information and views to consider when deciding best interests; this is broader than the traditional singular 'medicalized' perspective, as it includes the following:
  - the patient's general welfare
  - multiprofessional working
  - the views of family and carers, who gain the legal right to be consulted

The MCA enables people to put plans in place to ensure their healthcare wishes are still adequately represented if they later lose capacity by:

- specifying the process to make a written statement to refuse treatment (an advance decision)
- specifying the appointment of substituted decision-makers:
  - lasting power of attorney (LPA)
  - independent mental capacity advocate (IMCA)
  - court-appointed deputy
- stipulating that a person's known wishes and feelings are still considered

Realizing the complexity of end-of-life treatment decisions, the uniqueness of each scenario, and how a lack of capacity further clouds the picture, it is inevitable that the MCA contains limitations. The MCA's guidance cannot resolve the following:

- differing opinions on best interests, where consensus cannot be reached despite all reasonable attempts at resolution, e.g. differing religious beliefs within the same family or conflicts between HCPs and LPAs, when it is questionable who is best representing the patient's views
- disputes as to the applicability of advance decisions:
  - some doubt will be unavoidable in view of the potential for different interpretations of a patient's actual meaning (particularly if an advance decision uses vague or lay terms or was written by a third party)
  - the inherent difficulty for anyone to reliably predict their wishes for an unfamiliar future event; patients with capacity can and do change their minds when actually facing situations; many patients, despite lacking the capacity for complex treatment decisions, may have a quality of life that is acceptable to them that they wish to continue for as long as possible

MCA 2005 and assessing capacity

Everyone normally has the mental capacity to make everyday decisions for themselves, e.g. what to eat and where to live. This self-determination extends to deciding whether to accept or refuse medical treatments.

The MCA clarifies that anyone from the age of 16 years is assumed to have the capacity to make their own decisions. However, a judgement of capacity must be made if it is felt that a person is unable to make a decision for themselves as a result of a specific brain or mind dysfunction (e.g. dementia, learning difficulties, mental health problems, stroke, brain injuries, or intoxication). The MCA specifies the best practice approach (optimistically described as the 'single clear test') to assess whether a person lacks capacity.

A person lacks capacity on an issue if, because of their brain or mind dysfunction, they cannot understand, retain, and use the relevant information to reach and then communicate their decision on that specific task at that specific time.

The burden of proof lies with confirming that, even after receiving all practical assistance, someone lacks capacity and, crucially, this adjudged lack of capacity is specific only to that decision at that time.

To demonstrate capacity, a person must meet all five required domains:

- believe the relevant information
- understand the relevant information
  - information must be given in a clear and understandable way; appropriately tailored to a person's needs, e.g. using simple language, a translator, or visual aids
  - 'relevant information' includes the nature and need for a decision, in particular the likely consequences of any accepting or refusing a treatment, of any alternative options, or of not deciding
- retain that information
  - for sufficient time to reach a decision, i.e. not necessarily any longer
- use or weigh the relevant information
  - to reach a balanced decision
- communicate their decision
  - this can be by any means; thus 'failure to express wishes' should rarely be given as the sole justification of incapacity, i.e. only where all help to communicate has failed

A lack of capacity cannot be established merely by reference to, or the presumptions around,

- age, appearance, or behaviour
- underlying medical conditions
- the likely duration of brain dysfunction

MCA and deciding best interests

The concept of a patient's 'best interests' is difficult to define precisely. Historically, it has appeared sufficient that any intervention should potentially offer a net benefit to the patient.[2]

A central tenet of the MCA is that any decisions made for people without capacity must be in their best interests. It is down to the person providing the care or treatment to decide what is in the best interests of the person lacking capacity.

Although the MCA does not define 'best interests' directly, it does provide a checklist of factors that any decision-makers must consider when deciding the best interests for a person they reasonably believe lacks capacity. In addition to the relative medical merits, consideration of broader ethical, social, and moral components is required. These requirements to determine best interests apply equally to donee(s) of LPA, court-appointed deputies, independent mental capacity advocates (IMCAs), and professionals within healthcare and social services.

Background to advance decisions to refuse treatment (previously advance directives or living wills)

Historically, it was accepted by most patients with life-threatening illnesses that doctors would make many treatment decisions on their behalf, and doctors would typically presume that most patients would want all available treatments. However, this is no longer the case, with patient-led care, increased emphasis on autonomy, greater access to information previously held within the medical community, and ongoing technological advances within medicine shifting the balance.

In advanced disease, some interventions may offer relatively little meaningful survival or symptomatic benefit, but may result in a significant burden to patients and families. Many patients may not desire a prolongation of life that is only possible through what they would see as 'unacceptable' means. Open discussion with patients usually results in an agreed management plan that prevents the pursuit of inappropriate and undesirable medical interventions.

Respect for patient autonomy is a fundamental aspect of medical professionalism; it is a prerequisite of the doctor-patient relationship and is enshrined in UK law. A patient with capacity can refuse any treatment for any or no reason, rational or not, even if their life may be shortened. A doctor may not enforce any treatment, intervention, or investigation upon them without their consent. However, there are exceptions; consent has not been needed in common law if there is necessity or in an emergency.

- doctrine of necessity: acting in the best interests of a patient who is not competent to give valid consent (now reflected in the MCA)
- emergency: to prevent immediate serious harm to a patient or to others or to prevent a crime

Doctors are not legally obliged to follow patients' requests for a specific treatment. Patient choice cannot force HCPs to give treatments against their best judgement, i.e. if it appears clinically unnecessary, futile, or inappropriate, or lacks any reasonable expectation of cost-effectiveness.

Advance decisions (or advance directives/living wills) allow a patient with capacity to formally express and register their wishes about future treatment decisions in the event that they may lose capacity (and then be unable to consent to or refuse treatment). Following proposals dating from the late 1960s, the first legal decision to validate an advance directive occurred in New Jersey Supreme Court, USA, March 1976.

Karen Ann Quinlan

In 1975, 21-year-old Karen Ann Quinlan lapsed into a persistent vegetative state after coming home from a party (as a result of hypoxic brain damage, following two respiratory arrests). Without the legal option for non-treatment (as she was not brain-dead), the hospital refused to stop her artificial ventilation, despite the request of her parents. Subsequently, in 1976, the Supreme Court found that her ventilation could be discontinued, on 'privacy' grounds, if the hospital ethics committee believed her condition was irreversible. The court regretted that it could not discern her supposed choice based on her previous conversations, but had no doubt that Karen would decide to stop the life-support if she could,

even if it led to her death. Once off the ventilator, she unexpectedly continued to breathe on her own and remained in a PVS until she died from infection in 1985.

At appeal, the judicial principles upheld were the following:

- when a patient lacks capacity, someone else may exercise their right to make treatment decisions, preferably their families with medical input (rather than the courts)
- end-of-life care decisions should balance any treatment invasiveness against the likelihood of recovery

Patients can refuse treatment even if this refusal might lead to death.

A similar high-profile debate on the role of advance decisions took place in the UK in 1993, following the case of Tony Bland, the first patient to be allowed to die following the decision of an English court to allow the withdrawal of life-prolonging treatment.[3]

Tony Bland

Tony Bland was left in a persistent vegetative state aged 18 years, following the crush at the Hillsborough football stadium disaster in 1989. Subsequently, the hospital, with the support of the Bland family, made an application to the court to lawfully withdraw all life-prolonging treatment, because such action at that time would otherwise have amounted to the crime of murder in UK law. On appeal the court decided the following:

- though at no time had Mr Bland actually given 'any indication of his wishes', it was felt that he would not have wished to continue living in the circumstances of being in a PVS
- artificial nutrition and hydration were to be counted as treatment and not basic care (as previously), so they could be withdrawn legally

MCA 2005 and advance decisions to refuse treatment

Advance decision

According to the MCA, an 'advance decision' describes the formal provision of clear instructions to cover any future loss of capacity, so a person can specify which treatment(s) should be then stopped or not started and under which circumstances.

By formalizing anticipatory decision-making, the MCA brings statutory rules and clear safeguards to improve the process. Though no set instructions for preparing an advance decision have been formalized (because of their inherently individualized nature), the MCA clarifies the necessary content and ramifications of an advance decision.

In summary, advance decisions:

- can only be made by informed, adult patients with specific capacity
- must stipulate the relevant treatments and circumstances

- to be valid, must be consistent with other behaviours, conversations, and wishes expressed by the patient
- only cover refusal of treatment
- can be oral or written, unless authorizing refusal of life-sustaining treatment, when they must also comply with further formalities, i.e. written, signed, witnessed, and clarifying 'even if life is at risk'

Open discussions with relevant HCPs will help ensure that the patient has the relevant information to complete an advance decision. Advance decisions to refuse treatment are the outcome from—and are not a substitute for—ongoing communication with HCPs and careful deliberation. To make informed choices, patients need to be aware of the predictable phases of their disease, the diagnosis, prognosis, rehabilitation potential, and all available treatment options. Patients also need to know what will happen if no treatment is carried out.

Advance decisions do not encompass other anticipatory decision-making:

- advance statements describing a patient's preferences for treatment
- oral or unwitnessed refusals of life-sustaining treatment
- general commentaries on a patient's fundamental values
- a non-specific desire not to be treated

Though these areas (even if documented) are not legally binding in the same way as specific advance refusals, they remain relevant to deciding 'best interests' and therefore still need to be incorporated into decision-making. However, nothing in an advance decision (formal or not) can force HCPs to give treatments against their best judgement.

Similarly, an advance decision from a patient under the age of 18 years should be taken into account and accommodated if possible, but a court or a person with parental responsibility can overrule it.

The legal weighting of any undocumented verbal advance decisions may prove uncertain if contested. Where possible, HCPs should record any verbal advance decisions to refuse treatment in the patient's medical notes as fully as is practical.

Healthcare professionals

- are liable to follow an advance decision to refuse treatment if it appears valid and applicable to the prevailing circumstances, just as if the person had made a contemporaneous decision with capacity (failure to comply could risk a claim of battery)
- carry no liability for the consequences of giving or not giving a treatment according to an advance decision that the HCP has sufficient grounds to reasonably believe to be valid and applicable
- can provide a treatment that has been 'refused' by the patient in an advance decision if they are not satisfied that the advance decision is both valid and applicable, and as long as the treatment is in the patient's best interests
- are protected from any liability if a failure to comply with an advance decision results from their lack of awareness of its existence

If an advance decision is contested, the court can be asked to decide if it exists, if it is valid, and if it is applicable to a proposed treatment. Specifically, life-sustaining treatment to prevent a serious deterioration can be provided while awaiting the court's decision. If the validity or applicability of an

advance decision remains uncertain, common law suggests the court would be likely to favour continuing with life-sustaining treatments.

Guidance on a written advance decision

Though there is no set format for written advance decisions, as with any legal document, it should be clear, comprehensive, and unambiguous. It must be readily accessible when needed, it should be reviewed regularly (to appear as up-to-date as possible), and all stakeholders should be kept aware of the contents to prevent avoidable distress and disputes when implemented. Meticulous preparation and adherence with the additional requirements is needed for any refusal of life-sustaining treatments, to prevent any doubts around validity or applicability, which may otherwise undermine the patient's expressed wishes if the advance decision were to be contested in court.

Possible format of written advance decisions

- patient's full name, address, and date of birth
- document name and address of GP, and any other key HCPs, stating whether they have a copy
- clarify the extent of HCP advice sought when writing the advance decision; give any additional names and addresses
- clear statement that the document should apply if the patient lacks capacity to make their own treatment decisions
- if potentially open to question, seek HCP confirmation and documentation of capacity at the time of writing
- make a clear statement of the patient's decision
  - clarify the specific treatment(s) to be refused
  - clarify the specific circumstances when the refusal would apply
  - confirm the decision stands 'even if life is at risk' if refusing life-sustaining treatments
- date of first and any subsequent drafts and the current review
- clarify whether an LPA has been appointed and any other nominated persons who should be consulted
  - document names, addresses, and telephone numbers
  - clarify their awareness of the contents of the document
- signature of patient or of their nominee (confirming signing for the patient, in the patient's presence)
- signature of the witness: clarify that it has been signed with the patient present, to witness both the signing and that the signature confirms that the document reflects the patient's wishes
- witness's full name, address, and relationship to the patient
- accessibility: details should be given of where all copies of the advance decision are expected to be kept
- attach a statement to better inform future 'best interests' decisions (not binding, but still must be taken into consideration)
  - set out the patient's general wishes, feelings, and values
  - make any specific requests for treatment, or a general request to receive all medically reasonable efforts to prolong life
  - state where the patient would like to be cared for

MCA 2005 and designated decision-makers to act for someone who lacks capacity

- A competent person can appoint someone they trust as an 'LPA', who can then have full legal powers to act on their behalf on matters of health, welfare, and finances, should they lose capacity (as detailed subsequently).
- Independent mental capacity advocates (IMCAs) are an extra safeguard for particularly vulnerable people in specific situations. An IMCA is appointed to represent and support any person who lacks capacity when there is no one available (as is practicable) to speak on their behalf. An IMCA is required in decisions of 'serious medical treatment' or decisions of significant changes of residence (e.g. discharge from hospice to nursing home). The IMCA brings all the factors relevant to a decision to the attention of the decision-maker, including the person's wishes, feelings, beliefs, and values. The IMCA can challenge the decision-maker. The Department of Health website provides a list of IMCA providers (from local authorities or NHS bodies).
- The Court of Protection will appoint a deputy when facing a series of decisions where the Court cannot resolve the issues with a one-off 'court order'. As specified, deputies can then make decisions on welfare (including health) and/or financial matters, but deputies cannot refuse consent to life-sustaining treatment or override an LPA, and they must act in the person's best interests.

MCA 2005 and lasting power of attorney (LPA)

A 'power of attorney' is a legal document that enables a person to choose someone else to act on their behalf. The MCA has updated and extended the scope of the previous UK statute on '(enduring) power of attorney' which covered only finances, replacing it with 'lasting power of attorney' (LPA) which can, in addition, cover decisions on health and welfare. The new documents allow a person, the donor, to choose one or more representative(s), the 'donee(s)', to officially act on their behalf. The scope of legal authority passed within an LPA can cover any or all aspects within either or both types of LPA.

Two types of LPA

- property and affairs:
  - replaces the previous enduring power of attorney
  - can be activated either before or after capacity is lost, as specified
- personal welfare:
  - a new option to appoint someone to 'consent' on health and other welfare matters
  - can only be activated once the donor has lost capacity

Thus, a patient can now appoint a trusted representative to cover not only relatively mundane decisions such as access to medical records, diet, and daily care routine, but also to accept or decline potentially life-sustaining treatment on their behalf should they lose capacity. Such a role carries a

'very heavy burden'; an LPA may have to make potentially life-and-death decisions for someone they care about, with, in practice, limited clear-cut instructions.

Creating an LPA requires:

- the appropriate appointment of a donee(s)
  - donees must be aged 18 years or more (or a trust corporation if only covering property and affairs)
  - donees must not be bankrupt, if the LPA conveys authority over property and affairs
  - two or more persons may act as an LPA jointly (shared role) and severally (independent roles)
  - a replacement donee can only be appointed by the donor
- that the document is drawn up in accordance with the MCA
  - donor had reached 18 years of age and had the required capacity at the time
  - written and complies with further specific requirements; for an LPA to be able to authorize the giving or refusing of consent to life-sustaining treatment, the document must contain explicit authority
- that the LPA is registered with the Office of the Public Guardian (OPG) before it can be used

The authority conferred by an LPA is subject to the following:

- confirmation that, even after receiving all practical assistance, the person lacks capacity for that decision at that time
- the LPA, in the prescribed form, has been registered with the OPG
- the donee has been fully informed of the nature, risks, and consequences to the donor of accepting or refusing any proposed treatment
- as applicable, consultation with any donee with 'joint' responsibility to reach agreement (by contrast, if multiple donees carry 'several and joint' responsibility, then they can all independently give the needed authority)
- any specified limitations to the scope of powers, as set by the donor
- compliance with all the provisions within the Act. In particular, donee(s) must adhere to 'the principles' and so they must make decisions that are in the donor's 'best interests'. Thus, no one person can act as a true patient proxy (i.e. able to give consent); in being obliged to follow best interests, if contested in court, the scope of a donee's authority may not prove comparable to that of a patient with capacity or an accepted advance decision.
- consensus with HCPs and other relatives/carers; if conflict cannot be resolved, the case will need referral to the Court of Protection. While discord around 'best interests' decisions should be infrequent, it is not yet clear whether LPAs will convey the power of veto to overrule clinicians. For example, could an LPA refusal prevent the necessary hoisting of a patient lacking capacity, despite the potential health and safety issues for staff (but crucially not the patient), pending any decision by the Court of Protection?

A donee of an LPA cannot authorize restraint unless:

- the LPA reasonably believes the donor lacks the necessary capacity
- the LPA reasonably believes that restraint is necessary to prevent harm to the donor
- the restraint is proportionate to the likelihood and seriousness of harm.

MCA 2005 and restraint/deprivation of liberty

The MCA's protection of patients' rights includes guidance on the 'restraint' of people lacking capacity.

- Restraint is defined as any restriction to the liberty or movement of an incapacitated person or the use or threat of force should the person resist.
  - Restraint is only permitted if the person using it reasonably believes it is necessary to prevent harm to the incapacitated person.
  - Any restraint must be proportionate to the likelihood and seriousness of potential harm.
  - Any restraint must represent the least restrictive option.
- To prevent incompatibilities with the European Convention on Human Rights, there was a need to ensure these patients had recourse to adequate formal legal procedures if admission were needed. Consequently, the MCA makes any deprivation of liberty unlawful unless there is 'Bournewood authorization' or Court of Protection support. In an 'emergency', an institution (e.g. hospice) can issue urgent authorization for any patient felt to be at risk of deprivation of liberty while obtaining standard authorization through a local authority. These situations are often complex, and the official implementation of the safeguards seems to still vary nationally.

Bournewood case

Amendments to the MCA in 2007 came after the case of patient HL. HL had a severe learning disability and a background of autism. He had spent many years living in Bournewood Hospital. As part of a resettlement scheme, he moved into the community and was cared for by Mr and Mrs E. In 1997, after becoming agitated at a day centre, and displaying self-harming behaviours, he was readmitted to Bournewood Hospital. There was no formal detainment in place, but if he were to attempt to leave (which he never did), it was stipulated that he should be detained under the Mental Health Act 1983. His carers were prevented from visiting for fear he would want to go with them. Mr and Mrs E took the case to court on the basis that HL was deprived of his liberty. In 2004, it was deemed by the European Court of Human Rights that HL had been deprived of his liberty, and this lack of regulation was recognized as the 'Bournewood gap'. This prompted an update of the MCA in 2007.

References

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2. BMA (2007). Withholding and Withdrawing Life-prolonging Medical Treatment (3rd edn). Oxford: Blackwell.
3. Airedale NHS Trust Bland (1993). All England Law Rep; Feb 1993; 1:821–96.

Clinical negligence

Claims of clinical negligence will result when doctors are deemed to have acted outside of sound medical practice. While clinical opinion may vary, in medical litigation the central question is whether or not a doctor attained the standard of care as required by law, although the definition of what this is has changed over the last 60 years. Until recently, the UK legal standard expected is one of 'reasonable care' as defined by case law; this standard was founded on the Bolam case (1957).

Bolam (1957)

Mr Bolam underwent electroconvulsive therapy (ECT) for clinical depression. At that time, medical opinion differed on how best to minimize the risk of injuries possible from convulsions induced by ECT. In Mr Bolam's case, the technique of manual restraint was ineffective, and as a result fractured his pelvis. He subsequently argued that the doctor had been in breach of the standard of care in providing treatment and that the hospital had been negligent.

The judge in his direction to the jury said that a doctor is not guilty of negligence if he has acted in accordance with the practice accepted as proper by a responsible body of medical opinion skilled in that particular art. If, therefore, a medical practice is supported by a body of peers, then the Bolam test is satisfied, and the practitioner has met the required standard of care in law. This test has been used on numerous occasions in cases of medical litigation.

Subsequently, the judgment from the 'Bolitho' case has imposed an additional requirement above the standard of clinical care as was defined by the Bolam test. The courts must now take a more enquiring stance, testing the medical evidence offered by both parties in any litigation, to determine whether such opinion is 'reasonable', 'respectable', and 'responsible'. The courts must be satisfied that the medical experts have considered all the risks and benefits to reach a defensible and logical conclusion. Thus, though unlikely, a doctor acting in line with the accepted practice could still be found to be negligent if the court believes the accepted medical practice in question is not sufficiently balanced or logical. That is, just the occurrence of similar medical practices is no longer a sufficient defence in itself; to be defensible, clinical care must also reflect balanced, comprehensive, and logical decision-making.

Bolitho (1998)

In 1984, a two-year-old boy was readmitted to hospital with breathing difficulties a day after discharge, following a four-day admission for croup. During this stay, a doctor failed to attend when called by nurse colleagues to assess further episodes of breathing difficulties. Subsequently, the child arrested and sustained severe brain damage. By the time of the court case, the child had died.[1] A breach of duty from the non-attendance was established, while the doctor's defence that they would not have intubated the child if they had attended to it was not considered germane.

The question of negligence rested with the need for intubation and whether this intubation could have prevented the arrest. Conflicting medical evidence was given on whether intubation would have been the proper course of action. In line with the Bolam test, the doctor was initially deemed not negligent, since not intubating was supported by one of the two sets of responsible medical opinion.

Though the courts ultimately dismissed the case, it went to appeal and the House of Lords. The Bolam principle was perceived as being excessively reliant upon the medical testimony supporting the defendant. Contrary to the spirit of Bolam, the presence of expert medical opinion supporting the defendant was deemed insufficient in itself to avoid a claim of clinical negligence. Rather, the court had to be satisfied that *any* body of medical opinion relied upon by the defence had demonstrated that it had a logical basis, having weighed all the competing risks and benefits. Reassuringly, it was deemed 'very seldom' that a judge would question a competent medical expert opinion.

The most recent significant change to the expected standard was founded on the outcome of the Montgomery case. This case has elevated the standard of what is expected of doctors and has shifted the emphasis.[2]

Montgomery (2013)

In 1999, Mrs Montgomery gave birth in a Lanarkshire Hospital. There were complications during the delivery, and consequently the baby suffered serious disability. Mrs Montgomery sought damages on the basis of negligence of the doctor responsible for her care during delivery. As Mrs Montgomery had diabetes, there was increased risk of having a larger baby, and consequently the complications of vaginal delivery were potentially greater. The doctor involved did not routinely advise women with diabetes about the additional risks associated with vaginal delivery. It was deemed that Mrs Montgomery was not informed of all the risks, specific to her, that would potentially shape her decision-making process with respect to mode of delivery. The court found in favour of Mrs Montgomery, stipulating that she should have been informed by her clinician of the risk of shoulder dystocia.

This case has resulted in a shift in the paradigm to one that is patient-centred. The question clinicians should ask as a result of this case is not 'What would my colleagues do in this case?' but 'What would a patient expect to know about the case?'.

References

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2. Montgomery v Lanarkshire Health Board (2013) CSIH 3. Accessed 20/12/2018. https: //www.scotcourts.gov.uk/search-judgments/judgment?id=ddbd8aa6-8980-69d2-b500-ff0000d74aa7

Further reading

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Death certification and referral to the coroner

Registration of death

Every death occurring in the UK has to be registered in the Register of Deaths local to the place of death. This chapter relates to procedures in England and Wales, although other jurisdictions, e.g. Scotland, have very similar procedures.

The information recorded in the register comprises personal details of the deceased person and medical information as to the cause of death. The death must be formally registered (within 5 days) at the Register Office for Births, Deaths and Marriages local to the place of death, although it is now possible to provide the personal details needed to register at any registry.

Personal details

The relevant personal details (including the deceased's full name, home address, dates and places of birth and death, occupation, matrimonial/partner status, etc.) will be provided by the 'informant' (normally a close relative who has personal knowledge of the deceased) who attends the register office, and is able to respond to the various questions asked by the registrar.

Medical details and completion of the Medical Certificate of Cause of Death

The medical details will be provided by the registered medical practitioner who has been in attendance on the deceased during their last illness. They are required to furnish a certificate in the prescribed form (Medical Certificate of Cause of Death or MCCD). It should be completed by the certifying doctor, with the cause of death to the best of the doctor's information, knowledge, and belief.

The MCCD should be completed promptly, giving clear statements that set out the sequence of the disease process that led to death. It should not give a 'mode' of death as the only entry, nor should abbreviations be used. The doctor is legally responsible for delivering the MCCD to the registrar, although normally the informant acts as the doctor's agent and hands it to the registrar.

The registrar will copy all the medical details from the MCCD (using the identical words and spelling) into the register.

Changes to the certification system in England and Wales have been debated for several years following the inquiry into serial murders by Dr Harold Shipman. The new medical examiner's role began in April 2019.

The changes in the system are to ensure equality and improve transparency and efficiency within the system. In Scotland, new MCCD forms were introduced in 2015; this has eliminated the need for cremation forms.

Referring deaths to the coroner

In 2016, just under half of all deaths in England and Wales were reported to the coroner.[2] Deaths that cannot be readily certified as due to natural causes should be referred to the coroner. Once a death has been reported

to the coroner, they have a duty to investigate the cause of death. This may be done by way of informal inquiry carried out by the coroner or a coroner's officer, by a post-mortem examination made to establish a cause of death, or by an inquest. If the family objects to the post-mortem, whether for religious or other reasons, an appeal can be made, but this may delay the funeral.

The registrar of births and deaths (but no one else) has a statutory duty to report any death to the coroner if, on the basis of information coming to the registrar's notice, it may be one that, by law, the coroner is required to investigate (see following). Nevertheless, doctors are encouraged to report voluntarily any death that the registrar may subsequently refer to the coroner. This will save time and reduce uncertainty for the family. Coroners and their officers are always prepared to discuss individual cases and, in this way, ensure that families are neither inconvenienced nor troubled unnecessarily.

Coroner's inquiries

If the case is one where an inquest is held, the registration in the Register of Deaths is completed by the coroner when the inquest is finally concluded.

A coroner's inquest is a limited public inquiry, convened by the coroner, to find factual answers as to who the deceased person was, and how, when, and where the death occurred. The coroner does not address matters of blame (liability).

Registrar's duty to report to the coroner

The registrar is required to report the death to the coroner in the following situations:

- it appears to the registrar that the deceased was not attended during their last illness by a registered medical practitioner
- the registrar has been unable to obtain a duly completed MCCD
- the deceased was not seen by the doctor
  - after death, or
  - within 14 days before death
- the cause of death appears to be
  - unknown
  - unnatural
  - the death was caused by
    —violence
    —neglect
    —abortion
  - the death occurred in suspicious circumstances
  - the death occurred
    —during an operation
    —before recovery from the effect of an anaesthetic
  - the death appears to have been due to
    —industrial disease
    —industrial poisoning

24 hours

It is sometimes argued that if the deceased was under the care of the doctor for less than 24 hours before death ensued, that the doctor may not

have sufficient knowledge as to the cause of death to complete the MCCD. The coroner's office will always advise informally about this.

Certifying deaths in the hospice setting

In a hospice setting, it is not uncommon for a patient to die with a pathological fracture or to die within a short time of arrival at the hospice. The local coroner will be happy to discuss these cases.

Other points

Burial and cremation

The registration process also provides authorization for burial or cremation. The authorization issued by the registrar should be handed to the funeral director to be used by the family. If the case is one where an inquest is held, the authorization of the burial or cremation is given by the coroner.

Cremation

New regulations were applied to cremation in the UK as of January 2019.

If a body is to be cremated, a Certificate of Medical Attendant (Form 4) and a Confirmatory Medical Certificate (Form 5) should be completed. In Form B, if the doctor has not attended the deceased within 14 days of death, the coroner should be notified. The doctor must see the body after death.

Form C must be completed by a registered medical practitioner of not less than 5 years standing, who shall not be a relative of the deceased or a relative or partner of the doctor who has given the certificate in Form B. The doctor must see and examine the body after death. In addition, the doctor must have seen and questioned the medical practitioner who completed Form B.

The applicant for cremation has a new right to inspect Cremation form 4 or 5. Some of the information may have been given to the doctor by the deceased in confidence. If it is included in the form, it may be disclosed to the applicant for cremation if they choose to inspect the form. If this would be a breach of confidence, information may be given to the medical referee on a separate sheet of paper attached to the form with explanatory reasons.

Death certificate

When completed, the entries in the Register of Deaths will form 'the death certificate', the proof of death required for the various legal and social processes as well as overall statistics of causes of death. Copies of the death certificate can be obtained from the registrar.

Wills

If there is a will, the executors named in the will (or if there is no will, the deceased's personal representative) is responsible for arranging the funeral and looking after (and subsequently disposing of) the person's assets and property.

If there is a will, the executor should 'prove' this to obtain probate of the will.

If there is no will, the deceased's personal representative should apply for letters of administration.

Funeral director

The funeral director will need to know whether the body is to be buried or cremated (over 75% of deaths in the UK are now followed by cremation).

They will need to know of any religious customs or rituals that might be necessary.

Bodies may be 'partially' embalmed routinely, or this might be discussed with the family. Traditionally, embalming involves draining blood from the body and replacing it with formaldehyde plus a pinkish dye pumped under pressure, which has a hardening and disinfecting effect. Nowadays, the blood is not drained, but a small amount of embalming fluid is infused to help prevent the body smelling and to make the face more presentable; this is particularly relevant for hygienic reasons or if the families wish to view.

References

1. Department of Health (2016, May) Guidance: An overview of death certification reforms. DoH.
2. Ministry of Justice (2017, May) Coroners Statistics Annual 2016: England and Wales. Ministry of Justice statistics bulletin. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/613556/coroners-statistics-2016.pdf

Further reading

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Fitness to drive

In the interests of road safety, those who suffer from a medical condition likely to cause a sudden disabling event at the wheel or inability to safely control their vehicle from any other cause should not drive.

The Secretary of State for Transport, acting through the medical advisers at the Drivers Medical Group at the Driver and Vehicle Licensing Agency (DVLA), has the responsibility to ensure that all licence holders are fit to drive. It is the duty of the licence holder to notify the DVLA of any medical conditions which may affect safe driving. Most patients are sensible and responsible, and, with the support of family members, are safe on the roads. They will avoid driving when their physical or mental condition begins to affect their judgement and ability to react quickly to unpredictable circumstances.

Driving is often seen as an important factor in maintaining the struggle for independence. It may be very hard for the patient, on both a practical and emotional level, to agree to letting go of the last vestiges of control over their lives. Very sensitive handling is needed. A crucial component of any patient-doctor relationship it that of trust. It is important that patients do not avoid seeking medical help for fear that their doctor will disclose personal information without consent. It is therefore important, if at all possible, to be open and honest with patients. Most patients understand why it may not be safe for them to drive. However, in the circumstance where public safety is at risk, it is a doctor's responsibility to divulge this information to the DVLA.

If a patient is obviously unfit to drive for any reason and refuses to comply, the GMC issues the following guidelines:

- The DVLA is legally responsible for deciding whether a person is medically unfit to drive. They need to know when driving licence holders have a condition which may, now or in the future, affect their safety as a driver.
- Therefore, where patients have such conditions, the doctor should make sure that the patient understands that the condition may impair their ability to drive. If a patient is incapable of understanding this advice, e.g. because of dementia, you should inform the DVLA immediately.
- Explain to patients that they have a legal duty to inform the DVLA about their condition. If the patient refuses to accept the diagnosis or the effect of the condition on their ability to drive, you can suggest that they seek a second opinion, and make appropriate arrangements for this. You should advise patients not to drive until the second opinion has been obtained.
- If patients continue to drive when they are not fit to do so, you should make every reasonable effort to persuade them to stop. This may include telling their next of kin.
- If you do not manage to persuade patients to stop driving, or you are given, or find, evidence that a patient is continuing to drive contrary to advice, you should disclose relevant medical information immediately, in confidence, to the medical adviser at DVLA.
- Before giving information to the DVLA, you should inform the patient of your decision to do so. Once the DVLA has been informed, you should also write to the patient to confirm that a disclosure has been made.

Driving and drugs that might impair cognitive and motor skills

Doctors have a duty to inform patients when they are prescribed medication which may impair their driving (GMC guidelines, see Table 34.1). Patients should be reminded that motor insurance may become invalid if there are changes in medical circumstances.

Patients on longer-term stable doses of opioids show only minor effects in terms of diminished cognition, perception, coordination, or behaviour related to driving.

Patients, however, who are newly started on opioids or who are prescribed an increase above their 'normal' stable dose may show cognitive impairment for a few weeks or so. These patients should be advised not to drive during this period.

Driving and brain tumours

The regulations for restrictions of driving vary depending on the type of brain tumour and how it has been treated. However, in the case of high-grade primary or secondary brain tumours, whether or not a convulsion has occurred, the DVLA must be notified. Patients will not be allowed to drive for at least 2 years after treatment.

Driving and heart/vascular conditions

Patients with heart failure are usually be safe to drive provided that there are no symptoms that may distract the driver's attention. Following PCI, patients may resume driving after 1 week, and following CABG may resume after 4 weeks. There are restrictions for those with intracardiac defibrillating devices. Patients with an abdominal aortic aneurysm of >6.5cm will be disqualified from driving. Patients must not drive for at least 1 week after pacemaker implantation, and must also inform the DVLA. Patients with an implantable cardioverter defibrillator may not drive for 6 months after implantation.

Patients with NYHA Class IV must not drive.

Driving and dementia

Patients with poor short-term memory, disorientation, or lack of insight and judgement will almost certainly not be fit to drive. There is acknowledgement, however, that presentation and progression of dementia are variable; in early dementia, while sufficient skills remain and progress is slow, the medical adviser may allow driving but will require a yearly review.

Table 34.1 Drugs in palliative care that may impair cognitive and motor skills

Opioid analgesics	Morphine, oxycodone, etc.
Benzodiazepines	Diazepam, lorazepam
Antidepressants	Amitriptyline
Phenothiazines	Levomepromazine
Antihistamines	Cyclizine

Driving and seat belts

Exemption from having to wear a seat belt may be sought if it is thought to pose a danger to the patient's safety, such as in the situation of significant intra-abdominal disease.

Application forms for a Certificate of Exemption from compulsory seat belt wearing in the UK may be obtained through the NHS Response telephone line (0300 123 1002).

Useful contacts

Drivers Medical Group
DVLA
Swansea SA99 1TU
Tel: 0179 276 1104
DVLA At a Glance—Current medical standards of fitness to drive http://www.dvla.gov.uk (reviewed 6 monthly) medadviser@dvla.gsi.gov.uk

References and further reading

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DVLA (2017, June) Assessing fitness to drive: a guide for medical professionals. Last updated August 2018. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/618072/assessing-fitness-to-drive-a-guide-for-medical-professionals.pdf https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/618072/assessing-fitness-to-drive-a-guide-for-medical-professionals.pdf
GMC guidance (2017) Confidentiality: patients' fitness to drive and reporting concerns to the DVLA or DVA.

If in any doubt concerning the latest legal requirements in relation to driving and palliative care issues, access the DVLA website.

Useful figures

Dermatomes

See Fig 34.1 and Fig 34.2.

Genograms

See Fig 34.3.

Peripheral nerve assessment

See Fig 34.4.

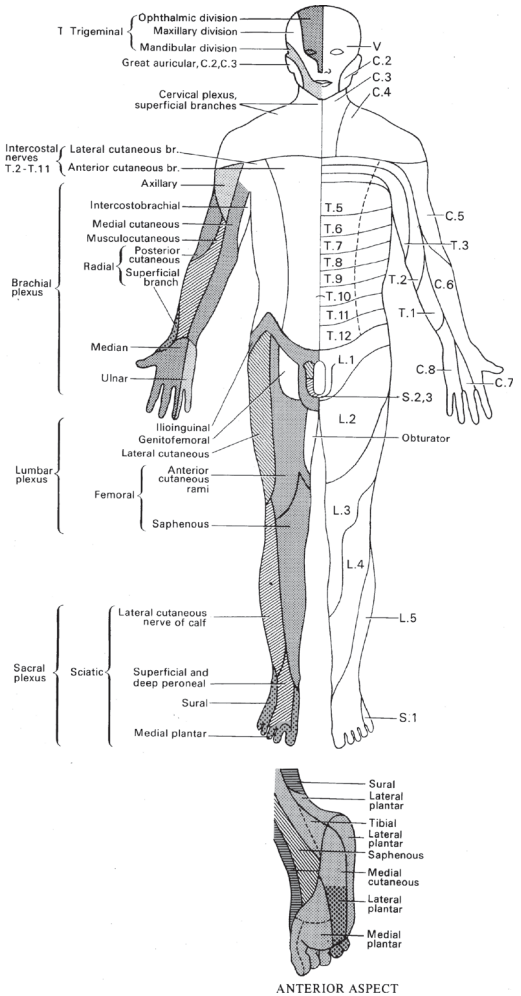


Fig 34.1 Dermatomes posterior aspect. Reproduced from Longmore M., Wilkinson I., and Rajagopalan S., (2004) Oxford Handbook of Clinical Surgery 6th edition pp. 338–9: Oxford University Press with permission from Oxford University Press.

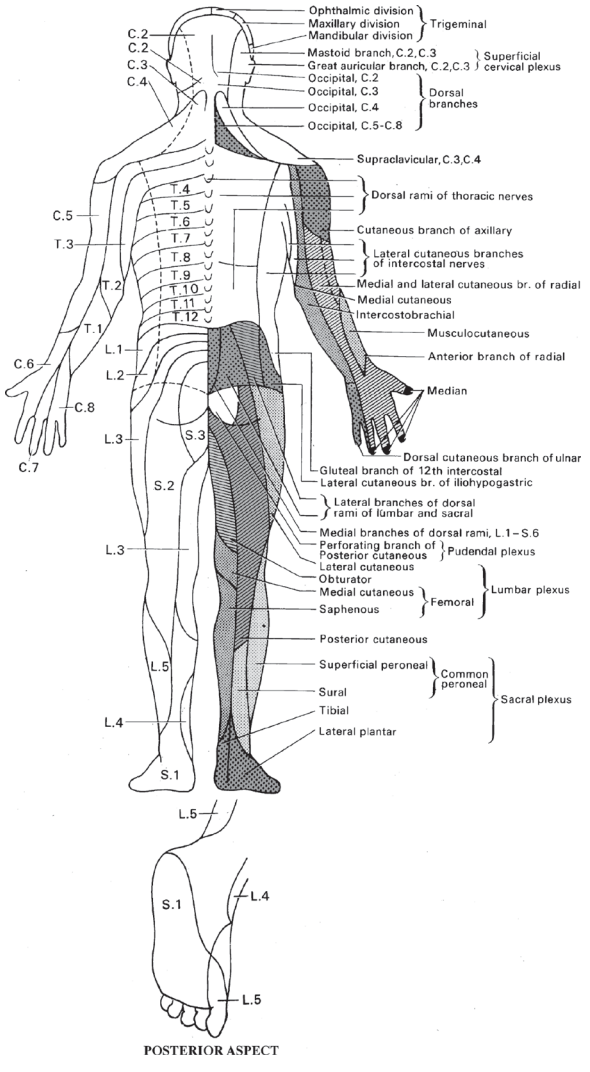


Fig 34.2 Dermatomes anterior aspect. Reproduced from Longmore M., Wilkinson I., and Rajagopalan S., (2004) Oxford Handbook of Clinical Surgery 6th edition pp. 338–9: Oxford University Press with permission from Oxford University Press.

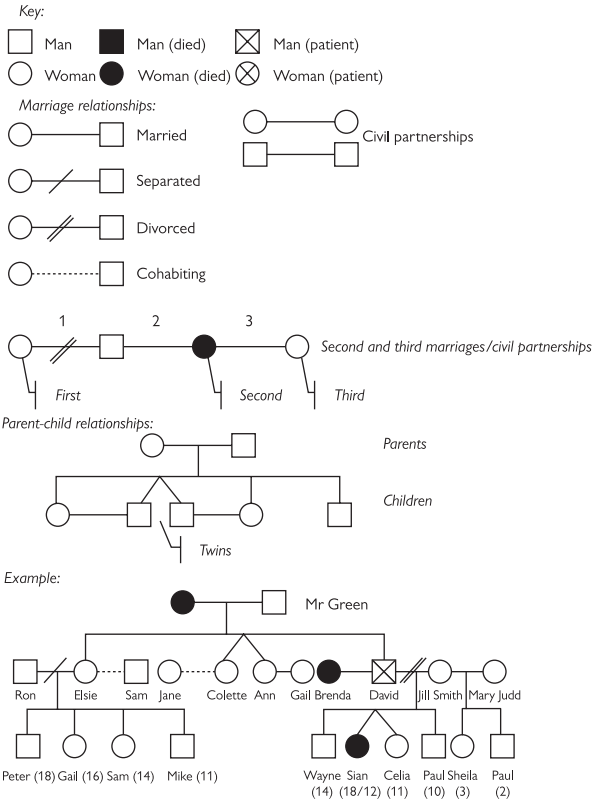


Fig 34.3 Genograms.

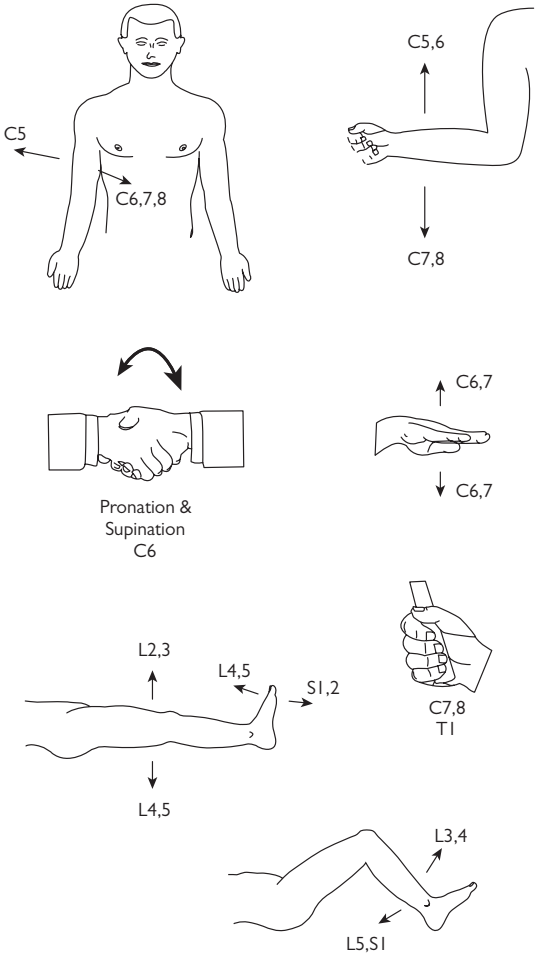


Fig 34.4 Peripheral nerve assessment.

Travelling abroad

It is not uncommon for terminally ill patients to want to travel abroad in order to see family or to die in their home country. A wish to travel by air needs to be balanced against the risk to the individual and the inconvenience and cost to fellow passengers and airlines in the event of unscheduled changes to flight plans. If there is any doubt, the airline medical officer, who will give the final authorization, should be contacted well in advance of travel.

In flight

Changes in air pressure occur during flight, and PO_2, may be reduced. For this reason, patients with marked breathlessness (who are unable to walk more than 50 metres), with Hb less than 7.5g/L, ischaemic heart disease or cardiac failure, or those who are oxygen-dependent may have difficulty.

In-flight cabin oxygen is inadequate for such patients. Extra supplies of oxygen may be made available as necessary if the airline is aware in advance.

Air expands at lower atmospheric pressures, and for this reason patients with a pneumothorax, large bullae, ear/sinus disease, or recent surgery or colonoscopy should not fly without advice. Other conditions to consider carefully are intracranial tumours and confusion.

Patients will be at risk of thromboembolism on long-haul flights, especially if they are unable to mobilize adequately; the use of support stockings or foot rocking devices may be appropriate.

Special arrangements

Transport to and from airports is arranged by the patient. If a stretcher is required, nine economy class seats are required, the cost of which is borne by the patient.

Cabin staff are not authorized to look after personal care needs, medical treatment, or specialized medical equipment. An escort for a patient who is flying will be needed if:

- a patient is relatively dependent
- a patient has a syringe driver
- a patient has surgical drains
- emergency management of symptoms may be needed
- medication might need to be given by injection
- the journey is long and interrupted by several transfers

It is important to remember that all medication or equipment that might be needed during the flight are kept as hand luggage. This includes all regular medication, including analgesics, anti-emetics, anticonvulsants, steroids, insulin, inhalers, and any medication such as glyceryl trinitrate which might be needed on an as-required basis. Syringes, needles, spare batteries, and a sharps disposal box, if appropriate, should be remembered. All controlled drugs need to be in their original packaging and carried in hand luggage.

Controlled drugs

If a patient is taking regular controlled drugs, a Home Office licence will be required if the trip is longer than 3 months. If the dosage, and therefore total quantity of drug, is high, a licence may be required for less time away.

An up-to-date letter from the prescribing doctor is required, which must be carried by the patient. The letter should contain the following information:

- the patient's name
- address
- date of birth
- outward and returning dates of travel
- the country being visited
- the drugs being carried, including dosages and total amount
- generic (not brand names) should be used

It is also advisable to contact the embassy, consulate, or high commission of the country being visited to ensure that they will not refuse entry to someone with controlled drugs.

Travel insurance

Any patient travelling abroad should be advised to obtain travel insurance in the event of them becoming unwell. Getting travel insurance when a patient has an advanced disease can be difficult, so they should be encouraged to look as early as possible. There are companies which specialize in providing cover for individuals with medical problems.

Further reading

https://www.macmillan.org.uk/information-and-support/organising/travel-and-holidays/travelling-abroad/taking-medicines-abroad.html

Tissue donation

Human organ and tissue transplantation has proven to be a successful method for treating many medical conditions. However, the demand for organs and tissues continues to exceed supply. The intensive care unit is generally considered the only clinical area where individuals can donate organs and tissue. However, individuals who die in other clinical areas can potentially donate a variety of tissues, including, occasionally, their kidneys. Although tissue donation does not enjoy the same high public profile as organ donation, it nevertheless holds many significant benefits for recipients. For example, the transplantation of new heart valves to patients with diseased or infected heart valves can be life-saving. Skin donation can be used to treat severe burns, and corneal transplantation has the ability to improve or even restore sight for those with diseased corneas, enhancing the recipient's quality of life. Tissue donation is also subject to fewer contraindications and restrictions than is associated with solid organ donation. Collection times are less urgent, varying from 24 hours after death for corneas to 48 hours for heart valves. Thus, many patients who die in environments outside intensive care have the potential to be non-heart-beating donors.

There is evidence that donation, far from increasing relatives' distress, may help in bereavement, families gaining comfort and meaning to the death. Studies have shown that relatives are generally happy to talk about donation and to feel some good has resulted from the death. Some professionals feel that there is a 'duty to ask' for tissue donation and, indeed, some families have felt cheated by not being given the opportunity to discuss the issue. The subject of tissue donation may be straightforward if it has been discussed with the patient prior to death and if a donor card is available. However, even in this situation, consent should always be sought from the next of kin.

In practice, it is easiest for corneas to be donated since this can be organized (it must be within 24h) at the location of death without the need for transfer to a hospital pathologist. The transplant coordinator will arrange for the eyes to be removed. (The eye sockets are packed and shields inserted to ensure the original appearance of the donor is restored.)

A fear in popular culture that mutilation of the body, particularly the eyes, affects the deceased's beauty, identity, or personhood, and the idea that vision is necessary for the after-life, may be some of the reasons cited for families being reluctant to agree to donation. Debate continues on presumed consent with an 'opt out' clause. There is evidence that those who consent to donation do so not out of social duty but out of altruism and generosity, from which they gain positive rewards. The subject of tissue donation remains a very individual and sensitive issue which needs careful handling in inevitably vulnerable families.

There are various practical considerations, some of which are outlined in Table 34.2.

Table 34.2 Practical considerations for tissue donation

	Cornea	Heart valves and trachea	Kidneys
Max. age of donor	Any age	60 years	70 years
Max. time from asystole to tissue removal	24h	72h	1h

Contraindications

The criteria for the acceptability of tissues for donation are inevitably becoming more stringent. There are few absolute contraindications, but certain cancers or a diagnosis of CJD or HIV would be contraindications to donation. In the UK, a donor coordinator is available 24h a day to provide very helpful advice.

Follow-up

The donor coordinator writes an acknowledgement letter to the family informing them of how the tissues have been used. Families usually find this very comforting.

Help and advice for patients

UK national resources

Macmillan Cancer Support
Macmillan Cancer Support funds Macmillan nurses—referral via GP or hospital information line. Financial help through patient grants—applications through hospital and hospice nurses, social workers, and other healthcare professionals.
Macmillan Cancer line: 0808 808 0000
http://www.macmillan.org.uk/

Marie Curie Cancer Care
Hands-on palliative nursing care, available through the local district nursing service. Also runs inpatient centres: admission by referral from GP or consultant. Both the services are free of charge.
Marie Curie support line: 0800 090 2309
http://www.mariecurie.org.uk/

Tenovus Cancer Information Centre
Information and support for patients, their families, and carers. Helpline staffed by experienced cancer-trained nurses, counsellors, and social workers. Individual counselling service; free literature.
43 The Parade, Cardiff CF24 3AB
0808 800 1010
http://www.tenovus.com/

Bereavement

Asian Family Counselling Services
Includes bereavement counselling.
020 8813 9714

Cruse Bereavement Care
Bereavement counselling
0808 808 1677
http://www.cruisebereavementcare.org.uk

Samaritans/Age Concern/Citizens Advice Bureau
From local telephone directory

The Compassionate Friends
A self-help group of parents whose son or daughter (of any age, including adults) has died from any cause.
0345 123 2304
http://www.tcf.org.uk

Carers

Carers UK
Information and support to people caring for relatives and friends. Free leaflets and information sheets.
0808 808 7777

Children

Together for short lives
0117 989 7820

Complementary therapies

British Acupuncture Council
020 8735 0400
http://www.acupuncture.org.uk

Institute for Complementary and Natural Medicine
020 7922 7980
http://www.i-c-m.org.uk

Conditions other than cancer

Alzheimer's Society
0330 333 0804
http://www.alzheimers.org.uk

British Brain and Spine Foundation
Helpline provides information and support about neurological disorders for patients, carers, and health professionals.
0808 808 1000
http://www.brainandspine.org.uk

Motor Neurone Disease Association
Professional and general enquiries:
01604 250505
Helpline: 0808 802 6262
http://www.mndassociation.org

National dementia helpline
0300 222 1122

Parkinson's Disease Society
0808 800 0303
http://www.parkinsons.org.uk

Stroke Association
0303 303 3100
http://www.stroke.org.uk

Specific cancers

Breast Cancer Care
0808 800 6000
http://www.breastcancercare.org.uk/

Lymphoma Association
0808 808 5555 (Mon–Fri 9am–6pm)
http://www.lymphoma.org.uk/

Oesophageal Patients Association
0121 704 9860
http://www.opa.org.uk

Ovacome
A support organization for women with ovarian cancer.
0800 008 7054 or 020 7299 6654 (Mon–Fri 9am–4pm)
http://www.ovacome.org.uk/ovacome

Prostate Cancer Charity
0800 074 8383 (Mon–Fri 10am–4pm)
http://www.prostate-cancer.org.uk/

Prostate Cancer Support Association (PSA)
0800 035 5302
http://www.prostatecancersupport.co.uk

The Roy Castle Lung Cancer Foundation
0333 323 7200
http://www.roycastle.org/

Specific health problems

Changing Faces
Offers information, social skills training, and counselling for people with facial disfigurements.
0300 012 0275
http://www.changingfaces.org.uk/

Colostomy Association
0118 939 1537
Freephone: 0800 32842 57/0800 587 6744
http://www.colostomyassociation.org.uk

Let's Face It: Support Network for the Facially Disfigured
A contact point for people of any age coping with facial disfigurement.
0777 583 2597
http://www.lets-face-it.co.uk

Lymphoedema Support Network
020 7351 4480
http://www.lymphoedema.org/

National Association of Laryngectomee Clubs
020 7730 8585
http://www.laryngectomy.org.uk

Sexual Advice Association
http://www.sexualadviceassociation.co.uk/

Urostomy Association
01889 563 191
http://www.uagbi.org

Specific patient groups

Chai Lifeline
Emotional, physical, practical, and spiritual support to Jewish children, their families, and friends.
020 8731 6788
http://www.chailifeline.org

LGBT cancer support
http://www.lgbtcancer.org.uk

National LGBT Cancer Network
https://cancer-network.org

National Network for Palliative Care of People with Learning Disability
0207 387 3976

Laboratory reference values

These are guides only—different labs use different ranges. Pregnant women and children also have different normal ranges—consult the lab.

Haematology

Measurement	*Reference interval*
White cell count (WCC)	$4.0–11.0\times10^9$/l
Red cell count (RCC)	Men: $4.5–6.5\times10^{12}$/l Women: $3.9–5.6\times10^{12}$/l
Haemoglobin	Men: 13.5–18g/dl Women: 11.5–16.0g/dl
Packed cell volume (PCV) or haematocrit	Men: 38.5–50.1% Women: 36.0–44.5%
Mean cell volume (MCV)	76–97fl
Mean cell haemoglobin (MCHC)	32.7–34.6 g/dl
Neutrophils	$2.0–7.5\times10^9$/l *40–75% WCC*
Lymphocytes	$1.3–3.5\times10^9$/l *20–45% WCC*
Eosinophils	$0.04–0.44\times10^9$/l *1–6% WCC*
Basophils	$0.0–0.1\times10^9$/l *0–1% WCC*
Monocytes	$0.2–0.8\times10^9$/l *2–10% WCC*
Platelet count	$150–400\times10^9$/l
Reticulocyte count	$25–100\times10^9$/l *0.8–2% RCC**
Erythrocyte sedimentation rate (ESR)	Depends on age
International normalized ratio (INR)	0.8–1.2 Ranges for warfarin therapy depend on indication
Prothrombin time (PTT)	12–17 sec
Factors I, II, VII, X	
Activated partial thromboplastin time	28–40 sec
Factor VIII, IX, XI, XII	
Red cell folate	180–300 ng/mL

* Only use percentages as reference interval if red cell count is normal. Otherwise use absolute value.

Biochemistry		
Substance	P	Reference interval
Adrenocorticotrophic hormone	P	<80ng/L
Alanine aminotransferase (ALT)	P	5–35iu/L
Albumin	P	35–50g/L

Measurement		*Reference interval*
Alkaline transaminase (AST)	P	30–150u/L
α-amylase	P	0–180u/dl
Aspartate transaminase (AST)	P	5–35iu/L
Bicarbonate	P	24–30mmol/L
Bilirubin	P	3–17μmol/L
Calcium (total)	P	2.12–2.26mmol/L
Creatine kinase (CK)	P	Men: 25–195iu/L Women: 25–172iu/L
Creatinine	P	70–≤150μmol/L
Ferritin	P	12–200μg/L
Folate	P	2.1μg/L
Follicle stimulating hormone (FSH)	P/S	2–8u/L>25u/L post menopause
Gamma-glutamyl transpeptidase (GGT, γGT)	P	Men: 11–51iu/L Women: 7–33iu/L
Glucose (fasting)	P	3.5–5.5mmol/L
Iron	S	Men: 14–31μmol/L Women: 11–30μmol/L
Luteinizing hormone (LH)	P	3–16u/L
Osmolality	P	278–305mosmol/kg
Phosphate (inorganic)	P	0.8–1.45mmol/L
Potassium	P	3.5–5.0mmol/L
Prolactin	P	Men: <450u/L Women: <600u/L
Prostate specific antigen (PSA)	P	0–4ngrams/mL
Protein (total)	P	60–80g/L
Sodium	P	135–145mmol/L
Thyroxine (T_4)	P	70–140nmol/L
Total iron binding capacity	S	54–75μmol/L
Triglyceride	P	0.55–1.90mmol/L
Urate	P	Men: 210–480μmol/L Women: 150–390μmol/L
Urea	P	2.5–6.7mmol/L
Vitamin B_{12}	S	0.13–0.68nmol/L (>150ng/L)

P = plasma (e.g. heparin bottle); S = serum (clotted—no anticoagulant)

Lab reference values. Reproduced from Longmore M et al. (2007) The Oxford Handbook of Clinical Medicine, 7th edn. Oxford University Press. with permission

Further reading

Book

Sque M., Payne S. (eds) (2007) *Organ and Tissue Donation: An Evidence Base for Practice*. Maidenhead: Open University Press.

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