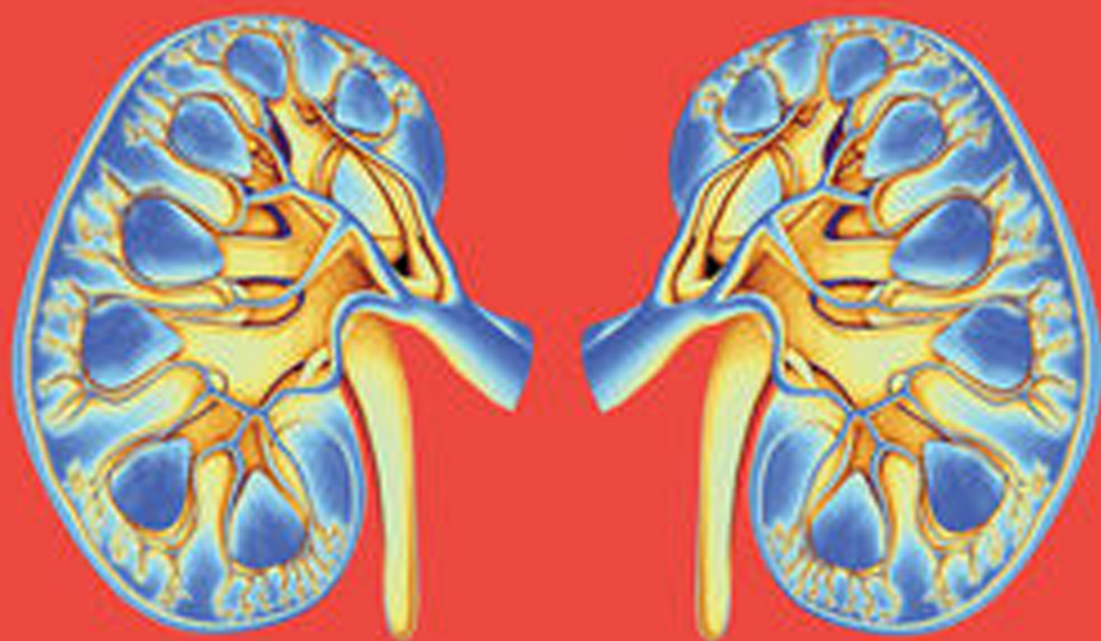


FIFTH EDITION

RENAL NURSING

CARE AND MANAGEMENT OF
PEOPLE WITH KIDNEY DISEASE



EDITED BY
NICOLA THOMAS

WILEY Blackwell

Renal Nursing

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*Care and Management of People
with Kidney Disease*

Fifth Edition

Edited by

Nicola Thomas

London South Bank University
London, UK

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This edition first published 2019 © 2019 by John Wiley & Sons Ltd
Edition History [4e, 2014]

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9600 Garsington Road, Oxford, OX4 2DQ, UK

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Library of Congress Cataloging-in-Publication Data

Names: Thomas, Nicola, editor.

Title: Renal nursing : care and management of people with kidney disease /
edited by Nicola Thomas.

Description: Fifth edition. | Hoboken, NJ : Wiley-Blackwell, 2019. | Includes
bibliographical references and index. |

Identifiers: LCCN 2018060334 (print) | LCCN 2018061627 (ebook) |
ISBN 9781119413165 (Adobe PDF) | ISBN 9781119413158 (ePub) |
ISBN 9781119413141 (pbk.)

Subjects: | MESH: Kidney Diseases--nursing | Nephrology Nursing

Classification: LCC RC918.R4 (ebook) | LCC RC918.R4 (print) | NLM WY 164 |
DDC 616.6/140231--dc23

LC record available at <https://lcn.loc.gov/2018060334>

Cover Design: Wiley

Cover Image: © ALFRED PASIEKA/SCIENCE PHOTO LIBRARY/Getty Images

Set in 9.5/11.5pt Sabon by SPi Global, Pondicherry, India

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Foreword

Kidney disease is common, harmful, often treatable and preventable. Although much progress has been made in identifying chronic kidney disease earlier and delaying the need for dialysis and transplantation, the number of people affected by kidney disease continues to grow each year. Chronic Kidney Disease is a global health burden and has become a major public health issue.

Over 2 million people worldwide currently receive treatment with dialysis or a kidney transplant to stay alive, yet this number may only represent 10% of people who actually need the treatment to live. Acute Kidney Injury accounts for 8–16% of hospital admissions, with >1% of health service expenditure being attributed to AKI in the UK. The International Society of Nephrology has an ambitious aim to prevent all avoidable death from AKI worldwide by 2025. Nurses play a key role in the early recognition and treatment of AKI and renal nurses are no exception and have a crucial role in adding quality to care.

People with Chronic Kidney Disease have a wide range of physical and emotional needs. These include encouragement to achieve behavioural change goals they have set themselves, support with decision making, education about their condition, traditional basic care needs individually delivered with compassion and an understanding of the complexity of kidney disease along with other comorbidities. The skills and competencies required to address these needs are the foundation of high-quality care delivered by both registered and non-registered nurses. Caring for people with kidney disease is a ‘hands-on’ job requiring an understanding of psychology – the person, the carers and the families and your own; knowledge of the biology and pathophysiology of the kidney; expertise in the nursing of the acutely unwell and the management of complex long-term conditions; as well as emotional resilience.

Renal nurses recognise the patients they care for have a common disease, but each individual’s experience is unique, requiring support and encouragement appropriate to his/her age, cultural background and degree of health literacy. As such, nurses specialising in kidney care are pivotal to the multi-professional team. Not only do they bring their understanding of kidney disease and experience of managing others in a similar situation, they are also the advocate for holistic care, and act as a catalyst for shared decision-making. To achieve such high standard of care the appropriate education and training is needed to develop this vast knowledge base and practical skills.

Nurses’ access specialist knowledge in a variety of formats be it e-learning, text books such as this or even social media. Since the dissolution of national renal courses there is a lack of educational standardisation for renal nursing, something which the newly formed Association of Renal Nurses UK (ANN-UK) is keen to address. By bringing the renal nursing community together under one national organisation we have the opportunity to create an educational framework for all nurses working in kidney care. The future will include access to a national curriculum via e-learning.

As part of the educational framework, this 5th edition of *Renal Nursing* will provide you with the information you need to understand the fundamentals of kidney care. Use this textbook in conjunction with gaining practical hands-on experience in dialysis units, inpatient wards, outpatient settings and home therapies and you will have the knowledge and skills to make a vast difference to many people with kidney disease.

Karen Jenkins

President of the Association of Nephrology Nurses, UK

Preface

I have very much enjoyed editing the fifth edition of this successful book for nurses and allied health care professionals working in nephrology, dialysis and transplantation, along with colleagues who are all experts. The past five years have again seen tremendous changes in renal care in the UK, particularly in the area of patient and public involvement. The *Kidney Patient Involvement Network* (KPIN), launched in 2018, is a network of kidney organisations, charities and individuals committed to quality patient, public involvement and engagement (PPIE), who are willing to work collaboratively on initiatives to improve standards in PPIE and develop patient leaders of the future. It is so important that people with experience of kidney disease contribute to renal nursing education, both in the classroom and also in writing. Chapter Three of this textbook was very warmly received last time as it is provided a patient and carer perspective on care, and encouraged us to think in the 'patient's shoes'.

This book is mostly for those who are new to the renal specialty. Nurses who are studying on preregistration courses and practitioners who are commencing a post-registration course in renal nursing will find it particularly helpful. It also serves as a good foundation for nurses who wish to refresh their knowledge in a part of the renal field in which they are currently not practising, or for other members of the multi-professional team who are commencing a career in nephrology. This new edition is again written in a style that promotes kidney care for what it is: a dynamic, varied and rewarding specialty.

Each chapter has been written by an expert in his or her field. Recognition must go to those authors who wrote chapters for the previous edition but were unable to contribute to this edition. They are Annette Davies, Paul Challinor, Claire Main and Fliss Murtagh.

Renal nurses in the 21st century face a constant challenge to keep abreast of developments in care and management. What does not change is the constant physical and psychosocial challenges that patients and their families have to face. This must always be in our minds. In my thirty-five years of practice as a renal nurse the repeated request from patients is that we should emphasise what *can* be done rather than what cannot. The word 'restriction' should not be part of a renal nurse's vocabulary: why not fluid or dietary *allowance*? As in the fourth edition, I have endeavoured to use a language in this book which puts patients at the centre of care.

I am delighted that the Association of Nephrology Nurses, UK (ANN-UK), launched in 2018, might reintroduce a framework for renal nursing education in the near future. I hope that this latest edition will complement that vision and will continue to encourage renal nurses to care for their patients with compassion, sensitivity and understanding.

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CHAPTER 1

The History of Dialysis and Transplantation

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Learning Outcomes

- to understand the evolution of haemodialysis (HD), peritoneal dialysis (PD), and transplantation.
- to appreciate the challenges that healthcare professionals have had to overcome in the development of the nephrology specialty.
- to evaluate the changing focus of renal care in the twenty-first century.
- to identify the opportunities for nephrology nursing in the future.

Introduction

The introduction of dialysis as a life-saving treatment for kidney failure was not the result of any large-scale research programme; rather, it emerged from the activities of a few pioneering individuals who were able to use ideas, materials, and methods from a range of developing technologies.

Haemodialysis, as a routine treatment for renal failure, was initiated in the 1960s, followed by continuous ambulatory peritoneal dialysis (CAPD) in the late 1970s. The recognition of the need for immunosuppression in transplantation in the 1960s enabled it to become the preferred treatment for many patients.

Haemodialysis

The beginning

It was the Romans who first used a form of dialysis therapy by giving hot baths to patients to remove urea. The action of the hot water made the patient sweat profusely and this, together with the toxins diffusing through the skin into the bath water, would temporarily relieve symptoms. However, the Romans did not understand

why the treatment worked. The effect was to leave the patient fatigued but, as the only hope, this treatment was still used on occasion into the 1950s.

The first time that the term 'dialysis' was used was in 1854, by Thomas Graham, a Scottish chemist (Graham 1854). He used dialysis to describe the transport of solutes through an ox bladder, and this was the catalyst for other researchers working in a similar field to focus on the membrane.

Membranes were made from a variety of substances, including parchment and collodion (Eggerth 1921). Collodion is a syrupy liquid that dries to form a porous film, and allows the passage of small-molecular-weight substances, whilst being impermeable to substances with a molecular weight greater than 5 kDa. In 1889, B.W. Richardson referred to the use of collodion membranes in the dialysis of blood. So, by this method, living animals were dialysed in experimental conditions (Richardson 1889), but the limiting factor that prevented the treatment being used in humans at this time was the lack of suitable materials.

Pre-1920

It was not until 1913 that the first article on the technique of HD, named the 'artificial kidney', was reported. Experimental dialysis was performed on animals by using variances in the composition of dialysis fluid (Abel et al. 1914). Substances could be added to the solution to avoid their net removal. The main aim of the experiments was the removal of salicylates. The removal of fluid and toxins accumulated due to kidney disease was not, at this time, considered.

In 1914, Hess and McGuigan were experimenting with dialysis in a pharmacology laboratory in Chicago. As a result they were able to transfer sugar from tissue to blood and from the blood across a collodion membrane. The design of the dialyser minimised the length of tubing from the patient, and a high blood flow was achieved by connection to the carotid artery in an effort to minimise the necessity to use an anticoagulant. A single U-shaped collodion tube was inserted into a glass cylinder with a rubber stopper at one end. The blood flow both to and from the dialyser was at one end, with a port for adjusting the pressure inside the tube. These experiments were still only performed on animals. The only anticoagulant available was in the form of an extract obtained from crushed leech heads, called hirudin. This was far from satisfactory, even though leeches were plentiful and readily available from the corner shop for around \$25 per 1000.

The 1920s

The first dialysis performed on a human was carried out by the German physician, Georg Haas, in Giessen in the latter half of the 1920s. He performed six treatments in six patients. Handmade collodion membranes were used, and clotting was prevented by using hirudin and, later, a crude form of heparin. Haas used multiple dialysers to increase the surface area of blood exposed to the dialysis fluid. This necessitated as many as six dialysers arranged in parallel and he found that the arterial pressure of the blood was insufficient to propel the blood through the entire extracorporeal circuit. He therefore introduced a pump into the circuit. Haas was aware of the lack of support given to him by the hospital and his colleagues, and by the late 1920s he gave up and the work was stopped. Georg Haas died in 1971, aged 85 years, and was honoured as the pioneer of dialysis.

Despite these treatments, carried out from the 1920s to the 1940s, those with uraemia suffering from poor appetite and vomiting could be offered nothing more than bed rest and a bland salt-free diet composed mainly of vegetables, carbohydrate, and fat to reduce protein metabolism. Dialysis was not considered a realistic option and the conservative therapy was only offered as a palliative measure.

Heinrich Necheles was the founder of the contemporary dialyser. In 1923, he experimented with the sandwiching of membranes, thus giving an increased surface area without the necessity for multiple dialysers. The membrane used was the peritoneum of a sheep. As the membrane was prone to expansion, support sheets were placed between the layers of membrane, thus allowing a large surface area of membrane to come into contact with the dialysis fluid. Other features introduced by Necheles were a heater, the priming of the pathway for the blood, and a filter to prevent clots returning to the patient.

The 1930s

The 1920s and 1930s saw great advances in synthetic polymer chemistry, resulting in the availability of cellulose acetate, which could be used as a membrane for HD. It was in 1937 that the first synthetic membrane was used by the American scientist William Thalhimer. The material, cellophane – a form of cellulose acetate, which was used extensively in the sausage industry – had potential that was not recognised for some years. In the mid-1930s came the purification of heparin (Thalhimer et al. 1938), which could be used as an anticoagulant. Together, these two advances gave rise to the next stage of development, which took place in 1943 in occupied Holland.

The 1940s and 1950s

Willem Kolff, a physician working in Groningen in Nazi-occupied Holland, had his attention drawn to the work of a colleague who was concentrating plasma by using cellulose acetate as a membrane and immersing it in a weak solution of sugar. Kolff noticed that toxins in the blood were altered by this method (Kolff 1950). He built a rotating drum dialyser, which provided sufficient surface area for his first attempt at human dialysis (Kolff and Berk 1944). His machine consisted of 30m of cellophane tube that was wound round a large cylinder. The cylinder was placed in a tank containing a weak solution of salts – the dialysate. The patient's blood was passed through the cellophane tube, the walls acting as a semipermeable membrane. Blood flow was achieved by the addition of a circuit containing a burette, which, when filled with blood, could be raised high enough to allow the blood to flow into the dialyser. The burette was then lowered, allowing the blood to drain back, and raised again to allow the blood to return to the patient. The slats in the construction of the cylinder were of wood due to the shortage at this time of materials such as aluminium – in retrospect, this was fortunate because the toxicity of aluminium is now appreciated. Six hours were required for the treatment, and it is interesting to note that, with this method, the efficiency of dialysis that could be achieved was similar to that which is possible with the dialysers in use today: a clearance of 170 ml min^{-1} urea could be achieved. Fluid could only be removed by increasing the osmotic pressure of the dialysate fluid by the addition of sugar, as an increase in pressure on the membrane would result in rupture (Kolff 1965).

The whole procedure was very time consuming and labour intensive, as the process required attention at all times to raise and lower the burette and observe the membrane for rupture, which happened frequently. Repairs to the membrane were carried out by inserting a glass tube at the point of rupture.

Kolff's first clinical experience was gained with a 29-year-old woman with chronic nephritis. The blood urea was kept stable for 26 days, but after 12 sessions of dialysis, her blood urea began to increase, and she subsequently died.

After the war, in 1945, Kolff's technique was widely used, particularly in Sweden and the United States. The treatment was initially for acute kidney injury, when

kidney function could be expected to return to normal following a short period of dialysis treatment. It was widely used in the Korean war in 1952 to treat trauma-induced renal failure. The group, led by Paul Teschan, trained to use the rotating drum dialyser and saved many lives by lowering the high potassium levels of the victims (Teschan 1955).

Some of the earliest research carried out on fluid removal from the blood using negative pressure was conducted by M.R. Malinow and W. Korzon at Michael Reese Hospital in Chicago in 1946 (Malinow and Korzon 1947). The device used was the earliest version of a dialyser with multiple blood paths and negative pressure capacity. It had parallel sections of cellulose acetate tubing and, by adding layers of tubing, the surface area of the device could be increased. The diffusion properties of this device were not considered, as it was intended only for removal of water from the blood. The device required a low priming volume and the circuit included a blood pump.

In the 1940s, interest in dialysis as a treatment for renal failure had spread throughout Europe and across to Canada as the need was becoming widely recognised by the medical profession. After obtaining drawings of the Kolff dialyser, Russell Palmer and a colleague from Vancouver, in Canada, built a replica and dialysed their first patients in September 1947 (Palmer and Rutherford 1949).

Kolff was invited to take his artificial kidney to New York where he trained physicians in the operation of the life-saving device. There was resistance from hospital staff at Mount Sinai Hospital, who only permitted the treatment to be administered in the surgical suite after normal surgical schedules were completed for the day. The first patient scheduled for treatment was a victim of mercuric chloride poisoning, but treatment was cancelled when a spontaneous diuresis occurred.

The first successful dialysis in Mount Sinai Hospital was in January 1948, in a female admitted to hospital having inserted mercury tablets into her vagina to induce an abortion (Fishman et al. 1948). Eight hours after the first dialysis using the Kolff machine, the patient passed urine. The treatment had been a success. Victims of drug overdose were then regularly treated by use of the rotating drum dialyser until 1950.

To expand the use, the rotating drum would have to be modified to become easier to use. Kolff enlisted the help of Dr. Carl Walter, who worked at the Peter Brent Brigham Hospital. Together with Edward Olson, an associate engineer from Fenwal, they set about designing and building a new version of the Kolff device. Stainless steel was used for the drum, and refinements included a hose for filling the pan with the 100l of dialysate fluid, which was heated, and a hood to cover the drum. A tensioning device was used on the cellophane membrane as it had a tendency to stretch during use. The split connection for the patient's tubing was introduced, and this allowed the patient's tubing to remain stationary whilst the drum rotated. This was made leakproof, and a Lucite hood was added to overcome heat loss from the extracorporeal blood (Figure 1.1). These improvements paved the way for wider acceptance of the use of dialysis treatment (Merrill et al. 1950).

When the Kolff–Brigham kidney was used, the heparin dose ranged from 6000 to 9000 units, and was infused prior to the start of the treatment. The dialyser was primed with blood, and the blood flow to the dialyser was limited to 200 ml at a time to prevent hypotension. To assist blood flow a pump was inserted in the venous circuit rather than the arterial side, to minimise the probability of pressure buildup in the membrane, which would cause a rupture.

This version of the Kolff–Brigham dialysis machine was used in 1948, and in all, over 40 machines were built and exported all over the world. Orders for spare parts were still being received as late as 1974, from South America and behind the Iron Curtain.



Figure 1.1 Artificial kidney machine (Kolff–Brigham), France, 1955. Source: With kind permission from Science and Society Picture Library.

The 1950s

The Allis-Chalmers Corporation was one of the first companies to produce dialysis machines commercially. They were prompted into manufacture when an employee developed renal failure. There was no machine available and so the firm turned its attention to producing a version of the Kolff rotating drum. The resulting machine was commercially available for \$5600 and included all the sophistication available at the time. Allis-Chalmers produced 14 of these machines and sold them all over the United States into the early 1950s.

In October 1956, the Kolff system became commercially available, so the unavailability of equipment could no longer be used as an excuse for nontreatment of patients. Centres purchased the complete delivery system for around \$1200 and the disposables necessary for the treatment were around \$60. The system was still mainly used for reversible acute renal failure drug overdose and poisoning.

The development of the dialyser

Jack Leonards and Leonard Skeggs produced a plate dialyser, which would permit a reduction in the priming volume and allow negative pressure to be used to remove fluid from the patient's system (Skeggs et al. 1949). A modification to this design included a manifold system, which allowed variation of the surface area without altering the blood distribution. Larger dialysers followed, which necessitated the introduction of a blood pump.

In the late 1950s Fredrik Kiil of Norway developed a parallel plate dialyser, with a large surface area (1 m^2), requiring a lower priming volume. A new cellulose membrane, Cuprophane, was used, and this allowed the passage of larger molecules than other materials that were available at that time. The Kiil dialyser could be used without a pump. Kiil dialysed the patients using their own arterial pressure. This dialyser was widely used because the disposables were relatively inexpensive when compared with other dialysers available at that time.

A crude version of the capillary-flow dialyser, the parallel dialyser, was developed, using a new blood pump, with a more advanced version of the Alwall kidney (MacNeill 1949). However, it was John Guarino who incorporated the important feature of a closed system, a visible blood pathway.

To reduce the size of the dialyser without reducing the surface area, William Y. Inouye and Joseph Engelberg produced a plastic mesh sleeve to protect the membrane. This reduced the risk of the dialysis fluid coming into contact with the blood. This was a closed system, so the effluent could be measured to determine the fluid loss of the patient. It is the true predecessor of the positive- and negative-pressure dialysers used today.

The first commercially available dialyser was manufactured by Baxter and based on the Kolff kidney. It provided a urea clearance of approximately 140 ml min^{-1} , equivalent to today's models, and was based on the coil design. The priming volume was 1200–1800 ml and this was drained into a container at the end of treatment, refrigerated, and used for priming for the next treatment. It was commercially available in 1956 for \$59.00.

The forerunner of today's capillary-flow dialyser was produced by Richard Stewart in 1960. The criteria for design of this hollow-fibre dialyser were low priming volume and minimal resistance to flow. The improved design contained 11 000 fibres which provided a surface area of 1 m^2 .

Future designs for the dialyser focused on refining the solute and water removal capabilities, as well as reducing the size and priming requirements of the device, thus allowing an even higher level of precise individual care.

The emergence of home haemodialysis

It was Scribner's shunt which provided vascular access, at the start, leading to the first dialysis unit to be established for patients at the University of Washington Hospital. Belding Scribner also developed a central dialysate delivery system for multiple use and set this up in the chronic care centre, which had 12 beds. These beds were quickly taken and his plan for expansion was rejected. The only alternative was to send the patients home, and so the patient and family were trained to perform the dialysis and care for the shunts. Home dialysis was strongly promoted by Scribner.

Stanley Shaldon reported in 1961 that a patient dialysing at the Royal Free Hospital in London was able to self-care by setting up his own machine, initiating, and terminating dialysis (Figure 1.2); so home HD in the UK was made possible. The shunt was formed in the leg for vascular access, to allow the patient to have both hands free for the procedures. Hence Shaldon was able to report the results of his first patient to be placed on overnight home HD in November 1964. With careful patient selection, the venture was a success. Scribner started to train patients for home at this time, and his first patient was a teenager assisted by her mother. Home dialysis was selected for this patient, so that she would not miss her high-school education. The average time on dialysis was 14 hours twice weekly. To allow freedom for the patient, overnight dialysis was widely practised. At first, emphasis was on selection of the suitable patient and family, even to the extent of a stable family relationship, before the patient could be considered for home training (Baillod et al. 1965).

From these beginnings, large home HD programmes developed in the United States and the United Kingdom, thus allowing expansion of the dialysis population without increasing hospital facilities. Many patients could now be considered for home treatment, often with surprisingly good results, as the dialysis could be moulded to the requirements of the individual, rather than the patients conforming



Figure 1.2 Patient and nurse with dialysis machine and Kiil dialyser, 1968. Source: With kind permission from Science and Society Picture Library.

to a set pattern. However, with the development in the late 1970s and early 1980s of CAPD as the first choice for home treatment, the use of home HD steadily dwindled. It is now however seeing renewed interest. The National Institute for Clinical Excellence (NICE) published guidance on home versus hospital HD (NICE 2002) and recommended all suitable patients should be offered the choice between home HD or HD in a hospital/satellite unit.

Vascular access for haemodialysis

It was Sir Christopher Wren, of architectural fame, who in 1657 successfully introduced drugs into the vascular system of a dog. In 1663, Sir Robert Boyle injected successfully into humans. Prison inmates were the subjects and the cannula used was fashioned from a quill. For HD to become a widely accepted form of treatment for renal failure, a way to provide long-term access to the patient's vascular system had to be found and until this problem was solved, long-term treatment could not be considered. In order for good access to be established, a tube or cannula had to be inserted into an artery or vein, thus giving rise to good blood flow from the patient. The repeated access for each treatment quickly led to exhaustion of blood vessels for cannulation. The need for a system whereby a sufficiently large blood flow could be established for dialysis, without destroying a length of blood vessel every time dialysis was required, was imperative.

In the 1950s, Teschan, in the 11th Evacuation Hospital in Korea, was responsible for developing a method of heparin lock for continuous access to blood vessels. The cannulae were made from Tygon tubing and stopcocks, and the blood was

prevented from clotting by irrigation with heparinised saline. It was not a loop design, as the arterial and venous segments were not joined together.

In 1960, in the United States, George Quinton, an engineer, and Belding Scribner, a physician, made use of two new synthetic polymers – Teflon and Silastic – and, using the tubing to form the connection between a vein and an artery, were able to reroute the blood outside the body (usually in the leg). This was known as the arteriovenous (AV) shunt. The tubing was disconnected at a union joint in the centre, and each tube then connected to the lines of the dialysis machine. At the end of treatment, the two ends were then reconnected, establishing a blood flow from the artery to the vein outside the body. In this way, repeat dialysis was made possible without further trauma to the vascular system.

This external shunt, whilst successful, had drawbacks. It was a potential source of infection, often thrombosed, and had a restrictive effect on the activity of the patient. This form of access is still occasionally used for acute treatment, although the patient's potential requirements for chronic treatment must be considered when the choice of vessels is made, so that vessels to be used in the formation of an AV fistula are not scarred. In 1966, Michael Brescia and James Cimino developed the subcutaneous radial artery-to-cephalic vein AV fistula (Cimino and Brescia 1962), with Cimino's colleague, Kenneth Appel, performing the surgery.

The AV fistula required less anticoagulation, had reduced infection risk, and gave access to the bloodstream without danger of shunt disconnection. Subsequently, a number of synthetic materials have been introduced to create internal AV fistulae (grafts). These are useful when the patient's veins are not suitable to form a conventional AV fistula, such as in severe obesity, with loss of superficial veins due to repeated cannulation or in the elderly or those with diabetes.

Venous access by cannulation of the jugular or femoral veins has now replaced the shunt for emergency dialysis.

Further developments

Monitoring and total control of the patient's therapy became more important as dialysis became widespread, and so equipment development has continued. Sophisticated machines incorporated temperature monitoring, positive-pressure gauges, and flow meters. Negative-pressure monitoring followed, as did a wide range of dialysers with varying surface areas, ultrafiltration capabilities, and clearance values. Automatic mixing and delivery of the dialysate and water supply to the machine greatly increased the margin of safety for the procedure, and made the dialysis therapy much easier to manage. The patient system that has evolved provides a machine that monitors all parameters of dialysis through the use of microprocessors, allowing the practitioner to programme a patient's requirements (factors such as blood flow, duration of dialysis, and fluid removal) so that the resulting treatment is a prescription for the individual's needs. Average dialysis time has been reduced to four hours, three times weekly, or less if a high-flux (high-performance) dialyser is used.

The early 1970s saw the overall number of patients on renal replacement therapy (RRT) increase due to the increased awareness brought about by the availability of treatment. Free-standing units for the sole use of kidney dialysis came into being, leading to dialysis becoming a full-time business. Committees for patient selection were disbanded, and the problems concerned with inadequate financial resources came to the fore. Standards for treatment quality have now been set. Attempts continue to reduce treatment duration, to enhance the patient's quality of life. Good nutrition has also emerged as playing a vital role in reducing dialysis morbidity and mortality. Dialysis facilities are demanded within easy reach of

patients' homes, and this expectation has led to the emergence of small satellite units, managed and monitored by larger units, as a popular alternative to home HD treatment.

Peritoneal Dialysis

Peritoneal dialysis (PD) as a form of therapy for kidney disease has been brought about as a result of the innovative efforts and the tenacity of many pioneers over the past two centuries. It was probably the early Egyptian morticians who first recognised the peritoneum and peritoneal cavity as they embalmed the remains of their influential compatriots for eternity. The peritoneal cavity was described in 3000 BC in the Ebers papyrus as a cavity in which the viscera were somehow suspended. In Ancient Greek times, Galen, a physician, made detailed observations of the abdomen whilst treating the injuries of gladiators.

The earliest reference to what may be interpreted as PD was in the 1740s when Christopher Warrick reported to the Royal Society in London that a 50-year-old woman suffering from ascites was treated by infusing Bristol water and claret wine into the abdomen through a leather pipe (Warrick 1744). The patient reacted violently to the procedure, and it was stopped after three treatments. The patient is reported to have recovered, and was able to walk 7 miles (approximately 13 km) a day without difficulty. A modification of this was subsequently tried by Stephen Hale of Teddington in England: two trocars were used – one on each side of the abdomen – allowing the fluid to flow in and out of the peritoneal cavity during an operation to remove ascites (Hale 1744).

Subsequent experiments on the peritoneum (Wegner 1877) determined the rate of absorption of various solutions, the capacity for fluid removal (Starling and Tubby 1894) and evidence that protein could pass through the peritoneum. It was also noted that the fluid in the peritoneal cavity contained the same amount of urea that is found in the blood, indicating that urea could be removed by PD (Rosenberg 1916). This was followed by Tracy Putnam suggesting that the peritoneum might be used to correct physiological problems, when he observed that under certain circumstances fluids in the peritoneal cavity can equilibrate with the plasma and that the rate of diffusion was dependent on the size of the molecules. Research also suggested at this time that the clearance of solutes was proportional to their molecular size and solution pH, and that a high flow rate maximised the transfer of solutes, which also depended on peritoneal surface area and blood flow (Putnam 1923).

George Ganter was looking for a method of dialysis that did not require the use of an anticoagulant (Ganter 1923). He prepared a dialysate solution containing normal values of electrolytes and added dextrose for fluid removal. Bottles were boiled for sterilisation and filled with the solution, which was then infused into the patient's abdomen through a hollow needle.

The first treatment was carried out on a woman who was suffering acute kidney injury following childbirth. Between 1 and 3 l of fluid were infused at a time, and the dwell time was 30 minutes to 3 hours. The blood chemistry was reduced to within acceptable limits. The patient was sent home, but unfortunately she died, as it was not realised that it was necessary to continue the treatment in order to keep the patient alive.

Ganter recognised the importance of good access to the peritoneum, as it was noted that it was easier to instil the fluid than it was to attain a good return volume. He was also aware of the complication of infection, and indeed it was the most

frequent complication that he encountered. Ganter identified four principles, which are still regarded as important today:

- there must be adequate access to the peritoneum.
- sterile solutions are needed to reduce infection.
- glucose content of the dialysate must be altered to remove greater volumes of fluid.
- dwell times and fluid volume infused must be varied to determine the efficiency of the dialysis.

There are reports of 101 patients treated with PD in the 1920s (Abbott and Shea 1946; Odel et al. 1950). Of these, 63 had reversible causes, 32 irreversible, and in 2 the diagnosis was unknown. There was recovery in 32 of 63 cases of reversible renal failure. Deaths were due to uraemia, pulmonary oedema, and peritonitis.

Stephen Rosenak, working in Europe, developed a metal catheter for peritoneal access, but was discouraged by the results because of the high incidence of peritonitis. In Holland, P.S.M. Kop, who was an associate of Kolff during the mid-1940s, created a system of PD by using materials for the components that could easily be sterilised: porcelain containers for the fluid, latex rubber for the tubing, and a glass catheter to infuse the fluid into the patient's abdomen. Kop treated 21 patients and met with success in 10.

Morton Maxwell, in Los Angeles in the latter part of the 1950s, had been involved with HD, and it was his opinion that HD was too complicated for regular use. Aware of the problems with infection, he designed a system for PD with as few connections as possible. Together with a local manufacturer, he formulated a peritoneal solution, and customised a container and plastic tubing set and a single polyethylene catheter. The procedure was to instil 2 l of fluid into the peritoneum, leave it to dwell for 30 minutes, and return the fluid into the original bottles. This would be repeated until the blood chemistry was normal. This technique was carried out successfully on many patients and the highly regarded results were published in 1959. This became known as the Maxwell technique (Maxwell et al. 1959). This simple form of dialysis recognised that it was no longer necessary to have expensive equipment with highly specialised staff in a large hospital to initiate dialysis. All that was required was an understanding of the procedure and available supplies.

The catheter

Up to the 1970s, PD was used primarily for patients who were not good candidates for HD, or who were seeking a gentler form of treatment. Continuous flow using two catheters (Legrain and Merrill 1953) was still sometimes used, but the single-catheter technique was favoured because of lower infection rates.

The polyethylene catheter was chosen by Paul Doolan (Doolan et al. 1959) at the Naval Hospital in San Francisco when he developed a procedure for the treatment to use under battlefield conditions in the Korean War. Because of the flexibility of the catheter, it was considered for long-term treatment. A young physician called Richard Ruben decided to try this procedure, known as the Doolan technique (Ruben et al. unpublished work), on a female patient who improved dramatically, but deteriorated after a few days without treatment. The patient was therefore dialysed repeatedly at weekends, and allowed home during the week, with the catheter remaining in place. This was the first reported chronic treatment using a permanent indwelling catheter.

Catheters were made from tubing available on the hospital ward and included gallbladder trocars, rubber catheters, whistle-tip catheters, and stainless-steel sump drains. However, as with the polyethylene plastic tubes, the main trouble was kinking

and blockage. Maxwell described a nylon catheter with perforations at the curved distal end, and this was the catheter which became commercially available. Advances in the manufacture of the silicone peritoneal catheter by Palmer (Palmer et al. 1964) and Gutch (Gutch 1964) included the introduction of perforations at the distal end, and later Tenckhoff included the design of a shorter catheter, a straight catheter, and a curled catheter. He also added the Dacron cuff, either single or double, to help to seal the openings through the peritoneum (Tenckhoff and Schechter 1968). He was also responsible for the introduction of the trocar that gave easy placement of the catheter. Dimitrios Oreopoulos, a Greek physician, was introduced to PD in Belfast, Northern Ireland, during his training and he noted the difficulties encountered with the catheters there. He had been shown a simple technique for inserting the catheter by Norman Dean from New York City, which allowed the access to be used repeatedly.

Peritoneal dialysis at home

In 1960, Scribner and Boen (Boen 1959) set up a PD programme that would allow patients to be treated at home. An automated unit was developed which could operate unattended overnight. The system used 40l containers that were filled and sterilised at the University of Washington. The bottles were then delivered to the patient's home, and returned after use. The machine was able to measure the fluid in and out of the patient by a solenoid device. An indwelling tube was permanently implanted into the patient's abdomen, through which a tube was inserted for each dialysis treatment. The system was open, and therefore was vulnerable to peritonitis. A new method was then used, whereby a new catheter was inserted into the abdomen for each treatment, and removed after the treatment ended. This was still carried out in the home, when a physician would attend the patient at home for insertion of the catheter, leaving once the treatment had begun. The carer was trained to discontinue the treatment and remove the catheter. The wound was covered by a dressing, and the patient would be free of dialysis until the next week. This treatment was carried out by Tenckhoff et al. (1965) in a patient for three years, requiring 380 catheter punctures.

The large 40l bottles of dialysate were difficult to handle and delivery to the home and sterilisation were not easy. Tenckhoff, at the University of Washington, installed a water still into the patient's home, thus providing a sterile water supply. The water was mixed with sterile concentrate to provide the correct solution, but this method was not satisfactory as it remained cumbersome and dangerous due to the high pressure in the still. Various refinements were tried using this method, including a reverse osmosis unit, and this was widely used later for HD treatment.

Lasker, in 1961, realised the potential of this type of treatment and concentrated on the idea of a simple version by instilling 2l of fluid by a gravity-fed system. This proved to be cheaper to maintain but was labour-intensive. Later that year, he was approached by Ira Gottscho, a businessman who had lost a daughter through kidney problems, and together they designed the first peritoneal cyclor machine. The refinements included the ability to measure the fluid in and out, and the ability to warm the fluid before the fill cycle. Patients were sent home using the automated cyclor treatment as early as 1970, even though there was a bias for HD at that time.

In 1969, Oreopoulos accepted a position at the Toronto Western Hospital and, together with Stanley Fenton, decided to use the Tenckhoff catheter for long-term treatment. Because of a lack of space and facilities at the hospital, it was necessary to send the patients home on intermittent PD. He reviewed the Lasker cyclor machine and ordered a supply, and by 1974 was managing over 70 patients on this

treatment at home. Similar programmes were managed in Georgetown University and also in the Austin Diagnostic Clinic in the USA.

The beginning of continuous ambulatory peritoneal dialysis

It was in 1975, following an unsuccessful attempt to haemodialyse a patient at the Austin Diagnostic Clinic, that an engineer, Robert Popovich, and Jack Moncrief became involved in working out the kinetics of 'long-dwell equilibrated dialysis' for this patient. It was determined that five exchanges each of 2 l day⁻¹ would achieve the appropriate blood chemistry, and that the removal of 1–2 l of fluid from the patient was needed per day. Thus came the evolution of CAPD (Popovich et al. 1976).

The treatment was so successful that the Austin group was given a grant to allow it to continue dialysing patients with CAPD. Strangely, the group's first description and account of this clinical experience was rejected by the American Society for Artificial Internal Organs. At this time the treatment was called 'a portable/wearable equilibrium dialysis technique'. The stated advantages compared to HD included:

- good steady-state biochemical control;
- more liberal diet and fluid intake;
- improvement in anaemia.

The main problems were protein loss (Popovich et al. 1978) and infection. It was recognised that the source of infection was almost certainly related to the use of the bottles. Oreopoulos found that collapsible polyvinylchloride (PVC) containers for the solution were available in Canada. Once the fluid was instilled, the bag could then be rolled up and concealed under the clothing. The fluid could be returned into the bag during draining by gravity, without a disconnection taking place (Oreopoulos et al. 1978). New spike connections were produced for access to the bag of fluid, and a Luer connection for fitting to the catheter, together with tubing devised for HD, greatly reduced the chances of infection. The patients treated on an intermittent basis (by intermittent peritoneal dialysis or IPD) were rapidly converted to CAPD and evaluation of the new treatment was rapid, due to the large numbers being treated. Following approval by the US Food and Drug Administration, many centres were then able to develop CAPD programmes.

The first complete CAPD system was released on to the market in 1979, giving a choice of three strengths of dextrose solution. Included in this system were an administration line and sterile items packed together to form a preparation kit, to be used at each bag change in an attempt to keep infection at bay. The regime proposed by Robert Popovich and Jack Moncrief entailed four exchanges over a 24-hour period, three dwell times of approximately 4 hours in the daytime, and 1 dwell overnight of 8 hours. This regime is the one often used today.

The systems are continually being improved, with connectors moving from spike to Luer to eliminate as far as possible the accidental disconnection of the bag from the line. A titanium connector was found to be the superior form of adaptor for connection of the transfer set to the catheter, and probably led to a reduced infection rate for peritonitis. A disadvantage of this technique is the flow of fresh fluid down the transfer set along the area of disconnection, thus encouraging any bacteria from the disconnection to be instilled into the abdomen. The development of the Y-system (flush before fill) in the mid-1980s in Italy resulted in a further decrease in peritonitis.

Automated peritoneal dialysis

Automated PD in the form of continuous cyclic peritoneal dialysis (CCPD) was further developed by Diaz-Buxo in the early 1980s to enable patients who were unable to perform exchanges in the day to be treated with PD overnight.

Advances in peritoneal dialysis for special needs

Even more recently advances in CAPD treatment include a dialysate that not only provides dialysis but which contains 1.1% amino acid, to be administered to malnourished patients. This is particularly useful for older people on CAPD, in whom poor nutrition is a well-recognised complication.

Those with diabetes were initially not considered for dialysis, because of the complications of the disease. Carl Kjellstrand, at the University of Minnesota, suggested that insulin could be administered to those with diabetes by adding it to the PD fluid (Crossley and Kjellstrand 1971). However, when this suggestion was first put forward, it was not adopted because the 30-minute dwell did not give time for the drug to be absorbed into the patient. It became viable later, when long-dwell dialysis was initiated, and this gave the advantage of slow absorption, resulting in a steady state of blood sugar in the normal range, thus alleviating the need for painful injections (Flynn and Nanson 1979).

The realisation that patients are individuals, bringing their own problems associated with training, brought many exchange aid devices onto the market to assist the patient in the exchange procedure. These exchange devices were mainly used to assist such disabilities as blindness, arthritis (particularly of the hands), and patients prone to repeated episodes of peritonitis.

The present

In some centres PD is usually the first choice of treatment for established renal disease. In many countries, because of the lack of facilities for in-centre HD, it will remain so. However, the relative prevalence of PD in the United Kingdom has been declining since its peak in the early 1990s, possibly because of the availability of satellite HD and a high level of PD technique failure. In 2016 only 20.5% of people who required RRT were on PD (at 90 days after starting dialysis) compared with 69.8% of patients on HD (Byrne et al. 2018).

Transplantation

In the beginning

Kidney transplantation as a therapeutic and practical option for RRT was first reported in published literature at the turn of the twentieth century. The first steps were small and so insignificant that they were overlooked or condemned.

The first known attempts at renal transplantation on humans were made without immunosuppression between 1906 and 1923 using pig, sheep, goat, and sub-human primate donors (Elkington 1964). These first efforts were conducted in France and Germany but others followed. None of the kidneys functioned for long, if indeed at all, and the recipients all died within a period of a few hours to nine days later.

Of all the workers at this time, the contribution made by Alixis Carrel (1873–1944) remains the most famous. His early work in Lyons, France, and in Chicago involved the transplantation of an artery from one dog to another. This work later became invaluable in the transplantation of organs. In 1906, Carrel and Guthrie, working in the Hull Laboratory in Chicago, reported the successful transplantation of both kidneys in cats and later a double nephrectomy on dogs, reimplanting only one of the kidneys. He found that the secretion of urine remained normal and the animal remained in good health, despite having only one kidney (Carrel 1983). Carrel was awarded the Nobel Prize in 1912 for his work on vascular and related surgery.

While at this stage there was no clear understanding of the problem, some principles were clearly learned. Vascular suture techniques were reviewed and the possibility of using pelvic implantation sites was investigated and practised. No further renal heterotransplantations (animal to human) were tried until 1963 when experiments using kidneys from chimpanzee (Reemtsma et al. 1964) and baboon were tried, with eventual death of the patients. This ended all trials using animal donation.

The first human-to-human kidney transplant was reported in 1936, by the Russian Voronoy, when he implanted a kidney from a cadaver donor of B-positive blood type into a recipient of O-positive blood type, a mismatch that would not be attempted today. The donor had died six hours before the operation and the recipient died six hours later without making any urine. The following 20 years saw further efforts in kidney transplantation, all without effective immunosuppression (Groth 1972). The extraperitoneal technique developed by French surgeons Dubost and Servelle became today's standard procedure.

The first successes

The first examples of survival success of a renal transplant can probably be attributed to Hume. Hume placed the transplanted kidney into the thigh of the patient, with function for five months. Then at the Peter Bent Brigham Hospital in Boston, USA, in December 1954, the first successful identical-twin transplant was performed by the surgeon Joseph E. Murray in collaboration with the nephrologist John P. Merrill (Hume et al. 1955). The recipient survived for more than two decades. The idea of using identical twins had been proposed when it was noted by David C. Miller of the Public Health Service Hospital, in Boston, that skin grafts between identical twins were not rejected (Brown 1937). The application of this information resulted in rigorous matching, including skin grafting, prior to effective immunosuppression.

Over the period between 1951 and 1976 there were 29 transplants performed between identical twins, and the survival rate for 20 years was 50%. Studies of two successfully transplanted patients, who were given kidneys from their nonidentical twins, were also reported (Merrill et al. 1960). The first survived 20 years, dying of heart disease, and the second 26 years, dying of carcinoma of the bladder. Immunosuppression used in these cases was irradiation.

Immunosuppression

It was Sir Peter Medawar who appreciated that rejection is an immunological phenomenon (Medawar 1944), and this led to research into weakening the immune system of the recipients to reduce the rejection. In animals, corticosteroids,

total body irradiation, and cytotoxic drug therapy were used. Experiments in animals were still far from successful, as were similar techniques when used in humans. It was concluded that the required degree of immunosuppression would lead to destruction of the immune system and finally result in terminal infections.

A few patients were transplanted between 1960 and 1961 in Paris and Boston, using drug regimens involving 6-mercaptopurine or azathioprine, with or without irradiation. They all died within 18 months. Post-mortem examination of failed kidney grafts showed marked changes in the renal histology, which at first were thought unlikely to be due to immunological rejection, but later it was convincingly shown that this was indeed the underlying process.

In the early days of kidney transplantation, the kidney was removed from either a living related donor or a cadaver donor and immediately transferred to the donor after first flushing the kidney with cold electrolyte solution such as Hartman's solution. In 1967, Belzer and his colleagues developed a technique for continuous perfusion of the kidney using oxygenated cryoprecipitated plasma, which allowed the kidney to be kept up to 72 hours before transplantation. This machine perfusion required constant supervision, and it was found that flushing the kidney with an electrolyte solution and storage at 0 °C in iced saline allowed the kidney to be preserved for 24 hours or more (Marshall et al. 1988). This was a major development in transplantation techniques.

During the 1950s it was recognised that many of the survivors of the Hiroshima atomic bomb in 1945 suffered impairment to their immune system. It was concluded that radiation could therefore induce immunosuppression, and clinical total body irradiation was used to prolong the survival of renal transplants in Boston in 1958. This did improve the survival of some transplants; however, the overall outcomes were poor. There was clearly a need for a more effective form of immunosuppression than irradiation.

A breakthrough in immunosuppressive therapy occurred in 1962 in the University of Colorado, when it was discovered that the combination of azathioprine and prednisone allowed the prevention and in some cases reversal of rejection (Starzl et al. 1963). Transplantation could at last expand. A conference sponsored by the National Research Council and National Academy of Sciences in 1963 in Washington resulted in the first registry report, which enabled the tracing of all the early non-twin kidney recipients. In 1970, work commenced on the development of ciclosporin by Sandoz in Basel, Switzerland, following recognition of the potential (Borel et al. 1976). Clinical trials carried out in Cambridge, United Kingdom (Calne et al. 1979) showed that outcomes on renal transplantation were greatly improved, both with graft and with patient survival. Ciclosporin revolutionised immunosuppression treatment for transplant patients, even though it is itself nephrotoxic and its use needs close monitoring.

Tissue typing is a complex procedure and, as yet, is far from perfect. The use of the united networks for organ sharing has increased the efforts of matching donor and recipient, and data available from these sources show a significant gain in survival of well-matched versus mismatched cadaver kidneys. Cross-matching remains as important today as it was at its conception. None of the immunosuppressive measures available today can prevent the immediate destruction of the transplanted organ by humoral antibodies in the hyperacute rejection phase. This was recognised as early as 1965 (Kissmeyer-Neilsen et al. 1966), and it may be that this phenomenon holds the key to the future of successful heterotransplantation.

Blood transfusions

It was observed in the late 1960s that patients who had received multiple blood transfusions before organ transplantation did not have a poorer graft survival than those who had not been transfused. Opelz and Terasaki (1974) observed that patients who had received no transfusions whatsoever were more likely to reject the transplant. It became evident, therefore, that a small number of blood transfusions resulted in an improved organ survival and so the transfusion policies for nontransfused recipients were changed throughout the world. This 'transfusion effect' is of much less importance in the ciclosporin era.

The present

Renal transplantation has been a dramatic success since the 1980s, with patient survival rates not less than 97% after six months' transplantation for both living related and cadaver transplants. Although short-term survival for the graft is good – at least 90% expectation of survival of the graft at one year – cadaveric graft survival at five years is around 70%, with a substantial minority losing their renal graft after 15 years.

The future

There is no doubt that renal transplantation is the treatment of choice for many patients requiring RRT giving, in general, a better quality of life than dialysis. However, organs are in short supply. A change in the law may result in more kidneys becoming available for transplantation, by allowing easier access to donors or removing the need for relatives' consent, but until a significant breakthrough is achieved there will continue to be a waiting list for transplantation and it will be necessary to continue to improve the techniques of dialysis. However, the number of people waiting for a kidney transplant has dropped slightly in recent years (down from 6300 in 2012 to 5118 in December 2017) whilst the number of kidney transplants has increased, with 2568 being carried out in 2011/2012 and 3173 being carried out in 2016/2017 (NHS Blood and Transplant 2018). Reasons for this increase are discussed further in Chapter 13.

Conclusion

Dialysis has come a long way from the small beginnings of the hot baths in Rome. Refinements and improvements continue, most recently with the emergence of erythropoietin in the late 1980s to correct the major complication of anaemia in people with ERF (established renal failure). The challenge of adequate dialysis for all who need treatment remains.

Transplantation is still not available for all those who are eligible, and changes in the law may help with availability of donor organs. The multidisciplinary teams will continue to strive to give patients the best possible quality of treatments until a revolutionary breakthrough in prevention of ERF happens.

UK Renal Registry data report that in the United Kingdom, the incidence rate in the UK decreased from 120 per million population (pmp) in 2015 to 118 pmp in 2016 reflecting RRT initiation for 7759 new patients (Byrne et al. 2018). Figure 1.3 shows the RRT modality at the end of 2016.

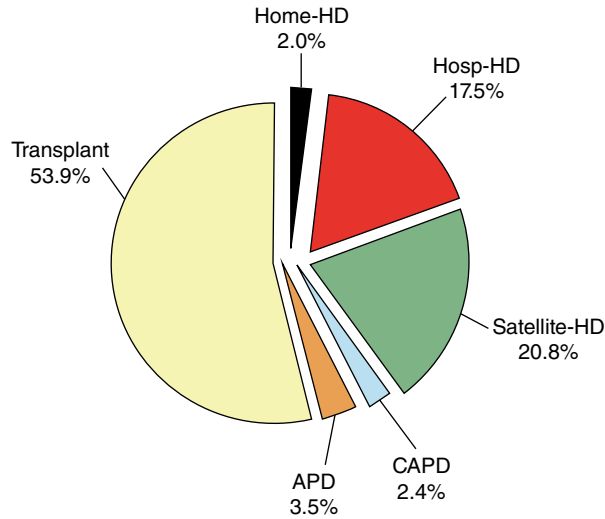


Figure 1.3 Renal replacement therapy modality in the UK at 31/12/16. Source: The data reported here have been supplied by the UK Renal Registry of the Renal Association. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the UK Renal Registry or the Renal Association.

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CHAPTER 2

Applied Anatomy and Physiology and the Renal Disease Process

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Learning Outcomes

- to understand the structure and main functions of the kidney.
- to explain the basic renal processes of filtration, reabsorption, and secretion.
- to identify the main conditions causing advanced kidney disease.
- to analyse the clinical features of these conditions and explain the principles of care management.

Introduction

This chapter provides the reader with a detailed discussion of all aspects of renal physiology and its relationship to important pathophysiological processes in renal disease, and some brief discussion on related nursing observations. The first part of the chapter explores the normal renal anatomy and physiology and the second part deals with disease processes causing advanced kidney disease. This is not intended as a complete reference to all kidney diseases; rather, it illustrates how altered renal physiology can affect the whole body and, indeed, how other diseases can affect kidney function.

Structure and Functions of the Kidney

The kidneys are paired organs lying behind the peritoneum, on either side of the vertebral column. The upper pole of the kidney is at the spinal level of T12 and the lower pole at approximately L3. The right kidney is a little lower due to the presence of the liver on that side. Usually, the kidneys are oriented with the concave surface facing the spine. However, due to developmental aberrations, other orientations of the kidney may occasionally exist (e.g. lying in the pelvis), but these do not usually affect function. Each kidney is approximately 11 cm long and weighs about 150 g (Figure 2.1).

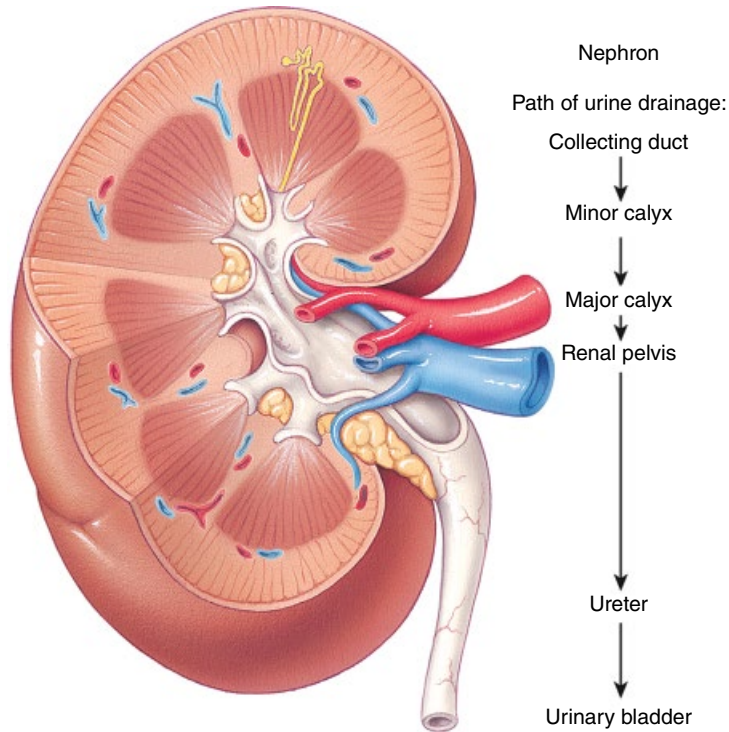


Figure 2.1 Structure of the kidney. Source: Tortora and Derrickson (2007). This material is reproduced with permission of John Wiley & Sons, Inc.

On the concave surface of the kidney lies the hilum, from which the ureter and the main blood vessels and nerves access the kidney. The cut surface of the kidney reveals two distinct regions: a dark outer region called the cortex, and a pale inner region called the medulla. The outer cortex is covered by a fibrous capsule and the whole kidney is surrounded by a pad of fat that offers some protection against injury. Broadly speaking, the cortex contains the filtering and reabsorptive components of the nephrons, whilst the medulla contains the concentrating and diluting components of the nephrons and a system of collection ducts. These ducts funnel the urine into the pelvis at the heart of the medulla, from where it moves down the ureter into the bladder (Figure 2.2).

The nephron

The nephron is the functional unit of the kidney and each kidney contains approximately one million nephrons (Figure 2.3). The unique structure of the nephron is critically related to its complex functions and contains five components, each performing a distinct process:

- the Bowman's capsule – forming a blind-ending capsule around a knot of capillaries called the glomerulus (the site of filtration);
- the proximal convoluted tubule (the site of bulk-phase reabsorption and some secretion);
- the loop of Henle (where the concentration and dilution of urine mainly occur);

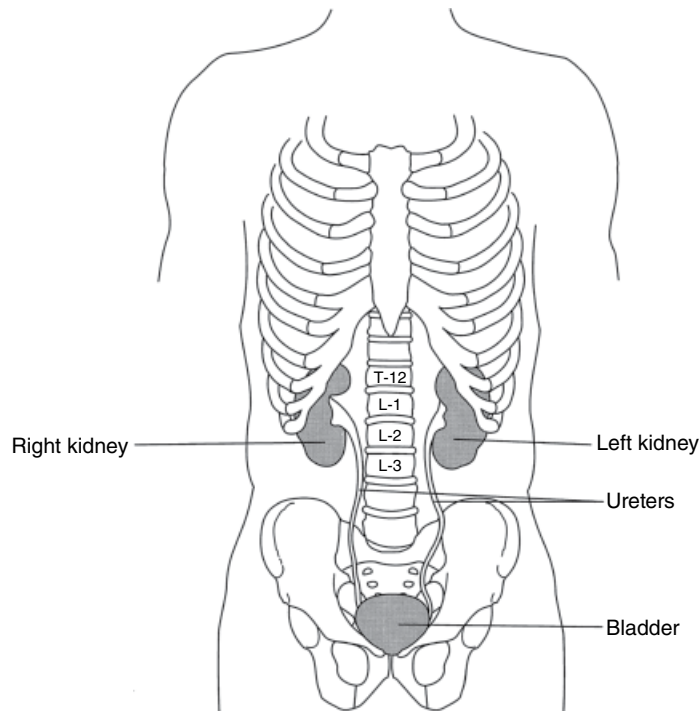


Figure 2.2 Relative position of the kidneys in the body.

- the distal convoluted tubule (the site of ‘fine-tuning’ reabsorption and more secretion);
- the collecting duct (also important for the concentration of urine and for carrying urine into the renal pelvis).

These processes do not occur in isolation but are interdependent and intimately related to each other by the shape of the nephron. The importance of this fact will become clear when the renal processes are discussed in more detail.

There are broadly two types of nephron found in the kidney (Figure 2.4). Approximately 85% of nephrons are cortical nephrons, which have short loops of Henle that are contained in the cortex of the kidney. The other 15% of nephrons are called juxtamedullary nephrons and they have long loops of Henle, which extend deep into the medulla of the kidney. It is the long loops of Henle that enable concentration of urine; animals adapted to arid environments have long loops of Henle compared with those that have a lesser requirement to conserve water. It is the loops of Henle, together with the collecting ducts which also pass through the medulla, that give the pyramids of the medulla a striated appearance.

The main functions of the kidney are to rid the body of the end-product of metabolism and to regulate the electrolytes found in the body fluids. A more detailed list of the functions of the kidney can be found in Box 2.1. Before looking at how the kidney achieves its functions, there follows a discussion on the impressive versatility of urine.

The versatility of urine

When the immense variability in the qualities of urine that can be produced in order to control our internal environment is considered, one cannot fail to be

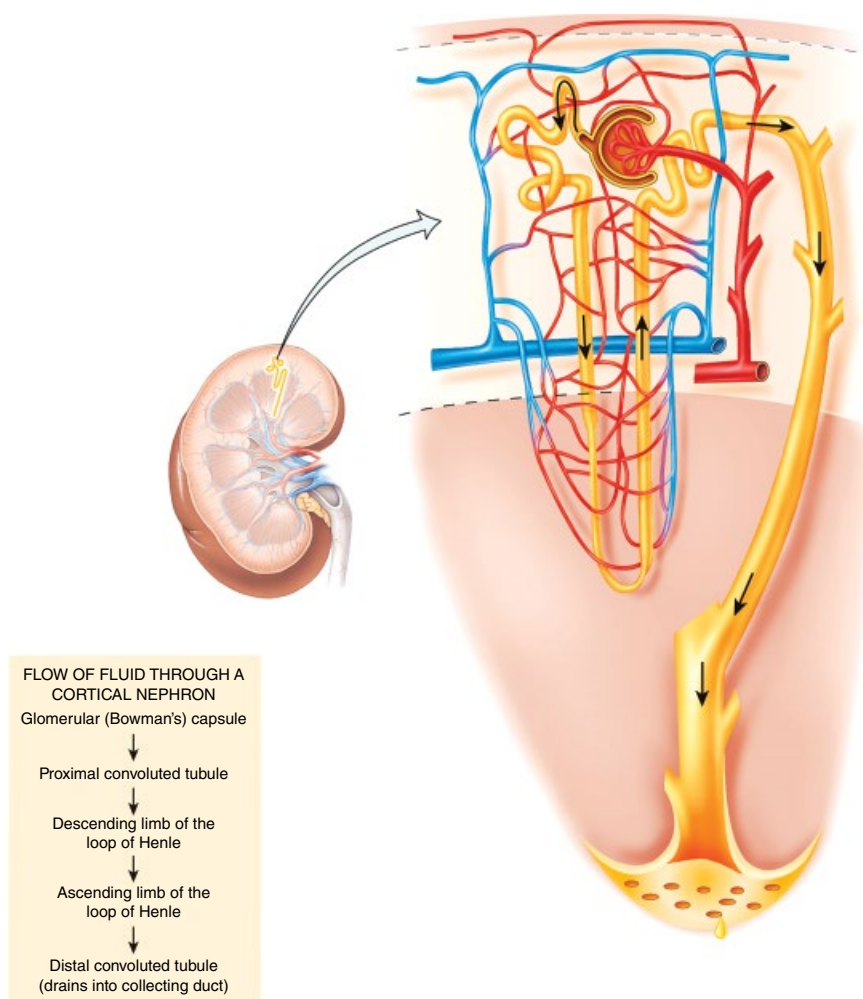


Figure 2.3 The parts of a nephron, collecting duct, and associated blood vessels. Source: Tortora and Derrickson (2007). This material is reproduced with permission of John Wiley & Sons, Inc.

impressed by the complexities of the workings of the kidney. Broadly speaking, there are three parameters that can be varied in order to maintain the constancy of our bodily fluids: urinary volume, urinary concentration and urinary content.

Urinary volume

In a healthy person, the volume of urine produced per day can vary from as little as 300 ml, if no water is ingested or there is excessive water loss from the body (as in diarrhoea), up to a maximum of 23 l in cases of excessive fluid ingestion. In health, urine output should not drop below 300 ml day⁻¹ because this is the absolute minimum water volume required to excrete the daily load of toxic waste products. If the amount of waste products to be removed by the kidney rises, then the minimum urine volume must also rise. However, the average urine output per day is approximately 1500 ml. The kidneys' ability to vary the volume of daily urine output over such a wide range is essential if we are to maintain a constant

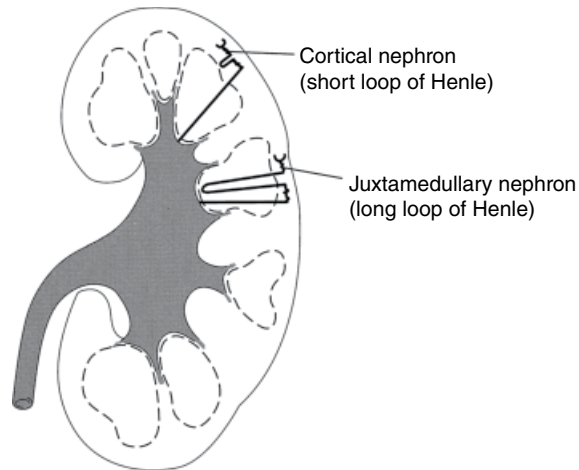


Figure 2.4 The position of the nephrons in the kidney.

BOX 2.1

The functions of the kidney

Excretory

- excretion of metabolic waste products, e.g. urea and creatinine.

Regulatory

Regulation of:

- body water volume;
- body fluid osmolality;
- electrolyte balance;
- acid–base balance;
- blood pressure.

Metabolic

- activation of vitamin D.
- production of renin.
- production of erythropoietin.

body fluid volume in the face of adverse factors such as excessive heat, which causes sweating; colonic infections causing diarrhoea; or excessive thirst and water ingestion, as seen in the condition psychogenic polydipsia (Table 2.1).

Urinary concentration

Though the volume of urine can vary over a wide range, the amount of solutes to be excreted by the kidney each day is much less variable. Thus, in order to excrete a fairly fixed volume of solutes each day in a very variable volume of water, the kidney must have the ability to concentrate or dilute the urine. On a hot summer's day when very little fluid has been drunk, urine is dark in colour and of low volume, whereas if liberal amounts of beer have been consumed at a party, large volumes of watery urine are passed all evening. In fact, this diuretic effect of beer is not wholly due to the volume imbibed, but also to the fact that the alcohol

Table 2.1 Normal fluid inputs and outputs.

Inputs (ml)		Outputs (ml)	
Water	1500	Urine ^a	1500
Food	500	Insensible loss	lungs 400
			skin ^b 400
Water of metabolism	400	Faeces ^c	100
Total	2400		2400

^a Urinary volume is the only factor that can be regulated by the body to balance fluid inputs.
^b This insensible loss of fluid through the skin is by simple evaporation (not sweat). Sweat is called 'sensible loss' and may reach up to 5 l h⁻¹, for example, when a person is exercising excessively.
^c Loss of fluid with the faeces can be as high as several litres per day in the presence of severe intestinal infections such as cholera.

present in the beer suppresses the secretion (from the posterior pituitary gland) of antidiuretic hormone (ADH), also known as vasopressin, a hormone that would normally prevent diuresis. The hangover suffered the next day is therefore caused by dehydration.

The ability of the kidneys to excrete all the body's excess solutes in varying amounts of water by concentrating or diluting the urine is essential for maintaining a constant body osmolality (Box 2.2). The mechanism in the kidney that controls the concentration or dilution of urine is often affected early on in renal disease, making it difficult for the individual to control both body fluid volume and osmolality in response to changes in fluid inputs and outputs. This can result in the individual tipping back and forth from states of dehydration to fluid overload.

BOX 2.2

Concepts of osmosis and body osmolality

- water can move between the different body fluid compartments across semipermeable membranes by the process of osmosis.
- the more concentrated a solution, the more water will be drawn into this solution.
- any solute that can cause the movement of water across a semipermeable membrane is said to be 'osmotically active'.
- the osmotic activity of substances in solution is dependent on the number of dissolved particles in the solution and not on their size or charge.
- sodium chloride (NaCl) dissociates in solution into Na⁺ and Cl⁻ ions, so the number of osmotically active particles is almost double the number of NaCl molecules (but not exactly double because the dissociation is not complete; the solution consists of NaCl, Na⁺, and Cl⁻ particles).
- osmotically active particles in solution are measured by the unit called the osmole or milliosmole (mosmol).
- osmolality is measured in mosmol kg⁻¹ water and is a measure of the potential osmotic activity of dissolved solutes in solution.
- normal body fluid osmolality is 285 mosmol kg⁻¹ water.
- the concentration (rather than the osmotic activity) of individual electrolytes is measured in mmol (millimoles) or μmol (micromoles) rather than mosmol

Urinary content

The range of substances that can be constituents of urine is varied and includes:

- ions: sodium, potassium, calcium, magnesium, chloride, bicarbonate, phosphate, and ammonium;
- metabolic waste: urea, creatinine, and uric acid;
- drug metabolites: most metabolites of pharmacological agents are eventually excreted from the body through the kidneys; many are detoxified in the liver first;
- other products of normal metabolism: metabolites of hormones can be detected in the urine by appropriate assays and may be a diagnostic aid; for example, the appearance of human chorionic gonadotrophin (hCG) in the urine in the early stages of pregnancy forms the basis of the pregnancy test.

Normal urine is clear in appearance, though it may vary in colour from pale to dark amber, depending on its concentration. It has no unpleasant odour, though urine that has been standing a long time may develop a strong ammonia smell. Finally, normal urine has a pH that is slightly acidic – around pH6 – though urine can have a pH in the range 4.0–8.0 in cases of severe acidosis or alkalosis respectively.

Basic Renal Processes

Glomerular filtration

This is a process of filtration of plasma across the glomerular basement membrane from the glomerulus into the Bowman's capsule (Figure 2.5). The glomerular filtration surface is a unique structure composed of three layers:

- the endothelial lining of the glomerular capillaries;
- the basement membrane;
- the epithelial cells of the Bowman's capsule, or podocytes. Filtration occurs between the slits formed by the finger-like processes of these cells (called pedicels) which surround the glomerular capillaries.

These three layers are fused together and act as a barrier to the filtration of large-molecular-weight molecules such as proteins.

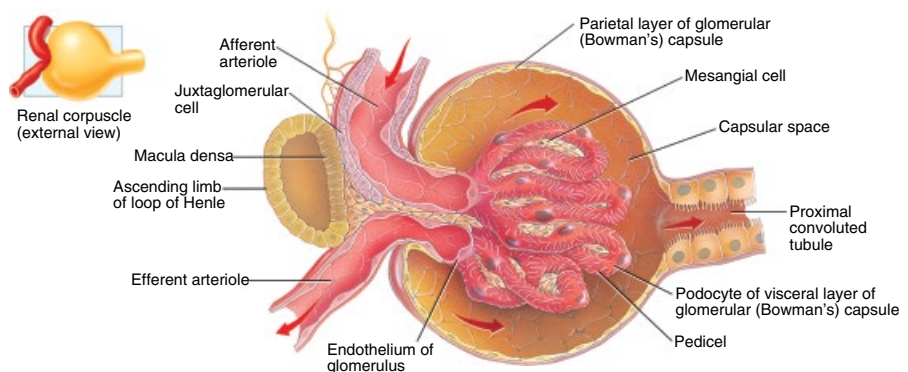


Figure 2.5 Structure of the glomerulus and Bowman's capsule. Source: Tortora and Nielsen (2009). This material is reproduced with permission of John Wiley & Sons, Inc.

Blood enters the glomerulus from a series of branches of the renal artery, ending in the afferent arteriole. Blood then leaves the glomerulus through the efferent arteriole rather than a vein. In the majority of nephrons (those situated in the cortex), the efferent arteriole from the glomerulus divides up into capillaries, which cover the surfaces of the convoluted tubules. The capillaries finally empty into the venous system. In the deeper juxtamedullary nephrons, the efferent arteriole from the glomerulus divides to form loops which lie parallel to the loops of Henle and so run down into the medulla. These vessels are called the vasa recta and are concerned with the process of concentration of the urine. Blood then leaves the kidney through a series of larger converging veins, ending in the renal vein which returns the blood to the vena cava.

In effect, the nephrons contain two capillary beds, one within the glomerulus and a second which surrounds the convoluted tubules of the nephrons. This unusual arrangement of two capillary beds in tandem enables a pressure gradient to exist within the nephron, with high pressure in the glomerulus, favouring filtration, and a relatively low pressure in the peritubular capillaries, favouring reabsorption.

The formation of a filtrate from plasma flowing through the glomerulus occurs due to Starling's forces. These are the same forces that cause the filtration and reabsorption of tissue fluid in other capillary beds in the body, but with some important adaptations. In the glomerulus, filtration depends on three main pressures. One type of pressure promotes filtration, and the other pressures oppose filtration. Fluid is forced across the glomerular basement membrane because of the high hydrostatic pressure of blood flowing through the afferent arteriole. This pressure is greater than the sum of the blood colloid osmotic pressure (BCOP) and the pressure in the Bowman's capsule (capsular hydrostatic pressure) opposing it (Figure 2.6). In an ordinary capillary bed, this filtrate would be almost entirely reabsorbed back into the capillary at the venule end because the hydrostatic pressure would have fallen to below the colloid osmotic pressure of the capillary, which would then pull the fluid back in by osmosis. However, in the glomerulus, because blood leaves via another arteriole (the efferent arteriole) rather than a venule, a high hydrostatic pressure is maintained and the sum of the BCOP and capsular

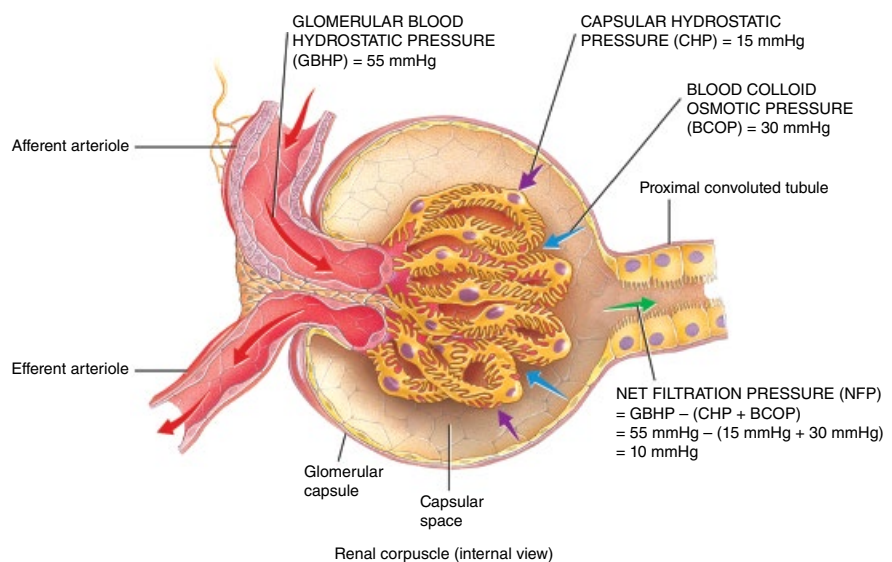


Figure 2.6 The formation of filtrate in the glomerulus. Source: Jenkins and Tortora (2013).

hydrostatic pressure is insufficient to move fluid back into the capillary. This situation is obviously desirable so that large amounts of filtrate can be made. All of the filtrate formed in the glomerulus passes into the Bowman's capsule and is often referred to as tubular urine.

Amount and composition of glomerular filtrate

The amount of glomerular filtrate formed per minute is referred to as the glomerular filtration rate (GFR), and in the average healthy person is approximately 125 ml min^{-1} . This volume is the sum amount from all two million nephrons in the kidneys and thus the amount from each nephron is relatively small. A quick calculation shows that at a GFR of 125 ml min^{-1} , the total amount of filtrate formed per day is 180 l – approximately 60 times the circulating plasma volume. Obviously, the majority of this must be reabsorbed to prevent severe dehydration.

The 'average' GFR quoted is generally only average for a young adult. Children have a lower GFR than this because their nephrons are still increasing in size (all nephrons are present at birth). After the age of about 30 years the number of functioning nephrons starts to decrease because of the ageing process, thus the GFR decreases proportionately. However, this only becomes significant to health when the GFR falls to around 5 ml min^{-1} – a situation that only occurs in a diseased kidney. An estimated GFR (eGFR) can be calculated clinically by measuring serum creatinine and applying a formula. The principles of the eGFR test are described more fully in Chapters 6 and 7.

The composition of the initial glomerular filtrate is that of a plasma ultrafiltration; that is, without proteins. The main determinant of what can pass through the glomerular basement membrane is molecular size, although the molecular shape and charge are also important. The passage of strongly negatively charged molecules such as albumin tends to be retarded because of the presence of fixed negative charges in the basement membrane which repel their movement. Albumin, a small protein, has a molecular weight of 69 000, a weight just below the cut-off point for filtration. It can therefore cross the filter, but does so only in minute quantities since it is also hindered by its negative charge. Similarly, haemoglobin, with a molecular weight of 68 000, is small enough to be filtered, whereas intact erythrocytes are too large to cross into the Bowman's capsule. The appearance of haemoglobin in urine therefore indicates haemolysis, with the release of the protein into the blood. It is because of this free permeability of small molecules that the composition of the initial glomerular filtrate is the same as that of the plasma, and will include the major ions sodium, potassium, chloride, bicarbonate, calcium, and phosphate; glucose; amino acids; and the toxic waste products of urea and creatinine. Any albumin filtered is reabsorbed through the proximal tubule into the renal lymph system and returned to the bloodstream.

Selective reabsorption

Reabsorption is a process that involves the movement of water and dissolved substances from the tubular fluid back into the bloodstream. The term 'selective' infers a regulatory function to this process, as indeed not all of the filtered substances are returned to the blood. Any substances not reabsorbed will pass with the urine into the bladder to be excreted from the body. The main sites for reabsorption in the nephron are the proximal and distal convoluted tubules.

Mechanisms of reabsorption

Broadly speaking, there are three mechanisms in the nephron for the reabsorption of water and solutes: osmosis, diffusion, and active transport. Osmosis is the

movement of water from an area of low concentration to a more concentrated solution across a membrane which allows water molecules through but is selectively permeable to solute molecules (a semipermeable membrane).

Diffusion occurs where a concentrated solution meets one which is less concentrated. The solute will equilibrate throughout the solvent. This may occur across a membrane so long as the membrane is permeable to the solute. Diffusion may also occur through specialised 'protein carriers' in the membrane. This is sometimes known as 'facilitated diffusion'. In these cases, the number of protein carriers in the membrane is limited, meaning that movement of the solute will be limited. This is true for tubular reabsorption of glucose (which is also linked to sodium transport). Once all the carriers are active, reabsorption of glucose has reached its maximum. If the filtered load of glucose is excessive, not all can be reabsorbed and glucose will appear in the urine, as happens in untreated diabetes mellitus.

Active transport is so named because it is an energy-requiring process. The energy source is adenosine triphosphate (ATP). Active transport can move solutes against a concentration gradient. Cells which carry out a lot of active transport will have a lot of mitochondria present (the 'power-generating' organelles of cells).

In the proximal tubule cells, where most reabsorption is by active transport, the cells are packed with mitochondria. Proximal tubule cells also have a large brush border on their luminal surface (the surface facing into the tubule) to increase their surface area for reabsorption. In contrast, cells lining the descending loop of Henle are comparatively thin, have no brush border, and have relatively few mitochondria. This suggests that these cells are not very metabolically active and are adapted for reabsorption by passive diffusion. The epithelial cells of the distal tubule are similar to those of the proximal tubule but with a less well-defined brush border and fewer mitochondria. This suggests that these cells are capable of active transport of substances but in much lesser quantities than in the proximal tubule. This again illustrates how each segment of the nephron is anatomically adapted to carry out its unique functions. The different cell types lining the tubules are illustrated in Figure 2.7.

Reabsorption in the proximal convoluted tubule – the site of bulk-phase reabsorption

Approximately 65% of all reabsorption occurs in the proximal tubule (hence the term 'bulk phase') and is obligatory rather than regulatory. Most substances here are reabsorbed by active transport mechanisms, including sodium, chloride, potassium, glucose, amino acids, phosphate, and bicarbonate. Urea is absorbed by passive diffusion and water is reabsorbed by osmosis. Some substances are reabsorbed almost entirely in the proximal tubule, such as glucose and amino acids, which do not appear in the urine, whereas others have only between 60 and 70% reabsorption, such as sodium, water, and potassium. Approximately 50% of urea is reabsorbed here but creatinine is not reabsorbed at all. However, for all substances that are reabsorbed, the proximal tubule is the site where the bulk of this reabsorption occurs.

Reabsorption in the distal convoluted tubule – the site of fine-tuning reabsorption

This is the site where more specific regulation of substances occurs according to the needs of the body. In order for the distal tubule to be aware of precisely what the body's reabsorptive needs are, there needs to be some method of communication between the cells of the distal tubule and the rest of the body. This communication system is via a range of hormones that form part of a negative-feedback system for

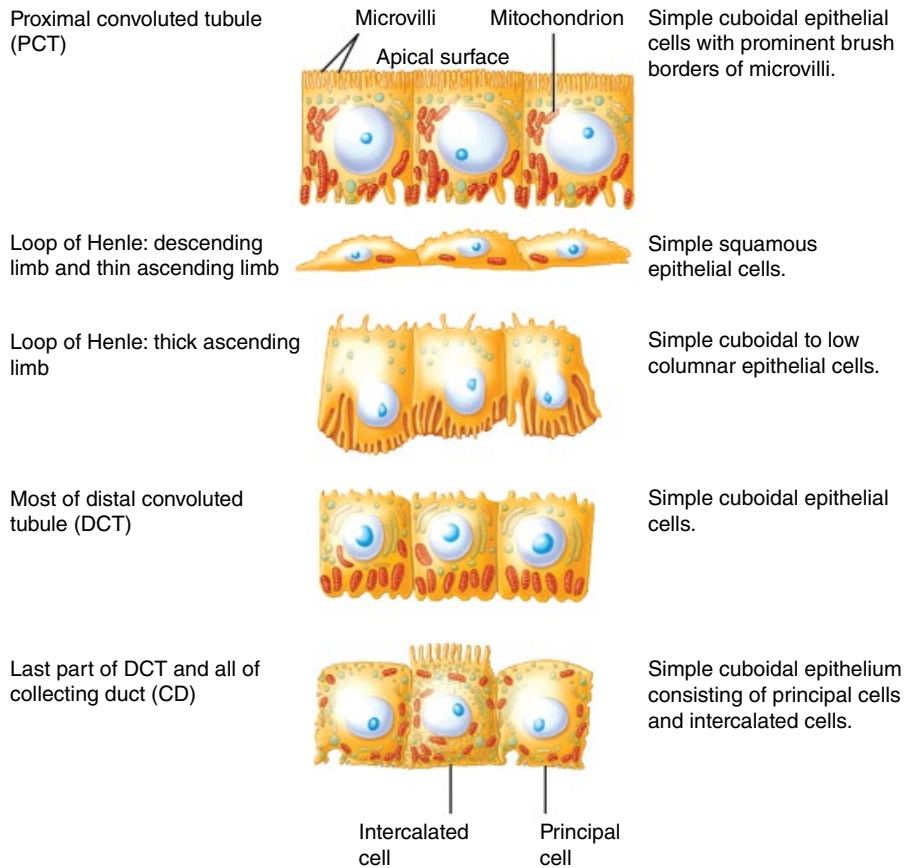


Figure 2.7 Histological features of the renal tubule and collecting duct. Source: Tortora and Nielsen (2009). This material is reproduced with permission of John Wiley & Sons, Inc.

the homeostatic control of ions and water. For example, sodium and water reabsorption are under the control of aldosterone (secreted by the adrenal cortex) and ADH secreted by the posterior pituitary gland. Potassium reabsorption is also controlled by aldosterone, whereas calcium and phosphate are controlled by parathyroid hormone (PTH). The precise mechanisms for controlling the electrolytes outlined above will be dealt with in later sections in this chapter.

Secretion

The process of secretion occurs in both the proximal and distal tubules and involves the movement of substances from blood flowing through the peritubular capillaries, through the tubule wall cells, and into the tubular fluid. In this respect, secretion is the opposite process to reabsorption. Substances that are secreted into the tubules are excreted in the urine. Though creatinine is freely filtered at the glomerulus, total creatinine excretion is increased by 20% by the process of secretion. Ions that are transported into the tubules by secretion are hydrogen, which is secreted in both the proximal and distal tubules and is important in acid–base control, and potassium, which is secreted in the distal tubule in exchange for sodium reabsorption. The hormone involved is aldosterone.

Excretion of drugs and drug metabolites

Many drugs and their metabolites are finally excreted from the body through the kidneys by the processes of glomerular filtration and secretion. Like other filtered substances, the rate of filtration of drugs will depend on their molecular size and charge: smaller molecules are filtered more rapidly than larger ones. Drugs that bind to plasma proteins are filtered very slowly because of the size of the complex. Some drugs are cleared from the blood purely by glomerular filtration and thus the rate of clearance cannot exceed the GFR of 125 ml min^{-1} , whereas other drugs are excreted by a combination of filtration and secretion, such as benzylpenicillin, which achieves a total clearance rate of 480 ml min^{-1} (Shitara et al. 2006; Bennett et al. 2012).

Concentration and dilution of urine

The components of the nephron that are involved in the concentration and dilution of the urine are the loop of Henle and the collecting ducts. The concentration of urine is measured in units of osmolality (mosmol kg^{-1} water). The most dilute urine that humans can produce is approximately $60 \text{ mosmol kg}^{-1}$ water, but this situation occurs in the pathological condition of diabetes insipidus in which the pituitary gland fails to produce ADH. The most concentrated urine that can be produced is approximately $1400 \text{ mosmol kg}^{-1}$ water, which is greater than four times more concentrated than plasma (plasma osmolality = $285 \text{ mosmol kg}^{-1}$ water) and requires maximum ADH secretion. The average range of urine osmolality in people with normal kidneys is between 300 and $500 \text{ mosmol kg}^{-1}$ water.

Countercurrent mechanism of urinary concentration

The countercurrent mechanism is a complex physiological process that will not be discussed in great detail.

In order to concentrate the urine the following factors are required:

- the creation and maintenance of a local environment in the kidney that allows large quantities of water to be reabsorbed by osmosis from the collecting duct back into the blood;
- a mechanism that can influence the opening and closing of water channels in the collecting ducts in order to control the exact amount of water reabsorbed.

Creation of the local environment

This local environment consists of an increasing hyperosmotic medullary interstitium as one moves towards the tip of the loops of Henle. In other words, the tissue spaces between the loops of Henle in the medulla of the kidney must be made hyperosmotic compared to the fluid in the collecting duct. As the collecting ducts pass through the medulla on their way to the renal pelvis, water can be pulled out by osmosis, resulting in less water entering the urine.

This hyperosmotic environment is created by the active and passive transport of ions (mainly sodium and chloride) out of the tubular fluid as it passes through the loop of Henle into the medullary interstitium. The buildup of ions here gradually increases and becomes more concentrated as the loop of Henle descends into the medulla. The tip of the medulla can reach osmolalities of up to $1400 \text{ mosmol kg}^{-1}$ water. Water does not follow the transport of ions into the medullary interstitium by osmosis because the thick ascending limb of the loop of Henle is impermeable to water. Urea also makes an important contribution to the creation of the hyperosmotic environment. Urea can diffuse passively through the

walls of the tubules at most points along the nephron, but urea diffusion is greatly enhanced across the collecting tubule wall in the presence of even small amounts of ADH. Therefore large amounts of urea become concentrated in the medullary interstitium.

Maintenance of the local environment: the countercurrent mechanism

It could be thought that as fast as the hyperosmotic environment is created it will be washed out by processes of diffusion and reabsorbed back into blood. However, the environment is maintained because of the unique arrangement of the looped vasa recta capillaries around the loops of Henle. The vasa recta are only supplied with 1–2% of the blood entering the kidneys, so there is very little blood flow for ions to be reabsorbed back into. In addition, the vasa recta lie with their ascending and descending limbs in very close proximity. This close proximity allows for rapid exchange of water and solutes between the two limbs. So, as blood flows down the descending limb of the vasa recta, the high concentration of ions in the medullary interstitium enables ions to diffuse into the vasa recta (markedly increasing their concentration), and water to move out by osmosis, but as the blood moves into the ascending limb of the vasa recta, the high concentration of ions in the blood then enables ions to diffuse back out into the medullary interstitium (and water back into the blood), maintaining the hyperosmotic environment.

The regulation of body fluid volume and osmolality

Sodium is the main extracellular cation (positively charged ion) and is intimately related to extracellular volume. An increase in body sodium content could lead to an increase in extracellular fluid volume, leading to hypertension and oedema; and a decrease in body sodium content could lead to a decrease in extracellular fluid volume, leading to hypotension and dehydration. Thus, it is vitally important that body sodium content is kept at a constant level if body fluid volume is to remain constant. Fortunately, the healthy kidney conserves sodium very efficiently in short-age, and can excrete $10\text{--}150\text{ mmol day}^{-1}$ when sodium is in excess.

Sodium levels, and hence fluid volume, are regulated by three hormones:

- ADH;
- aldosterone;
- atrial natriuretic peptide.

Antidiuretic hormone

ADH is secreted from the posterior pituitary gland in response to a rise in plasma osmolality. Osmoreceptors in the hypothalamus detect small changes in the plasma osmolality and send signals to the posterior pituitary to secrete more or less ADH. Since sodium, along with its associated anion (negatively charged ion) chloride (Cl^-), contributes approximately 95% of the extracellular fluid osmolality, sodium concentration of extracellular fluid is obviously important in determining ADH secretion.

ADH receptors are found in the collecting ducts of kidney tubules and ADH acts to open water channels found here. Remember that the collecting ducts pass through the inner medulla of the kidney – a region of high osmolality. If water channels in the walls of the collecting ducts open, water will move out of the collecting duct into the medullary interstitium and finally into the circulation. The fall in plasma osmolality then leads to a slowing down of ADH secretion by negative feedback (Figure 2.8).

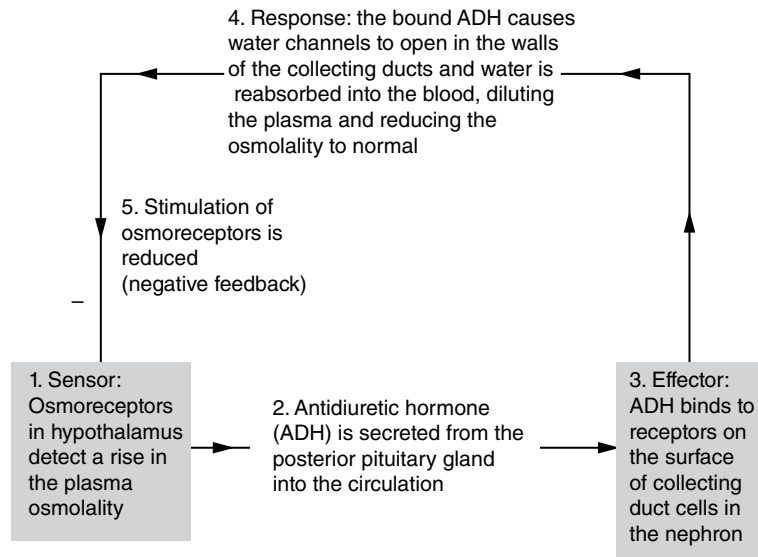


Figure 2.8 Negative-feedback loop for antidiuretic hormone (ADH) release and control of plasma osmolality.

Aldosterone

Aldosterone is a steroid hormone secreted from the adrenal cortex. It has its effect on the distal tubule of the nephron: the more aldosterone is secreted, the more sodium is reabsorbed. Aldosterone, however, is not the sole determinant of body sodium balance, although in extreme cases of oversecretion of aldosterone, such as in Cushing's disease, hypertension may result from over-retention of sodium and water.

The secretion of aldosterone, unlike ADH, is not directly triggered by extracellular osmolality, but is regulated by a peptide, angiotensin II. See Figure 2.9.

Atrial natriuretic peptide

This peptide is released from cardiac atrial cells in response to an increased atrial stretch. It has five known major effects:

- inhibition of aldosterone secretion by the adrenal cortex;
- reduction of renin release by the kidney;
- reduction of ADH release from the posterior pituitary;
- vasodilation;
- natriuresis and diuresis.

All of these effects result in the excretion of sodium and water through the kidney, reducing the extracellular fluid volume back to normal. Other factors which may be important in sodium regulation are renal prostaglandins, kinins, and the renal nerves. Failure to regulate the extracellular fluid volume occurs commonly in people with renal disease and leads to hypertension.

The renin–angiotensin–aldosterone pathway

The distal convoluted tubule forms a unique contact with the glomerulus, passing in the angle between the afferent and efferent arterioles. At this point, specialised cells called the macula densa in the wall of the distal tubule make contact with cells in the endothelium of the arterioles which release a hormone called renin.

The macula densa and the renin-releasing cells are collectively called the juxtaglomerular apparatus or complex (see Figure 2.5).

The juxtaglomerular apparatus is responsible for maintaining a constant blood flow through the glomerulus, and thus a constant GFR despite fluctuations in arterial pressure. This is achieved through a tubule feedback mechanism in which a fall in GFR results in a fall in the chloride ion concentration in the distal tubule. This stimulates the macula densa cells which send 'signals' to the renin-secreting cells to release renin. Renin acts via the renin–angiotensin system (Figure 2.9) to produce both local vasoconstriction of the efferent arteriole (increasing GFR) and peripheral vasoconstriction to increase arterial blood pressure. In addition, salt and water retention increase due to the effects of aldosterone.

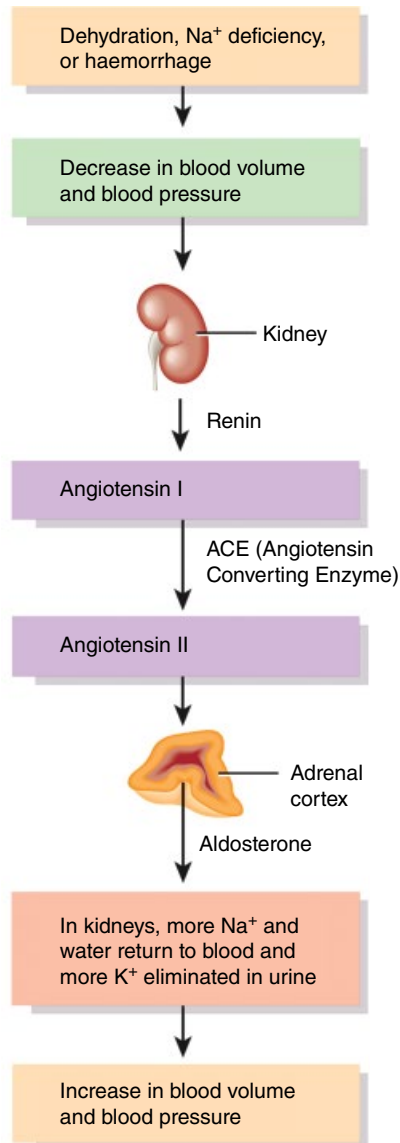


Figure 2.9 The renin–angiotensin–aldosterone pathway. Source: Tortora and Derrickson (2007). This material is reproduced with permission of John Wiley & Sons, Inc.

Aldosterone and the control of body potassium content

Potassium is the main intracellular cation. Only about 2% of the total body potassium content is extracellular. Potassium ions are freely filtered at the glomerulus: 65% of reabsorption takes place in the proximal tubule. However, the renal handling of potassium ions is not as efficient as that of sodium, nor is potassium conserved so well when there is a shortage. The secretion of potassium is also linked to that of sodium and hydrogen ions. Unlike sodium regulation, where aldosterone is just one factor in the regulation of sodium content, aldosterone is the only hormone involved in the control of potassium content and thus has a very important regulatory role. Small increases in extracellular potassium concentration directly stimulate aldosterone secretion from the adrenal cortex. The effect of aldosterone in the distal tubule of the nephron is to increase the secretion of potassium into the urine. When aldosterone levels fall, the reverse occurs and less potassium is secreted. The release of aldosterone stimulated by rises in extracellular potassium concentration is strongly controlled by a negative-feedback system. Once the potassium concentration returns to normal the stimulus to secrete aldosterone is quickly switched off.

The hormone aldosterone increases sodium reabsorption in exchange for potassium or hydrogen ions. If excess potassium ions need to be secreted, then fewer hydrogen ions can be secreted and vice versa. Clinically, this phenomenon results in an association between metabolic acidosis and hyperkalaemia (or conversely, metabolic alkalosis and hypokalaemia), because in patients with acidosis the distal tubules will increase the rate of hydrogen ion secretion (to prevent a fall in plasma pH) by reducing the rate of potassium ion secretion, resulting in the retention of potassium ions in the blood, leading to hyperkalaemia.

Hypokalaemia and hyperkalaemia

Potassium is important in maintaining the membrane potential of nerve and muscle cells and hence affects their excitability. Disturbances in potassium balance show their effects in abnormal nerve and muscle function and may be life threatening.

Changes in muscle tone and in the electrocardiogram (ECG) may indicate an altered potassium balance. The diet almost invariably contains adequate potassium, so hypokalaemia generally occurs due to excessive losses. Persistent vomiting, diarrhoea, or the use of certain prescribed diuretics are the most likely causes of low blood potassium. Dialysis using an inappropriate concentration of potassium in the dialysate may also result in hypokalaemia. Treatment of hypokalaemia by the administration of a potassium salt must be undertaken with care since this may result in hyperkalaemia. The uptake of potassium into cells is also dependent on the acid–base balance in the patient. Acidosis (low blood pH) causes the release of potassium from cells so acid–base disturbances must first be corrected.

Hyperkalaemia can occur as a result of decreased potassium excretion in the renal patient. Insulin promotes uptake of potassium into cells, so insulin deficiency may lead to hyperkalaemia, as can a variety of prescribed drugs (McDonald et al. 2015) and excessive tissue breakdown following trauma.

Regulation of calcium, phosphate, and magnesium

Calcium and phosphate are the main mineral constituents of bone and thus the majority of calcium and phosphate in the body is found in the skeleton. However, small amounts of both these ions are found in extracellular fluid. Calcium exists in the plasma in two forms. Approximately 50% exists in the free ionised form

(1.25 mmol l⁻¹), and the other 50% in a bound form, mainly bound to protein, particularly albumin (1.25 mmol l⁻¹). Usually when serum calcium levels are measured, the total calcium concentration is measured (2.5 mmol l⁻¹). This total calcium is then 'corrected' depending on the blood albumin level, since it is the ionised form of the calcium that is important in the extracellular fluid in controlling nerve and muscle conduction. Any condition which leads to a fall in the ionised calcium concentration (even if total calcium remains normal) will lead to the classic symptoms of hypocalcaemia – tetany, muscle cramps, and even convulsions. In situations of hypercalcaemia, the main effects seen are pruritus, extraskeletal calcification, renal calculi, peptic ulceration, and changes in mental function such as memory loss and depression.

Inorganic phosphate (i.e. those ions carrying a charge) exists in several forms – 'acid' phosphate (H₂PO₄⁻) and 'alkaline' phosphate (HPO₄⁻). The normal plasma range of total inorganic phosphate is 0.87–1.45 mmol l⁻¹. Phosphate is important in buffer systems to maintain the plasma pH and exists in equilibrium with calcium.

Both calcium and phosphate are freely filtered at the glomerulus. When the plasma phosphate level is below 1 mmol l⁻¹, all the filtered phosphate is reabsorbed in the early proximal tubule. However, once the plasma phosphate level rises above 1 mmol l⁻¹, the amount of phosphate excreted in the urine rises in proportion to the plasma concentration. Further excretion of phosphate in the distal tubule (by secretion) can occur in response to the rise in the circulating level of PTH. Calcium reabsorption is very similar to that of sodium, in that approximately 65% occurs in the proximal tubule, and a further 20–25% in the ascending limb of the loop of Henle, leaving around 10–12% of filtered calcium being delivered to the distal tubule. How much more calcium is reabsorbed in the distal tubule depends on the levels of circulating PTH.

Magnesium is an important intracellular cation involved in energy storage and production. In all, 55% of total body magnesium is found within bones, so it is not surprising that magnesium balance is linked to that of calcium.

PTH increases tubular reabsorption of magnesium. Under normal circumstances, gastrointestinal absorption and urinary excretion of magnesium are equal. Gastrointestinal disorders may therefore decrease magnesium uptake, but this is matched by a decrease in renal excretion. Most diuretics, and alcohol, increase renal magnesium excretion.

The renal handling of calcium and phosphate – the roles of PTH, vitamin D, and calcitonin

The mechanisms by which plasma calcium and phosphate are regulated are closely interrelated. The two major regulators are PTH and vitamin D. Calcium and phosphate can enter the plasma from the gut and from the bone. Indeed, almost all of the approximately 1 kg of calcium in a 70 kg person is found in the bone. Of this, a few grams exchange daily with the plasma calcium pool. Calcium and phosphate can leave the plasma by being redeposited in bone, or by renal excretion.

PTH is secreted by the parathyroid glands situated next to the thyroid. Secretion is stimulated by a decrease in plasma calcium concentration, and reduced when plasma calcium levels rise. Its effect is to raise plasma calcium concentration, mainly by increasing bone breakdown (resorption) and releasing calcium ions. PTH also acts in the kidney, stimulating one step in the conversion of vitamin D to its active metabolite, calcitriol or 1,25-dihydroxycholecalciferol, also known as 1,25-hydroxyvitamin D.

Vitamin D is a steroid that enters the body either through dietary intake or by the effect of sunlight on the skin. However, this is an inactive form of the vitamin

called cholecalciferol. To become activated it needs to undergo two metabolic conversions, one in the liver and one in the kidney. These conversions result in the formation of calcitriol. This active form has its effect in the gut, kidney, and (in the presence of PTH) on bone, raising plasma calcium levels. The actions of vitamin D are summarised in Figure 2.10.

The effects of both vitamin D and PTH are to increase the plasma calcium concentration. However, these effects are carefully controlled by a negative-feedback system which prevents the calcium level rising too high. The negative-feedback system is outlined in Figure 2.11. Only if calcium levels suddenly rise high (as after a high-calcium meal) is calcitonin stimulated to be released from the C cells of the thyroid gland, causing calcium to be redeposited in the bone. This is a rapid and relatively short-acting effect. The control of calcium and phosphate levels is essential for the maintenance of normal bone. In renal disease the production of calcitriol is reduced, thus removing the negative-feedback effect on PTH. The result is a rise in PTH leading to loss of calcium from bone and the complications of renal bone disease. Renal bone disease is discussed in Chapter 7.

Calcium ions play an important role in the regulation of nerve and muscle function and in blood clotting. Hypocalcaemia is characterised by increased excitability of muscles leading to tetany, when skeletal muscles go into spasm. Hypercalcaemia is a common finding in an individual with renal failure.

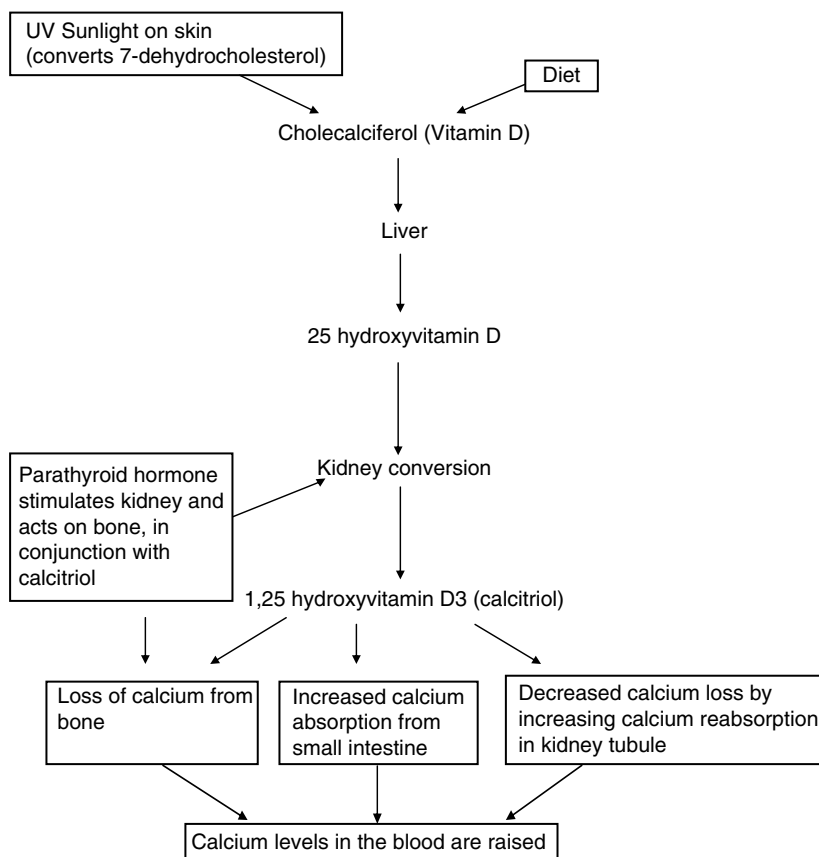


Figure 2.10 The actions of sunlight, vitamin D and parathyroid hormone (PTH) on blood calcium.

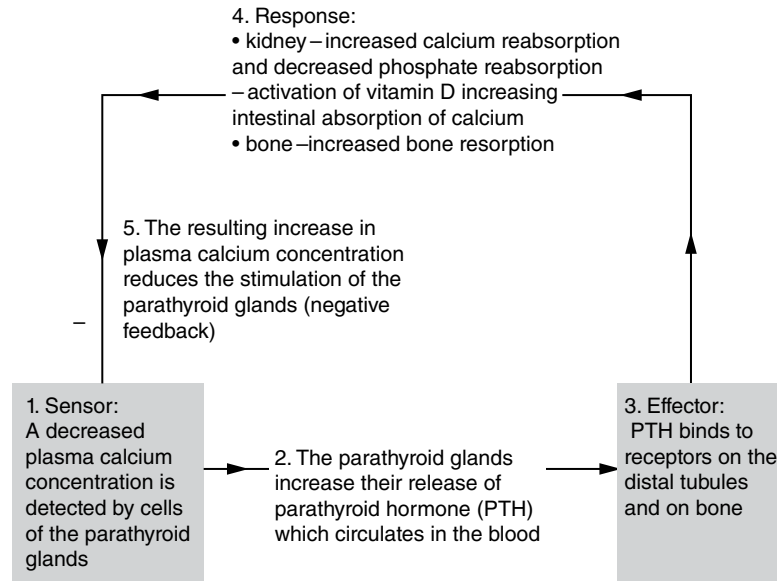


Figure 2.11 Negative-feedback loop for parathyroid hormone (PTH) release and calcium and phosphate control.

Acid–base control

Acid–base balance is about maintaining the constancy of the pH of the body's fluids. The pH scale is a logarithmic scale (range 1–14) that measures the concentration of free hydrogen ions in a fluid. In fact the scale is reciprocal, which means that as the pH becomes lower, the hydrogen ion concentration gets increasingly greater. Thus at acidic pHs (below 7), the hydrogen ion concentration of the fluid is very high relative to that at basic pHs (above 7). In fact, for each point on the scale there is a 10-fold difference in the hydrogen ion concentration. When we consider that the normal pH range of our bodily fluids is between 7.35 and 7.45, this appears very narrow but actually represents over a 20% difference in the hydrogen ion concentration! It is doubtful we would tolerate a 20% change in our sodium ion concentration with such ease.

So what are acids and bases? Simply put, acids are molecules that in the right environmental conditions will give up or donate a hydrogen ion to the solution they are in, and a base is a molecule that mops up or accepts free hydrogen ions from the solution. Thus, in order to maintain a constant hydrogen ion concentration (and hence constant pH), both acids and bases need to be present in the solution to donate or accept free hydrogen ions as required. Acids and bases working together in this way to minimise changes in pH are called buffers.

Though there are several buffering systems in the body, including haemoglobin, plasma proteins, organic, and inorganic phosphates, the most important one physiologically is the bicarbonate buffering system, and it is this one that will be described.

Bicarbonate buffering system

To understand the bicarbonate buffering system, the following reaction sequence needs to be understood:



This equation explains how the components of the buffering system are generated in the plasma. Carbon dioxide is generated by cells as an end-product of metabolism and diffuses into the plasma. The CO_2 dissolves in water to form carbonic acid (H_2CO_3), which is the acid component of the buffering system. The carbonic acid, in turn, is in equilibrium with the hydrogen (H^+) and bicarbonate ions (HCO_3^-). This forms the basic component of the buffering system. This reaction sequence can run in either direction, thus if there is a build-up of CO_2 in the plasma then more carbonic acid will be formed and the reaction will be driven to the right in order that more bicarbonate ions can be formed to minimise changes in the pH. However, if an excess of hydrogen ions builds up (from metabolic processes) then the reaction will be driven to the left, resulting in CO_2 and water forming. The excess CO_2 can then be blown off in the lungs. Since this reaction sequence constantly runs backwards and forwards to maintain a constant pH, it follows that pH must be dependent on the relative proportions of CO_2 to bicarbonate ions. This can be shown in the following equation:

$$\text{pH} \propto \text{HCO}_3^- / \text{PCO}_2$$

Both components of this equation can be controlled by the body. The bicarbonate ion concentration is carefully controlled by the kidneys, whereas the PCO_2 is controlled by the lungs. Thus the lungs and the kidneys are the two main organs that together control the acid–base balance of the body.

Control of bicarbonate ion concentration by the kidney

Bicarbonate ions are freely filtered in the glomerulus. When the plasma bicarbonate concentration is normal (25 mmol l^{-1}) then all of the filtered bicarbonate is reabsorbed: 90% reabsorption occurs in the proximal tubule and 10% in the distal tubule. However, if plasma bicarbonate concentration is higher than normal then this excess bicarbonate is lost in the urine.

The reabsorption of bicarbonate ions in the nephron is not a straightforward transport of ions from the tubular fluid into the plasma as with other ions, but involves various chemical reactions inside the tubular wall cells. The filtered bicarbonate in the tubule undergoes the whole reaction sequence identified above for the bicarbonate buffering system so that CO_2 and water are formed. This is catalysed by the enzyme carbonic anhydrase, which is found in the brush border of the proximal tubular cells. The resulting CO_2 then diffuses into the tubular cell where it undergoes the same reaction sequence, reforming the bicarbonate ion plus a hydrogen ion. The hydrogen ion is secreted into the tubule to be excreted and the bicarbonate ion diffuses into the plasma. This process is sometimes referred to as bicarbonate ‘trapping’ (Figure 2.12).

This process preserves bicarbonate ions in the blood, but to excrete excess hydrogen ions, substances must take up these ions in the kidney tubule to prevent their reabsorption into the blood. This is the role of the phosphate ions HPO_4^{2-} and the ammonia ions (NH_3), both of which take up one hydrogen ion to form H_2PO_4^- and NH_4^+ respectively. The process also generates HCO_3^- ions which can be reabsorbed. NH_4^+ ions cannot readily diffuse back across cell membranes, so the H^+ ions are effectively trapped in the tubule lumen.

Correcting acid–base fluctuations in the healthy individual

Fall in plasma pH

This is a condition called acidaemia or, more commonly, acidosis. This problem arises when there are excess hydrogen ions in the body fluids. In the absence of respiratory or renal disease, the initial response to control pH is for the excess

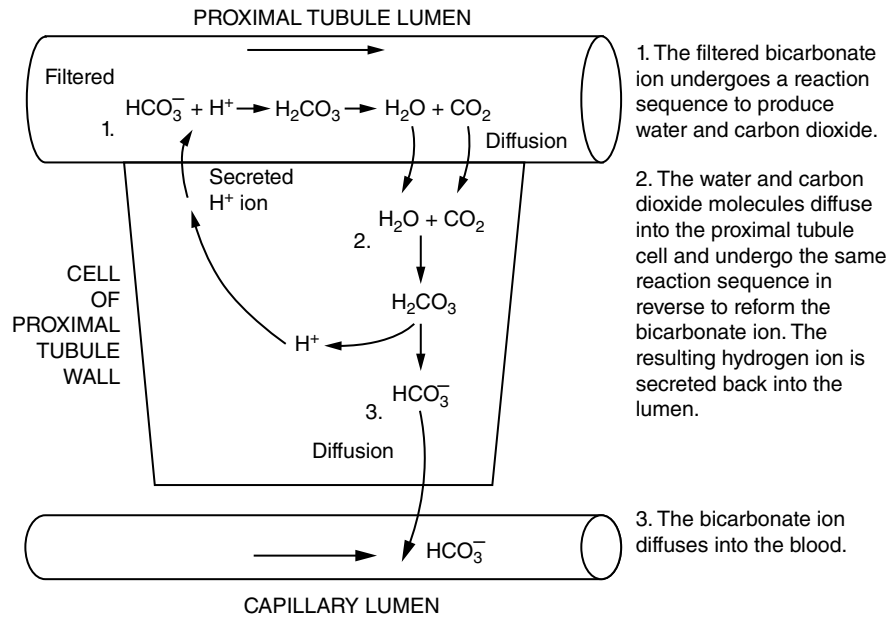


Figure 2.12 Bicarbonate reabsorption in the kidney tubules.

hydrogen ions to drive the bicarbonate reaction sequence to the left to produce CO_2 and water. The lungs can then deal with this excess CO_2 by increasing the respiratory rate to 'blow off' the CO_2 . This process gives a quick short-term compensation to the problem but not long-term correction. The rise in hydrogen ion concentration is then corrected by the kidneys secreting the excess hydrogen into the urine and in the process generating further bicarbonate for reabsorption into the plasma.

Rise in plasma pH

This condition is called alkalaemia or alkalosis, and arises when there is a reduction in the hydrogen ion concentration of the body fluids. The kidney plays the main role in correcting this problem by reducing the amount of hydrogen ion secretion. However, because hydrogen ion secretion and bicarbonate reabsorption are coupled together, this also results in a reduction in the plasma bicarbonate level. The plasma bicarbonate concentration is then corrected by a reduction in ventilation rate by the lungs, which leads to a build-up of CO_2 , which drives the reaction sequence to the right to generate more bicarbonate ions.

Though the above compensatory and correction processes buffer the small fluctuations that occur in the acid-base balance in the healthy individual, larger fluctuations in acid-base balance tend to occur when there is either respiratory or metabolic disease. This is because the normal correction mechanisms are blocked. For example, in disorders of ventilation, a respiratory acidosis or, rarely, alkalosis may develop, whereas in disorders of metabolism (including renal disease) a metabolic acidosis or alkalosis may develop. Descriptions of these disorders are beyond this chapter, but the reader is referred to Box 2.3 for a brief outline of the causes and symptoms of the metabolic acidosis of kidney disease.

Erythropoietin production by the kidney

The final important role that the kidney has is the production of the hormone erythropoietin. Erythropoietin is a glycoprotein that promotes the proliferation and differentiation of erythrocyte precursors in the bone marrow. Thus,

BOX 2.3**Metabolic acidosis****Causes of acidosis in established kidney disease**

- reduced renal excretion of acids.
- reduced renal reabsorption of bicarbonate.

Markers and symptoms

- fall in plasma pH (as hydrogen ion concentration rises).
- fall in plasma bicarbonate concentration.
- increased anion gap (difference between the plasma concentration of cations Na^+ and K^+ and anions Cl^- and HCO_3^-).
- possible hyperkalaemia which may lead to fatal cardiac arrhythmias.
- depressed central nervous system causing coma.
- respiratory compensation, hyperventilation (Kussmaul's breathing).
- possible development of renal bone disease.

erythropoietin is necessary for the maintenance of a normal red cell count and prevention of anaemia. The erythropoietin-producing cells of the kidney have been identified (at least in mice) as being intercalated cells of the collecting ducts in cortical nephrons, with peritubular cells apparently being involved in hypoxic conditions (Nagai et al. 2014). Erythropoietin production is stimulated by hypoxia and inhibited when the hypoxia is corrected, thus its production is controlled by the negative-feedback principle. The kidney is not the only site of erythropoietin production. Approximately 20% of erythropoietin is produced at extrarenal sites, thought mainly to be the liver. However, in the presence of severe renal disease, this extrarenal production of erythropoietin is insufficient to maintain the red cell count at normal levels, achieving only one-third to one-half the normal level. Anaemia is therefore a problem in most patients with chronic and advanced kidney disease, although this has now been overcome with the use of recombinant erythropoietin. See Chapter 6 for nursing management of anaemia in renal disease.

The relationship between blood pressure and renal function

Despite normal fluctuations in the systemic blood pressure, the kidneys are to some extent able to autoregulate the pressure of blood entering the glomerular capillaries. This ensures that the glomerular hydrostatic pressure remains constant and GFR is maintained. In addition the kidneys are the source of the hormone renin, which has a direct effect on blood pressure via the renin–angiotensin pathway (see Figure 2.9). If the blood pressure entering the glomerulus drops then more renin is released, resulting in a rise in systemic blood pressure.

If the filtering mechanism of the kidney is impaired by a drop in hydrostatic pressure within the glomeruli or by damage to glomerular tissue, the ability of the kidney to excrete nitrogenous waste products, and to regulate water and electrolytes, may be impaired. This will ultimately result in symptoms associated with renal failure, including fluid retention which leads to hypertension.

Conversely, if blood pressure is persistently raised (hypertension), there is a risk of damage to blood vessels throughout the body, but particularly those in the brain (leading to stroke), coronary vessels, and renal vessels. The renal artery (Figure 2.13), or smaller renal arteries, may become narrowed by arteriosclerosis (e.g. renal artery stenosis or renovascular disease). This will lead to impaired renal blood flow which will stimulate the release of renin, and the cycle of hypertension is worsened. Hypertension may therefore be both the cause and the result of kidney disease.

Blood pressure control

The control of hypertension is the treatment of priority in patients with chronic kidney disease in preventing the progression of renal failure and cardiovascular complications. Health education pertaining to cessation of smoking and alcohol, healthy eating, and regular exercise for weight control is just as important in patients with chronic kidney disease as in other patients with hypertension.

Conditions Causing Chronic and Advanced Kidney Disease

In this part of the chapter the reader is introduced to some of the common causes of chronic kidney disease and the altered physiology that results from, or may lead to, renal dysfunction. It is not intended as a complete guide to chronic kidney disease but as a starting point for understanding how important the kidneys are and how their function interacts with other body systems.

Chronic kidney disease is a result of a number of pathological processes causing irreversible damage to kidney tissue. There is a mass destruction of nephrons, so that the kidneys are unable to maintain fluid and electrolyte balance and excrete waste products from the body.

Chronic kidney disease is caused by a slow progressive decline over a course of many years (perhaps 10–20). There may be an insidious onset of renal failure with the minimum of symptoms developing in the patient on the approach to advanced kidney disease. Unlike acute kidney injury, where a full recovery of renal function can occur, in chronic kidney disease the kidneys are permanently damaged and the disease is usually progressive. According to the National Kidney Foundation Kidney Disease Quality Outcome Initiative (K-DOQI), chronic kidney disease is diagnosed when tests have persistently (for three months or more) shown a reduction in kidney function (eGFR less than $60 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$), or the presence of proteinuria, with an urinary albumin:creatinine ratio persistently greater than 3 mg mmol^{-1} (KDIGO 2012). See Chapter 6 for further explanation of stages 1–5 of chronic kidney disease.

The most common causes of advanced kidney disease resulting in renal replacement therapy in the UK are diabetes mellitus, glomerulonephritis, hypertension, pyelonephritis, polycystic kidney, and renal vascular disease (UK Renal Registry 2016).

Renal artery stenosis

Renovascular hypertension is high blood pressure due to narrowing of the arteries that carry blood to the kidneys (Marshall et al. 2014). This condition is also called renal artery stenosis. In renal artery stenosis there is a major reduction in renal perfusion. This alteration results in increased renin secretion and activation of the renin–angiotensin system. If left untreated, accelerated hypertension will develop, resulting in further pathological changes and damage to the kidneys. Conditions causing renal artery stenosis include:

- atherosclerosis: lipids and fibrous tissue lining the main renal artery and its larger branches.
- fibromuscular dysplasia: narrowing of arteries in the kidney (and other vessels including the carotid arteries). This principally occurs in young women.
- hyaline arteriolar sclerosis: thickening vessel walls due to the deposition of hyaline material, narrowing the lumen. This occurs naturally after 50 years of age

but is also seen earlier in diabetes. Obstruction to the renal blood flow can also be caused by:

- vasculitis: necrosis and inflammation of the vessel walls because of immunological changes.
- embolism: the kidney is a common site of embolism from circulating cardiac thrombi.
- thrombosis: intravascular coagulation in the arterioles and glomerular capillaries of the kidney, which will result in renal tissue infarction (Figures 2.14-2.15).



Figure 2.13 Conventional angiogram showing a normal right renal artery. Contrast material has been injected into the renal artery by means of a catheter, seen just to the right of the vertebral column.

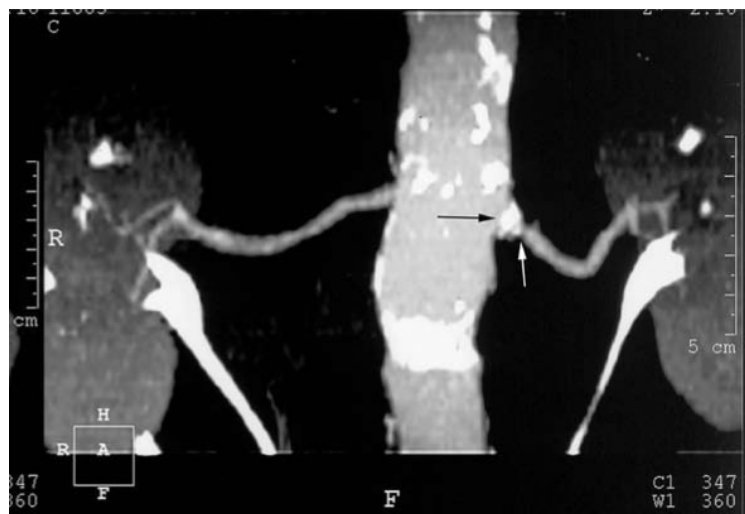


Figure 2.14 Computed tomography scan showing left renal artery stenosis. The black arrow points to a calcified plaque at the origin of the artery with narrowing of the artery distal to the plaque (white arrow). Heavy calcification is seen in the aorta (bright patches).

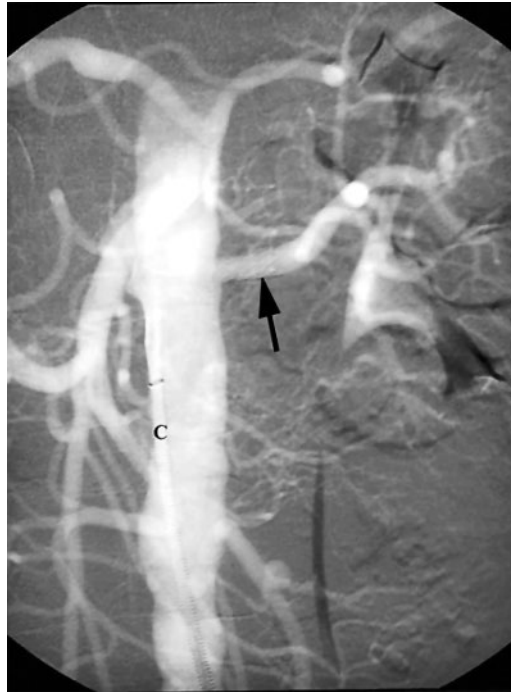


Figure 2.15 Digital subtraction angiogram of the same patient shown in Figure 2.14 following treatment by insertion of a metallic stent (black arrow) to improve the blood flow to the left kidney. C, catheter.

Disease Progression and Prognosis

Hypertension resulting from renal artery stenosis may be treated by drugs to reduce blood pressure or by lipid-lowering treatment. The stenosis itself can be treated by angioplasty of the renal artery with intra-arterial balloon catheters, by insertion of a stent, or by surgical bypass of the narrowed vessel (McLaughlin et al. 2000). A Cochrane review of medical therapy versus balloon angioplasty (with or without stenting), carried out in 2014, did not identify significant differences between the treatments (Jenks et al. 2014). The European Society of Cardiology (2017) has produced guidelines on treatment.

Nephrosclerosis

Hypertension can cause nephrosclerosis and is a major precipitating factor of renal disease. Hypertension that is not treated leads to sclerosis of the renal arterioles and the blood supply to glomeruli, tubules, and interstitium gradually decreases. Scar tissue develops in the kidney, resulting in loss of renal function and eventually chronic kidney disease.

Nephrotic syndrome or nephrosis

The nephrotic syndrome is not a disease, but a collection of symptoms. It is characterised by:

- heavy proteinuria (greater than 3.5 g in 24 hours)
- serum albumin $<25 \text{ g l}^{-1}$
- protein:creatinine ratio $>350 \text{ mg mmol}^{-1}$
- severe and generalised oedema.

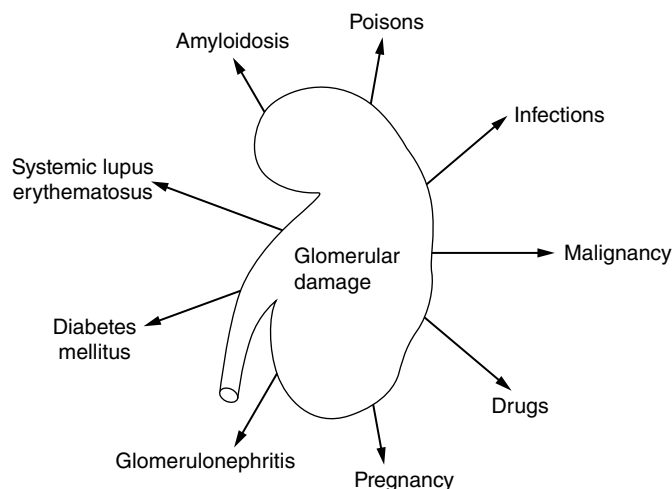


Figure 2.16 Causes of the nephrotic syndrome.

The nephrotic syndrome may develop in a patient with a primary renal disease of unknown cause (idiopathic nephrotic syndrome) or it may be associated with other conditions in which kidney involvement is secondary, such as amyloidosis or diabetes mellitus (Figure 2.16).

Pathology of nephrotic syndrome

The nephrotic syndrome is the result of glomerular damage increasing the glomerular basement membrane permeability, allowing large amounts of small albumin molecules to pass through into the urine. It should be remembered that the size of the albumin molecule is just at the cut-off point in size of particle which may pass through the glomerular filter (see Figure 2.5). As the disease progresses, larger-molecular-weight proteins leak through the glomerular basement membrane and GFRs may also reduce as the glomerular damage increases.

As the protein continues to be excreted, the serum albumin decreases (hypoalbuminaemia). This in turn leads to a low BCOP and diffusion of fluid into the tissue spaces causing generalised oedema.

A reduction in the circulating blood volume stimulates the release of renin from the kidney, resulting in more aldosterone being released from the adrenal cortex, which is responsible for the retention of sodium and water. Retained fluid also passes out of the capillaries into the tissue, causing more oedema (Figure 2.17).

In the early stages of the nephrotic syndrome, the protein leak may be the only disorder of renal function, but with some glomerular lesions, the disease progresses and nephrons are destroyed. This will lead to established renal failure and the patient will require dialysis.

Clinical features and management of care of nephrotic syndrome

Oedema

In the early stages of the nephrotic syndrome, swollen eyes at the start of the day and swollen feet and ankles at the end of the day may be observed. As the disease progresses, or as a result of poor symptom control, the oedema becomes more generalised, causing pleural and peritoneal effusions resulting in breathlessness and congestion of the gastrointestinal tract.

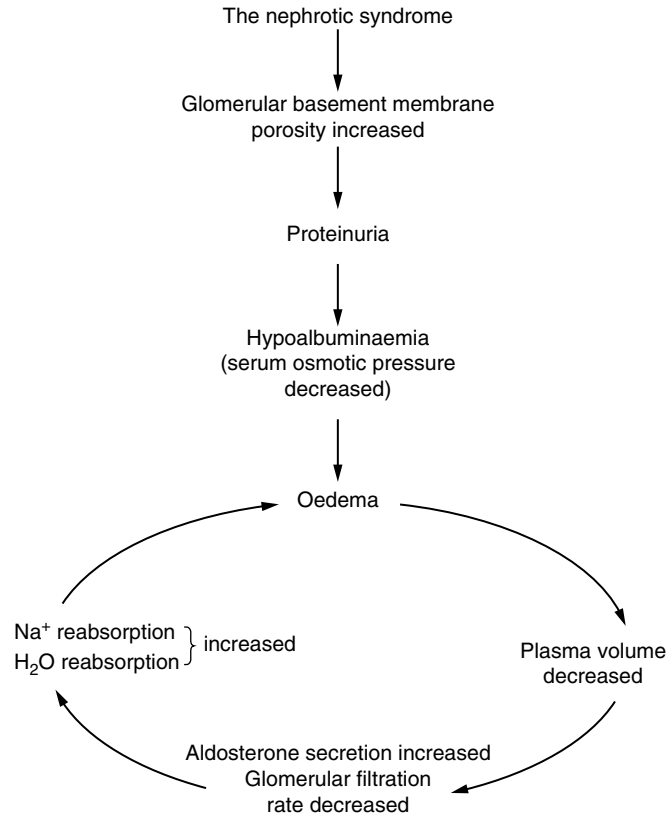


Figure 2.17 Oedema formation in the nephrotic syndrome.

Fluid removal will be the treatment of priority for patients, but diuretic therapy needs to be administered carefully as profound hypoalbuminaemia may cause a reduced circulating blood volume, triggering a hypotensive response in some patients following the administration of large doses of intravenous diuretics. Infusions of small volumes of intravenous salt-poor albumin prior to the administration of diuretics will increase plasma volume and restore a diuretic response in the patient. In the majority of patients the albumin is excreted after 24–48 hours.

All patients with severe oedema and receiving aggressive diuretics should be weighed daily and have four-hourly lying and standing blood pressure recordings to observe for deficits caused by a reduced plasma volume.

Proteinuria

Urine has a frothy appearance due to the high protein content (losses greater than 3.5 g in 24 hours) and as a consequence hypoalbuminaemia develops. The loss of immunoglobulins increases the risk of infection. Hyperlipidaemia is also a clinical sign of the nephrotic syndrome, as a result of the liver synthesising more cholesterol and lipids. This makes the plasma milky in appearance.

Muscle wasting

The loss of skeletal muscles becomes apparent when the generalised oedema has subsided. Muscle wasting is a result of protein mobilisation into the blood to counteract protein lost in the urine.

Weight loss and malnutrition

Chronic nausea, vomiting, and poor appetite may result from congestion in the gastrointestinal tract due to oedema. Weight loss also results from proteinuria and muscle wasting.

A dietetic referral should be made, and the patient encouraged to take a high-calorie diet with a protein allowance compensating for the protein loss.

Tiredness and lethargy

These symptoms may be attributed to a combination of reduced calorie intake, muscle wasting, and the generalised oedema which may increase body weight by up to 10 kg. Patients should be encouraged to take plenty of rest.

Intravascular clotting

There is a risk of spontaneous intravascular clotting in a patient with nephrotic syndrome due to the increase in circulating clotting proteins along with venous stasis in the legs and a reduction in plasma volume.

During episodes of hospitalisation and immobility, prophylactic anticoagulants may be used (for example, subcutaneous heparin). The use of antiembolic stockings increases venous return and reduces venous stasis.

Care for those with nephrotic syndrome can be very challenging for the renal care team.

Children

Nephrotic syndrome in children can lead to frequent infections, hypoproteinaemia, and oedema. The use of corticosteroids has reduced mortality rates to around 3% (Hodson et al. 2007), although some cases are resistant to steroid treatment, in which case immunosuppressants may be used (Ulinski and Aoun 2012).

Diabetic kidney disease

Diabetic nephropathy is the term used to describe damage to the kidney structure and function that occurs as a result of the long-term complications of diabetes mellitus. Type 1 and Type 2 diabetes mellitus are characterised by raised blood glucose levels and sustained hyperglycaemia. High glucose concentrations induce specific cellular effects, which affect various kidney cells including endothelial cells, smooth muscle cells, mesangial cells, podocytes, cells of the tubular and collecting duct system, and inflammatory cells and myofibroblasts (Forbes and Cooper, 2013). There is evidence of a heritable susceptibility to developing diabetic nephropathy, but as yet no identifiable genetic cause has been identified (Brennan et al. 2013). Glycosylation of proteins occurs, glycosylated haemoglobin (HbA_{1c}) being an example. These biologically active molecules are known as advanced glycosylation endproducts or AGEs, and it is thought that these compounds contribute to vascular tissue damage. Patients with diabetes are therefore at increased risk of suffering micro and macro vascular damage resulting in a range of cardiovascular, renal, and other sequelae. Diabetic kidney disease develops in 30–40% of patients with Type 2 diabetes and in 2015, diabetic renal disease remained one of the single most common cause of renal failure (UK Renal Registry, 2016).

Pathology

Patients initially develop microalbuminuria, i.e. 30–300 mg 24 h⁻¹. This may not occur for up to 10 years after diagnosis of type 1 diabetes mellitus, but diabetes

mellitus may go undetected for so long that microalbuminuria or proteinuria is present at diagnosis of diabetes. After one to five years, proteinuria becomes clinical, even to nephrotic levels ($>3.5 \text{ g day}^{-1}$). With good blood pressure and glycaemic control, and with prescription of ACE inhibitors or angiotensin receptor blockers (ARBs), it is possible to delay the progression from micro to macroalbuminuria and to slow the decline in GFR. The first line of treatment for controlling the progression of diabetic nephropathy is tight glycaemic control, along with the use of angiotensin-converting enzyme inhibitors (ACEI) to control blood pressure (Thomas and Karalliedde 2015).

The kidneys may be of normal size or slightly larger than normal. In Type 1 diabetes the most important structural changes involve the glomerulus, whereas in patients with Type 2 diabetes, tubulo-interstitial and vascular lesions are more common (Vestra and Fioretto 2003). The pathologies associated with diabetes mellitus are:

- pyelonephritis, the most common lesion found in those with diabetes mellitus, causing chronic kidney disease and a result of autonomic neuropathy in the bladder;
- diffuse intercapillary glomerulosclerosis, causing thickening and sclerosis of the basement membrane of the glomerular capillary and proliferation of the mesangial cells;
- the glomerulus becoming increasingly replaced and destroyed by the deposition of nodules of a glycoprotein material – nodular glomerulosclerosis (or Kimmelstiel–Wilson nodules);
- arteriosclerosis develops in the arteries supplying the glomerulus due to hyaline deposits in the afferent and efferent arterioles, causing ischaemia and accelerating the disease process;
- papillary necrosis.

Diabetic nephropathy and glucose control

The kidneys have an important role in the metabolism of insulin and, as the GFR decreases in renal failure, so does the delivery of insulin to the proximal tubule cells where it is metabolised. Consequently, the circulating half-life of insulin increases with higher levels in the body after any given dose. Insulin requirements or oral hypoglycaemic agents should therefore be decreased so that hypoglycaemia does not occur.

Intensive diabetes management with the goal of achieving near-normal blood glucose levels has been shown to delay the onset of microalbuminuria in Type 1 and Type 2 diabetes. The American Diabetes Association (2016) has published a position statement on diabetic nephropathy which has useful care recommendations. Early diagnosis of diabetes is also important. Finne et al. (2005) found that children diagnosed with diabetes before the age of five years have the most favourable prognosis in terms of progression to established renal failure.

Glomerulonephritis

The term glomerulonephritis covers a group of conditions in which inflammation in the glomerulus occurs, either as a primary disease, or as part of a systemic illness. It is therefore important to consider the possibility of an underlying systemic condition if glomerulonephritis is diagnosed. See Cunard and Kelly (2003) for further reading.

Glomerular disease occurs when the structure or function of the glomerular capillary network has been damaged as a result of antigen–antibody reactions in the glomeruli.

There are contributions from lymphocytes, macrophages, antibodies, immune complexes and inflammatory mediators. The glomerular cells may proliferate, basement membrane thicken or exudates of leukocytes and platelets build up in the glomerulus. These tissue reactions result in changes in the filtration properties of the glomerulus, leading to proteinuria, haematuria, impaired excretory renal function and hypertension.

Any age group may be affected, though some types are particularly common in children. The estimated incidence of glomerulonephritis is 0.2–2.5/100 000 year⁻¹, rising to 6.2–15.6/100 000 year⁻¹ for minimal change disease in Asian children (McGrogan et al. 2011). See Box 2.4 for histopathology.

Treatment

In some cases, an underlying cause of the autoimmune response can be identified and eradicated. For example, drugs, tumours, or infectious agents (e.g. streptococci) may result in glomerulonephritis, which may resolve on removal of the tumour or drug. Treatment for glomerulonephritis tends to involve anti-inflammatory and/or immunosuppressive drugs. In rare conditions with rapid deterioration of renal function, plasma exchange may be used.

The prognosis depends to a large extent on the particular subtype of glomerulonephritis, identified by the pattern of glomerular injury involved.

Subtypes of glomerulonephritis

- minimal-change glomerulonephritis (renal biopsy normal by light microscopy).
- membranous glomerulonephritis.
- mesangial proliferative nephritis.
- focal segmental glomerulosclerosis.
- crescentic glomerulonephritis (associated with syndrome of rapidly progressive glomerulonephritis).
- mesangiocapillary glomerulonephritis (MCGN).
- post-infection glomerulonephritis.

Minimal-change glomerulonephritis

The condition is so named due to the essentially normal appearance of the glomeruli under the light microscope. It most often presents in children aged between two and four years of age, and accounts for 90% of cases of nephrotic syndrome in children. The condition is very rarely associated with impairment of excretory renal function and is occasionally secondary to drug use (particularly nonsteroidal anti-inflammatory drugs [NSAIDs]) or malignancy (e.g. lymphoma).

Severe oedema may be present but without associated hypertension.

Management of care Diuretic therapy will clear the oedema. Most patients respond to high-dose corticosteroids, but relapse is common as the dose is reduced, and up to 50% of patients remain corticosteroid-dependent. In these patients, alkylating agents such as cyclophosphamide are sometimes successful. Ciclosporin is also effective (Macanovic and Mathieson 1999).

Prognosis Subsequent relapses in the condition can be treated with similar protocols. Patients do not usually develop chronic kidney disease.

Membranous glomerulonephritis

These patients typically present with proteinuria which may be asymptomatic or severe enough to cause nephrotic syndrome. Microscopic haematuria, hypertension, and/or impaired excretory renal function may also be associated. It is seen in adults rather than in children. Onset is insidious and the disease develops slowly, over the course of 20 years in some cases.

BOX 2.4**Glomerular disease**

Glomerulonephritis is the term used to describe a variety of disorders that principally affect the glomeruli in the kidney. Such glomerulopathies may arise as primary disorders of the glomerulus, or as part of a systemic disorder such as systemic lupus erythematosus (SLE) or diabetes mellitus.

Histopathology

Glomerular damage may be manifest as one or more of the following tissue reactions:

- cellular proliferation – leading to an increase in the number of cells in the glomerular tufts.
- leukocyte infiltration of inflammatory cells – mainly neutrophils and monocytes.
- basement membrane thickening – as occurs in diabetes mellitus, or this may be a response caused by precipitated immune complexes.
- hyalinisation and sclerosis – hyalinisation is the accumulation of homogeneous, amorphous substance in the glomerular tuft composed of mesangial matrix, basement membrane, and plasma protein. Sclerosis is the total obliteration of structural detail in the glomerular tuft and is the end result of glomerular damage.

Clinical manifestations

Clinical presentation of glomerular disease may range from an acute onset of disease with a reversible outcome, to a chronic insidious onset that eventually leads to renal failure after several decades. A number of syndromes of glomerular disease are defined:

- proteinuria – occurs if the glomerular basement membranes are damaged so that they leak protein.
- nephrotic syndrome – occurs if the basement membranes are damaged more severely and increase the protein leak to greater than 3.5 g protein 24 h⁻¹. This in turn induces a low serum albumin and generalised oedema. Hyperlipidaemia usually also occurs.
- haematuria – occurs if capillary walls are disrupted, allowing red cells to pass into the urine. This may be microscopic or macroscopic. However, most forms of haematuria are non-glomerular in origin.
- nephritic syndrome – occurs when basement membrane damage and red blood cell leakage are present together, leading to proteinuria and haematuria, accompanied by generalised oedema and mild hypertension.
- established renal disease occurs when damage to the glomeruli is severe enough to impair the normal filtering function of the glomerulus, resulting in an accumulation in the blood of substances such as urea, creatinine, and potassium.

Specific nursing observations

Parameter	Rationale
Temperature	Patients with nephrotic syndrome are prone to infection, which exacerbates the disease if not detected and treated promptly.
Blood pressure	Hyper- or hypotension may be present, dependent on the patient's fluid and cardiac status. One should also monitor for a postural drop.
Respiration	Rapid, shallow breaths may indicate pulmonary oedema. Severely acidotic patients may develop Kussmaul's respirations (deep, sighing hyperventilation).
Daily weight	Serial measurements of the patient's weight (at the same time each day) give the clearest indication of changes in fluid status.
Urinalysis	The urine should be tested for protein and blood as indicators of glomerular disease. Urinary volume should also be monitored, and the urine sent for culture if infection is suspected.
Skin	The skin should be observed for oedema, dehydration, pruritus, flaking and dryness, pressure sores, and rashes. A skin rash may indicate a systemic disease such as SLE, vasculitis, or Henoch–Schönlein purpura.

There is widespread thickening of the capillary wall in the glomerulus (but without proliferation of the cells), which seems to result from the deposition of immune complexes in the kidney. This can occur as a result of drug use (particularly NSAIDs, gold, and penicillamine), secondary to tumours (e.g. carcinoma of bronchus or breast), infection (particularly hepatitis B), or hypothyroidism.

Management of care The prognosis of the secondary forms of the disease depends on the prognosis of the underlying condition. Complete resolution may be expected on withdrawal of the offending drug, whereas membranous glomerulonephritis, which is secondary to a tumour, has a poorer prognosis unless the tumour is eradicated.

At least 25% of patients undergo spontaneous remission of proteinuria without treatment. For those with a poorer prognosis, a combination of treatment with a steroid and an immunosuppressant (chlorambucil) given in alternating cycles may prove beneficial. There is a particular risk of thrombosis in membranous glomerulonephritis, so anticoagulants may also be prescribed (Macanovic and Mathieson 1999).

Prognosis GFR may be normal for the first few years, but then may slowly deteriorate as the sclerosis of the glomerulus increases. If no primary cause of the disease is found and eradicated, dialysis or organ transplant may be inevitable in the long term.

Mesangial proliferative nephritis

This is the most common type of glomerulonephritis worldwide. Patients present with haematuria, sometimes with associated proteinuria, hypertension, and impaired renal excretory function. The immunoglobulin IgA is deposited in the glomerulus, and there is sometimes proliferation of the glomerular cells. The cause of the deposits is not known, but it seems the problem is in the IgA system rather than in the kidney. An associated glomerular change is seen in Henoch–Schönlein purpura, a condition more common in children which is associated with a purpuric rash, joint, and gastrointestinal involvement.

Management of care There is no proven treatment for this form of glomerulonephritis, although in patients with heavy proteinuria, steroids may be used successfully to reduce the protein loss. Antihypertensives (for example, ACEI) may also be used.

Focal segmental glomerulosclerosis

This condition is named after the areas of scarring which occur in the glomeruli. The sclerotic changes affect some glomeruli but not others (focal) and may affect only parts of each glomerulus (segmental). The patient will typically present with nephrotic syndrome (hypertension, haematuria, impaired excretory renal function).

Management of care and prognosis for the patient Treatment with prolonged courses of corticosteroids may induce remission of nephrotic syndrome, but the disease often progresses and established renal failure develops in about 50% of patients within 10 years.

Crescentic glomerulonephritis

Also known as rapidly progressive glomerulonephritis, this condition is associated with rapid but progressive deterioration in renal function and the presence of oliguria or anuria. Haematuria and proteinuria also occur. In Goodpasture's syndrome, auto-antibodies are directed against collagen – a major structural component of the glomerular basement membrane. Up to half of those with Goodpasture's disease also have pulmonary haemorrhage. Without effective treatment, established renal failure will develop in weeks and months, rather than years.

Acute inflammation in the glomerulus is the underlying cause, sometimes with the formation of crescents when the glomerulus is squashed by cells which fill the Bowman's space. In some cases, antibodies to the glomerular basement membrane are present but, in most cases, no immunoglobulin is identified in the glomerulus.

Management of care and prognosis Plasma exchange followed by corticosteroid and immunosuppressant therapy will remove the offending antibodies and prevent further proliferation. The prognosis in these cases is directly related to the amount of damage already done to the glomeruli.

Mesangiocapillary or membrane-proliferative glomerulonephritis

Three subtypes of this condition are recognised, identifiable only by electron microscopy. In all cases the presentation of the patient is similar, with proteinuria, haematuria, hypertension, and impaired renal function. There are no known causes. All types tend to have a progressive course, and up to 50% of patients develop chronic kidney disease within 10 years.

Treatment focuses on blood pressure control and use of corticosteroids.

Post-infection glomerulonephritis

Poststreptococcal glomerulonephritis (for example, following a throat infection) was a common cause of renal failure in the preantibiotic era and is still common in some parts of the world. Immune complexes which arise following infection with group A haemolytic streptococci deposit in the glomerular capillary wall, resulting in proteinuria, haematuria, and hypertension.

Glomerulonephritis may complicate infection with a range of organisms. Infection with *Staphylococcus*, influenza B, hepatitis B and C, and human immunodeficiency virus (HIV) may all result in renal damage.

Pyelonephritis

This is a bacterial infection of kidney tissue, with the infection beginning in the lower urinary tract and ascending to the kidney(s). Acute pyelonephritis is commonly associated with pregnancy, obstruction, instrumentation, or trauma to the urinary tract and in patients with a chronic illness.

Chronic pyelonephritis is the result of repeated infections of the urinary tract. There is widespread destruction of nephrons and replacement with scar tissue, which eventually causes established renal failure. For the majority of patients, the disease starts in early childhood and is due to ureteric reflux and infection, but symptoms of the disease may not present clinically until adulthood. In adults, chronic pyelonephritis is a complication of obstruction in the renal tract, because stone formation and structural abnormalities both cause stasis of urine.

Clinical features and management of care

The patient will present with pyrexia and rigours and loin pain over the affected kidney(s). Symptoms of a lower urinary tract infection may also be present.

Antibiotics can be given to treat the acute phase of the infection, but there is little evidence to prove that prophylactic antibiotics slow down the onset of chronic kidney disease. A high fluid intake (up to 3 l day⁻¹) is important.

Disease progression and prognosis

If the chronic infections are only affecting one kidney, the disease is usually prolonged but benign. Bilateral chronic infection will ensure that chronic kidney disease is of rapid onset.

Reflux nephropathy is a congenital anatomical abnormality where there is incompetence of the sphincter at the junction of the ureter with the bladder, allowing the reflux of urine back up the ureter and into the renal pelvis. Infection may develop and the formation of scar tissue will eventually cause chronic kidney disease. If identified early, surgical correction will be needed. Recurrent urinary tract infection during childhood should always be fully investigated and treated.

Polycystic kidney disease

Polycystic kidney disease is one of a number of cystic diseases of the kidney. Polycystic disease refers to two hereditary cystic diseases: autosomal recessive polycystic kidney disease (ARPKD) and autosomal dominant polycystic kidney disease. Both conditions may occur in children, although the recessive disease is more commonly seen in this age group. The following descriptions will refer to autosomal dominant polycystic kidney disease, one of the most common genetic disorders, which is responsible for approximately 10% of patients with end-stage renal failure.

Genetics

The autosomal dominant form of the disease is one of the most common genetic disorders, affecting an estimated 1:400–1000 of the population. The condition occurs equally in men and women and is transmitted by both sexes. Whilst most patients have an affected parent, 10% of cases can be traced to a *de novo* mutation (Harris and Torres, 2014). Symptoms may not develop until patients reach their 20s; the mean age of starting dialysis treatment is 57 years. However, by the age of 80, virtually all individuals who carry the gene will manifest some form of the disease. Mutations in either of two genes PKD1 or PKD2, which code for proteins polycystin-1 and 2, are responsible for the condition (Calvet and Grantham 2001).

ARPKD is a severe, inherited disorder of the kidney that typically presents in the neonatal period with an incidence of approximately 1/20 000. Most affected children die within the first few hours of life, although a number of patients present in later childhood, or as adults. To date, only one gene (PKHD1) has been identified in the inheritance of ARPKD, although there is evidence for locus heterogeneity, making interpretation of genetic screening complex (Bergmann 2015).

Pathology

Both kidneys are considerably enlarged and consist of a compact mass of cysts which are scattered equally throughout the cortex and medulla (Figure 2.20). The cysts increase in size and eventually rupture, allowing infection and scar tissue formation, and reducing the number of functioning nephrons. The enlarged cysts compress the normal renal tissue and hypertensive changes and glomerulosclerosis occur. Cysts are filled with watery fluid which may be clear, blood-stained from a recent haemorrhage, brown from an old haemorrhage, or filled with pus (Figures 2.18–2.20).

Liver cysts may be found in patients with polycystic kidneys and there is also a significant association with aneurysms of the cerebral arteries.

Clinical features and management of care

- pain: the patient may complain of abdominal distension or discomfort following minor physical trauma and this may cause frank or microscopic haematuria. Pain in the flank is associated with the large cysts rupturing and any blood clots that are passed will cause the patient to experience colic. Mild analgesia may be sufficient to relieve discomfort, but pain caused by cysts rupturing or from clot retention may require opiates.

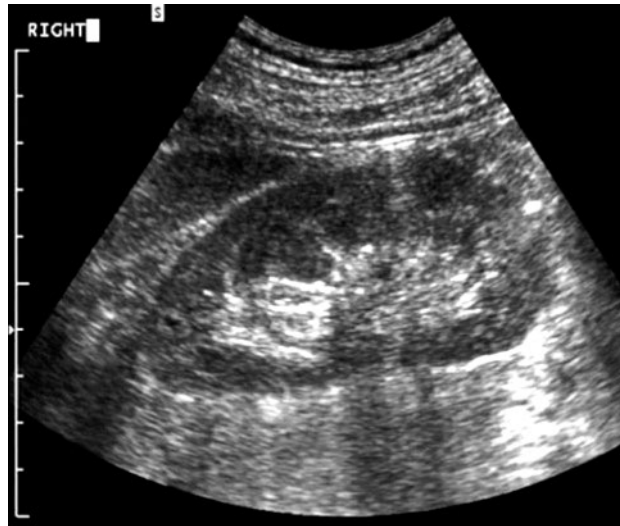


Figure 2.18 Ultrasound of a normal right kidney.

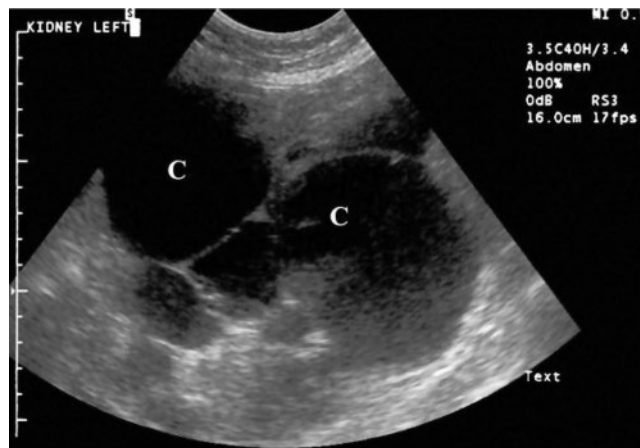


Figure 2.19 Ultrasound of a polycystic kidney showing how the normal tissue is replaced by multiple fluid-filled cysts (C).

- haematuria and proteinuria: microscopic or frank haematuria is seen in more than 50% of patients. Chronic blood loss does not usually result in anaemia because the erythropoietin production by the kidneys is increased. Patients may be advised to alter their lifestyle if they are prone to physical abdominal trauma which may cause cysts to rupture. Mild proteinuria is always present in the mid to late stages of the disease and may be the first abnormality that draws attention to the condition during a routine medical examination.
- urinary tract infections: repeated urinary tract infections are common complications, and may affect the cysts. Unnecessary urological investigation should be avoided and female patients should receive health education regarding perineal hygiene. All patients should be advised on the importance of a high fluid intake to prevent urinary stasis and how to recognise the signs of a urinary tract infection.
- hypertension: secondary hypertension is common in patients with polycystic disease and may deteriorate as established renal failure approaches. It is treated

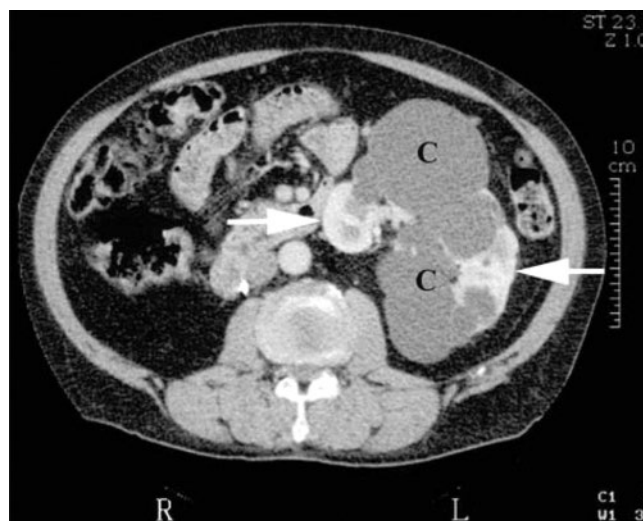


Figure 2.20 Computed tomography scan showing a polycystic left kidney; the cysts are marked by C. The white arrows point to normal renal tissue. The right kidney has been removed.

aggressively, not only because it may accelerate deterioration of renal function, but because it may increase the risk of intracerebral haemorrhage in these patients (Ecder et al. 2000).

Multisystem diseases affecting the kidney

The kidney may be affected in many ways by disease processes that are not directly associated with renal function. This vulnerability is, in part, due to the high blood supply of the kidneys; together the kidneys receive 25% of the cardiac output. The glomerular capillaries, because of their filtering properties, come into close contact with all blood constituents.

The effects of diabetes mellitus and of systemic infections in the kidney have already been mentioned. The following are some more examples of multisystem diseases which may affect the kidney.

Systemic lupus erythematosus

This is an autoimmune inflammatory disease which affects joints, blood vessels, skin, and the nervous system, as well as the kidneys. Glomerular inflammation may result in proteinuria, haematuria, and hypertension; renal involvement often occurs within three years of diagnosis of the disease. Nonrenal manifestations of the disease are usually present, such as arthralgia, rash, and haematological disorders. It can be treated using immunosuppressants and steroids (Bertsias et al. 2012)

Renal amyloidosis

Amyloidosis is the term given to a group of chronic infiltrative disorders characterised by the presence of deposits of an abnormal protein called amyloid. Two groups of protein deposit exist – AL amyloid or AA amyloid – but renal involvement occurs with both. AA amyloid deposits are a complication of many chronic inflammatory diseases, occurring in up to 10% of patients with rheumatoid arthritis; AL amyloid deposits may occur secondary to myeloma or as the primary condition, AL amyloidosis. This is a systemic disease which affects the heart, peripheral nervous system, liver, and kidney. AL accounts for up to 86% of renal amyloidosis cases (Kidd and Carl, 2016).

A common site of deposition of the insoluble amyloid fibrils is in the walls of the renal arterioles and glomerular capillaries. The result is usually nephrotic syndrome followed by progressive renal failure. Ten-year individual survival rate is about 20% (Sasatomi et al. 2007).

Scleroderma or systemic sclerosis

This is a multisystem condition which causes gradual hardening and tightening of the skin and increased binding to subcutaneous tissue. Renal involvement is one of the less common but most serious complications of the disease and, in the past, was a major cause of mortality. Patients often present with the features of malignant hypertension and rapidly deteriorating renal function. Diastolic pressure may exceed 130 mmHg. Antihypertensives, particularly ACE inhibitors, improve the renal outlook of these patients, but there is no treatment for the underlying condition.

Polyarteritis nodosa

More common in men than women, this condition usually presents in later life. It is characterised by widespread inflammation of small and medium arteries and aneurysm formation. Thrombosis in these arteries can lead to complications which particularly affect the gut, peripheral nervous system and kidneys. The renal presentation is that of progressive renal impairment caused by renal infarction and hypertension. Treatment is with corticosteroids, and renal prognosis depends on early diagnosis and treatment since organ damage is irreversible.

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Resources

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CHAPTER 3

Patient and Carer Involvement in Renal Nursing Care, Education, and Research

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Learning Outcomes

- to explain what is meant by patient involvement.
- to understand the challenges faced by patients and carers during predialysis, dialysis, and transplantation.
- to identify how patients and carers can be involved in renal nursing education.
- to review the policy guidance on involving patients and carers in renal nursing research.

Introduction

This chapter aims to provide the reader with an insight into how patients and carers can have a more participatory role, not only in the planning, delivery, and evaluation of their care but also in the teaching of nurses and involvement in renal research and quality improvement programmes. It has been written by people who have kidney disease and who feel passionate about improving the nursing care that is given to everyone with the condition, whether they be contemplating dialysis options, undergoing dialysis, or receiving a kidney transplant. Parts of the chapter have been written in the first person as they are based on personal experiences and it was felt that key messages in this chapter are more powerful if described in this way.

The chapter includes case studies and learning activities that will assist the reader to make sense of, and learn about, patient and carer partnership and involvement. The driving theme is that there should be ‘no decision about me, without me’, epitomised in the White Paper, *Equity, and Excellence: Liberating the NHS* (Department of Health 2010), which emphasised shared decision-making and promotion of partnership.

Patient Involvement in Care

‘Patient involvement’ is a complex concept, and the term is sometimes used interchangeably with ‘partnership’ and ‘participation’, although these similar terms are slightly different. Generally, patient involvement can be described as ‘approaches which engage individual patients in the management of their health and healthcare and in the decisions that are made in the course of it’ (National Voices 2018).

Recently, the Care Quality Commission in England has published a report ‘Better Care in My Hands’, which looks at how people are being involved in their own care (CQC 2016). The report’s key conclusions were that just over half of patients definitely felt involved in decisions about their health care and treatment, although there has been little change in people’s perceptions of how well they are involved in their health or social care over the last five years. A significant minority of people have consistently reported only feeling involved in their care to some extent or not at all over this period.

Patient-Reported Experience Measures

In 2016 a pilot patient experience survey was developed by Kidney Care UK and the UK Renal Registry. The questions to be asked were devised by patients, ranging from access to the renal team, being treated with dignity, and quality of transport. 8500 patients across 39 units responded to the paper survey, which showed a reasonably positive experience but transport, the environment, and sharing decisions about care showed the most variation and came out lowest.

The survey was repeated in 2017, with the questions having been validated by the University of Hertfordshire and the survey available in paper and online form and translated into Welsh, Urdu, and Gujarati. This time 56 of the 57 units in England and Wales (11 500) completed the survey and the key finding was that the unit in which a patient is treated is the most important thing influencing experience of care. Analysis by age, sex, ethnicity, and stage of disease showed no significant difference in experience based on those characteristics.

In 2017, ‘sharing decisions about your care’ was the lowest-rated item, even lower than transport experience and needling, a new item introduced for 2017. Patients are encouraged to discuss their unit’s results with their medical team but the strongest encouragement is for clinicians to consider what they can learn from the PREMs (Patient-Reported Experience Measures) work and look to improve patient experience. This survey is planned to run every year from now on. Full results can be found at <https://www.renalreg.org/projects/prem> (accessed 23 June 2018).

Although most nurses, if questioned, have welcomed the idea of patient involvement in their care, many patients may not see it that way. The chapter includes three case studies (Case Studies 3.1–3.3) where the patients, and in one instance a carer, describe care and management that did not always involve them and discuss ways in which the nursing care could have been improved. It also includes a case study (Case Study 3.4) on patient and carer involvement in research and quality improvement.

Case Study 3.1: Thoughts of a patient undergoing dialysis and a transplant

I have had kidney disease for 37 years. Having been diagnosed with renal arteriolar stenosis in 1977, I received my first kidney transplant from my mother in 1988. That kidney settled down within 12 months and I was fortunate to spend the following 18–19 years in relative good health, working, helping my wife bring up a young family, and travelling the world over. In 2006, my kidney began to fail and I took early retirement from my job in June 2007. I went into end-stage renal failure in 2008 and began what turned out to be three-and-a-half years of haemodialysis. Late in August 2011, I received a call to say that there was a possibility of a kidney for me. Twelve months after the operation, I began to lead a new life again with my wife, with the opportunity once again to travel and to do those things that I have been unable to do for so long.

I would like to share my experiences of the care I have received over the years, both of the good things, of which there have been many, but also those things that I believe could be improved.

Renal care has different requirements from many other medical conditions, as it very often supports a situation that is chronic and does, therefore, enable a whole life relationship to develop between the patient and the medical team. This, to me, should be the core of renal care. Over the years I have received excellent care, but there have been occasional lapses. It is rarely due to a lack of medical knowledge or experience; it is much more a straightforward lack of understanding of the patient's needs and concerns. Although I will largely restrict myself to my more recent experiences, it is worth recalling my shock and horror when I was told, having been an outpatient for a number of years in the mid-1980s and fully believing that I could happily continue as an outpatient, that I would have to receive dialysis or a kidney transplant relatively soon in the future. I had had no idea about this and was convinced that my life was at an end. I had two very young boys at the time and I found it very difficult to come to terms with this news sitting on my own facing the consultant and with no idea what to ask, what to say, and how to respond. We have come a long way since those days, but some of the lessons today are not that different.

Predialysis

My first kidney began to deteriorate in late 2006 and the standard of care I received was excellent. I was then transferred to a different section of the renal team, whose expertise was in attempting to preserve failing kidney function for as long as possible. My wife was fully involved in the discussions and we were both kept informed of the progress, or otherwise, of the kidney. I knew long before it was required that I would need dialysis. Of the various options for dialysis, it was explained to me that haemodialysis was likely to be the only reasonable option for me and although I understood the medical mechanics of dialysis, that it purified the blood and removed excess fluid, I had no appreciation of the psychological impact of dialysis and I was given very little help in trying to understand its impact. My introduction to haemodialysis was a brief visit to an acute dialysis unit where I was shown patients attached to bleeping machines, all looking pretty poorly. The unit was full, noisy, and it appeared to me to be barely organised chaos. I was not given the opportunity to talk to any patients in a similar position to mine and I found the visit quite disturbing. I think it was predominantly for that reason that I delayed the decision to start dialysis for longer than was medically advisable.

At each of my visits to the unit in the months leading up to starting dialysis in May 2008, I was asked how I felt and I would say I was OK, but I knew in my heart of hearts that I wasn't. I was very tired all the time. I was not able to do much around the house. I slept most of the time. My feet and legs, particularly, were very swollen and I became very breathless every time I walked more than a few hundred metres, but making that final, irrevocable decision to commence dialysis was something that I wanted to put off for as long as possible. It seemed such a big and irreversible step to make. It was my wife, at one of our regular visits, when I had responded, again, to the doctor that I was OK, who said, 'No, you are not. It is time to start dialysis'. She was right but I had left it very late and I was found to be carrying in excess of 10 kg of fluid when we tried to establish my dry weight.

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Starting dialysis

There is more than one means of vascular access and the options were explained to me well. In my particular set of circumstances, there was a possibility of receiving a kidney from my brother and it was therefore suggested to me that I have a permcath installed, which is a simple procedure and which enables the patient to begin dialysis immediately. After some discussion, I accepted this option and the procedure took place in mid-May 2008 and I began dialysis that same day.

It was always made clear to me that I would receive a couple of sessions at the main hospital before a more permanent slot was found for me elsewhere. Within a month I was given Tuesday, Thursday, and Saturday evening slots at a local hospital, which were convenient for me and enabled me to drive to and from the hospital. Although it would be ideal for patients to be given a choice as to which slots they might prefer, in reality that is not possible. Each of the units I attended over the years was simply too busy and, if you were to be relocated, the choice of slot was determined by what was available, not necessarily what was ideal for the patient. I did, however, request an alternative time, since I found the evening slot difficult to adjust to. I often suffered from cramp and found it difficult to sleep when I arrived home. I was eventually given morning slots on Mondays, Wednesdays, and Fridays and that was to be my schedule until I moved to home dialysis.

My experience at the hospital was not always good. Renal care enables a closer relationship between patient and provider to develop than is often the case with other medical disciplines. This is particularly the case with patients on dialysis, where they will see the same nurse or group of nurses, week in, week out. A good relationship between patient and nurse is, therefore, desirable and it should, self-evidently, be combined with care and compassion. None of these qualities requires intensive training; all require a particular attitude of mind and this, in my experience, was not always there. In addition, I could see how some simple changes could improve the lot of patients on the ward but I became increasingly frustrated at my inability to get any changes introduced while I was on dialysis.

Communication and empowerment

It is important for patients to feel that they are more than just an object that needs to be treated. It can help a patient gain some self-respect if he or she assists in preparing for their treatment. This might mean taking their weight, their temperature, and perhaps their blood pressure. It could also mean learning a little about lining the machine, getting your tray ready with dialyser, needles, swabs, and so forth. Although this might mean a small investment in training from the nurses in the short term, it will help them in the longer term and it will also give patients a feeling of empowerment, which is so important for long-term treatments such as dialysis. This, though, was not my experience and it was left to patients as to whether or not they were able to assist. The view from the nurses was that they were too busy to do anything other than connect and disconnect the patients.

Because the patients are likely to see the same nurses, week in, week out, it is not only possible but also desirable to develop a good relationship between the nurse and patient. In my experience, this did not happen until I was transferred to the self-care unit prior to dialysing at home. It was often the practice of nurses, having put the patient 'on', to sit at the computer where it was clear that they were not always working! All I am suggesting is that the nurses talk to their patients and get to know them better. It will help the nurses understand the concerns of their patients better and it will certainly help the patients feel that they 'matter' and are not simply objects to be processed.

Monitoring

Regular visits from the consultant did not take place. Those consultations that did take place invariably took place at the bedside, rather than in the more discreet confines of the consultant's room. Although I was told I had a nominated nurse, which is a sensible concept, even when she was on duty she did not look after her nominated patients. I never managed to understand what the role of my nominated nurse was. I was on the transplant list for the time I was dialysing and was told that I should have antibody checks carried out regularly. This was not done and I found it very difficult to get these blood tests done in the satellite unit although I was told it was important to monitor them.

Infection control

Insufficient care and attention was given to monitoring for infection. In my case, I developed a nasty infection around my permcath but, despite regular attention given to that area by the nurses, as they attached and detached my line to/from the machine three times a week, it was my wife who noticed the infection, as a result of which I was immediately admitted to hospital as an inpatient and was given large doses of antibiotics to stem the infection. I had the old line removed from my right jugular vein and a new one installed in my left jugular vein. How is it possible for a nurse not to notice something that he or she looks at so regularly when they should be specifically trained to be aware of the risk of such infections in a patient with a permcath?

Cannulation

Cannulation protocols vary considerably between nurses. It was only when I started training for home dialysis that this issue was explained to me. The two main techniques are 'button hole' and 'rope ladder'; each has its advantages and disadvantages but none of this was explained to patients in my unit. Without careful needling, a patient can end up with very 'lumpy' access points, which may not be necessary and can be cosmetically very disturbing. It appeared to me that the nurses would 'needle' wherever they could, rather than following one or other of the main techniques.

Holidays

Holidays are very important for dialysis patients. It is, reasonably enough, a patient's responsibility to organise whether or not a slot is available at a particular centre, but procedures were not in place when this initial research had been done, to set the medical requirements in place. It was often not clear which nurse was responsible for liaising on my behalf with the holiday centre and it happened more than once that my unit contacted me on the eve of a short visit away for information on exactly where I was staying, who the contacts were, and what was needed. This is very frustrating, given that trips have to be arranged at least six weeks in advance and dialysing away from your main base can itself be stressful.

Home dialysis

After two years or so of increasing frustration, I asked one of the nurses if there were any alternatives to dialysing at the hospital three times a week. One of the better-informed nurses suggested that I might enquire about dialysing at home. This seemed to me to be an excellent option and I was able to get the assistance of a nurse recently transferred from another hospital to teach me to line the dialysis machine and, much more importantly, to needle myself. It was only then that I learnt the differences between the various needling techniques, which, in my view, all renal nurses should know about and discuss with their patients. Training was slow at the satellite unit and there were various parts of the process that I could not be taught as there was never enough time between the am/pm and pm/evening dialysis sessions for the nurses to take the time to explain to me what I needed to do.

I was, however, finally transferred to the main hospital and I became part of the local self-care unit. Dialysis patients there were able to manage their own care at a level that suited them. Some patients dialysed at the unit independently of the nurses who simply kept a watching brief over their patients, while others were at various stages of training prior to beginning dialysis at home.

Since I had already had some basic training, I quickly completed my training and, having arranged through the hospital for an appropriate machine to be installed at home and all the necessary kit to be delivered, I began dialysing at home in November 2010, and I can quite honestly say it that it changed my life. I was given excellent care from both the nursing staff and the technical support team. Each month a nurse would visit me at home and take my blood for analysis. I was also able to arrange regular visits with the consultant. More importantly, I felt I had regained a greater control over my own life, which is so important for patients with chronic conditions. I began dialysing every other day, which meant I'd be doing a Monday, Wednesday, Friday rota one week and a Sunday, Tuesday, Thursday, Saturday rota the following week. I was, therefore, dialysing one session per fortnight more than previously, which helped me to feel a little better and relax a little more with my fluid and dietary allowances. Dialysing at home also meant that I could set my own dialysis times to suit myself and my wife, rather than following a hospital routine, which enabled us to manage our lives better and helped me to 'dialyse to live', rather than 'live to dialyse'.

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It was a very positive step for me to be able to dialyse at home. It is not an option for all patients, however, and it is dependent partly on the patient's willingness to take greater control over their lives, but also on their particular domestic situation.

I would recommend that the renal nurses should be trained always to consider which of their patients might be suitable for dialysing at home and to broach the subject with suitable patients. Many patients will not want to go down this path but, with the help also of patients who are already dialysing at home, it is always worth discussing it because it is clear that the long-term outcome for home dialysis patients can be better than for those in hospital. This may require an investment in terms of time and money but it is one that I believe will pay dividends in the medium to long term.

I found the most difficult thing to come to terms with was self-needling but this is not always essential. In the self-care unit it was possible to do everything for yourself, except self-cannulation. At home it is possible to train your carer to undertake the cannulation if he or she is prepared to take on the responsibility.

In my case my wife was not involved in my training until I actually came home, when she learnt from me how to line the machine, prepare the tray, and so forth. Because dialysis takes up so much of one's life together it is important, in my view, to involve one's partner in the training from the beginning. It is easier to learn with someone else and it also gives two heads the opportunity to learn what to do should something go wrong.

Patient choice and shared decision making

As I researched options for dialysis, it became clear that other options to dialysing three times a week in hospital did exist – home dialysis (as I have discussed above), but also nocturnal dialysis and using a portable dialysis machine, for example. In addition, there are options available for patients to improve their chances of receiving a transplant through the swap, or paired, scheme. It may be unreasonable to expect all nurses to have knowledge of all these issues but in my experience, none of the nurses knew about any of them. It was only when I asked some specific questions that I was told about home dialysis. This information ought to be included in basic nursing renal training, in my opinion.

Best practice and peer review

As a dialysis patient I visited the units in Penzance, Truro, Jersey, Norwich, Edinburgh (the Holiday Dialysis centre), Inverness, and Elgin. All the units were different, in a number of ways, from my home base and in each case each unit could have benefited in some way from the experiences of others. In my view, periodic meetings of senior nurses with their peers could only be beneficial and they could discuss a whole range of issues such as exercising while on dialysis, transport, the provision of food during dialysis sessions, how personal care plans are used, the role of the social worker, and whether there might be a role for a patient representative. I am sure that there are many other subjects that would be of relevance to both nurses and patients.

Transplantation

When I finally received the call from the hospital in August 2011, it came as a complete shock. After so many years of dialysis, it was no longer at the forefront of my mind and I was pretty much resigned to leading a life of dialysis. After a mad rush through the night, my wife and I arrived at the hospital at 7:00 in the morning and we spent a whole day undergoing a variety of tests. We were also aware that another couple had been called. Depending on the outcome of the blood tests, one of us would be offered the kidney. This was very difficult for both of us and for some of the time both couples even shared the same waiting room. During the day we were given a little information about the donor and the family and the circumstances surrounding the donor's death. It was explained that there was a risk, albeit a very small one, that the kidney might not work and that, if it did work, it might take some time to 'wake up' – possibly six weeks or more. This presented my wife and me with a bit of a problem. I was pretty stable on dialysis and we were managing our lives as well as could be expected. Our concerns were that, having waited nearly four years for this kidney, if it did not work, this might have an impact on my antibody levels and my chances of getting another kidney in the future. These were impossible questions to answer but they had to be asked. The general view, however, from the doctors was that there was only a small risk of the kidney not working. I should go for it. Thus, when it became clear that I was to be the fortunate recipient, we did go ahead and I went up to theatre at about 21:00 that evening.

My experiences as an inpatient immediately post my transplant operation, and during the follow-up clinic appointments were generally good.

Care as an inpatient

On the wards, the 'three Cs' are of paramount importance: Care, Compassion, and Communication. The standard of nursing care on the wards varied considerably from shift to shift and from day to night. In general, the day staff were more proficient than the night staff. They had a better understanding of the patient's illness, were more likely to talk to their patients (although this was still uncommon in my experience), they were more attentive, responded better to patient requests, and often had a little more time to spend with their patients.

Hygiene standards on the ward were mixed. Not all nurses or doctors wore gloves when taking blood, for example. Blood pressure cuffs were never wiped before taking a patient's blood pressure. What most shocked me, however, was when breakfast was handed out, and my Weetabix was handled with bare hands.

Some nurses would offer the patient a bed bath, but most did not. Some would actively encourage the patient to move, get up from the bed, and walk around the ward, but most did not. One nurse only in my experience went to the trouble of introducing herself to me as the patient. This is such a simple issue but so important from the patient's perspective. You really want to know who is looking after you so that you can speak to the right nurse if you want some advice, help, and so forth.

Outpatient care and immunosuppression

As an outpatient, I was very well treated and felt in good hands most of the time. When it is time to be discharged, there are always delays, which often seem to be the responsibility of pharmacy. This, I am sure, is difficult to avoid but I am also sure that there must be a better, more efficient way of organising a patient's departure. This is in the interests of the patients themselves but must also be in the interests of the ward in freeing up a bed promptly.

The importance of taking one's antirejection drugs is paramount. If you fail to take them you may lose your kidney. This needs to be stressed over and over again. I am constantly amazed at the number of patients who 'forget' to take their drugs! In addition, it is always important to emphasise the side effects of the drugs. Again, in my experience, this is done but particular attention should be given to the effect the antirejection drugs can have on one's skin and on one's susceptibility to infection.

Rejection is a constant worry. There are no guarantees with transplantation. This is another issue that needs to be highlighted. In my experience, this is done competently. My one additional comment in this area is that there is very little attention given to the psychological needs of the patient post-transplant. Initially, it is a very worrying time. You attend clinic three times a week and there can so often be setbacks, that the whole process can be a real rollercoaster. Little thought, however, is given to this area. The appointments concern themselves with the medical side of things only. I do not know whether a counsellor is even available.

As visits to the clinic become less frequent, it becomes increasingly important for a patient to be able to monitor his or her blood results. Patients are understandably concerned about their progress and, although I was told that the hospital would contact me if there were any issues, there are sometimes occasions when issues escape the attention of the experts and, in my case, my very low white cell count was not picked up sufficiently quickly and I ended up attending hospital on a Saturday morning for an emergency procedure.

In 2013, I became a member of Renal Patient View (now abbreviated to Patient View <https://www.patientview.org>), which is run by the Renal Registry and which allows a patient access to a range of information about his or her care. The most critical aspect to me was being able to monitor my blood results the day following my appointment. No longer am I dependent on a call from the unit. This must ease their workload as well as helping me. For anyone with computer access and a basic understanding of how systems work, I would recommend investigating the possibility of accessing Patient View. Nurses should also inform and encourage patients to sign up.

Seven years post-transplant, my kidney function is relatively stable and I attend outpatient appointments every three months, which I am hoping is a situation that continues for as long as possible.

Case Study 3.2: Thoughts of a carer

I met my husband in 1977, just three months after his initial diagnosis, so my experience of living with a partner who has kidney disease has been long and varied. He told me about his medical condition right at the beginning of our relationship, but I think we were both very naïve about the implications for our future together. His condition was managed conservatively for the next nine years. It was always there in the background but did not impact hugely on our life.

The big change came when he was told his kidney function was deteriorating and he should start on a low-protein, low-sodium, and low-potassium diet. This was quite hard to manage whilst providing for our two young children, as we had very little advice about how to do this. Essentially just a few diet sheets and prescriptions for the relevant special foods required. These foodstuffs were mostly unpalatable and difficult to prepare. I remember crying over the first meal that I made because it looked so meagre and awful. Thankfully these (Giovanetti) diets are no longer used.

Transplantation

Transplantation followed about nine months later, in January 1988, when my husband's mother donated one of her kidneys. Living transplants at the time were very unusual, with only about 5% of the total being performed in this way. Two major operations within six weeks and various complications over the following year, resulting in a third operation, finally stabilised my husband's condition. It was a rollercoaster, never knowing what would crop up next and not quite daring to believe that eventually it would be alright.

I can remember a mother at the school gate saying that she didn't know how I could cope with all that was happening. I thought to myself that I didn't know either, but I didn't have much choice! We did have kind friends and family but it was still a challenging time, trying to be supportive to my husband who was struggling to maintain a positive outlook, balanced with keeping life as normal as possible for our children aged 4 and 2. The culture at the time was very much 'stiff upper lip and get on with it'. In retrospect it would have been lovely to have someone to voice my concerns to, who understood the road we were travelling.

Eventually we went on to have 19 wonderful years of normal family life, the only reminder of the transplant being the various medications that my husband took daily and the three-monthly hospital visits. However, transplantation does not cure kidney disease; it only gives respite from dialysis for the lifetime of the replacement kidney.

Advanced kidney disease

By 2006 my husband's kidney function began to deteriorate and with it his overall condition. Having to take early retirement on health grounds in 2007 was a real blow to his self-esteem; he had loved his working life. Early retirement can be a difficult transition in normal circumstances but when you feel unable to enjoy the new freedom that retirement brings because you are too tired it is very frustrating. As his condition worsened, our lives became very restricted. We were unable to do much because he felt so unwell and tired all the time. Just climbing the stairs was making him breathless and he began to dread the short walk to the station to travel for his fortnightly hospital appointments.

My husband developed sleep apnoea, which meant we could not share the same bedroom. Snoring is often joked about but sleep apnoea is not funny – it gets to the point where you spend your whole time lying there waiting for the person next to you to take their next breath. A 24-hour monitor revealed that he was suspending his breathing up to 40 times per hour. No wonder he was exhausted all the time when he could not get any proper rest. It was not until dialysis commenced that this problem began to resolve itself, as the large amount of excess fluid he carried was gradually removed.

Hospital-based haemodialysis

Starting dialysis is a huge step for both the patient and the carer and should not be underestimated by clinicians. Psychologically it feels like the end of normal life, no matter how limited that 'normal life' has become. The thought of being dependent on a machine for the rest of your life unless you are fortunate enough to receive a new kidney is very daunting. The information that you receive at this stage is critical to the way that you adjust to your new life and how you cope physically and emotionally. I'm sure most patients at this stage will feel depressed, quite justifiably.

Once the decision was taken to dialyse it all happened very quickly but with little preparation in terms of what we could expect. It was very bewildering and scary. I tried to be positive and encouraging because my husband was too poorly to do it for himself.

In retrospect I felt totally unprepared for it all. I knew that it was the right thing to be doing and hoped that my husband would feel better soon, but I felt totally out of my depth. A perm-cath line was put in and looked a mess with bleeding and bruising all around the site for almost a week. Dialysis started immediately with the first sessions being unpleasant because he suffered from bad cramps. I dreaded asking how it had gone because I knew it was probably painful. He could not tolerate having much fluid removed in one go, so it took quite a while to establish his 'dry weight'. I felt helpless and didn't know what to do or say to support him, except that it could only get better.

If we had been able to talk to a patient who was living well with dialysis at that time it would have made all the difference – to see that one can regain control of one's life and return to a reasonable level of health.

For two years my husband attended the local hospital for treatment and became increasingly frustrated with the time it took and the lack of interest in him as a person. There was no attempt to get to know him or anything about his life outside. It was as if he was a body on a bed that needed to be attached and then detached from a machine at a time that suited them. This may sound very harsh, but I can't understand why you would choose to be a dialysis nurse if you have no interest in your patients as people when by the nature of the job you are spending long periods of time with those people every week!

In stark contrast we have met some wonderful dialysis nurses throughout various parts of the country as my husband received treatment on holiday. Without exception, they were kind, caring, proficient, and, crucially, interested in him as an individual. Those nurses learnt more about him in a week as a holiday dialysis patient than most of those at the home unit learnt in the whole time he was there.

Home haemodialysis

We were eventually made aware that home dialysis might be an option and this was a real turning point. From a slow start, we eventually reached the stage where my husband could start dialysis at home. A spare room in the house was adapted and the relevant equipment was installed by the hospital. We had wonderful support from the home dialysis team but it was still quite nerve wracking when we dialysed for the first time on our own. I would say that it took about three months for us to gain confidence.

It was a big change for me as my life became much more restricted. Before, my husband would leave for the hospital at 07:00 and return at about 13:00, which did not affect me at all. I would either be at work or doing my own thing. Once the home dialysis began, I had to be at home and available the whole time that my husband was attached to the machine. I had not fully considered the implications of this and it was quite hard to adjust. He was advised that increasing the amount of dialysis he performed would improve his overall condition, which made sense, so he decided to dialyse every other day. This meant that we were on a two-week rotation, which was fine, but it also meant that I could not have the freedom to attend a regular evening class or meeting because I would not be free on the same evening every week. As I was working part time we had to dialyse in the evening when I got home. This also meant that I spent every other evening by myself as my husband preferred to be on his own during his sessions. I would be downstairs with a two-way radio so that he could call me if he needed anything. He was always hungry whilst dialysing and I would provide sandwiches, toast, and biscuits as required!

Having said all of that, home dialysis brought huge benefits and we were so pleased to be able to take advantage of the opportunity offered. The freedom to dialyse to suit our life gave us the ability to travel and visit friends and family more easily. Taking control of the treatment rather than being dependent on the hospital was very liberating. We were free of the risk of hospital-acquired infections and, apart from the occasional visit from the home dialysis sister to take blood samples and follow-up hospital checks, we were living our own lives again. Life was at home rather than the hospital.

My husband had been on the transplant list for over four years and, having exhausted all other potential options, we began to accept that dialysis might have to be a permanent part of our lives. We decided to try and do as much as we possibly could within its constraints,

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including travelling to America to visit family. We continued to travel within the UK receiving hospital dialysis in the local units. We found an equilibrium that gave us a good quality of life.

Transplantation

When a call finally came I felt totally unprepared. My husband had gone away on a walking trip for a couple of nights and I took the call in the early hours of the morning. My first reaction was that one of our elderly relatives must have been taken ill. As soon as the caller said that she was a doctor from the hospital and asked for my husband, I realised what this might mean. The range of emotions that I experienced at that moment included, shock, excitement, fear, disbelief, anxiety and, most strongly of all, sadness for the donor's family.

My husband has already described the hours that we waited to find out if the kidney would be suitable. We decided not to tell any friends or family what was happening, not wanting to raise anyone's expectations, let alone our own, just in case it did not go ahead. Then the huge sense of relief and the ensuing anxiety when we were told it was a suitable match, with the excitement of contacting everyone. Thank goodness for text messaging and email! The operation went ahead that night and I remember saying goodbye to my husband in the anaesthetic room, thinking 'please God let it all go smoothly'. To my amazement I received a call at about 1:00 from my husband saying that it was all done and he was back in the ward. When I visited him the next morning he had no recollection of making the call!

From then on I spent every day driving to and from the hospital, spending as much time with my husband as was allowed. At home I was receiving all the wonderful calls with enquiries and good wishes but it was very tiring. Unfortunately, both of my sons and most of our good friends that I might have called on were away at the time, so it was a great relief when they all began to return and I didn't feel so alone.

My husband recovered well and focussed on getting mobilised as quickly as possible, but every day we were hoping for that precious moment when he needed to pee! It finally came on day six after the operation. I was at home and received a text from my husband as he was too emotional to speak. It is difficult to explain the relief that I felt at that moment, but it was as though a huge burden was being lifted from my shoulders. I sent out a mass text message around the world to friends and family. My son's girlfriend was on holiday with her family and burst into tears when she read it, as did her mother and sister! Never were a few millilitres of urine so welcomed! My husband continued to make a good recovery and was discharged home nine days after the operation. It was so good to have him at home and be able to care for him myself.

Post-transplant follow-up

Follow-up for patients after transplantation is very intense, requiring hospital visits three times per week for blood tests, weight, and blood pressure measurement. This was tiring for my husband and he was anxious about travelling by train and being exposed to all the coughs and colds of other passengers with his immune system suppressed.

Over the following weeks and months there were various setbacks, mainly related to getting his immunosuppression drugs properly balanced, but eventually my husband's condition stabilised and we began to enjoy the new-found freedom that the transplant gave us. To be able to enjoy the simple things, like going out for a lovely cup of coffee and a cake! The fluid restriction and low-potassium diet had meant this was impossible before. We were able to visit friends and family when we liked for as long as we liked and it was, and still is, wonderful.

My thoughts to you as nurses

Kidney disease is with the patient and their families for the rest of their lives and each one has their own individual circumstances. Learn as much as you can about them as individuals and their particular condition and you will help transform how they cope with their disease.

As a patient on hospital-based dialysis it is very difficult to comment if things are not right, as you feel very vulnerable. Criticism, however constructive, is not always well received and therefore things that could be improved go unchanged because of lack of trust.

Being confident that those who care for you really know you will develop a sense of trust that will enable concerns to be raised and addressed.

- in the early days of diagnosis and dialysis, patients may feel very unwell, frightened, depressed, that their life is over. There may be anxieties about their employment, finances, housing, family, and so on, which may affect their overall health.
- spend time to get to know your patients as well as possible, understanding their home and family circumstances, their fears and concerns. Understand what they enjoy and what they can do, and focus on these things and not on the negative
- use language that can be easily understood.
- become their advocate.
- encourage independence, teaching them all the things they can do to help themselves. Many patients could manage some or even most of their dialysis given the right encouragement. Some could have dialysis at home with the right support.
- recognise that renal disease, and dialysis in particular, has a huge impact on the patient's partner and immediate family.
- encourage and enable the patients to take holidays by facilitating dialysis at other centres.
- be knowledgeable about what is available. If the patient is on the transplant register make sure they are aware of the various options available through live transplantation. Encourage discussion with friends and family.
- emphasise that you 'dialyse to live, not live to dialyse'. There is still so much that they can do.

Being the partner/carers for someone with kidney disease can be very challenging and lonely at times, as it can be hard for friends and family to understand the complexities of the disease and all the challenges that it brings. My plea would be to ensure that the carers are looked after too. Small acts of kindness and a comforting word will go a long way. Information about the local KPA, support groups, and online forums can provide a lifeline.

We are now seven years on from the transplant and our life is very busy and wonderful. One of our sons has married and we now have a gorgeous grandson that we are both able to enjoy to the full. We are so grateful to the family who had the courage to donate the organs of their loved one. I do hope that knowing other lives can continue restored to good health will be of some comfort to them.

Case Study 3.3: Communication

I have been a patient with kidney disease for over 20 years and have been on dialysis for a large part of that time. As a result of my scientific background, I took interest in renal failure and haemodialysis by reading up on it further and asked nurses and doctors about different aspects of renal medicine. I have learned a lot and gained an insight into renal care and medicine. In addition, there are aspects of renal practice which I have been able to identify that can be improved and enhanced, thus addressing the importance of the continuity of care.

One aspect that I feel could be improved is communication. On a haemodialysis unit, there seems to be a setup where there is a peak time when the nurses put patients on the machine and then promptly return to the nurses' station. After this period, there is a length of time where the nurses update their work and each nurse is assigned a particular duty, e.g. stock, transplantation bloods. The other peak-time rush starts again when patients start to come off the machine. On some days, this can be more hectic than other days, due to staff pressures, but the question is why some nurses do not seem to want to engage with the patients when they are less busy during the middle of the dialysis shifts.

Each patient is assigned a named nurse in the dialysis unit. In my experience, it seems that many patients do not know who their named nurses are. The nurses should be introduced to their respective patients since it is the nurses who have the most interaction with the patient as opposed to other healthcare professionals. Nurses should be able to explain the results of monthly bloods (e.g. full blood count, urea, and electrolyte levels) to their patients and time

(Continued)

should be taken for this. I feel nurses could give us a brief session explaining the parameters of the haemodialysis machine, e.g. what is a good pump speed for efficient dialysis, reasons why the machine alarms. Once patients are more comfortable about their knowledge of renal care and medicine, nurses can encourage them, depending on the patient's circumstances, to undergo self-care.

Transfer between dialysis units

As a dialysis patient of 12 years, I have moved between dialysis units twice. When it came to the first move, no meeting about the move was arranged with the patients and it was as if we were to accept the move without having enough time to process all the information. Dialysis becomes a way of life for the time they are on this routine so just like moving house is stressful, moving dialysis units has its own anxieties. Due to such moves, transport can be a concern as well, especially getting to the dialysis on time, safely, and smoothly. Nurses should be able to alert patients in good time of when such changes are likely to occur so that patients can be reassured that the running of any procedures will be smooth.

Psychosocial issues

Many patients are not aware of the kinds of help that are available to them, which is the reason why renal social workers should come to the dialysis unit regularly, to avoid patients making separate trips to the hospital to see them. Renal social workers should come at least twice a week to accommodate the patients who come on different days and conduct a ward round like doctors do, so each patient is aware of their service.

Some patients have the right to hospital transport for their treatment so when administrators are not available to sort out issues such as delayed transport, the nurses should be able to have involvement in such situations.

Reflection

After reading the case studies above, think about similar situations when you might have been the provider of the care to these patients. Reflect carefully and consider the following points:

- what skills do you have (or what do you need to acquire) to enable a true partnership with patients?
- how far do you actively include patients and family members in decisions about their care?
- how could you make the best use of quiet times during a dialysis shift (such as assessment, supporting self-management, education, decision-making with patients)?
- in what ways could you engage with patients and their families to measure the level of patient involvement in your unit?
- how far does your unit give a true choice to patients when they are contemplating long-term renal replacement therapy?

Patient Involvement Using Social Media: The Renal Patient Support Group, Facebook, Twitter, BlogSpot, and Instagram

Background to social media

Since the 1990s, technology such as the Internet, email, and instant messaging (IM) facilities on mobile phones, digital cameras, and computer scanners, have provided a way to communicate, produce original media footage and access information at a

rapid pace. Using technology has advanced the way we gather data and information such that we no longer really require to be at a specific place at a given time. Now, many people are equipped with smartphones, which have applications ('apps'). The majority of us are now becoming more knowledgeable in the way we retrieve information and connect with family, friends, and colleagues on a daily basis using such media as Facebook and Twitter. This section provides some insight on the variety of social media forms that are useful in healthcare, and describes the very successful Renal Patient Support Group (RPSG) on Facebook, BlogSpot, and ResearchGate.

Facebook

Facebook is a modern social media/networking platform, which has massive capacity allowing people to communicate and interact. Facebook launched in 2004 and has over 900 million active users; more than half of them utilise the Facebook app on a smart or android phone. Facebook can be used personally or for business to reach a larger audience in a much shorter time. The NHS has recently joined Facebook and this has helped to

- engage with followers in order to share information on the NHS, their products, services, and latest news;
- share advice and information about important health issues, and where appropriate, may link to major health stories in the news;
- point people to the correct channels to get opinions heard. NHS Blood and Transplant (NHSBT) are also using Facebook to highlight the importance of organ donation.

Twitter, Blogspot, and Instagram

Twitter is an online social networking service and micro-blogging service that enables its users to send and read text-based posts of up to 280 characters, known as 'tweets'. A blog can be a personal journal published on the Internet consisting of discrete entries (or 'posts'). A typical blog combines text, images, and links to other blogs, web pages, and other media related to its topic. The ability of readers to leave comments in an interactive format is an important part of many blogs. Most blogs are primarily textual, although some focus on art (art blog), photographs (photo blog), videos (vlogging), music (MP3 blog), and audio (podcasting). Instagram is a social networking app made for sharing photos and videos from a smartphone. Like Facebook or Twitter, anyone who creates an Instagram account has a profile and newsfeed. When you post a photo or video on Instagram, it will be displayed on your profile. Perhaps one of the most attractive features of Instagram is its hashtag facility. Placing a word or phrase preceded by a hash mark (#) within a message to identify a keyword or topic of interest can help facilitate a search for it. Whenever a user adds a hashtag to a post, it's able to be indexed by the social network and becomes searchable/discoverable by other users. In some regard, Instagram perhaps functions better than Twitter owing to its flexible photo posting and visual nature.

The Renal Patient Support Group on Facebook

The RPSG is a voluntary (non-funded) Facebook group co-founded by three individuals in 2009 – two long-time patients and one long-time carer. The initial intention of the RPSG developers was to help support other patients with kidney

disease, relatives, and carers following routine clinical outpatient appointments at the North Bristol NHS Trust. The RPSG developers knew that it would be a challenge to provide support to fellow patients face to face in the outpatient setting owing to the limited time and the general rush in the clinical environment. The RPSG developers decided to explore an online platform, and Facebook was a fitting choice because it is a social media platform recognised on a global scale and allows the sharing of ‘real-time’ lived experiences. The RPSG offers online peer support globally, with members sharing and caring.

Since the RPSG allowed the co-founders to interact with patients from the local NHS Trust, using Facebook further attracted patients, family members, and friends from various regions of the UK and beyond, thus allowing everyone to gain a better understanding of chronic kidney disease (CKD) and end-stage renal disease (ESRD) from various parts of the world and thus where everyone is able to interact, ask questions, and post messages, retrieving instant responses. The RPSG developers also want to see that patients become more active with their local kidney patient associations (KPAs), as they support renal patients via the requests of health professionals in a given NHS Trust.

The great advantage of the RPSG has now been that other patients from the UK can gain more insight into CKD in other parts of the world and vice versa. The RPSG Admin/Research team consist of eight members who have several roles. Representatives from UK, Italy, and USA, respectively, give their time and dedication in seeing that the group is moderated. The RPSG on Facebook had in March 2018 nearly 8000 members internationally and is recognised as one of the most reputable evidence-based support groups, owing to its research and support activity.

Renal Patient Support Group statistics

To provide basic statistics of membership activity and engagement, in a 60-day period (January–March 2018) there were 285 posts, 2300 comments, and 4700 reactions to different group posts. Table 3.1 below provides a table of RPSG membership by top countries and cities.

Table 3.1 Membership of the Renal Patient Support Group (RPSG) January–March 2018.

Top Countries	No. of Users	Top Cities	No. of Users
United Kingdom	3089	London, England, United Kingdom	296
United States	2050	Bristol, England, United Kingdom	120
Egypt	312	Alexandria, Alexandria Governorate, Egypt	110
India	231	Manchester, England, United Kingdom	84
Canada	174	Cairo, Cairo Governorate, Egypt	80
Saudi Arabia	138	Birmingham, England, United Kingdom	62
Ireland	135	Kent, England, United Kingdom	59
Pakistan	132	Riyadh, Riyadh Region, Saudi Arabia	54
Australia	116	Leeds, England, United Kingdom	50
Algeria	109	New York, NY, United States of America	49

What's on the Renal Patient Support Group?

- patients sharing real-life experiences and supporting each other.
- helpful links for all.
- video links that may be of interest.
- Academic/Research Papers that may be of interest.
- research Folder consisting of supporting projects and collaborations.
- voluntary patient activity opportunities.
- a list of KPAs and related groups and pages.
- event Posters/Flyers folder. Some of the RPSG's projects and activities include the following:
 - renal Patient View service evaluation (NHS Kidney Care Project Support).
 - record access (Royal College of General Practitioners/NHS Connecting for Health Project Support).
 - improving Shared Decision Making for Renal Dialysis – A Call to Action (NHS Institute for Innovation and Improvement Project Support).
 - patients Receiving Kidney Care: How Technology Helps (University of Brighton Project Support)
 - bringing Carers into Kidney Care Project (NHS Kidney Care Project Support)

The Renal Patient Support Group on Blogger

The RPSG blog was launched in 2012. In addition to some of the material and information already on the Facebook page, the RPSG blog allows members and non-members of the RPSG to gain more insight into CKD.

In planning, the co-founders thought to also provide opportunities for an 'external crowd' insight on RPSG activities, thus promoting the group via a second platform. On the blog there are a number of website links to documents/guidelines, RPSG activity updates, and much more. This social media platform allows general internet users to understand more about what is happening surrounding kidney health. The RPSG developers would like to see more people use this facility widely. It is a very successful platform for research collaborations, especially where service providers want to get a better understanding of what gaps in CKD need to be bridged and where there are mutual interests between patients and health professionals. The RPSG blog has had near to 12 000 views worldwide since its launch.

The Renal Patient Support Group on ResearchGate

ResearchGate is a social networking site for scientists and researchers to share published work, ask, and answer questions, research networking, and identify collaborators with mutual interests. Owing to the expansion of RPSG research and publication activity, the RPSG team identified that in addition to sharing efforts via the RPSG Facebook and BlogSpot platforms, it would also be advantageous to share its publications and outcomes on ResearchGate. In 2015 the RPSG team officially began adding its research onto ResearchGate to share activities amongst the academic and research community. Over three years (2015–2018), the RPSG ResearchGate page now has over 100 publication items in various formats.

The Renal Patient Support Group on Instagram

In anticipating reaching 8000 members worldwide, in April 2018 the RPSG administration/research team discussed what better way to highlight more activities than to implement an Instagram account. Specifically, the team wanted to initiate its

'CKD *through Art*' initiative. Owing to a variety of art posted on the RPSG Facebook group in several formats, it would be sensible to highlight this on another form of social media, and Instagram seemed a fitting platform to share. The plan behind the 'CKD *through Art*' action is to have all RPSG CKD art, flyers, posters, research posters, charity events, banners, and words of encouragement on Instagram to prompt more discussion and engagement.

The RPSG continues to expand. Health professionals should grab opportunities provided by social networks to improve the health of their patients and do their utmost to ensure that the highest quality of health information and access to treatment is there for all.

The RPSG does have a general disclaimer informing members not to provide any specific clinical or medical advice. The RPSG has also successfully allowed a platform for interaction, providing insight to 'little-heard' populations and thus also distributing information on CKD/ESRD to general Facebook users. The RPSG raises CKD issues and awareness at all stages of chronic illness.

Over time, patients and carers have become more aware of self-management and are continuing to learn from the RPSG membership. Owing to access to electronic health records, patients want to engage in communication relating to laboratory test results. The RPSG continues to expand; the group prides itself on being a reputable evidence-based support group and an organisation that prompts people and patient involvement. Professionals should seek to grab opportunities provided by social media to improve the health of patients and do their utmost to ensure that the highest quality of health information and access to treatment is available. This will also help bridge gaps in inequalities of long-term conditions like CKD.

Information on the RPSG can be found at

RPSG Facebook

<http://www.facebook.com/groups/RPSGroup>

RPSG Blog

<http://shahidrpshg.blogspot.co.uk>

RPSG ResearchGate

https://www.researchgate.net/profile/Shahid_Muhammad

RPSG Instagram

<https://www.instagram.com/rpsginsta>

Patient and Carer Involvement in Renal Nursing Education

Many providers of higher education are involving patients and carers in curriculum planning and teaching activities. The value of involving users and carers in the education of health and social care professionals has long been recognised (Levin 2004). Research on the involvement of users in education has demonstrated that it can challenge entrenched perceptions and attitudes of health professionals (Katan and Prager 1986) and help break down barriers of hierarchical and paternalistic services, and produce practitioners capable of delivering improved and more relevant outcomes for users and their carers (Tew et al. 2004). Service user involvement in curricula development was analysed in a recent review (Morgan and Jones 2009) and it was found that, despite a limited and weak traditional evidence base on impact on students' knowledge and practice, both students and service users identify benefits from engagement. Another paper (Gutteridge and Dobbins 2010), which was part of a larger evaluation study, described how members of staff in a faculty of health were interviewed about the impact of service user and carer involvement on learning and teaching. Semi-structured interviews were used to

explore current levels of involvement, barriers, and solutions, and findings suggested that staff recognised the need to involve service users and carers in their learning activities but a number of barriers were found.

One example of a renal user and carer group in higher education is the Kidney Research and Education Initiative (KREI) at City University London (Chamney et al. 2012), which later developed into the Kidney Research User Group (KRUG) at London South Bank University. The main aim of the KREI was to become a centre of excellence for kidney care, education, and research that had a particular focus on patient involvement in research and teaching. KRUG activities now focus on involvement of patient members in designing research questions, grant applications, development of research methods, and dissemination of findings.

Pre-registration teaching

An interesting teaching session had taken place which was designed for year 2 student nurses and taught by a renal nursing lecturer. Patients and carers from the advisory group were invited to review what was taught and how the lecture was conducted. Patient and carer participation was encouraged at this session as it was felt that the student nurses required examples of first-hand experiences from renal patients and carers in order to supplement and enhance their learning. An evaluation was carried out following the session where the patients and carers were able to provide feedback with regards to the format/structure of the modules based on renal care. Such evaluations provided positive changes to the renal care modules and encouraged motivation and interest in renal care from student nurses.

After further discussions, the members of the KREI decided to involve patients in all future teaching sessions. The first teaching session that involved patients and carers followed a few months later. The views on all sides of patient, carer, and students were very positive. All enjoyed the session and the evaluation from students felt it was very useful since it gave them a strong insight into what it is like to have kidney disease.

Of the 48 students attending the lecture, 46 gave feedback, and 100% of the feedback was positive. Examples of the comments made include:

‘I felt like I was present in the treatment and now know how it feels to be a renal patient’.

‘It was interesting, concrete. It should be done as much as possible to give a human face to conditions’.

‘It brings the subject to life. It teaches me more than what the lecturer teaches’.

‘It was really helpful to have an insight into the patient’s experience’.

‘If we are to become good nurses we need to listen to our patients. This should start now as we train’.

The response to the involvement of patient and carer in all the lectures was overwhelmingly positive. The nurses were able to obtain a first-hand view of the experiences of an individual with kidney disease together with a carer, enabling them not only to learn about renal disease from an academic perspective but also to learn the impact this has on patients from a personal level. Many students commented on the greater impact of a session where they could understand the patient’s journey and the involvement, and importance, of a carer in their life. It was also felt that the practice of involving a patient at such sessions should be extended to other medical disciplines. Felton et al. (2018) has supported this view by finding that the involvement of service users and carers in classroom learning is meaningful and relevant to nursing students’ education. One benefit was that the co-facilitation approach enabled students to understand the person, rather than the ‘patient’.

Overall, the sessions were enjoyable for the students and they appreciated patients and carers coming to their session and showed gratitude. For the patients and carers it was very positive to know that to the best of their ability, they helped give an informative outlook on what it is like to have kidney disease.

Summary

If setting up a similar project in your school or university, then it is important to consider the following:

- all lecturers/practitioners must be committed to the meaningful involvement of patients in teaching and learning;
- patients and carers need to be reimbursed for their time and expenses (see guidelines on this in the following section);
- a formal advisory group needs to be set up with written 'terms of reference';
- patients and carers may need support and/or training in teaching skills and techniques.

McKeown et al. (2010) have written a comprehensive guide to service user and carer involvement in education for health and social care if further information is required.

Patient and Carer Involvement in Renal Research

A review provided evidence of a range of benefits to researchers and participants of public and patient involvement (PPI) in health research (Staley 2009) and the importance of this approach to the NHS has long been recognised (Boote et al. 2002). There is a long history of PPI in particular fields, such as in mental health (Mental Health Research Network; Mental Health Foundation, SURE) and Cancer (National Cancer Research Network; Macmillan Cancer Support). However, user and carer research collaboration between members of the public, researchers, and clinicians in the field of kidney care is still quite new. Staley (2009) reports that one of the impacts of public involvement in health research is that members of the public and researchers develop a more constructive and ongoing dialogue.

Although there are national initiatives to involve patients in research, the number of health researchers actively involving the public in research appears to have been limited (Thompson et al. 2009). In addition, there is little research specifically addressing the attitudes of health researchers towards involving the public. One qualitative study (Thompson et al. 2009) suggested varying constructions of public involvement in research, based on moral and political principles.

A more recent study (Barber et al. 2011) investigated the process and progress of service user involvement in research and also identified perceived benefits to research, researchers, and service user researchers that endorsed previous findings. However, this study also demonstrated the benefits of allowing time for patients' structured reflection on their involvement and this is an important message for those working in renal care. A systematic review (Tong et al. 2015) of 16 studies found that the processes for identifying research priorities are broad ranging, but patient involvement is uncommon, and the processes are often not described well. Establishing research priorities, using a prespecified and transparent process that engages patients, is needed to ensure that resources are invested to answer questions that address the shared priorities in kidney disease.

Case Study 3.4: Patient and carer involvement in research/quality improvement

In 2010, Kidney Research UK, with a grant from the Health Foundation, led a project (named ENABLE-CKD) to improve the variability in managing early CKD by using a quality improvement intervention called a care bundle (a set of evidence-based activities grouped together and carried out at the same time) (Thomas and Loud 2012). The care bundle comprised three clinical interventions, plus one self-management intervention developed and delivered by a Patient Advisory Group.

A patient advisory group was set up and comprised six people with various long-term conditions (kidney, diabetes, heart disease). The group was led by an expert patient, previously known to the renal community and with a background in management. The members of the Patient Advisory Group had some common characteristics, including a shared goal of wanting to help others. The Chair of the patient group created role descriptions in conjunction with team members (see Box 3.1), setting expectations in both the project and patient

BOX 3.1

Role description for patient advisory group members

Duration

The term of office is the duration of the project.

Background

This group consists of people who support the aims of the project and who:

- have experience of kidney disease as service users or carers;
- represent kidney organisations;
- represent nonkidney organisations from related medical disciplines such as vascular care and diabetes care.

Role

- to guide and influence the effectiveness of delivery and propagation of educational tools for patients to improve patient care.
- assist with measurement methods of the quality and effectiveness of tools (with reference to the expected benefits).
- monitor and review output as tools are applied.
- alert core team to potential risks.
- contribute to possible practice training.
- use work from other disease areas.
- consider all work with reference to propagation in other disease areas.
- use personal networks to spread awareness of the programme.

The group will meet two or three times each year.

Principal responsibilities

1. To attend Patient Group meetings.
2. To contribute during Patient Group meetings.
3. To take part in group communications.
4. To deal with the associated paperwork related to the project.
5. Support others in the group.
6. Confidentiality.

Benefits to group members

- personal development: through involvement in the full range of patient group activities, members will be offered opportunities to develop knowledge and skills in areas related to the project.
- personal satisfaction in making a much-valued contribution to a project of potential benefit to kidney patients in the United Kingdom and beyond.
- payment: members can claim reimbursement of travel expenses and a daily fee in accordance with INVOLVE guidelines ([www.invo.org.uk/posttypepublication/payment-for-involvement] accessed 24 June 2018) for attendance at project meetings.

team that all were to be treated as equals and professionals in the project. Honoraria were paid at the same rate as professionals on the team, further demonstrating the value of working together in this way (Loud et al. 2013).

The members of the Patient Advisory Group themselves benefited from their participation in the ENABLE-CKD project, gaining skills in training of professionals, confidence in their own condition, and satisfaction from helping others. Regular communication between Advisory Group members was important to project success, as was understanding and support from each other when Advisory Group members had their own health challenges.

Over two years the team worked alongside the clinical team and the GP practices using a quality improvement approach: Plan, Do, Study, Act (Institute for Health Improvement 2012).

Training healthcare professionals

The team co-developed and delivered training to 29 GP practices in how to help people to self-care. Healthcare professionals appreciated the training and materials; as they were developed by people of long-term conditions it added a level of experience to the project. They valued learning how to explain kidney disease and how to support their patients to self-care.

An information booklet for patients

The team co-developed a patient information pack which the trained doctors and nurses would give to people with CKD who said they wanted the self-management information. A diet sheet was later added to the pack, on request from both patients and professionals. The pack included information about CKD and where to find further information and a DVD called 'Living with CKD'. At the end of the project all these materials were amended following patient evaluation

Education for people with CKD

The patient team co-developed and delivered patient education sessions (for people with stage 3 CKD) at selected GP practices, focusing on how people could help themselves. They explained what self-care is and what an individual can do to help themselves. The education session comprised:

- description of self-care and exploration of benefits;
- areas on which to focus for self-care;
 - blood pressure;
 - blood sugar;
 - smoking;
 - diet;
 - exercise;
 - taking medication and why it is important;
- limited consultation time with doctors/nurses – making the best use of it.

All the materials from this project including teaching slides, notes, and patient information materials are available for free download (following registration) from <https://www.kidneyresearchuk.org/packageofinnovation> (accessed 23 June 2018).

Many organisations have involved patients and the public in improving their services. NHS England (2018) has showcased a range of examples on their website: <https://www.england.nhs.uk/participation/success/case-studies/trusts> (accessed 23 June 2018).

Kidney Patient Involvement Network

Researchers, educators, and project creators should seek patient views and participation in their work. This is not always successful, especially if patients feel included only as a token and are not given requisite support and training in that role. In recognition of the need to build a stronger partnership between patients and professionals, the KPIN (Kidney Patient Involvement Network) team, which

commenced in 2018, has been created by patients and professionals together. It represents many different interests, from kidney research to redesigning services that influence and improve the quality of patient care. It aims to help the patient and carer voice to be stronger and provide adequate training to increase the number of patient/public leaders. KPIN plans over the next five years to measure and research what works, share best practice, capture impact, and embed high quality standards for patient and carer involvement. KPIN has been included as a testbed for INVOLVE standards: www.invo.org.uk/current-work/standards (accessed 23 June 2018).

INVOLVE

INVOLVE is a national advisory group that supports greater public involvement in NHS, public health and social care research. INVOLVE is funded by and part of National Institute for Health Research (NIHR). INVOLVE shares knowledge and learning on public involvement in research and has a useful resource centre to help researchers and clinicians involve patients and carers in their research programmes: www.invo.org.uk/resource-centre (accessed 23 June 2018).

Measuring the Impact of Patient and Public Involvement

Brett et al. (2014) published a review that included 66 studies that reported the impact of PPI on health and social care research. The positive impacts identified enhanced the quality and appropriateness of research at all stages of the research process. These included development of research questions that mattered to patients, development of user-friendly information, questionnaires, and interview schedules, more appropriate recruitment strategies for studies, and enhanced implementation and dissemination of study results. There is no doubt that PPI enhances any quality improvement or research project, but health care professionals must take care to evaluate the impact in order for PPI to become part of everyday practice. A study (Thomas et al. 2016) designed to understand the experiences of older people (>70 years) when making a decision about renal replacement therapy, was also a coproduced study, whereby patients and carers were involved in all aspects of the research process. This study also explored the impact of involving people with kidney disease on the research process and the individuals who were involved. One interviewee (who had kidney disease) said 'It helped because they (the participants) felt that you understood what they were telling you, there's almost that immediate bond' (p. 6).

Conclusion

This chapter has highlighted the critical importance of involving patients and carers in renal practice, education, and research/quality improvement programmes. It is hoped that nurses reading this chapter will reflect very carefully on what has been written and evaluate how far they facilitate a true partnership with patients and their families on a day-to-day basis.

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Resources

- HealthTalk Online offering patient information, patient stories and patient blogs: www.healthtalkonline.org (accessed 20 March 2019).
- INVOLVE supporting greater public involvement in NHS, public health and social care research: www.invo.org.uk/resource-centre (accessed 20 March 2019).
- MAGIC programme – Health Foundation: www.health.org.uk/areas-of-work/programmes/shared-decision-making (accessed 20 March 2019).
- Self-management support: <https://www.health.org.uk/publications/supporting-self-management> (accessed 20 March 2019).

CHAPTER 4

Psychological Perspectives

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Learning Outcomes

- to explore the psychological issues that patients may present with whilst preparing for and undertaking renal replacement therapy.
- to identify the means of support for patients and their partners/families/carers.
- to understand the management strategies that may assist patients and their partners/families/carers to cope with this long-term condition.

Introduction

The variety of psychological impacts that patients face when living with chronic kidney disease (CKD) is well documented. This chapter aims to address the psychological challenges that patients face, along with those that may be experienced by their partners/families/carers when living with CKD. It will highlight the various psychological effects that can impact upon patients, along with management strategies that may assist patients and their partners/families/carers to cope with this chronic illness. The role of the various members of the renal healthcare team will be highlighted, together with ways in which they can assist patients and families to cope with the various facets of treatment modalities for renal disease.

It is vital that the psychological perspectives of patients with renal disease are not underestimated. Hope (2012), a patient living with CKD in the United Kingdom (UK), identified the need for more action to support the reduction of mental health problems for those living with long-term conditions following the report from the UK Department of Health (2011). He identified the need for a robust campaign to highlight more awareness – amongst renal healthcare providers, patients, and carers – of the cause, prevalence, and frequency of renal replacement therapy (RRT) and its complications, including depression, anxiety, and poor coping mechanisms that some patients face. There must also be recognition of the interrelationship between mental and physical health.

Hope (2012) further calls on the need to target what really is relevant to all patients across the age divide, by concentrating on quality of life (QoL), both

physical and mental. This can be delivered to patients where it is relevant in their lives when they are not receiving direct care. There is also a need to prioritise treatment modalities such as self-care in satellite units, home haemodialysis (HHD), continuous ambulatory peritoneal dialysis (CAPD) and pre-emptive transplantation, which provides patients with improved control over their lives and enhances overall QoL, along with mental and physical wellbeing. Finally, there is a need to recognise that kidney failure is a family concern, as it can affect carers/family members' mental health, along with patients. It is important that patients and families/carers are all supported (Hope 2012). Loft (2017), a Communications Officer from Kidney Research in the UK, also discusses the relevance of the psychological impact of kidney disease, and narrates the story of a patient and his partner who identified that they required much more support from the initial diagnosis of CKD 'rather than having to wait until we're at rock bottom before we can get anybody to help us'. They maintain that other patients and their families are struggling also and advocate the need for specialised renal counsellors that can be accessed at the point of diagnosis to assist both patients and their families (Loft 2017).

Dixon (2012) identifies self-management and patient empowerment as familiar concepts in the management of CKD. It is untenable for the healthcare service not to prioritise and direct these concepts, given the ageing population along with the number of people diagnosed with CKD and their subsequent demand on healthcare service. Havas et al. (2015) asserts that the tenets of a patient-centred approach should surround the support provided by the healthcare team when supporting those patients with CKD to enhance their self-management. It is well documented that self-management promotes both physical and psychological wellbeing in individuals with chronic health illness. A meta-analysis of studies was conducted to appraise the effects of self-management in patients with CKD. The findings indicated that self-management programmes can enhance the outcomes of medical, role, health-related quality of life (HRQoL), and emotional management. There were substantial improvements observed in the management of interdialytic weight gain, self-efficacy (perceived competence), anxiety, depression, and HRQoL which advocate instigating self-management programmes for patients with CKD (Lin et al. 2017). Joboshi and Oka's (2017) Japanese randomised control trial tested the efficacy of the Encourage Autonomous Self-Enrichment (EASE) patient education programme with patients (mainly stages 3–5) not receiving RRT. This programme supports the autonomy and intrinsic motivations of patients with the intention of enhancing self-efficacy and maintaining self-management, on apparent self-efficacy, self-management behaviours, and physiological outcomes (blood pressure and renal function parameters). The findings indicate that the EASE programme demonstrated improvements in these patients' perceived self-efficacy and self-management behaviours.

There remains however a challenge for both patients along with healthcare providers to create sustainable strategies. Living with CKD involves many challenges apart from the psychological impact of having a noncurable and life-threatening illness; these include illness-induced interruptions to day-to-day activities, interests, and lifestyles. Patients need both psychological and social support to prevent them from assuming a fatalistic perspective and a view that they have no control over their circumstances – surrendering control. Emotional responses such as anxiety, depression, fear, and uncertainty are commonly expressed by individuals living with CKD. There are many patients who do not have the self-confidence to self-manage their illness (self-efficacy), which has been related to emotions such as powerlessness and depression. However, psychological and social supports are important factors in improving self-efficacy, which has been highlighted as the only

independent predictor of self-care/self-management. There is a need for a high input of psychosocial support, including practical and financial advice, for the many challenges that renal patients face daily if high levels of self-efficacy and sustainable self-care/self-management are to be achieved. It is important to recognise that both psychological and social support care delivery could be affected in favour of the physical aspects of renal care delivery. The relevance of self-care must not be underestimated in patients living with CKD as they are inescapably their own carers and they need this psychological support. If this area of support delivery is reduced it could negatively affect clinical care outcomes along with patients' overall wellbeing and QoL (Dixon 2012).

The National Health Service (NHS) England and the UK Renal Registry (2016) have worked in collaboration to create a national programme – Transforming Participation in CKD. This programme acknowledges the importance of empowering individual patients and their carers to be involved in the management of their care. Engaging with individuals through this manner can enhance their motivation and participating in healthy behaviours can have an influence on both their symptoms and clinical outcomes, as well as transform the means in which they interrelate with health service providers. Evidence-based literature would suggest that an individual's willingness to participate in self-management may be enhanced by specific, directed interventions. A main purpose of this programme is to establish whether the utilisation of intervention programmes can assist individuals living with kidney disease (Stage 3b or higher) to enhance their understanding, abilities, and self-confidence in empowering greater participation in the self-management of their well-being. These interventions are advocated for both healthcare teams and patients. Some of the interventions discussed include the use of asking three questions, which is a simplistic means of assisting patients to engage more in their treatment and care. Referring to these questions throughout a consultation can assist decisions concerning the best choice of action for each single patient. This concept endorses the NHS's objective of 'no decision about me, without me' (NHS and UK Renal Registry 2016). Jayanti et al. (2015) investigated decision-making preferences and their motivating factors in end-stage kidney disease (ESKD) patients. They assert that healthcare providers should move away from a standard 'one size fits all' style and be more mindful of the individual patients' preferences. See <https://www.thinkkidneys.nhs.uk/ckd> for further information (accessed 10 June 2018).

Further interventions supported by NHS England and the UK Renal Registry (2016) include the use of personalised care-planning, peer support, and motivational interviewing (MI). This is another vital aspect of efficient sustained self-management. Through the means of information-sharing, shared decision-making, goal-setting, and action-planning, patients must be supported to articulate their own requirements and act on their own priorities. The use of peer support also has the ability to enhance experience, psychosocial effects, behaviour, health outcomes, and service usage amongst individuals and their carers living with chronic physical and mental health conditions. According to experience and evidence, peer support is respected by those who participate; it can enhance how individuals feel and how they act. It may enhance motivation and self-confidence ('you are not alone'). The use of MI can improve patient self-efficacy. Patients can often feel overcome, despairing, or powerless, and subsequently experience reduced self-efficacy. MI can enable the patient and can impart optimism, confidence, and achievement. It assists patients to express their anxieties and obtain resolutions. It is a shared person-focused type of guidance to produce and reinforce motivation for change. MI utilises the patient's own influences and beliefs to ensure attainable and healthy lifestyle modifications including concordance to treatment. Those patients who participated in MI in comparison to the usual treatment have established they are

more likely to engage with their treatment, including attendance and participation in follow-up appointments, as well as creating vital enhancements in general health and wellbeing (NHS England and the UK Renal Registry 2016).

Psychonephrology

Psychonephrology is relevant to the psychological perspective of patients living with CKD, and established kidney failure (EKF). Psychonephrology has addressed nephrology and mental health, including psychiatry and psychosomatic medicine, since its inception in the 1970s (Levy 2008). Ohtake (2017) explains the rationale for psychonephrology. Firstly, patients living with CKD, especially those receiving dialysis, commonly experience increased levels of stress and have characteristics not found in patients with other illnesses. Secondly, patients with CKD commonly present with psychological reactions due to poor physical conditions from their primary disease, as well as the side effects from their medications. Finally, the close relationship amongst these patients and their family members and healthcare professionals can result in psychological stress in these other individuals. There are three main areas in psychonephrology: (i) care for patients with CKD, especially the psychological support associated with RRT; (ii) interventions for psychosomatic conditions in patients with CKD; and (iii) mental health provisions for healthcare providers in RRT. Patients often experience a variety of different types of psychological pain throughout the time approaching the commencement of RRT. They utilise a variety of defence mechanisms to cope with these types of pain. Many patients experience anxiety, anger, bitterness, apprehension, hopefulness, and depression before eventually coming to admit the necessity of undergoing RRT. However, some patients may remain in continual denial even after starting RRT; this often presents itself as physical symptoms or concordance issues to treatment. It usually takes around two weeks for CKD patients to recover their psychological equilibrium after being advised that they require RRT; this would be a normal psychological response. Some patients, however, may respond in a different manner which delays their psychological recovery; this is known as an adjustment disorder. This can vary depending upon the patient; he or she may be anxious or depressed long beyond the two-week window after having been notified of the need for RRT.

Chronic Kidney Disease

Most patients with CKD stage 4–5 (estimated glomerular filtration rate [eGFR] $<30 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$) or with CKD stage 3 and rapidly deteriorating renal function should be referred to a nephrologist for assessment. Ideally, patients should be referred at least a year before it is considered that they need RRT (Warwick et al. 2014). The Canadian Society of Nephrology clinical practice guidelines concerning the timing for commencing chronic dialysis identify that this should be based on when the patient presents with problematic uraemia symptoms or when the eGFR falls below $6 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$ (Nesrallah et al. 2014). Fischer et al. (2011) assert that interventions are badly needed to diminish late referrals for treatment and enhance patients' health when living with CKD. Smart and Titus (2011) assessed the impact upon clinical outcomes of early versus late referral of patients to renal services. They highlighted the advantages of early referral, including enhanced survival and reduced hospital stay. The UK Renal Registry (2016) highlighted a

reduction in the number of patients presenting as late referrals from 23.9% in 2006 to 16.4% in 2015. These late-referred patients were more likely to be younger (64.5 vs. 65.1 years), and of white ethnicity. They were also less likely to commence peritoneal dialysis (PD) and have a lower eGFR (7.7 vs. 8.6 ml min⁻¹ 1.73 m⁻²) than those patients who were early presenters. This reduction in late presentation may be as a consequence of several factors in the UK, including the Quality and Outcomes Framework (QOF) initiative (www.dh.gov.uk) which increases recognition of CKD amongst non-nephrologists, and the introduction of eGFR reporting which was supported with local and national guidelines (UK Renal Registry 2016).

The UK National Institute for Health and Care Excellence (NICE) (2011) clinical guidelines for PD highlight that patients and their families must be provided with both oral and written information concerning pre-emptive transplant, dialysis, and conservative care to enable them to make informed choices about their treatment. A systematic review of the readability of health-related information aimed at patients with CKD found that this written information is targeted above the average patients' literacy level. This is influenced by the cognitive decline of patients with CKD who may have a more reduced literacy level than the typical patient. This review suggested that healthcare providers need to be mindful of their target audience when preparing relevant patient information literature which should involve the pilot testing of same using patients with a reduced literacy level (Morony et al. 2015). Taylor et al. (2017) undertook a systematic review of quantitative studies of health literacy and clinical outcomes amongst adult patients with CKD. They found limited robust studies, however the available studies indicate correlations with adverse clinical events, increased use of healthcare, and mortality. There is a need, however, for prospective studies in this area.

Patient-centred care must take on board patients' unique needs and preferences. The management of care must be maintained by evidence-based information, which enables patients to make informed decisions concerning their care. There must be effective communication, with all the relevant parties involved. Patients and partners/families/carers must be given the opportunity to participate in decision making concerning their treatment and care (NICE 2011). Goovaerts et al. (2015) identifies that it is feasible to apply an education and support programme (renal replacement therapy option education [RRTOE]) that assists patients to choose a form of RRT that is most suited to their needs. This is through meticulous planning and efficient interdisciplinary collaboration, with the fundamental objective being the provision of knowledge and skills to enable patients to choose a modality that will advance their QoL. Campbell-Crofts and Stewart (2017) undertook interviews in two pre-dialysis clinics in Sydney, Australia, to ascertain patients' views concerning their decision-making experiences as they contemplated their transition to RRT. There were three overall themes that developed from the patients' perspectives which were outlined as the following questions: (i) Do I need RRT? (ii) What is the 'right' RRT for me? and (iii) When should I commence RRT? Interestingly the participants' feelings concerning their transition to RRT were affected by their apparent feelings of wellness and the viewpoint that RRT would not be required at any time in the near future. There is an onus on renal healthcare providers to fully comprehend the patient's journey throughout the pre-dialysis stages of CKD to create a space for shared understanding. This is required for the future planning and application of collective, person-focused educational approaches and long-term renal health outcomes (Campbell-Crofts and Stewart 2017).

There are many challenges facing individuals living with ESKD, particularly those receiving dialysis. Patients usually undertake haemodialysis (HD) three times per week for three to five hours each time, or undertake PD exchanges three to four

times daily or are attached to a machine at nighttime for many years consecutively. There can be problems related to the therapies themselves, the presence of comorbidities, constant uraemic symptoms, the requirement to conform to dietary and fluid restrictions, travelling to and from HD treatment, the burden of taking a large amount of daily medications, and the effect on employment, along with burden on family members (Speyer et al. 2016). This all indicates having to manage major stressors, including the symptoms of CKD, and the related problems and psychosocial consequences. A study by Rebollo Rubio et al. (2017) highlighted that about 30% of patients commencing RRT experience both anxiety and depression, which impacts on both the physical and emotional facets of HRQoL. These findings indicate the importance of close monitoring of patients' care throughout the first few weeks following the initiation of RRT. There is a need for a systematic complete evaluation as part of the treatment provided to patients in the pre-dialysis stage of CKD. The characteristics of anxiety and depression should be assessed for and addressed from their initial presentation, especially when RRT is been initiated. It is vital that interventions that ensure social support, including education concerning the emotional facets for patients with RRT as well as family participation, is addressed during the pre-dialysis discussions by the renal nurse. If this is not addressed, these issues could reduce the benefits to be acquired from RRT and exacerbate the patient's HRQoL (Rebollo Rubio et al. 2017).

Patient Choice

Chen et al. (2017) identifies that patients are often unsure as to which modality will be the best option for them, as there are advantages and disadvantages for each therapy which can be challenging for patients; this can result in decisional conflict. This can therefore increase the possibility of patients making decisions that are not founded on their values or preferences, which could lead to detrimental post-decisional outcomes. There are two main types of dialysis available: HD and PD. Each of these can vary – for example, there can be HHD, in-centre HD along with CAPD, assisted peritoneal dialysis (aPD) and automated peritoneal dialysis (APD). It is important to explain all the treatment options that are available. The major considerations that determine the best form of dialysis for individuals with CKD are their preferences concerning which therapy suits their daily lives best, the choices that are available within their renal unit, and clinical contraindications. Other considerations concerning PD that patients and families/carers should take into account include the skill to undertake this form of dialysis themselves; social support to assist them to undertake PD; incorporation of dialysis within personal and professional activities; opportunities to retain social connections; potential adaptations to their home; the time and distance journeying to hospital; flexibility of daily therapy; nutritional and medication regimens; and potential alterations to body image and physical pursuits due to dialysis access points (NICE, 2011).

According to Robinski et al. (2017) the role of psychosocial conditions as influencing factors in choosing a dialysis modality has been underestimated by research. These authors recently conducted a multicentre study in Germany with patients receiving HD and PD 6–24 months after the initiation of dialysis. The participants completed a questionnaire which referred to socio-demographic, psychosocial, physical, and shared decision-making facets; additionally, cognitive functioning was established. When patients had a good psychological state, and received shared decision-making, they were more satisfied. People receiving PD in contrast

to HD were more satisfied with their treatment and had enhanced cognitive functioning. They had a more autonomy-seeking character, and identified further satisfying shared decision-making. Treatment satisfaction was higher specifically in patients receiving HD when they had reduced cognitive functioning, a less autonomous personality, additional social support, and poorer physical and socio-demographic conditions. This study highlighted that psychosocial attributes play a pivotal role in treatment satisfaction in patients. The importance in clinical practice of concentrating on screening patient characteristics and shared decision making at an initial stage can promote patients' treatment satisfaction. Any changes to these initial findings will be investigated in a follow up in one year's time (Robinski et al. 2017).

Haemodialysis

Harwood et al. (2012) hypothesised that increased stressors and maladaptive coping responses would impact upon the selection of dialysis modality, specifically HHD. This study highlighted that individuals on HHD versus in-centre HD reported significantly fewer predialysis stressors, although coping was not associated with dialysis modality. The authors concluded that predialysis stress levels predicted dialysis modality and recommended further interventional studies to address CKD stressors with the aim to improve HHD usage.

An arteriovenous fistula (AVF) is the vascular access of choice for HD, followed by the arteriovenous graft (AVG), with the least preferred option being either tunnelled or non-tunnelled catheters placed in a central vein (Murphy 2011a). The specific timing for AVF placement will be governed by the rate of reduction in renal function, comorbidities, and by the surgical route. The AVF should be created at least six months, and AVG at least six weeks, before HD is required. However, it can be difficult to predict the rate of progression in some patients, thereby making the timing of access placement problematic (Kumwenda et al. 2015).

Patients should be involved in decisions about their management including pre- and post-vascular access insertion and long-term management. There can be significant problems related to vascular access resulting in increased morbidity and mortality if not properly treated. It can be very difficult for patients to adapt to having a chronic illness and the prospect of having HD. There must be continuous education and psychological support provided to the patients and partners/family members. Patients can experience body-image concerns, self-concept, and anxiety regarding their vascular access (Dinwiddie 2008). Patients must remain at the centre of care delivery as vascular access is their lifeline to HD treatment. The renal healthcare team, especially the nurse, play a vital role in the management of patients' vascular access (Murphy et al. 2011; Murphy, 2014).

According to Wadd et al. (2011) there is a paucity of literature that has examined the experiences of parents receiving HD. Related research has identified vital themes such as restricted lives, relationships, changes, ramifications, and outlook. Parents experience numerous illness-related symptoms, including fatigue and uraemia. These can impact upon their ability to provide both physical and emotional support to their children. The time spent with dialysis treatment can minimise time spent engaging with children in both play and school activities, along with other day-to-day activities such as work and household responsibilities. There is a necessity for further research in this area to ascertain the experiences from parents' viewpoints (Wadd et al. 2011). Interestingly Tu et al. (2014) identified patients receiving dialysis who had children or partners and were employed used considerably more coping strategies than those without any of these factors. Patients experienced more physiological stressors than psychosocial stressors such as limitations

in fluid and diet food and fatigue. The longer length of time that they received HD, the less stress experienced.

The Coping Strategy Inventory-Short Form (CSI-SF) is a recognised tool for investigating and clarifying cognitive and behavioural processes used by patients receiving HD to cope with stressors inflicted by their disease and therapy. The international sample of 7201 HD patients participated in this study using 9 languages, and were recruited in phase 4 of the Dialysis Outcomes and Practice Patterns Study (DOPPS). The CSI-SF measures four coping strategies, which were problem-focused engagement; problem-focused disengagement; emotion-focused engagement; and emotional-focused disengagement based on 16 items. An engagement strategy consists of an individual taking action by directly confronting his/her stressors. This can be regarded as a main influence in minimising the long-term psychological and physiological sequelae of environmental stressors. An avoidance or disengagement strategy is where the individual attempts to reduce his/her exposure to noxious stimuli. This can be regarded as generating enviable short-term effects but resulting in long-term concerns, including depressive symptoms. The importance is given to manage the stress-producing situation if the focus of the coping effort is problem-focused, whilst the importance is given to regulating an individual's affective response if the focus of the coping effort is emotion-focused. The results of this study indicate the support for the usage of the CSI-SF to assess coping strategies amongst English speaking patients in the United States, Canada, Australia, and New Zealand as well as Germany and Sweden (Speyer et al. 2016).

It has been highlighted that renal healthcare providers need to create strategies that promote patients to use humour effectively, along with positive thinking, whilst concurrently educating patients to use strategies that assist them to maintain normality within their life as much as feasible. It is also important that staff recognise those individuals that react more emotionally and demonstrate more stressors and less effective coping strategies. A collaborative team approach may assist these individuals using an educational and supportive care plan that can assist them to both adapt and manage their CKD (Harwood et al. 2009). It must be recognised, however, that those who are not coping do not always show emotion.

The empowering patients on choices for renal replacement therapy (EPOCH-RRT) study conducted interviews with 179 patients in the United States with advanced CKD not yet receiving dialysis (CKD-ND $n = 65$) as well as patients receiving HD ($n = 76$) and PD ($n = 38$). The transcripts of the interviews were categorised and established on the Coping Strategies Index (CSI) and were then contrasted across these patient groups by demographics, modality choice, and health status. The findings indicated that there were a number of concurrent coping strategies utilised by these patients that cross categories within every CSI subscale including problem-focused and emotion-focused strategies. The patients undergoing HD depended more upon social support in contrast to other patients. They utilised less types of disengagement strategies, with no patients receiving HD using approaches that were categorised as either social or wishful thinking. The findings indicated that the lives of patients are seriously impacted by kidney disease; patients have to cope with numerous chronic physical, psychosocial, and financial pressures. The CSI framework is applicable to the situation of coping with CKD and the qualitative approach used in this study highlighted this. The depictions of the lived experiences of patients coping with kidney disease may empower other patients with coping skills that match their own needs with the understanding that they have been successful for others in related situations. This understanding in the meantime may enhance targeted assistance provided by healthcare providers in order that patients can better cope with the many challenges they endure living with kidney disease (Subramanian et al. 2017).

Peritoneal dialysis

The UK Renal Association Clinical Practice Guideline (2017) on PD in adults and children acknowledge that the success of a PD programme is reliant upon specialised nurses, with relevant knowledge and skills in assessing and educating patients for PD therapy, supervising treatment and the appropriate resources to provide sustained community care (Woodrow et al. 2017). Keddo (2010) asserts that the nurse's attitude and confidence during the initial meeting with the patient and his or her family is vital, as it could make the difference between a successful PD assessment and one that is not. This could be said of any meeting with patients and their partners/families/carers to discuss treatment options. There are many psychosocial challenges whilst trying to adapt to PD. This includes language, literacy, limited memory, and family support. Language can be a challenge and an impediment to learning if, for example, the patient does not speak the native language (Thomas 2009). McClure (2010) concurs that there are additional challenges for those patients who do not speak the primary language that the nurse or trainer speaks. Factors such as previous learning experiences, ability to learn and repeat skills, uraemia levels when training occurs, comorbid problems, amount of fatigue, and current health beliefs may all contribute to patients' difficulties in learning the information required.

The physical environment where the teaching sessions are conducted must be quiet and free from disturbance and distraction. This environment can affect both the mental and emotional environment. The nurse must build a trusting relationship and achieve the means of communicating effectively using a culturally competent approach to enhance the chance of success. There can be limited resources available concerning translation services. This being the case, the onus is usually placed upon a younger member of the family such as a son or daughter to translate for the patient. This presents its own challenges as it can be difficult to ascertain whether the patient has grasped the information or whether it is the translator (family member) only (Thomas 2009). Various educational support materials can be used to support the information process including online materials, DVDs, technical manuals, and picture guides. It is important to ensure that renal healthcare providers have specialist knowledge concerning CKD and the essential skills to encourage decision-making. This can include skills in promoting and using decision aids to assist patients in making decisions concerning their care and treatment (NICE 2011).

Depression

Depression can be experienced in 2–10% of the general population; however, it is prevalent in 20–30% of patients receiving dialysis (Dobbels et al. 2010; Ossareh et al. 2014; Treadwell et al. 2017). Dobbels et al. (2010) assert that symptoms of depression, along with specific depressive conditions, are prevalent both in patients on dialysis as well as following kidney transplant. Patients that are depressed often have reduced QoL, further functional impairment, compounded pain, and worse concordance with medical treatments. Furthermore, they have more episodes of hospitalisation and greater mortality (Hedayati et al. 2012). Ossareh et al. (2014) maintain that patients who are depressed are three times higher in having concordance issues with their medical therapy in comparison to those patients that are not depressed.

Bossola et al. (2017) maintain that patients 'care little for PTH, Kt/V, and phosphate values but much about comfort, mobility, functionality, energy level, sleep

and mood'. This absence of consideration by healthcare providers to what patients regard as their quality objectives is challenging. Symptom burdens must be assessed and should be a significant component in the holistic evaluation of dialysis patients. Depression is diagnosed and managed only in a minority of patients, regardless of the high predominance and poor outcomes related to depression in dialysis (Holley 2013). Holley (2013) asserts that depression can impact upon the patient and their partner/family's response to management and participation in advance care planning. Recognising depression in a dialysis patient consequently can impinge upon overall treatment and QoL with physical symptoms and reactions to dialysis care.

It is worth considering screening for depression in patients on dialysis, due to the significant effect upon patient outcomes and overall goals for treatment. There are a number of recognised validated tools that are used for screening depression including the Beck Depression Inventory (Beck et al. 1961), and the Centre for Epidemiologic Studies Depression Scale (Radloff 1977). Most of these tools can be completed in a number of minutes and, with some individuals, this screening is an essential addition to screening for diminished cognition. Ossareh et al. (2014) identified that those patients that score higher than 10 have an increased risk of death compared to those with lower values. The physical symptoms that are typical of depression and may be more common in patients on dialysis include reduced energy, fatigue, sleep disorders, reduced appetite, and difficulty concentrating. However, to diagnose depression these physical symptoms must be accompanied by either feeling of sadness or lack of interest (Holley 2013).

Renal healthcare providers may play a pivotal role in establishing coping strategies. One of the treatment strategies for depression is to identify previously used coping strategies. Coping strategies are usually categorised as task oriented or emotion oriented. The individual must ascertain the stressor, initiate alternative solutions and reduce the expectations in task-oriented coping strategies. Some personality traits such as extraversion and frustration tolerance are related to task-oriented coping, whilst emotion-oriented coping strategies aim to influence the emotions affected by the stressors (Yeh et al. 2009). Keskin and Engin (2011) aimed to assess depression and suicidal ideation and coping strategies with stress in patients undergoing HD therapy. They found that patients firstly selected task-oriented coping strategies, followed by emotion-oriented coping strategies, and finally dysfunctional coping strategies. Both levels of depression and thoughts of suicide were high amongst patients who had lower education status and were receiving dialysis treatment for one to five years.

It is vital that nurses assess their patients using a holistic approach and consistently manage depression symptoms and suicidal ideation to improve quality care delivery. Nurses using integrated evaluation are vital in enhancing the mental health of patients living with ESKD (Keskin and Engin 2011). Treadwell (2017) suggests that Orem's Theory of Self-Care Deficit is suitable for recognising depression, discerning motivation for change, and inspiring self-care practices. Utilising the theoretical framework of Orem's nursing process, the capacity to highlight and address psychosocial concerns in patients may offer essential information to support patients with self-management skills to enhance concordance and QoL. There is a need for large clinical trials to ascertain the best method to manage depression in patients with ESKD (Treadwell 2017). Interestingly, recent research by Williams et al. (2017) highlights that male care providers of patients living with advanced kidney disease experience burden and symptoms of depression, as well as alterations in their physical health, as a result of their care provider role. The findings of this study suggest that the male care providers share similar experiences to female care providers of patients living with advanced kidney disease.

Sexuality

It has been identified that there is a high prevalence of sexual difficulties in patients with CKD, with 75% of men receiving dialysis experiencing erectile dysfunction and 30–80% of women with symptoms associated with sexual dysfunction. Navaneethan et al. (2010), in their systematic review and meta-analysis of observational studies, highlighted that, despite the incidence and clinical importance of this area, there were many limitations to the studies reviewed, including a poor response rate and lack of validated tools to assess sexual difficulties. There were also limited studies addressing this area in women with CKD who were not dialysis dependent. The development and expression of sexuality is influenced by biological and psychosocial factors. Sexuality can be a challenging concept to define. It is a multidimensional concept that incorporates a wide range of enjoyable sexual activities that may or may not include coitus but also touching, kissing, and embracing. It also includes body image, self-esteem, self-image, and how other individuals perceive us. It can be viewed that being a sexual individual is healthy. Therefore, participating in sexual intimacy might permit a means of helping individuals who are living with chronic illness to feel ‘normal’ (Sheils 2003; Lemieux 2004; Murphy 2011b, 2012; National Kidney Foundation 2011).

There are many contributory factors that can lead to the development of sexual difficulties in patients living with renal disease; these are medications, alterations in hormones, vascular, neurological, and psychological factors (Navaneethan et al. 2010). Table 4.1 indicates the numerous physical and psychosocial sexual concerns associated with living with renal disease. These sexual concerns do not just impact upon patients but also their spouses/partners/significant others. It can affect their overall QoL and can impact significantly upon their personal and overall family relationships. It can also be challenging for patients who are not in a relationship and who may be looking to meet a partner, or for those that are content not being in a couple, as overall body image can be altered when living with renal disease (Murphy, 2014).

Table 4.1 Male and female physical and psychosocial sexual concerns living with advanced kidney disease.

Men	Women	Both men and women
Tiredness	Tiredness	Anxiety, stress, and depression
Decreased libido	Decreased libido	Fear of failure
Sexual arousal difficulties	Sexual arousal difficulties	Struggle in relationship with spouse/partner
Erectile dysfunction	Absence of vaginal lubrication	Roles changes leading to reliance
Premature or delayed ejaculation	Pain during intercourse	Sense of guilt towards spouse/partner
Difficulty in achieving orgasm	Difficulty in achieving orgasm	Diminished confidence in sexual identity
	Altered menstrual patterns	Changes in body image and reduced self-esteem
	Anovulation	
	Fertility problems	

Source: Adapted from Auer (2008) and Levy et al. (2016).

Body image is intertwined closely with sexuality. Patients living with PD and HD require vascular access surgery, which can lead to scars and potential deformities. There is also the psychological impact on how patients feel with a potential foreign body in terms of a PD catheter inserted into their abdomen or living with a central venous catheter (CVC) in the neck or an AVF in the arm. Patients may feel that such vascular access is a constant reminder of living with their chronic illness. It has been regarded as the patient's 'lifeline' and therefore must be monitored carefully. Concurrently patients can feel unattractive and self-conscious of these 'lifelines' and may alter their self-image accordingly, for example avoiding wearing short-sleeve tops or keeping their shirts or tops buttoned up to avoid showing their central lines or fistulae when out in public, in case they attract stares. They may also find it difficult to undress in front of their spouses/partners or become intimate, for fear of being rejected by them. This may be a more significant issue in patients living with PD in terms of their abdominal catheter and positioning it when trying to be intimate with their spouses/partners/significant others (Murphy, 2014).

Furthermore, patients can complain of abdominal discomfort and distension with dialysate fluid, which can impair their body image regarding clothes size having to be increased to accommodate an extended abdominal girth. This can, again, impact their self-esteem and overall body image, leading to patients potentially feeling unattractive, unwanted, and depressed, and leading to social isolation. One could argue that there is a double-edged sword with regards to the use of some medications that patients must take to manage their treatment, such as antihypertensive drugs, and possible side effects such as erectile dysfunction (Murphy, 2014).

The use of immunosuppression medications with kidney transplant recipients can result in side effects that can affect body image such as hirsutism and weight gain. Female patients for example may be anxious to conceive post-transplant and may potentially risk their transplant if they do not concord to the recommendations of planning for conception and being carefully monitored by renal and maternity health care providers throughout the pregnancy (Murphy 2014).

Baker et al. (2017) identified that recipients of transplants should wait for one-year post transplant and have stable function before attempting conception. The advice concerning contraception should be comparable to the general population. Female recipients and their partners should be offered counselling regarding fertility and reproduction either before transplantation or soon afterwards. Prior to conception the immunosuppressant m-TORi should be discontinued and substituted as appropriate. The advantages and disadvantages of breastfeeding should be considered. It is suggested that there should be care pathways for managing sexual dysfunction. This issue should be discussed ideally at the annual review clinic. It is recommended that there should be close cooperation with local andrology facilities. In male kidney transplant recipients (KTR) the drug Sildenafil is safe and effective in males not prescribed nitrates (Baker et al. 2017). Sadeghian et al. (2016) maintain that the issue of body image has not been provided with enough attention for patients living with kidney disease. A disturbance in body image may increase the likelihood of psychological conditions amongst this group of patients.

Sexuality is not just relevant with patients who are receiving dialysis and kidney transplantation but also those that have chosen conservative management. It can remain an integral part of their lives and should not be assumed that it is not relevant towards end of life care. The concept of emotional connection may take priority over the physical aspect of sexuality at this stage of the patient's life (Murphy 2011b, 2012).

The management of these sexual difficulties includes optimising dialysis treatment, addressing dietary, anaemia, endocrine abnormalities, and hyperparathyroidism

issues, and reviewing drug therapy, erectile dysfunction, and psychosocial issues (Levy et al. 2016). It is important to broach this sensitive subject with patients. If members of the renal healthcare team, especially nurses, do not do so there can be a strong possibility that patients will not introduce this subject as they could feel embarrassed and uncomfortable in discussing it. Renal nurses must be comfortable with their own sexuality to discuss this subject and put aside their own preconceived ideas. They must be good communicators and be able to recognise when some patients do not want to discuss this subject, watching for verbal and nonverbal cues and being mindful of cultural issues and the physical environment at the time in terms of privacy. Not all patients identify sexual concerns as being an issue for them; this must be also acknowledged by nurses. However, the matter should be introduced and then it should be ascertained whether this is an issue for further discussion. It is important to involve the spouses/partners as much as feasible to enable them to feel included in this process and to ascertain their experiences. Patients must be educated in how to manage these sexual concerns and where to seek further assistance and advice, as nurses are usually not trained counsellors. The renal healthcare team needs to be educated in how to discuss this subject and to recognise that it is a real and valid concern for their patients. They must recognise that this area is an intrinsic part of patients' care delivery. If this vital aspect of patient care is not addressed and managed by nurses who are usually central in patients' care delivery; this could lead to patients suffering needlessly "in silence" (Murphy, 2012; Murphy, 2014).

Patient Education

Shared decision-making is vital for renal care delivery. A group was formed in the UK representing people living with CKD, including patient organisations, nurses, physicians, experts, and researchers in shared decision making. The aim of this group is to ensure that individuals with advanced CKD will be supported in making choices regarding their treatment. They and family members/carers they wish to include will receive information regarding every clinically appropriate option for the management of their kidney disease. There will be training and support provided to clinicians in the provision of decision support and information along with the usage of readily accessible tools (MacManus et al. 2012).

MacManus et al. (2012) assert that these aims will be readily accomplished if clinicians can act. The actions that will make a significant change include clinicians being prepared to use decision aids when discussing patients' treatment choices, along with the provision of this information using different formats. This will assist individuals with advanced kidney disease to comprehend the various clinically appropriate options available to them. Clinicians should also be able to assess the degree to which individuals are included in decision making concerning their care and to use this assessment to improve the service provided (MacManus et al. 2012). NHS Right Care (2017) decision aids for established renal failure and dialysis can be accessed online and can assist patients in deciding what the best choice is for them.

Shared decision making is relevant with the recent Standardised Outcomes in Nephrology (SONG) (2017) initiative. SONG is an independent and global initiative that brings collectively patients, care providers, and health professionals in collaboration to determine core outcome domains and outcome measures across the range of kidney disease for clinical trials and other types of research. The outcomes will be established based on the collective priorities of all the relevant stakeholders including patients, care providers, health professionals, researchers, and policy

makers. This will assist in ensuring that researchers convey outcomes that are significant and applicable to patients with kidney disease, their carers, and their health professionals; and consequently support decisions concerning treatment. Each SONG initiative is founded on the target group of patients which is determined by the appropriate stage of CKD/therapy stage (1–5): SONG-CKD, SONG-HD, SONG-PD, kidney transplantation SONG-Tx, age (i.e. paediatrics [SONG-Kids]), or diagnosis (e.g. polycystic kidney disease SONG-PKD) (SONG 2017).

The importance of early patient education cannot be underestimated. An Australian review by Strand and Parker (2012) compared the effectiveness of multidisciplinary care with traditional medical care on the progression of CKD stages 3–5. The multidisciplinary model of care is organised to provide individualised care to delay or prevent the advancement of CKD along with addressing the areas essential to attain a higher level of well-being or QoL for patients living with CKD. This review highlighted that education is a vital component that must be incorporated within multidisciplinary care.

Warwick et al. (2014) advocate that all patients should be encouraged to undertake home dialysis therapies where feasible, as part of an integrated management to RRT. They suggest that, where home dialysis is not feasible, patients and their partners/carers should be actively included in their dialysis treatment, be supported to perform as much self-care as feasible, and be engaged in every facet of their treatment including the management of medication and alterations in diet and lifestyle (Warwick et al. 2014). Power and Ashby (2014) suggest that both shared care and home dialysis therapies derive psychological and QoL benefits, as well as enhanced physiological effects for patients.

It is recommended that all patients with severe CKD (progressive stages 4 and 5), along with their families and carers, should be provided with a suitable education programme aimed at enhancing their knowledge and comprehension of their condition, and of the choices for treatment. Education programmes should be multidisciplinary, multifaceted, individualised to the needs of the patient, and grounded in adult learning principles. There are many educational methods that should be accessible, including individual conversations, group work, written and online resources, DVD/CDs, and contact with expert patients, along with opportunities for informal follow up. The information delivered must be pertinent to the individual, with the approach, balance, speed, and extent of the delivery being matched to the individual's learning style, ability, and preferences. The education programme must also include provisions for the education of patients who are referred late to dialysis, and commence dialysis in an unplanned way (Lecouf et al. 2013). Prerenal replacement therapy education programmes for patients and their families and carers should be sustained into the treatment period, with the purpose of enhancing patients. Involvement in their own care, increasing treatment concordance, and promoting good communication and cooperative relations with caregivers (Warwick et al. 2014). Mouelhi et al. (2017) identified that the majority of KTR in their study in France ($n = 1416$) were actively utilising the internet and social networks. They recommend that renal transplant units should create adaptable and web-based resources relevant to transplant information, which will permit a swift adaptation to changes in widespread practice, enhance patients' health, and indicate their preferences.

Self-Care

The concept of self-care is now extensively encouraged for the management of chronic illness. Some good examples of where self-care can be taught are those of home dialysis therapies (either HD or PD); where patients can learn to manage

their often complex treatment. This contrasts with many patients that attend both large centre and satellite HD units who can become very reliant on the renal healthcare providers and their partners/families. This may be partly associated with their comorbid conditions, but may also be pertinent to the concept of 'learned helplessness', which was highlighted in the initial days of dialysis; this concept is, however, more pertinent currently with the advancing age of the RRT population. The concepts of enhancing both self-care and self-efficacy have become more prominent in recent years amid patients with CKD.

There are several dialysis units in both the UK and Ireland where patients who have hospital-based therapies are encouraged to take greater involvement in their dialysis from the initial diagnosis and ongoing to patients undergoing RRT (Appleby 2013). Should patients not accept the gravity and the chronicity of their illness, it can lead to difficulties in accomplishing educational goals and concordance with the rigour of the treatment. Additionally, individuals learn more efficiently when information is accessible in a manner which concurs with their own learning style and choices; using several teaching methods should assist patients to learn (Warwick et al. 2014). SHAREHD is a Health Foundation-funded programme that aims to support patients receiving HD in hospital to be more independent and confident in participating in aspects of their own HD care. This programme has been extremely successful in demonstrating that greater patient engagement and helping people to manage their own health, is associated with better outcomes across a range of medical conditions. For more information see <https://www.shareddialysis-care.org.uk/sharehd> (accessed 10 June 2018).

Cove (2012) highlights the importance of psychological preparation in the care of patients in their adjustment to major changes in both health and treatment status from stages 4 and 5 CKD, to transition to RRT and renal transplant. The lack of psychological preparation can lead to adverse patient outcomes, including late initiation on RRT with related risks such as cardiovascular disease (CVD). Limited psychological preparation for renal transplantation can lead to acute rejection incidences along with the possible loss of the graft. Renal healthcare providers can assist patients through these challenges; however, there are patients that struggle. Adapting to their disease progression may require more intensive treatment (Cove 2012). The transtheoretical model of behaviour change, or stages of change model, ascertains a person's willingness to move towards healthier behaviour through a progression of psychological stages (see Box 4.1).

BOX 4.1

Transtheoretical model of behaviour change

- pre-contemplation (not ready): Here the patients do not plan to act concerning their health in the foreseeable future and are not aware that their behaviour will cause problems (for example a patient not accepting yet that he/she requires RRT soon).
- contemplation (getting ready): Here the patients are starting to identify that their behaviour is not helping them; they can begin to consider the advantages and disadvantages of their actions.
- preparation (ready): Here the patients intend to act soon and start taking small steps in changing their behaviour.
- action: Here the patients make precise overt behaviour modifications in attaining new healthy behaviours.
- maintenance: Here the patients can maintain action for a while and work towards preventing a relapse.

Conservative Kidney Management (Nondialytic Options)

It is important that patients with advanced CKD have all treatment options discussed with them and their partners/families. There are many older people presenting for dialysis who can be frail, require assistance, and have comorbidities such as heart disease and diabetes. With some older patients, dialysis may be a difficult treatment option and may not necessarily lead to an improved QoL along with prolonged survival (Murphy 2014).

Choosing a treatment option is a very personal decision. HD might be desirable for some patients, whereas others might prefer PD. Other patients who present with serious medical problems might be better advised to manage their symptoms. Conservative kidney management is where the patient opts not to have dialysis but will have continual assistance from the multidisciplinary team in terms of symptom management and control, along with palliative care and social work support (see Chapter 11 for further information).

Transplantation

It is recommended that kidney transplantation is the RRT of choice for those patients who are considered both suitable for major surgery and for chronic immunosuppression. Every individual that is expected to have an improved life expectancy post-transplantation should be assessed for transplantation. It is vital to maintain the patients' wellbeing whilst waiting for a kidney transplant (Murphy et al. 2011). All suitable patients should be listed for cadaveric transplantation six months prior to the expected commencement of RRT. The advantages of pre-emptive transplantation should be advised to all patients that are medically fit for surgery. There should be efforts made to detect a potential donor to enable pre-emptive transplantation prior an individual's requirement for RRT (Warwick et al. 2014). Burns et al. (2017) Australian study explored the lived experiences of patients waiting for a kidney transplant from a deceased donor whilst receiving RRT. This study highlighted that patients waiting for a transplant are overpoweringly hindered by their exposure to RRT. The concept of receiving a kidney transplant provides these patients with 'hope that one day they will be free'. However, uncertainty continues when patients are concerned as to the length of time waiting for a transplant as well as whether the transplant would really afford them with the freedom they covet. Social networks, including family members and fellow patients on dialysis, were identified as beneficial to patients whilst they wait. There were multifaceted emotions felt towards the deceased donor, with aspirations that an organ would be available quickly whilst valuing the immense cost to the donor and his/her family. 'Wishing for a transplant is like wishing for someone to die' (Burns et al. 2017).

Living kidney donors

The Kidney Disease: Improving Global Outcomes (KDIGO) (2017) Clinical Practice Guideline on the evaluation and care of living kidney donors recommends substituting decisions established on the assessments of singular isolated risk factors, instead using a comprehensive method in the assessment of risk factors utilising the best evidence available. Concurrently considering each candidate's demographic profile as well as health characteristics promotes a new framework for the assessment of donor candidate risk and for defensible shared decision making. KDIGO (2017) identifies that the evidence for the majority of guideline recommendations is scant

with numerous 'ungraded' expert consensus recommendations established to steer the donor candidate evaluation and management before, during, and after donation.

The potential living donor should not feel pressured to participate with the transplant procedure: who apart from the actual donor can establish that his/her consent to surgery is 'freely given'? It may be possible for the renal healthcare providers to recognise a donor who has visibly been put under pressure from either the potential recipient or from members of the applicable family. However, understated demands may exist in various situations that the donor does not disclose and the renal healthcare providers do not discover. This may make it challenging or unfeasible for a potential donor not to continue with the transplant procedure (British Transplantation Society and the Renal Association 2011).

It is vital to identify that there are numerous variants of informed consent 'freely given' as with paired donor-recipient. In a paired donor exchange, two kidney recipients essentially 'swap' willing donors. While medically eligible to donate, each donor has an incompatible blood type or antigens to his or her intended recipient. In most circumstances both the intentions and autonomy of the potential donor will be without question. However, there may be situations that could be more problematic to ascertain if consent is both cognisant and freely given.

This remit may be operated by a more formal independent third party, known as the Independent Assessor, or by a living donor coordinator. There is therefore a recommendation for independence between the healthcare providers responsible for the donor and the recipient; this may be known as a donor advocate. It is vital that this partition of responsibility remains customary and is applicable to every potential living donor. The donor advocate will be an informed renal healthcare professional who is not directly included with the recipients' care. He/she will answer any unresolved questions, worries, or challenging issues, and this empowers the donor to make a sincere autonomous resolution. It must be recognised that it may not always be feasible to isolate the donor and recipient healthcare professional teams even though it is regarded as best practice.

It is important for the potential donor to comprehend that he/she is not the only potential transplant source. This may be more specific when a potential recipient is deemed as unsuitable for inclusion on the deceased donor waiting list but is deemed as an acceptable risk for a planned living donor transplant. The donor in this situation must not feel obliged to donate. The donor may also feel that there would be family conflict if he/she does not wish to donate but remains anxious that refusing to donate would impact upon family dynamics. In this situation, the donor advocate must engage in discussions to reduce any potential damage to family relations. It is ideal from the start of this process to foster open and frank discussions between the donor and the recipient. This pre-emptive discussion assists in ensuring that both donor and recipient are fully aware of how information will be managed by their own renal healthcare teams and in reducing the possibility of conflict (British Transplantation Society and the Renal Association 2011).

KDIGO (2017) identifies that the psychosocial evaluation assists in determining if a donor candidate is psychologically fit for donation. There is a need for education and planning sessions with experienced healthcare professionals to discuss the psychosocial evaluation and the process involved with the donor candidate. These sessions will advise the donor candidate that he/she should have a good QoL following donation; however, the donor candidate should be advised that some individuals may experience psychosocial difficulties following donation. These sessions should concentrate on any worries that the donor candidate may have, and ensures that any possible psychosocial risks and benefits of kidney donation are revealed and understood. The psychosocial evaluation can also be used to devise a plan to assist the donor candidate in having a positive psychosocial experience during the

evaluation and donation procedures, and long-term following donation. Transplant programs should adhere to procedures for assessing psychosocial factors that either exclude donation or stop any further evaluation until there is a resolution.

It must be recognised that not all recipients wish to receive a living donor transplant. Healthcare professionals and family members may assume that the patient will be willing to accept a living donation, but this is not always the case. This decision should be respected by all concerned if the patient has made an informed choice. In these situations, the patient may require additional support and guidance to decline the offer without resulting in distress or relationship difficulties with the potential donor. There should be good support available where potential recipients have built positive relations with the transplant team. However, an independent third party provides a different facet; this may be more relevant with young adults. There can be an opportunity here for an environment where patients can potentially feel less pressured and be able to express their concerns regarding accepting a kidney (British Transplantation Society and the Renal Association 2011).

Support for the recipient of a transplant can be divided into two major components: the psychosocial evaluation for transplant candidacy and symptom management post-transplantation. There is a bidirectional association between mental illness and kidney disease. Poor transplant outcomes are related to co-occurring psychiatric conditions. This has been ascribed to behavioural influences such as nonconcordance (nonadherence), along with physiologic factors, for example alteration of immunologic and stress reactions.

There is a need for a biopsychosocial evaluation of patients post-transplant, addressing issues such as mood or worries, changes in perceptions, morose thoughts concerning self-harm or harm to other individuals, behavioural symptoms including concordance, taking risks, and substance abuse, along with environmental and personal stressors. These areas may be tempered by positive influences including social support, perception, spirituality, and the usage of adaptive coping methods (Danovitch 2010a). Ozcan et al. (2015) study utilised the Hospital Anxiety and Depression Scale (HADS) for evaluating depressive and anxiety symptoms and the Brief Cognitive State Examination (BCSE) for detecting probable cognitive impairment with patients receiving HD and PD, as well as those who had received a kidney transplant. They concluded that kidney transplant may have both a safeguarding and enhancing impact on cognition, and mood may be better enhanced.

It must be remembered that transplantation does not occur in clinical isolation, as the majority of patients pre-transplant have been exposed to CKD and all its associated complications (Danovitch 2010b). It is important that there is a continuous multidisciplinary alliance when discharging patients from the transplant unit home and into the primary care setting (Murphy 2011b, Murphy et al. 2011). There are two main stages in the first-stage management of kidney transplantation – avoiding acute rejection and avoiding opportunistic infection. The purpose of the second or later stage is to retain good graft function along with deterring the long-term consequences of immunosuppression such as infection, malignancy, and premature CVD (Baker et al. 2017). The foundation for the care of kidney transplant recipients is that of education, as patients need to acquire self-care skills (Murphy 2014).

Patients must be able to recognise and act upon the signs and symptoms of rejection. They must know to contact the transplant unit should they have any concerns. The self-care regime includes how to monitor their blood pressure, weight, temperature, urinary output, and glucose levels as applicable. It is vital that patients understand the signs and symptoms to look out for in terms of rejection (Wilkinson 2010).

Patients' experiences after transplantation are multifaceted. Prior to transplantation they have mixed emotions contemplating their current situation (i.e. dialysis

treatment) versus their concerns for their new life after transplantation, which are affected by their former experiences. Concerns include hope for a better quality of life after being advised that they will receive a kidney. They have mixed feelings such as shock, potential doubt, and uncertainty that the donor kidney will provide the desired effect for positive changes in their lives (Wiederhold et al. 2011). There were many themes described by Wiederhold et al. (2011), who discussed the patients' experiences after transplantation: experience of positive changes; dealing with the organ; experiences of impairment and worries; experience of self-confidence; experience of the need for support; and finally patient education.

Patients indicated that if the transplant is a success then this is a new phase in their lives and the transplant is viewed as a gift. They expressed their sincere appreciation towards the donor and his/her family who permitted the transplantation to proceed. The theme of the *experiences of positive changes* highlighted the joy and happiness for patients who experienced a newfound freedom from dialysis restrictions, along with hope for more independence and better performance in both personal health and professional lives. The theme of *dealing with the organ* addressed the difficulties that patients face in this initial stage trying to adapt emotionally and psychologically to the new situation. The patients realised that they must take care of themselves on a day-to-day basis, now with added responsibility of caring for the transplanted kidney.

The theme of *experience of impairments and worries* addressed the concerns that patients face, including resuming their previous employment if feasible, potentially minimising their working hours or even postponing the resuming of their working life to maintain the longevity of the transplant. The theme of *experience of self-confidence* highlights patients' abilities to adapt with the situation because of great self-confidence. In the first few weeks after transplantation there is a period of enjoyment with the new transplant, where patients reclaim their independence and quality of life. These positive changes empower patients to regard their new and unaccustomed situation with optimism and both family and the social environment support are regarded as vital in assisting patients to adapt.

This study showed that patients had little idea of how to adapt with their new kidney and there was a need for support and education in managing the transplant. Patients discussed the concept of trying to understand their new medications whilst the renal healthcare providers reiterated the importance of taking them constantly. In addition, there were many alterations concerning eating and drinking. The final theme discussed by these patients was *patient education*; this highlighted that patients identified the desire for real, substantial, and daily practice recommendations with educational sessions facilitated in either one-to-one or group sessions (Wiederhold et al. 2011).

Patients may encounter numerous psychosocial risks after transplant, which may have a negative impact upon all concerned. Patients' family dynamics and working background may be changing, with some patients finding it challenging to move away from the dependent 'sick role' that they experienced on dialysis. The new associated freedom that comes with a transplant could be a risk to those patients who identified themselves within the 'sick role', and it can be challenging to make the transition to health.

Guilty feelings may be expressed by patients who have received a kidney instead of another person. However, there is a need to re-emphasise to patients that these emotions are common and that they are worthwhile in terms of receiving this altruistic donation from the donor and his/her family.

The social aspects of dialysis sessions may be missed by some patients. These issues and concerns may result in personal relationship difficulties with partners and family members, along with anxieties about entering the workplace or genuine

concerns about losing financial assistance such as potential disability benefits (Hersh Rifkin 2010).

It can be uncertain how patients will adapt to the medication regime and the associated side effects. Physical side effects including hirsutism, possible weight gain, and gum overgrowth can all affect the body image of patients and how they relate to their partners/significant others. These side effects are usually temporary and can be managed but this must be explained to the patient and family. Body-image concerns may not always be obvious to patients and their spouses; they might not be discussed or addressed by either party or with the transplant unit. There is a need for sensitivity and open discussion by the renal healthcare providers (Hersh Rifkin 2010; Murphy 2012).

It is vital to prevent and identify nonadherence in KTR (Baker et al. 2017). The side effects highlighted above could cause patients to not take their medications as prescribed, so it is important to assess the patient's opinions towards these side effects. Some of the side effects can be reduced by concentrating on lifestyle, including diet and exercise. Patients can be encouraged to self-manage their care instead of expecting failure. The issue of concordance can be a major concern due to its high associated threat for both acute rejection and graft loss. It is recommended to identify factors (see Box 4.2) that are associated with nonconcordance and identify the necessity for a care pathway that would assist those patients who are regarded as an increased risk or with recognised nonconcordance. There should also be pathways in position for paediatric KTR in transition and for adolescents KTR (Hersh Rifkin 2010; KDIGO 2010; Kee-Low et al. 2015; Baker et al. 2017).

Education, prevention, and treatment strategies can be provided to minimise nonadherence. Individual counselling sessions may be necessary to assist patients and partners to deal with the life-changing event that transplantation presents. Patient support groups can also assist patients (Hersh Rifkin 2010). Kee-Low et al. (2015) conducted a systematic review to evaluate the efficacy of interventions to enhance medication concordance in adult kidney transplants.

Frame and Cronin (2017) set up a multidisciplinary annual review transplant clinic (ARTC) in London, UK, for long-term kidney transplant recipients (transplant > 7 years old) with a view to averting long-term transplant complications through evidence-based early recognition and prompt management. The ARTC's clinical model encompasses screening of both physical and psychological issues including renal transplant function, CVD, cancer risk, diabetes, anaemia, and bone metabolism. Health promotion and patient education is encouraged through the

BOX 4.2

Risk factors for nonconcordance of medication (KDIGO 2010)

- history of nonconcordance behaviour preceding transplantation.
- mental health illness.
- personality conditions.
- reduced social support.
- high risk behaviour such as substance abuse.
- high education level.
- teenager.
- period since transplantation.
- limited sufficient after care with transplant specialists.
- inadequate education prior to transplant.
- challenging medication regimens.
- numerous adverse effects from medications.

screening of patients' lifestyles such as body mass index (BMI), exercise, alcohol, and smoking consumption as well as medication concordance. These authors identified through a series of validated measures (Patient Health Questionnaire-9, Work and Social Adjustment Scale, Medicine Adherence Report Scale, and the Generalised Anxiety Disorder-7 scores) that were adjusted to patients' needs. An audit conducted by the ARTC in 2015 assisted in the facilitation of a clear pathway for psychological referral to a specialised renal psychologist or psychiatrist as applicable to the mental health services. It has also facilitated the re-referral of some patients back to their mental health team if they are currently under the auspice of same, involving the GP in the care process as appropriate. This is called the Integrating Mental and Physical Health Care in Research, Training, and Services (IMPARTS) referral pathway.

Conclusion

This chapter has addressed the various psychological challenges that patients and their partners/family members/carers face when trying to cope with CKD and the treatment options. The challenge is for renal healthcare providers to enable patients to learn to adapt and try their best to live with the treatment modality chosen. There must be appropriate care pathways for each individual patient. Positive partnerships with patients and their partners/family members/carers can foster increased shared decision making and self-care. Many patients do require psychological support from the renal healthcare team and it is important to recognise this from the onset.

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CHAPTER 5

Acute Kidney Injury

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Learning Outcomes

- to understand the different types and causes of acute kidney injury (AKI).
- to help and support the patient and family during an episode of AKI.
- to describe the signs and symptoms of AKI.
- to analyse the management of those with AKI.
- to evaluate the various treatment options for AKI.

Introduction

Acute kidney injury (AKI) results when there is an abrupt and rapid loss of kidney function which results in the retention of nitrogenous waste products (Jha 2016). AKI is recorded in around 2.5% of English hospital admissions, but laboratory data suggest that the true figure is nearer 15%, and numbers are believed to be rising (Kerr et al. 2014). AKI is associated with significantly increased mortality risk and patients who recover are at much increased risk of developing chronic kidney disease (CKD). Research by the National Confidential Enquiry into Patient Outcome and Death concluded that 30% of AKI cases that occur during hospital admission are avoidable, and only around half of patients with AKI were deemed to have received care that was regarded as good (NCEPOD 2009). Research in Kent by Kerr et al. (2014) concluded that around 60% of critical care bed days involved AKI, with critical care bed usage by AKI patients being over four times that of non-AKI patients. Costs to the National Health Service (NHS) of AKI have been estimated to be between £434 million and £620 million per year, exceeding the combined costs from breast, lung, and skin cancers (NICE 2013).

Poor recognition of patients at risk of developing AKI, and/or suboptimal care in the early stages of AKI, have been identified as significantly contributing to its prevalence within acute care (NCEPOD 2009). This is important because the prognosis for patients experiencing AKI can be significantly improved with early treatment, especially with respect to reduced risk of mortality and reduced risk of developing CKD. In response to this, the National Institute for Health and Care

Excellence (NICE) have developed a guideline for AKI detection and management (NICE 2013).

AKI can be seen as a spectrum of injury from impairment to failure, which may result in the need for renal replacement therapy (RRT). Clinically AKI is characterised by a rapid reduction in kidney function resulting in dysregulation of extracellular fluid volume, electrolytes, and acid–base balance (Jha 2016). Depending on its severity and duration, AKI is often transient in nature and, with careful nursing care, the patient can regain normal renal function. However, without appropriate specialised treatment, the patient may be denied the opportunity to make a full recovery and a precipitation of further impairment may lead to CKD and established renal failure (ERF).

The aim of this chapter is to emphasise the vital role the nurse plays in the prevention of progression to AKI and of the delivery of care for the patient in AKI. The nurse is vital to the wellbeing of the patient as the nurse monitors the patient for complications, participates in RRT, assesses the patient's progress and response to treatment, and provides physical and emotional support. In this central role the nurse can maintain close links with the patient's family, which can be instrumental to a family-centred approach to the patient's treatment. The alliance between the patient, the family, and the nurse is paramount in keeping the family informed of the patient's condition, assisting them to understand treatments, and providing psychological support. Figure 5.1 gives an overview of the signs and symptoms of AKI.

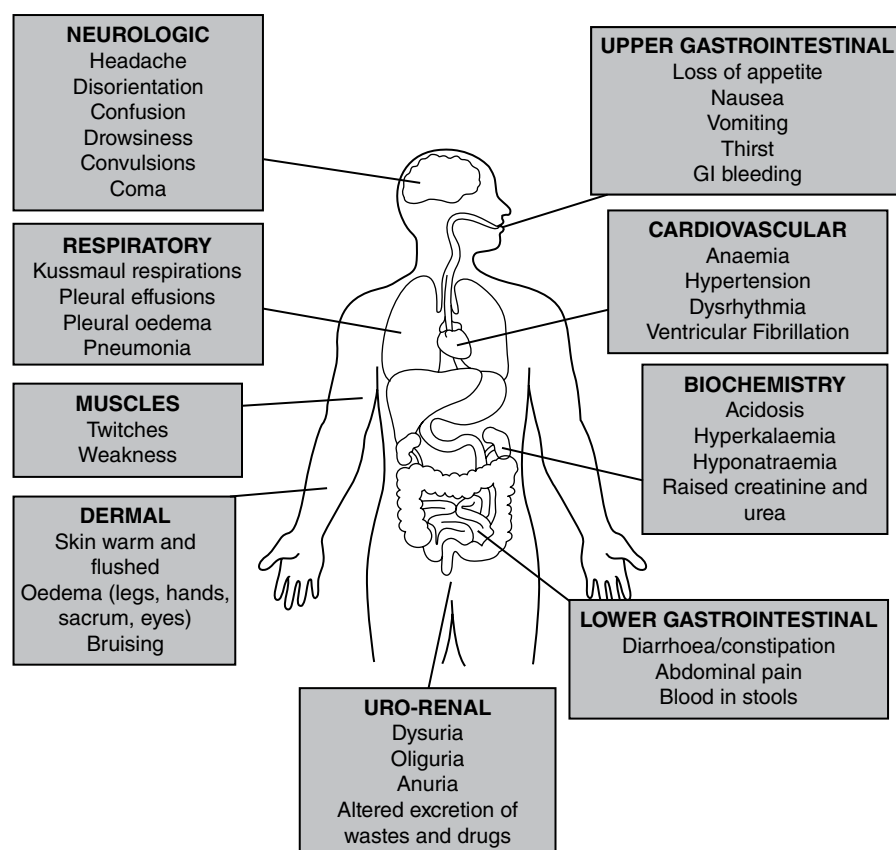


Figure 5.1 AKI – selected symptoms (O'Callaghan et al. 2004).

Due to the severity of symptoms involved in AKI, most patients are nursed in intensive care during the most severe phase to enable continuous renal replacement therapy (CRRT). Specific nursing activities for CRRT are beyond the scope of this book, but further reading can be found at the end of this chapter regarding the options available for RRT. However, renal nurses are likely to be involved in recognising AKI risks and onset, and in ongoing care for patients who may remain dependent on RRT and other specialist interventions after the most acute phase.

Mortality

There are a number of patient groups for which AKI has a particularly high mortality rate. For example, AKI occurs in around 40% of patients with severe sepsis and septic shock, and patients in this group are at greatly increased risk of mortality, ranging from 42% of patients in stage 1 AKI to as high as 85% in stage 3 AKI (Umbro et al. 2016). Early identification of the symptoms of AKI and rapid intervention with appropriate and evidence-based therapy is identified as essential in promoting maximal patient recovery and minimising long-term negative complications (NICE 2013). The nurse must therefore play a major role in assisting physicians and other members of the multidisciplinary team in optimising the treatment for this highly vulnerable group of patients. The development of new biochemical markers may enable a diagnosis to be made before changes are seen in either serum creatinine (SCr) or the urine output (UO).

It is important for nurses, patients, and carers to be able to understand that AKI is a serious condition that should never be underestimated. Constant improvements in dialysis technology, combined with a growing CKD population and limited funds, have put clinicians under pressure to try and predict the outcomes of treatment.

Classification

AKI may be divided into three major categories, in which each category has a physiological location of the insult (Table 5.1):

- **prerenal** – relates to the ineffective perfusion of the kidneys, which are structurally normal
- **renal (intrinsic)** – damage to the renal parenchyma, sometimes secondary to pre-renal problems
- **postrenal** – disordered urinary drainage of both kidneys or of a single functioning kidney.

An acute impairment may also present in the patient with existing CKD, which may lead to further structural damage; this presentation is often referred to as acute-on-chronic kidney disease and evidence would indicate that this is an increasing group (Jha 2016).

Prerenal renal failure

Prerenal causes of AKI are directly related to hypoperfusion states or a decline in the blood supply to the kidneys. Since the kidneys receive higher blood flow per unit mass than any other organ in the body, due to the complex capillary structure in the nephrons, they are especially sensitive to hypoperfusion. In prerenal failure the structure of the kidneys remains normal; however, when the renal blood supply is restricted, glomerular filtration is reduced, causing decreased perfusion of the kidneys. The net effect is a decreased blood flow to the glomeruli and the nephrons, which leads to ineffective filtration and disordered secretion and reabsorption

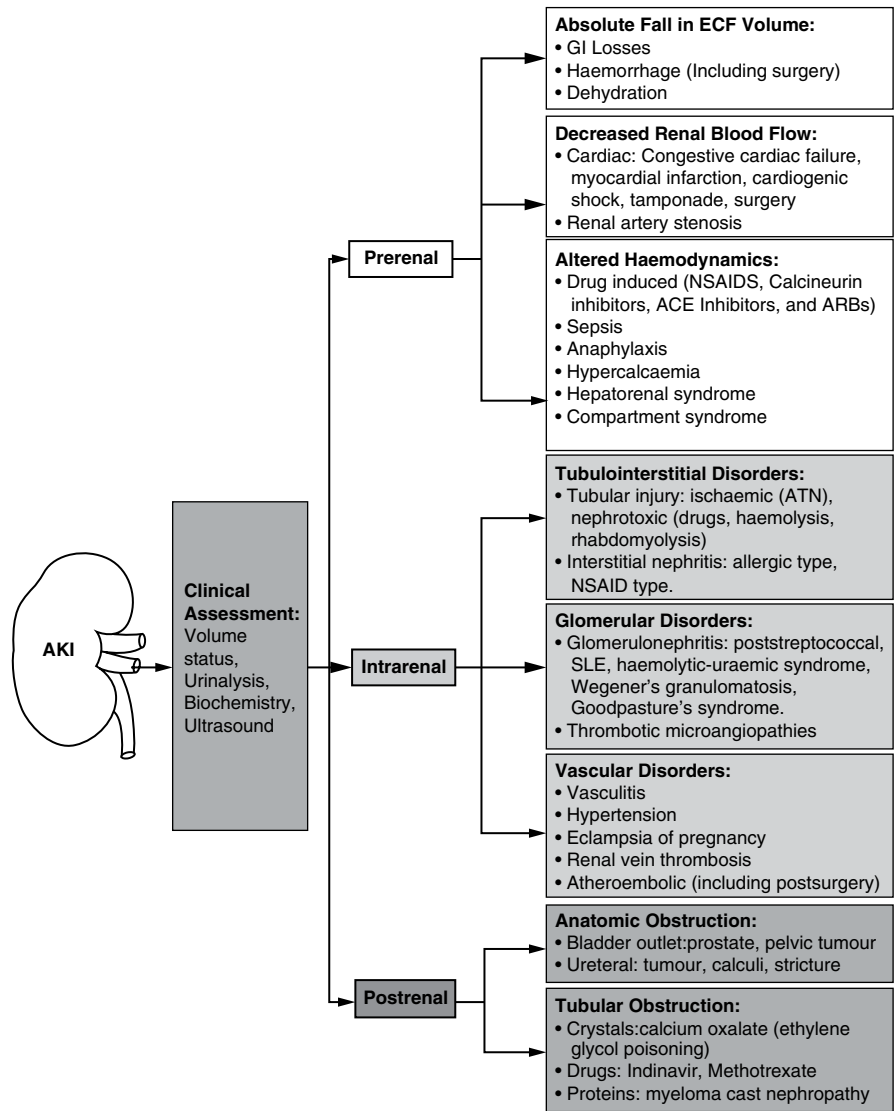


Table 5.1 Acute kidney injury (AKI): major causes and aetiology (Rennke and Denker 2014).

through the nephron because of inadequate blood flow. Without an effective renal plasma flow rate, the glomeruli are unable to filter waste from the blood, but the structure of the renal tubules remains intact (Figure 5.2).

In this prerenal state, urine osmolarity is high and sodium low, which is consistent with renal hypoperfusion and well-preserved renal function. If, at this stage, renal blood flow can be restored, then normal renal function will usually return. However, if the prerenal state is prolonged, then this may lead to ischaemic damage due to poor perfusion, which in turn may lead to acute tubular necrosis (ATN) (Pakula and Skinner 2016).

It is estimated that around 30% of cases of AKI occurring during hospital admission are both predictable and avoidable (Kerr et al. 2014). Early recognition, diagnosis, and treatment are vital in cases of prerenal disease, in order to prevent the condition progressing to renal failure with a degree of parenchymal damage. Nurses can play a large role in the recognition and management of this group of patients.

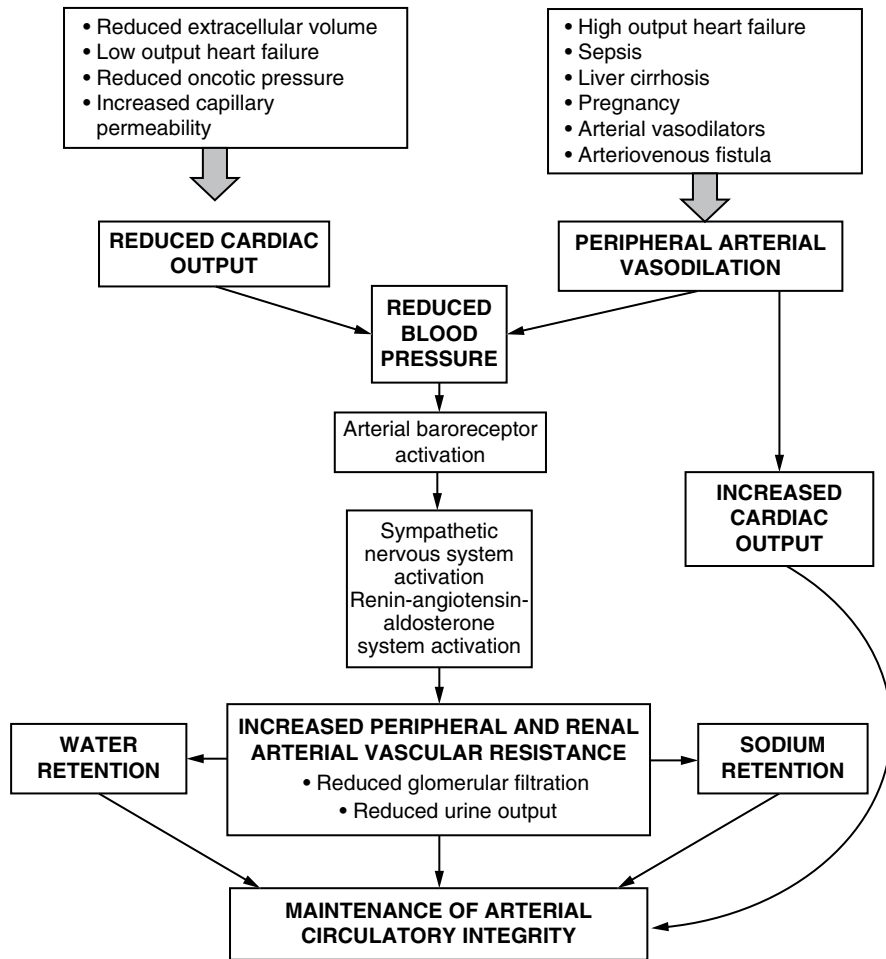


Figure 5.2 Prerenal failure progression (Steddon et al. 2014).

Renal (intrinsic) failure

This cause is sometimes referred to as intrinsic or intrarenal failure and is associated with structural damage to the glomeruli and renal tubules. The difference between pre- and postrenal failure and intrinsic failure is that in intrinsic failure, the correction of the aetiology will not guarantee the complete recovery of renal function, because of damage to the nephron itself. Here the episode of AKI may have a lengthy duration and can often lead to CKD.

The clinical course of intrinsic renal failure is often complex and, depending upon underlying disorders, the recovery may be prolonged for up to six weeks. As illustrated in Table 5.1, there are a wide variety of causes for intrinsic renal failure, which may involve multisystem disease or originate from a primary renal disorder, but often involve complicating severe illness that causes vasomotor nephropathy. Some specific causes are now discussed.

Acute interstitial nephritis

This condition often follows exposure to drugs in the form of antibiotics, analgesics, and nonsteroidal anti-inflammatory agents. Infections can cause a very similar

clinical and pathological picture and these include *Salmonella*, *Streptococcus*, *Meningococcus*, leptospirosis, and many viral disorders.

Other categories of interstitial nephritis are caused by systemic disease, such as systemic lupus erythematosus or sarcoidosis.

Clinical features

Fever, rash, arthralgia, back pain, and eosinophilia are clinical features of acute interstitial nephritis. AKI may not develop for some weeks but in some cases renal dysfunction may occur within a few hours after exposure to a causative drug.

Rhabdomyolysis

Rhabdomyolysis is a result of the release of muscle contents, including myoglobin, into the plasma. Causes include: crush injury, prolonged immobility, compartment syndrome, sickle cell disease, excessive exertion, shock, electrocution, status epilepticus, and intravenous drug abuse. These causes damage muscle tissue, allowing the pigment myoglobin to be released into the plasma. Myoglobin is an iron- and oxygen-binding protein and is only found in the bloodstream after muscle injury. At high plasma levels it becomes nephrotoxic. If treated early it can be successfully cured with fluid resuscitation, but failure to respond quickly can lead to permanent damage to both kidney tissue and the site of the trauma (Steddon et al. 2014).

Clinical features

The urine is often brown or coffee-coloured due to the presence of myoglobin. Patients often present with acute illness, with fever, weakness, pain, nausea, and vomiting.

Renal failure and liver disease

AKI is often associated with acute liver injury that may result from:

- paracetamol overdose;
- circulatory shock;
- severe leptospirosis sepsis.

It may also be seen in surgery on the biliary tract.

For the patient with advanced liver disease, the onset of kidney injury is often referred to as hepato-renal syndrome (HRS). This occurs in advanced liver dysfunction in conjunction with ascites and portal hypertension. Common causes of HRS include hypovolaemia, sepsis, nephrotoxic agents, and glomerulonephritis. Successful management relies on early recognition of risk factors such as existing cirrhosis and ascites, over diuresis, GI bleeding, sepsis, and major surgery. These patients often require intensive care and multi-system support. RRT is seen only as a bridge to potential liver transplantation (Steddon et al. 2014).

Cortical necrosis

Cortical necrosis may follow any course of intensive or prolonged ischaemia. The condition is also associated with sepsis, shock, transfusion reactions, and burns.

Renal biopsy reveals pathology of patchy necrosis of the glomeruli, tubules, and small vessels of the renal cortex. The renal medulla remains intact but the renal cortex becomes infarcted and calcifies, and this may be seen on plain abdominal X-ray.

The return of renal function is often slow but, if cortical necrosis is extensive, recovery is unlikely and the patient may become dialysis dependent.

Acute tubular necrosis

AKI due to ischaemic changes or toxic renal injury presents a clinical syndrome that is often referred to as ATN. It is a very common cause of AKI and has a high mortality rate of around 50%. It causes damage to the tubular portion of the nephron. Many years of improvements in dialysis technologies and other aspects of renal care have until recently done little to improve the prognosis for patients with ATN. Recent work has focused on the development of novel markers for prediction of renal recovery and it is thought that serum cystatin C may prove a better predictor than the traditionally used SCr (Gharaibeh et al. 2018).

Although the aetiology of ATN can vary, the common factor is that there is a reduction of oxygen and nutrients to the active tubular cells, which results in a lack of cell function and patchy necrosis. The tubular cells will regenerate at the basement membrane level. Treatment focus, in the absence of effective novel approaches, remains supportive care with dialysis allied with correction of electrolyte and metabolic disturbances (Rennke and Denker 2014).

Most intrinsic renal failure is caused by ischaemia through exposure to toxic agents, such as drugs or bacterial endotoxins.

Nephrotoxicity

In any patient with AKI, particularly ATN, a potential causative effect could be a therapeutic agent. Therapeutic agents can affect the kidney in any of the three categories listed, as illustrated in Table 5.2 (Perezella 2009, Steddon et al. 2014). Contrast-induced acute kidney injury (CI-AKI) occurs within 72 hours of the patient receiving the contrast media. AKI results from a combination of afferent arteriolar vasoconstriction and direct toxicity of the contrast media to the tubule epithelial cells. Patients with risk factors, including the elderly and those with diabetes, have a higher incidence. It is recommended that this group of patients receives appropriate fluid expansion before and after the procedure (Lewington and Kanagasundaram 2011).

Ischaemic ATN is often associated with inadequate perfusion to the kidney, in that the efferent and afferent arterioles are unable to maintain their autoregulatory function, and this leads to a fall in the glomerular filtration rate. This interruption in blood flow to the kidney may be due to surgical intervention, for example aortic repair, and is quite likely to cause ischaemia (Weldon and Monk 2000).

Table 5.2 Effects of therapeutic agents on the kidney.

Clinical syndrome	Causative agents
Prerenal	Ciclosporin, radiocontrast, amphotericin B, ACE inhibitors, NSAIDs
Intrinsic: acute tubular necrosis (ATN)	Aminoglycosides, amphotericin B, cephalosporins
Acute interstitial nephritis	Penicillins, cephalosporins, sulphonamides, rifampicin, NSAIDs, interferon, interleukin-2
Rhabdomyolysis	Amphetamines, statins, antimalarials, opiate abuse
Postrenal	Aciclovir, analgesic abuse
	Other heavy metals, including gold, lithium, mercury, silver
ACE, angiotensin-converting enzyme; NSAIDs, nonsteroidal antiinflammatory drugs.	

Postrenal failure

Postrenal conditions obstruct the flow of urine, so the obstruction has to be bilateral or located within the bladder or urethra in order to cause failure. The rapidity of recovery will depend on the duration and completeness of the obstruction. The urinary tract may be obstructed by three mechanisms:

- **intraluminal** (obstruction from within) – calculi, blood clots, renal papilla;
- **intramural** (disease of the wall) – transitional cell cancer, fibrosis, inflammation, infection;
- **extrinsic** (obstruction from outside) – trauma, prostatic hypertrophy, abdominal tumour, inflammation, fibrosis, haemorrhage.

The consequences in terms of progression to AKI include reduced GFR, reduced renal blood flow (following an initial rise), impaired renal concentrating ability, and impaired distal tubular function.

As with all types of kidney injury, it is important to find the cause and start treatment as soon as possible since, in theory, all postrenal failure is reversible. The initial recovery stage is usually characterised by a marked post-obstructive diuresis (Field et al. 2010).

AKI classification systems

The Acute Dialysis Quality Initiative (ADQI), in 2004, proposed the introduction of a diagnostic criterion for AKI using SCr levels and UO volumes over standardised periods of time. The system was called RIFLE (Table 5.3) (Ricci et al. 2007). The system provided a uniform standard for diagnosis and classification of AKI in order to optimise the treatment of patients with kidney disease. Many of the ADQI group collaborated at a later date to become the Acute Kidney Injury Network (AKIN), which modified RIFLE with regards the creatinine measure, due to the clinical significance of relatively small rises in SCr. As a result, the AKIN group modified RIFLE to the new AKI staging system, AKIN (Table 5.4), which reflects

Table 5.3 RIFLE classification of AKI.

Category	GFR criteria	Urine output (UO)
Risk	Increase in creatinine $\times 1.5$ or $\text{GFR} \geq 25\%$	$\text{UO} < 0.5 \text{ ml kg}^{-1} \text{ h}^{-1} \times 6 \text{ h}$
Injury	Increase in creatinine $\times 2$ or $\text{eGFR} \geq 50\%$	$\text{UO} < 0.5 \text{ ml kg}^{-1} \text{ h}^{-1} \times 12 \text{ h}$
Failure	Increase in creatinine $\times 3$ or $\text{GFR} \geq 75\%$	$\text{UO} < 0.3 \text{ ml kg}^{-1} \text{ h}^{-1} \times 24 \text{ h}$ or anuria $\times 12 \text{ h}$
Loss	Complete loss of kidney function ≥ 4 weeks	
ESKD	End stage kidney disease (≥ 3 months)	

Table 5.4 AKIN classification of AKI.

Category	Serum creatinine (SCr)	Urine output (UO)
Stage 1	$\text{SCr} \geq 150\text{--}200\%$ from baseline	$< 0.5 \text{ ml kg}^{-1} \text{ h}^{-1}$ for $> 6 \text{ h}$
Stage 2	$\text{SCr} \geq 200\text{--}300\%$ from baseline	$< 0.5 \text{ ml kg}^{-1} \text{ h}^{-1}$ for $> 12 \text{ h}$
Stage 3	$\text{SCr} \geq 300\%$ from baseline OR $\text{SCr} \geq 54 \mu\text{mol l}^{-1}$ with an acute rise of at least $44 \mu\text{mol l}^{-1}$ or commencement RRT	$< 0.3 \text{ ml kg}^{-1} \text{ h}^{-1}$ for $> 24 \text{ h}$ or anuria for $> 12 \text{ h}$

Table 5.5 KDIGO classification of AKI.

Category	Serum creatinine (SCr)	Urine output (UO)
Stage 1	$\geq 1.5\text{--}1.9 \times$ baseline or increase in SCr $\geq 0.3 \text{ mg dl}^{-1}$ ($\geq 26.5 \mu\text{mol l}^{-1}$)	$<0.5 \text{ ml kg}^{-1} \text{ h}^{-1}$ for 6–12 h
Stage 2	$\geq 2\text{--}2.9 \times$ baseline	$<0.5 \text{ ml kg}^{-1} \text{ h}^{-1} > 12 \text{ h}$
Stage 3	$3 \times$ baseline or increase in SCr $\geq 4 \text{ mg dl}^{-1}$ ($\geq 353.6 \mu\text{mol l}^{-1}$) or initiation of RRT	$<0.3 \text{ ml kg}^{-1} \text{ h}^{-1}$ for $\geq 24 \text{ h}$ or anuria for $\geq 12 \text{ h}$

these smaller changes, with the AKIN corresponding to the earlier RIFLE stages. Stage 1 relates to risk, while AKIN stage 2 relates to injury, and AKIN stage 3 corresponds to failure. The ‘loss’ and ‘end-stage kidney disease’ categories were dropped from the staging system but remain outcomes. The AKIN classification also introduced a baseline measure and dropped the use of eGFR as this is not an accurate measure of kidney function in AKI.

Lewington and Kanagasundaram (2011) recommend the use of the newest AKI staging system produced by International Kidney Disease: Improving Global Outcomes (KDIGO) staging classification (Table 5.5). All three systems provide guidance, and the use of one of these classification systems should promote earlier detection of AKI, leading to appropriate and timely treatment of AKI.

The NICE (2013) clinical guideline for AKI prevention, detection, and management recommends the use of the RIFLE, AKIN, or KDIGO definitions of AKI, which research indicates as being equally valid (Rodrigo et al. 2016). The NICE (2013) guideline specifically specifies the following as criteria for diagnosing AKI:

- a rise in SCr of $26 \mu\text{mol l}^{-1}$ or greater within 48 hours.
- a 50% or greater rise in SCr within the past seven days.
- a fall in UO to less than $0.5 \text{ ml kg}^{-1} \text{ h}^{-1}$ for more than six hours in adults and more than eight hours in children and adolescents.
- a 25% or greater fall in eGFR in children and young people within the last seven days.

Identifying The Cause(s) of Acute Kidney Injury

Urinalysis

NICE (2013) recommends performing urine dipstick testing for blood, protein, leucocytes, nitrites, and glucose in any patient in whom AKI is suspected as soon as possible. Diagnosis of acute nephritis should be considered and the patient referred to a nephrologist when a urine dipstick shows signs of haematuria and proteinuria in the absence of urinary tract infection or trauma, even if there is no obvious cause of AKI.

Ultrasound

NICE (2013) does not recommend routine use of ultrasonography of the urinary tract once the cause of AKI has been established. In cases where pyonephrosis (infected and obstructed kidneys) are suspected however, ultrasonography of the urinary tract should be performed within six hours of initial assessment.

Management of Acute Kidney Injury

Since normal kidney function is essential to homeostasis of the body, particularly with regard to volume, electrolyte balance, acid–base balance, and excretion of nitrogenous waste products, loss of these functions can lead to hyperkalaemia, volume overload, acidosis, and uraemia.

Prevention is better than a cure, so early detection and treatment of AKI will prevent rapid deterioration. Failure to identify deterioration in acutely unwell patients has been identified as a factor in many of the cases of hospital-acquired AKI. NICE (2013) recommend the use of early warning scoring systems such as the National Early Warning Score (NEWS) (RCP 2017) in order to improve the rate of early detection of patients at risk of developing AKI. Some people are at a greater risk of AKI – these include patients who have CKD, cardiac failure, liver disease, and diabetes, and those who are over 60 years of age. The clinical management goals for patients with AKI can be divided into three main categories:

- restoration of renal perfusion;
- minimising toxic effects;
- correction of metabolic derangements.

Relieve urological obstruction

All patients with upper tract urological obstruction should be referred to a urologist. Referral should be immediate in the presence of any of the following symptoms: pyelonephrosis, obstructed solitary kidney, bilateral upper urinary tract obstruction, or complications of AKI caused by urological obstruction. Nephrostomy or stenting, if required to relieve the obstruction, should happen within 12 hours of initial diagnosis (NICE 2013).

Hyperkalaemia

Hyperkalaemia is often a fatal complication in AKI. The failing kidney is unable to excrete potassium effectively when the patient is oliguric (<400 ml urine day) or, worse, anuric (no urine). It is further complicated by the very complex treatment of an individual who is often septic, hypoxic, and requiring blood transfusions and potassium-containing drugs.

RRT is the most efficient treatment for hyperkalaemia but this may take time to effect if vascular access is required. Other alternatives are available, but these are generally temporary solutions only, as they facilitate movement of potassium from the vascular compartment rather than removal:

- the administration of intravenous insulin and dextrose or nebulised salbutamol will help move potassium ions back into the intracellular compartment and away from the extracellular compartment. It is important to monitor the patient's blood sugar as hypo- or hyperglycaemia can occur. Also, it is important to measure the heart rate, which can increase in response to salbutamol.
- calcium carbonate is recommended in most cases to reduce the cardiotoxicity and decrease the cardiac membrane excitability.
- oral or rectal potassium exchange agents in the form of calcium resonium (which is a slower-acting treatment, often used as maintenance treatment for hyperkalaemia).

Volume overload

Successful volume homeostasis permits maintenance of a constant internal circulatory and extracellular volume despite consumption of varying quantities of water and salt intake and variable invisible losses of water.

The presence of oedema may be seen in the feet, legs, sacral area, and sometimes head and neck; as oedema follows gravity the location will depend largely on the positioning of the patient. The oedema is generally pitting in nature. The skin is particularly at risk at this stage and extra care must be taken. Shortness of breath and especially orthopnoea are indicative of pulmonary oedema.

Each patient in AKI should have an individual prescription for fluid and sodium intake. As a generalisation, the fluid intake volume should equal the daily UO plus 300–500 ml. Patients with a large insensible loss, such as happens with burns, obviously need a larger fluid intake and special care should be taken. It is important that the patient and family are involved in accurate fluid balance, as failure to maintain accurate fluid balance records has often been implicated in poor patient management.

Pharmacological management of fluid overload should not routinely use diuretics, although loop diuretics might be used while the patient is awaiting RRT or once renal function is recovering (NICE 2013).

Metabolic acidosis

The presence of AKI must not lead the nurse to think that it is the only cause of acidosis until other causes have been eliminated, for example ketoacidosis and/or lactic acidosis.

Acidosis in kidney injury occurs when the renal tubules fail to regenerate bicarbonate and secrete hydrogen ions into the urine, which in turn causes an acid–base imbalance.

As most acid comes from the breakdown of dietary protein, it is possible to reduce the level of acidosis by limiting the level of protein intake. Another alternative is to infuse sodium bicarbonate, but one has to be aware of fluid overload and hypernatraemia. The most efficient way of treating acute acidosis is via RRT.

Uraemia

The accumulation of nitrogenous waste products will produce acute uraemia. Symptoms of uraemia often include nausea, vomiting, hiccups, increasing bleeding, infection risks, neurological problems, irritability, confusion, and twitching. As previously mentioned, it is necessary to begin appropriate dialysis.

Nutrition

Patients with AKI are often very ill and their metabolisms are often under great stress, resulting in the need for extra calories and extra protein (Kariyawasam 2012). Protein calorie malnutrition is believed to be one of the leading factors in the high mortality rate seen in AKI (Murphy and Byrne 2010). AKI causes major stress-induced hormonal and metabolic derangements within the body which result in negative nitrogen balance and depletion of body energy reserves (Casaer et al. 2008). Nitrogen balance is exceptionally negative in AKI and is often linked to sepsis, surgery, multiorgan dysfunction syndrome, and renal factors such as uraemia, acidosis, inadequate protein intake, and parathyroid hormone (Murphy and Byrne 2010). Nutritional intake is therefore of particular importance.

Patients require an individualised nutritional assessment and feeding plan, which will require specialist input from a dietitian, taking into consideration their complex metabolic state, fluid balance, and current RRT. In the acutely ill patient, enteral nutrition, if tolerated, is considered to be the best treatment option by most experts (Cano et al. 2006) as it is cheaper, safer, and more physiologically normal. The development of concentrated low-electrolyte feeds has proven invaluable in allowing delivery of optimal protein and calories with the minimum of fluid and electrolytes. However, these special feeds are not normally needed if the patient is receiving continuous RRT. The aims of nutritional support are to:

- prevent protein energy wasting;
- preserve lean body mass and prevent or minimise malnutrition;
- avoid further metabolic arrangements;
- stimulate immunocompetence;
- repair tissue damage;
- preserve organ function;
- maintain biochemistry/fluid balance;
- enhance recovery.

KDIGO (2012) suggest the goal of any feeding regime should be to provide an energy intake of $20\text{--}30\text{ kcal kg}^{-1}\text{ day}^{-1}$. They advise against protein reduction with the aim of preventing or delaying initiation of RRT, recommending the administration of $0.8\text{--}1.0\text{ g kg}^{-1}\text{ day}^{-1}$ of protein in people who are noncatabolic with AKI, who do not require dialysis. They recommend $1.0\text{--}1.5\text{ g kg}^{-1}\text{ day}^{-1}$ for people with AKI on RRT, and up to a maximum of $1.7\text{ g kg}^{-1}\text{ day}^{-1}$ in patients on CRRT. In patients who are hypercatabolic, they recommend a maximum of $1.7\text{ g kg}^{-1}\text{ day}^{-1}$ of amino acids if on CRRT (Lewington and Kanagasundaram 2011). Hypokalaemia and hypophosphataemia might be observed once a patient has commenced CRRT, and supplementation of these electrolytes needs to be undertaken as required.

Patients with AKI are frequently anuric and hence monitoring of fluid balance and reduction of fluid intake is often necessary. In patients not requiring RRT it is likely that they will require dietary reductions in potassium, magnesium, and phosphate. The development of continuous RRT has allowed fluid and electrolytes to be more easily managed without the need for the reduced fluid allowances that previously meant having to limit nutritional support (see Chapter 13).

Infection

Infection is known to contribute to the high mortality of patients with AKI (Hall and Esser 2008). Many patients with AKI are immunocompromised due to uraemia (Perkins and Kisel 2005). They are therefore at an increased risk of developing infections such as pneumonia, urinary tract infections, and sepsis, due to the large numbers of invasive devices they may need *in situ*. To reduce some of these risks it is a priority to remove all unnecessary lines, and universal precautions and guidelines for maintaining asepsis should be adhered to at all times.

Sepsis

Sepsis is a systematic inflammatory response in the presence of infection and is associated with organ dysfunction, hypoperfusion, and hypotension. Symptoms include a body temperature in excess of 38°C or below 36°C , a rapid heart rate in excess of 90 beats per minute, hyperventilation in excess of 20 breaths per minute, and a white cell count in excess of $12\,000\text{ cells l}^{-1}$. Sepsis contributes to nearly 50% of AKI cases in intensive care units and is the most common contributory factor for

AKI in such patients (Umbro et al. 2016). Sepsis can develop extremely quickly and is associated with a very high mortality rate, and sepsis-induced AKI is often a significant contributory factor. The very high mortality rate in sepsis-induced AKI is in part explained by incomplete understanding of the pathophysiology. Key to minimising mortality and potential progression to AKI and other systems failures is early identification and management. NICE (2016) has produced a clinical guideline for the management of sepsis.

The Clinical Course of Acute Kidney Injury

The clinical course of AKI can be divided into four stages or phases:

- initiating stage;
- oliguric stage;
- diuretic stage;
- recovery stage.

Types of UO can be found in Table 5.6.

Initiating stage

This occurs when the kidneys are injured and when diagnosis is made and treatment established. It can last anything from hours to days. Accurate assessment and rapid intervention can be crucial at this stage to prevent progression to the latter stages. Key risk factors for development of AKI include existing CKD, liver cirrhosis, heart failure, diabetes, hypovolaemia, systemic infection, known use of nephrotoxic agents, symptoms or history of urological obstruction, falling early warning scores, advanced age, major surgery, and use of contrast media (NICE 2013).

Oliguric stage

This can last from 5 days to over 15 days. When AKI persists for weeks, endocrine problems, such as reduced erythropoietin production, are noticed. Functional renal changes occur, such as decreased tubular transport, reduced urine formation, and lowered glomerular filtration. Renal healing will begin to occur, with the basement membrane being replaced with fibrous scar tissue and the nephron clogged with inflammatory products. The patient is particularly susceptible to bleeding and infection during this stage.

Diuretic stage

With continued healing the kidney begins to regain most of its lost function, but this depends on the severity of the initial injury. The signs and symptoms of the original condition begin to disappear. UO can begin to increase back to normal

Table 5.6 Types of urine output.

Anuria	No urine output (UO)
Oliguria	<400 ml day ⁻¹
Nonoliguria	>400 ml day ⁻¹
Polyuria	Normal or high urine output

levels of up to $3\text{ l}^{-1}\text{ day}^{-1}$. Often a key sign of this phase will be a period of polyuria as the functions of filtration associated with the glomerulus and proximal nephron often recover prior to the reabsorption functions of the distal nephron. For this reason, careful fluid monitoring is essential and patients are likely to require fluid and electrolyte support.

Recovery stage

The recovery stage can last from several months to over a year. The basement membrane is restored to its previous structure; scar tissue will remain but is not clinically significant. The kidneys respond in a regulatory excretory function to the body's needs.

Further reading can be found in Lameire et al. (2008).

Renal Replacement Therapy (RRT) in Acute Kidney Injury

The purpose of RRT is to prevent morbidity and to support the kidney during its recovery phase. The amount, type, and frequency of RRT are dictated by the severity of the patient's condition (Levy et al. 2016).

Indications for RRT are:

- uraemic symptoms, such as pericarditis;
- volume overload;
- hyperkalaemia;
- metabolic acidosis;
- 'space-making' – for example, nutrition, transfusions;
- AKIN/KDIGO stage 3.

There are a variety of treatment options available for AKI and the choice will depend on physician preference, nurse expertise, and availability of the appropriate equipment. The options fall broadly into two categories: intermittent treatments (acute haemodialysis [HD] and haemodiafiltration [HDF]) and CRRTs, of which there are three basic types: continuous haemofiltration (HF), continuous HD, and continuous HDF. Treatments performed continuously over long periods of time allow optimal values to be obtained for urea and fluid exchange control, and electrolyte and acid–base balance. Historically there was more emphasis on the use of peritoneal dialysis in AKI, and there is some interest in reconsidering this as an option in certain circumstances.

Acute intermittent haemodialysis

In acute HD, certain factors need to be considered; these include time on dialysis (usually a maximum of two hours for the first treatment), frequency (daily dialysis may be required), potassium concentration of dialysate ($3\text{ mmol l}^{-1}\text{ K}^+$ dialysate may be necessary), a biocompatible dialyser, and good fluid balance control. For those patients who are too haemodynamically unstable for conventional HD, other forms of RRT may be appropriate.

Intermittent haemodiafiltration

Intermittent HDF can be a therapy option for patients with AKI or ERF. It combines the advantages of diffusion (dialysis) with convection HF, and it is suitable for use in patients with cardiovascular instability, especially those with fluid

overload. It has superior small solute clearance over HF. Blood flow rates are higher than those of continuous HDF and it requires an HDF membrane that is more permeable than a normal haemofilter. However due to the efficiency of small molecule clearance, this would not be a treatment of choice for the patient with severe uraemia at risk of disequilibrium. The high blood flow rates associated with HDF require excellent vascular access and this can be an issue in patients being treated acutely.

Continuous renal replacement therapy

The use of CRRT has developed enormously during recent years and involves either dialysis (solute removal using diffusion) or filtration (solute and water removal using convection) or a combination of treatments. The advantage of continuous therapy is the slower rate of fluid or solute removal, thus making it better tolerated by critically ill patients.

The nurses in the intensive care unit have developed their skills, taking on this responsibility to ensure holistic care. It is recognised that intermittent HD may be contraindicated in patients with AKI who are critically ill. Complications such as cardiovascular instability, sepsis, and multiorgan failure make conventional intermittent treatments impractical.

Continuous haemofiltration

Continuous HF provides solute removal by convection. It offers high-volume ultrafiltration using replacement fluid, which can be administered in a variety of concentrations according to the patient's biochemistry. The pump guarantees adequate blood flow to maintain required ultrafiltration rates. This method can be performed using several litres of replacement fluid each hour. This is dependent on the patient prescription, which is usually determined by their weight. The addition of a blood pump to the circuit removes the necessity for arterial access and provides a more reliable and controllable method of delivering treatment (Figure 5.3).

Continuous haemodiafiltration

To increase the efficiency of small-molecule clearance, a dialysis solution is continuously pumped through the filter in a countercurrent direction to the blood. Small molecule (urea) clearance by diffusion is more efficient. It is possible to use a standard blood monitor for the extracorporeal circuit and then use infusion pumps to administer dialysate and replacement fluid (Figure 5.4).

Continuous haemodialysis

This method incorporates the same principles as intermittent HD but operates at a greatly reduced rate. From the nursing perspective, the use of fully automated systems provides a reliable and easy method of monitoring the fluid balance of patients who are critically ill.

The machine comprises a basic blood module with blood pump, venous and arterial pressure monitoring, and an air detector. The fluid monitor has two integral pumps: one to remove fluid from the filter and the second to pump replacement fluid to the patient. The replacement fluid and the ultrafiltrate are suspended on a weigh scale, which calculates and controls a linear patient weight (Figure 5.5).

With such accurate fluid control, the nurse does not need to measure and record fluid loss and replacement constantly as with previous methods. The ultrafiltration rate and physiological solutions are prescribed by the physician based on available clinical data (fluid state, biochemistry).

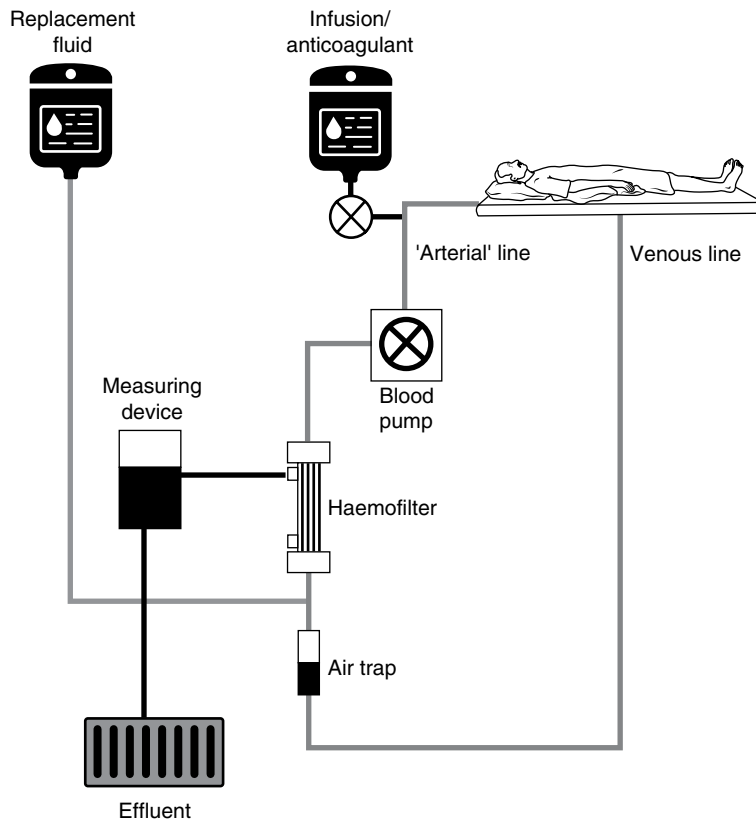


Figure 5.3 Continuous venovenous haemofiltration (HF).

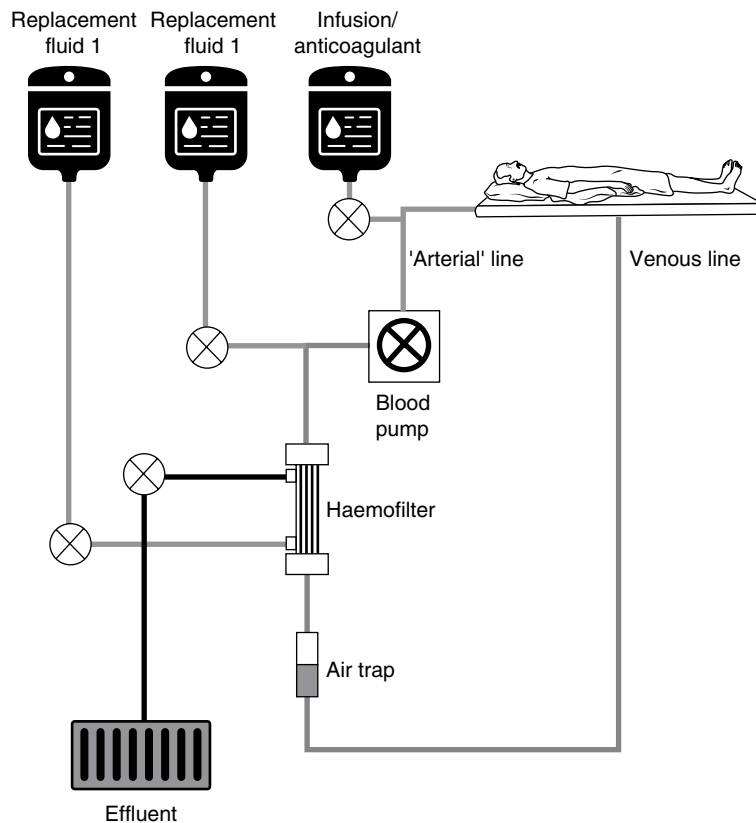


Figure 5.4 Continuous venovenous haemodiafiltration (HDF).

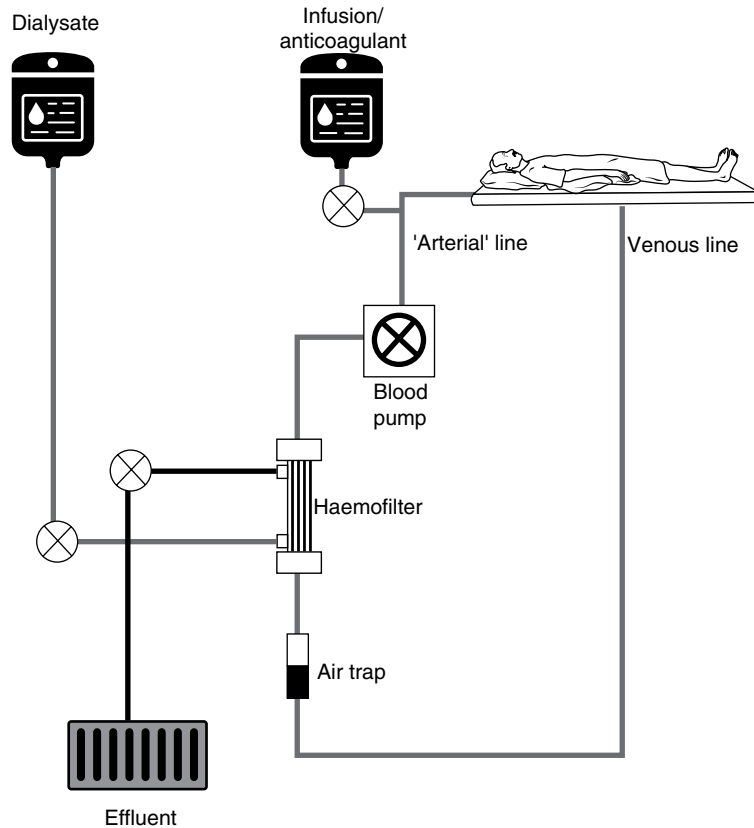


Figure 5.5 Continuous haemodialysis (HD).

Acute peritoneal dialysis

There has been renewed interest in the potential for the use of peritoneal dialysis in the treatment of AKI in recent years, and it has remained a much-used treatment option in many less-developed health economies because of its greater technical simplicity and lower cost. A systematic review of 24 studies into the use of acute PD found no significant difference in mortality between AKI patients treated with acute PD and those treated with extracorporeal blood purification (Chionh and Cruz 2014). One argument advanced in favour of the use of acute PD is that in the event of a patient failing to recover renal function it may facilitate the transfer of the patient to long-term PD therapy, rather than defaulting to HD.

Feasibility of acute PD depends very much on careful patient selection and the degree of experience with PD therapies in general in the centre in which the patient is being treated. Chionh and Cruz (2014) recommend the use of flexible PD catheters to minimise the chances of PD fluid leakage and infection, and the use of prophylactic antibiotic therapy prior to PD catheter insertion is also recommended. In patients with shock or liver failure, bicarbonate-based PD solutions are considered preferable to lactate-based solutions. Treatment is likely to need to commence with short dwell times (1–2 hours) in order to correct fluid overload, hyperkalaemia, and acidosis but dwell times can usually be lengthened to 4–6 hours after the first 24 hours of therapy.

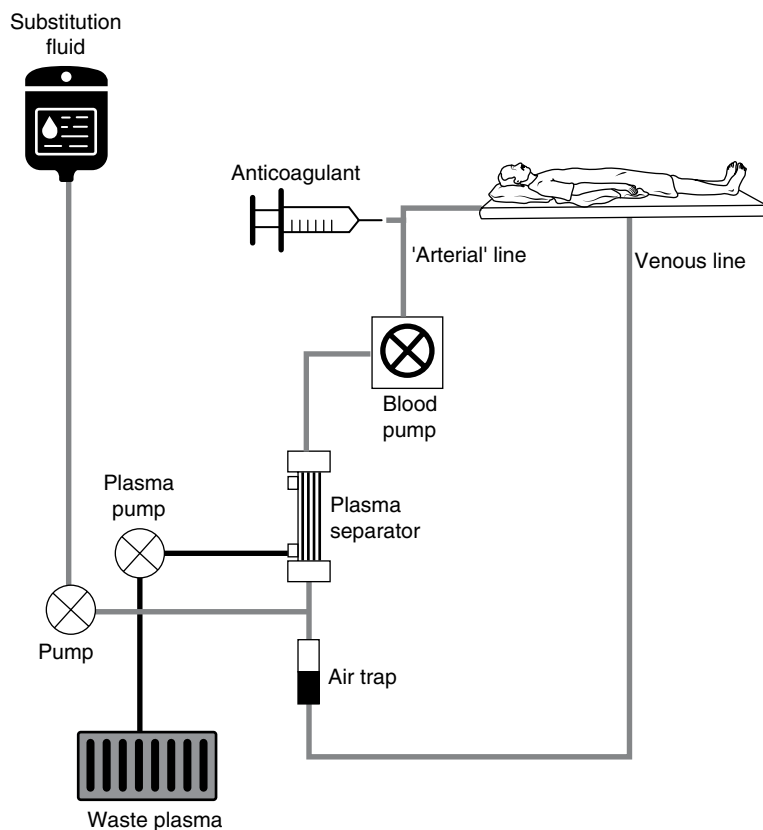


Figure 5.6 Plasma exchange.

Plasma exchange

Therapeutic plasma exchange (TPE) is an extracorporeal blood purification technique, designed for the removal of large molecular-weight substances from the plasma (Seck et al. 2011) (Figure 5.6). Most TPE procedures are performed for neurological, immunological, or haematological diseases, including anti-GBM disease, thrombotic thrombocytopenic purpura (TTP), Guillain-Barré syndrome, systemic vasculitis, AKI secondary to myeloma of the kidney, and haemolytic uraemic syndrome (HUS).

Plasma is separated from whole blood and then a replacement fluid is infused in equal volumes to the plasma that has been removed. It is a nonspecific therapy, removing all circulating substances within the plasma. A plasma filter is used to separate the plasma from all other cellular elements, using a semi-permeable membrane. As TPE removes all circulating substances in the plasma, care should be taken to avoid disturbances with clotting factors, calcium and magnesium levels, and any other substances that may be depleted as a result.

The fluid volume removed by TPE must be replaced to prevent marked volume depletion. Fresh frozen plasma (FFP) is usually given as the sole replacement solution, while albumin can be given alone or in conjunction with normal saline. The optimum choice depends on the disease being treated, for example saline and albumin for hyperviscosity and FFP for TTP.

Albumin

Albumin has the advantage that there is no risk of viral transmission and minimal risk of anaphylaxis.

Albumin-saline combination

When colloid and crystalloid solutions are used in combination, the amount of colloid should not be less than 50% of the total infusion. General recommendations are one-third saline, two-thirds albumin (UK Blood Transfusion and Tissue Transplantation Services 2005).

Fresh frozen plasma

FFP replaces the normal proteins that have been removed, therefore there is no depletion of coagulation factors or immunoglobulins. However, FFP can produce the most complications – including anaphylaxis, muscle cramps, and urticaria. FFP is the fluid of choice for TTP because it may provide a protein that diminishes platelet aggregation. Regimes for plasma exchange vary greatly depending on physician preference and clinical need.

Conclusion

The impact of AKI on patients and families is often unexpected and, despite new technology, it remains a serious disease with a high mortality rate. Unlike most patients who have had renal disease for some time, the patient with AKI who requires RRT will not have had the opportunity to have had counselling and the chance to evaluate their condition. The NICE (2013) AKI Clinical Guideline makes specific mention of the need to support patients psychologically and ensure the provision of appropriate patient information and education with regard to prognosis and future treatment options. The key aim of care is to balance humanistic caring skills with the technological and clinical expertise required to optimise the patient's survival and quality of life.

All patients with AKI require a high level of nursing management and the nurse therefore needs to understand the complexities of the illness and understand and manage electrolyte disturbances, disordered fluid status, and nutritional support to maintain protein stores and to reduce the infection risks. The renal nurse needs to understand the importance of the AKI classification systems and the relevant treatment guidelines, both national (NICE 2013) and local. The nurse also needs to be able to work with and advise colleagues working in general wards about patients who may have mild AKI (KDIGO stage 1), aiming to reduce the number that progress further along the AKI spectrum. It is imperative that renal nurses keep up-to-date with new technologies and initiatives so they act in a supportive role for their intensive care nursing colleagues.

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AKIN www.akinet.org (accessed 13 March 2018).

Hypertension, Dialysis and Clinical Nephrology, www.hdcn.com (accessed 27 February 2019).

KDIGO AKI guidelines, <http://kdigo.org/guidelines/acute-kidney-injury> (accessed 27 February 2019).

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Renal Registry www.renalreg.com (accessed 27 February 2019).

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CHAPTER 6

Chronic Kidney Disease

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Learning Outcomes

- to understand the classification of chronic kidney disease (CKD).
- to debate the scope of practice of primary care practitioners in managing CKD.
- to review the care and management of patients with mild to moderate CKD.
- to identify new innovations into identification and management of CKD.
- to evaluate best practice guidelines and strategies for predialysis care.

Introduction

This chapter will investigate care and management of those with mild to moderate kidney disease before renal replacement therapy (RRT) is required. Renal nurses are often involved with the technical, monitoring, and evaluative aspects of RRT for those with end-stage kidney disease (ESKD). However, many people may experience reduced renal function for years before needing RRT. This chapter will describe the care and management of people who have mild to moderate kidney disease and will discuss the published practice guidelines and strategies to guide care for this group. New healthcare roles are developing in this area of care, and so the potential for renal nurses to expand their scope of practice will be discussed.

Chronic Kidney Disease

It is estimated by a CKD Audit (Nitsch et al. 2017) that the prevalence of stage 3–5 CKD in the United Kingdom is currently around 5.5–6%, although only a very small minority of this group may eventually require dialysis or a renal transplant. Diabetes mellitus has become the most common cause of CKD, not only within the developed world but also increasingly within the emerging world, mainly due to the rise in the incidence of type 2 diabetes (Atkins and Zimmet 2010).

The National Service Framework and mild to moderate CKD

The National Service Framework (NSF) for Renal Services (Part Two) was published in February 2005. It identified four quality requirements covering CKD, acute renal failure, and end-of-life care. The two quality requirements of the NSF (Part Two) which relate to CKD are:

Quality requirement one: Prevention and early detection of chronic kidney disease
People at increased risk of developing or having undiagnosed chronic kidney disease, especially people with diabetes or hypertension, are identified, assessed and their condition managed to preserve their kidney function.

Quality requirement two: Minimising the progression and consequences of chronic kidney disease
People with a diagnosis of chronic kidney disease receive timely, appropriate and effective investigation, treatment and follow-up to reduce the risk of progression and complications.

One of the specific recommendations within the NSF made a huge change to the way in which kidney function was measured, and this change in practice will now be explained.

Kidney function and estimated glomerular filtration rate

Traditionally, kidney function has been assessed by measurement of serum creatinine. Serum creatinine is determined by the rate of production of creatinine, which is dependent on muscle mass, as well as the rate at which the kidney excretes it. Because of wide variation in patients' body size, weight, and muscle mass, serum creatinine is an inaccurate measure of kidney function. It is therefore recommended that kidney function in those with mild to moderate CKD (not including acute kidney injury) should be assessed by an estimation of glomerular filtration rate (eGFR).

The NSF for Renal Services recommended the use of the four-variable Modification of Diet in Renal Disease (MDRD) formula to estimate glomerular filtration rate (GFR). Clinical laboratories work out the eGFR based on the results of the serum creatinine, plus the gender and age of the patient. Once the eGFR is reported back to the primary care or renal clinic, an adjustment is made if the patient is African-Caribbean (not mixed race). If the patient is African-Caribbean then the eGFR result must be multiplied by 1.21. Assumption of Caucasian ethnicity can be made when using MDRD if ethnicity is unknown.

The use of eGFR enables healthcare professionals to evaluate kidney function within the accepted staging of CKD. It is important to note that an eGFR of 60–89 ml min⁻¹ is only indicative of CKD in the presence of other laboratory or clinical indicators. This reduces the possibility of inappropriately labelling people as having CKD. However, there are some cautionary notes to interpreting eGFR results. The following cautions are adapted from Renal Association guidance <https://renal.org/information-resources/the-uk-eckd-guide/about-egfr> (accessed 20 May 2018).

- eGFR is only an estimate of kidney function and a significant error is possible. The eGFR is most likely to be inaccurate in people at extremes of body type, e.g. patients with limb amputations, those who are severely malnourished, or those with extreme obesity.
- confidence intervals: The 90% confidence intervals are quite wide, e.g. 90% of patients will have a true GFR within 30% of their estimated GFR and 98%

have measured values within 50% of the estimated value. For an individual patient, however, serial values will be much more consistent than this just as creatinine values are – e.g. a 20% fall in a patient's eGFR is certain to reflect an important change.

- look at the trend in eGFR: Identifying trends in eGFR is often more informative than one-off readings, i.e. a progressive fall in eGFR across serial measurements is more concerning than stable readings which don't change over time.
- race: Some racial groups may fit the equations used to calculate the eGFR less well. This is mainly because the datasets used to derive these equations were predominantly white and black US citizens. There is usually a need to apply a correction factor for black people which varies depending on the formula used: add 21% if MDRD equation and 16% if CKD-EPI is used. In the UK population both the MDRD and CKD-EPI equations seem to work quite well.
- not-so-good near normal: The equations used for estimating eGFR tend to underestimate normal or near-normal function, therefore slightly low values (i.e. around the $60\text{ml min}^{-1} 1.73\text{m}^{-2}$ CKD 'cut-off' level) should not be over-interpreted. In this situation repeat testing, looking for a progressive decline in renal function over time.
- routine reporting of eGFR values >90 is not recommended and many labs are now reporting all values over 60 as >60 . Note, however, that a significant (e.g. 20%) rise in creatinine whilst eGFR is >60 may still be important as it will usually reflect a real change in GFR.
- values can differ between laboratories. Creatinine measurements can differ significantly between laboratories depending on the methods used to measure it. Furthermore, different laboratories may use a different formula to calculate the eGFR, further complicating comparison of eGFR measurements obtained from different laboratories.
- creatinine level must be stable: eGFR calculations assume that the level of creatinine in the blood is stable over days or longer, i.e. steady-state; they are not valid if it is changing. It is therefore not valid in patients with acute kidney injury or in patients receiving dialysis, for example.
- age: MDRD and CKD-EPI equations (see next paragraph) are not valid for individuals under 18 years of age.

In summary, a normal range for serum creatinine should no longer be given in isolation when assessing people with mild to moderate CKD, and the patient's management needs to be based on at least two eGFR results. The widespread use of eGFR has recently contributed to improved recognition of, and appropriate care of, individuals with CKD, including the reduction in late referral rates (now down to around 18%) from primary to secondary care (Byrne et al. 2018).

Since 2010 there has been increasing interest in the use of the CKD Epidemiology Collaboration (CKD-EPI) equation. The CKD-EPI equation was developed as a more accurate determination of the GFR (Levey et al. 2009) and one retrospective cohort study which compared the two equations found that the MDRD equation underestimated the prevalence of CKD amongst blacks and overestimated the prevalence of CKD amongst whites, compared with the CKD-EPI equation (Arora et al. 2012). Laboratories in the UK are increasingly using the CKD-EPI equation as recommended in NICE guidance (2014).

Staging of CKD

There is now worldwide acceptance of numerical stages or categories of CKD, based on the Kidney Disease Quality Outcomes Initiative (K/DOQI) classification (Kidney Disease Outcome Quality Initiative 2005). In general terms, categories 1–2

do not require specific interventions; categories 3a and 3b are managed in primary care; people with category 4 CKD may require referral to renal teams (this is the predialysis phase) and people with category 5 usually require some form of RRT (dialysis or transplantation) or conservative management.

In 2012 the international classification was amended and the GFR classification scheme remained with stages 1–5 (stage 3 is split into 3A and 3B), but stages for albuminuria were added: the guideline uses stages A1, A2, and A3 for the degree of albuminuria. This categorisation was adapted for the NICE guidance for CKD (2014). Table 6.1 shows the NICE (2014) categorisation of CKD.

Table 6.1 Classification of CKD using GFR and ACR categories (NICE 2014).

GFR and ACR categories and risk of adverse outcomes			ACR categories (mg/mmol), description and range		
			<3 Normal mildly increased	3–30 Moderately increased	>30 Severely increased
			A1	A2	A3
GFR categories (ml/min/1.73 m ²), description and range	≥90 Normal and high	G1	No CKD in the absence of markers of kidney damage		
	60–89 Mild reduction related to normal range for a young adult	G2			
	45–90 Mild–moderate reduction	G3a ¹			
	30–44 Moderate–severe reduction	G3b			
	15–29 severe reduction	G4			
	<15 Kidney failure	G5			

Increasing risk

Increasing risk

¹Consider using eGFR_{cystatinC} for people with CKD G3aA1 (see recommendations 1.1.14 and 1.1.15)

Abbreviations: ACR, albumin:creatinine ratio; CKD, chronic kidney disease; GFR, glomerular filtration rate

Adapted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group (2013) KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International (Suppl. 3): 1–150

General Medical Services contract

A contract for General Practitioners (GPs) in 2004 enabled GPs to be awarded points (related to income) if their surgery achieved specific indicators within a Quality and Outcomes Framework (QOF). The implementation of the General Medical Services (GMS) contract in 2004 coincided with the drive to implement measures in primary and secondary care for early detection and prevention of the progression of CKD. The inclusion of tests in the Diabetes QOF, such as measurement of microalbuminuria and annual testing of creatinine for people with diabetes, has increased the quality of screening and documentation, potentially allowing easier identification for those people with varying stages of CKD caused by diabetes (Roland et al. 2012).

The QOF for CKD was introduced in April 2006 and has been updated each year since. It is disappointing that in 2018 only one indicator (maintain a register of patients aged 18 or over with CKD with classification of categories G3a to G5) remains, as previously points were awarded for blood pressure control, urine ACR (albumin–creatinine ratio) testing, and medication prescription. Points are attached to each indicator and determine the sum paid to each practice.

Although recent years have seen an overall improvement in practices achieving blood-pressure and proteinuria targets, there is a large variation in GP practices recording the prevalence of CKD. The CKD Audit Part 1 (Nitsch et al. 2017) identified that there is considerable variation in coding for CKD between GP practices. The proportion of people with CKD stage 3–5 that were uncoded ranged from 0 to 80%, and on average this meant that approximately 70% of those with biochemical evidence of CKD (on the results available) had a CKD code. Amongst the 862 practices with available practice list size data, 4.4% of people over 18 were coded as having CKD stage 3–5. This gave a crude prevalence for coded CKD 3–5 of 3.5%.

The impact of clinical guidelines for managing CKD in primary care

Since the publication of the first guidelines for managing CKD in primary care in 2005, there remains scepticism about the impact and significance of diagnosing a patient with CKD, particularly as the concept of CKD is relatively new and patients with early disease are often asymptomatic (Brady and O'Donoghue 2010). One qualitative study (Crimson et al. 2010) found that primary care practitioners varied in their views of CKD. Some sought to implement the full clinical guidance, others only the pay-for-performance (QOF) targets. Nearly all practitioners had reservations as to whether CKD was really a disease and debated whether the diagnosis of CKD based on eGFR alone was appropriate. They also questioned whether CKD in older people was part of the natural ageing process. In addition, GPs had experienced difficulty in explaining the condition to patients without frightening them. These findings were supported by Greer et al. (2012) who found that practitioners in the United States reported several patient, provider, and system-level barriers that contributed to poor education about CKD in primary care. A study in the United Kingdom in 2012 found that there was still anxiety about the disclosure of early-stage CKD with patients. The tensions experienced in this study related to identifying and discussing CKD in older people and patients with stage 3A, embedding early-stage CKD within vascular care, and the distribution of work within the practice team (Blakeman et al. 2012). More recently Simmonds et al. (2016) suggested that the introduction of NICE guidelines in 2014, which focused on the meaning and purpose of CKD monitoring, may have helped to resolve some of the ethical and moral tensions clinicians expressed regarding the over-medicalisation of patients with a CKD diagnosis.

Innovation in Managing Mild to Moderate Kidney Disease in Primary Care

The aim of primary care management is to prevent or delay progression to ESKD and reduce cardiovascular risk. The Renal Association e-guide for CKD provides a comprehensive introduction to care and management of people with CKD and can be found here: <https://renal.org/information-resources/the-uk-eckd-guide> (accessed 20 June 2018).

Understanding the prevalence of CKD means that strategies for identification, assessment, and management need to be developed to help reduce the health burden that CKD poses in the United Kingdom. Around 6% of the population may have CKD stages 3–5, but not all patients with CKD need to be referred to or managed by nephrologists, although input from renal specialist nurses may be appropriate (Thomas 2011). These patients are at high risk of cardiovascular disease and should be managed appropriately, irrespective of referral to a nephrologist. Stable CKD and associated complications, such as cardiovascular risk and anaemia, can be managed in the community or general medical clinics, but timely referrals to renal services are crucial.

Examples of innovative projects to support primary care include employment of specialist renal nurses to work alongside practice and community nurses. The East London Community Kidney Service has instigated a system-wide change in community care of CKD, and employs one clinical nurse specialist for CKD, who educates people with mild to moderate CKD in community settings (Thomas and Rainey 2018). Renal nurses working within a community setting are still however in a minority in the UK.

Other initiatives, such as computerised systems, can identify patients most at risk of progressive CKD. The ASSIST-CKD project (Gallagher et al. 2017) is based on an intervention by Heart of England Foundation NHS Trust in Birmingham, whereby a community-wide CKD management system has contributed to a decline in the incident rate of RRT and the lowest percentage of patients presenting within 90 days of starting RRT in the UK (Renal Registry 2017). The intervention is based upon an offline database that integrates laboratory results from blood samples taken in all community and hospital settings relating to the same patient. Graphs of eGFR over time are generated for patients <65 years with an incoming eGFR <50 ml min⁻¹ 1.73 m⁻² and patients >65 years with an incoming eGFR <40 ml min⁻¹ 1.73 m⁻². Graphs where kidney function is deteriorating are flagged by a laboratory scientist or renal nurse and details sent to the GP with a prompt that further action may be needed.

In general terms, it appears that local and national initiatives have together contributed to the improved understanding and management of CKD in primary care in the United Kingdom and as Stevens et al. (2012) suggested, have shown signs of having made significant health gains. One such indicator is late referral to secondary care: the UK Renal Registry (2017) has reported that late presentation (within three months of requiring RRT) has continued to fall from 23.9% in 2006 to 15.6% in 2016.

Care and Management of Mild to Moderate Kidney Disease (Stages 3a–3b)

This section provides a general overview of the care and management of people with category 3a–b CKD, followed by a specific section on care and management of those with diabetes and CKD. The chance of developing CKD increases with age. People of African-Caribbean or South Asian ethnic groups are also more likely to

develop kidney disease. CKD appears to progress more rapidly in patients from lower socioeconomic groups. A family history of CKD is also a risk factor. Patients can be directed to the NHS Choices Kidney Disease checker to see if they might be at risk of CKD: <http://www.nhs.uk/tools/pages/kidneydisease.aspx> (accessed 20 June 2018).

Monitoring of CKD

Everyone at high risk should have an annual eGFR, to ensure that people with kidney disease are identified when the disease is still at an early stage. This is important because treatment of mild to moderate kidney disease with appropriate medicine management and changes in lifestyle can slow down kidney damage. Also, early detection and treatment of CKD lessens the chance of it leading to CVD (cardiovascular disease). An overview of testing frequency for CKD can be found in the NICE (2014) guidance (Section 6.1.3).

How to explain the diagnosis of CKD

Age-related decline in eGFR can be common, so it is important to note that an eGFR in the range 45–59, if stable over time and without any other evidence of kidney damage, is unlikely to progress or develop CKD-related complications.

Words used to explain this need to be chosen carefully. For example, it may be helpful to use the terms ‘kidney damage’ or ‘reduced kidney function’ rather than CKD, as the words ‘chronic’ and ‘disease’ can be frightening. It is also important to explain that kidney damage can be part of the normal ageing process. However, people with stage 3 CKD do need to be monitored and this will be carried out through an annual blood (eGFR) and urine (proteinuria) test. People with CKD should have a Read code, which means their names will appear on the CKD register in each practice. They should also be informed as such. There are many resources available to inform people about CKD. Kidney Care UK has a range of resources to support people who have been newly diagnosed with CKD: <https://www.kidneycareuk.org/about-kidney-health/newly-diagnosed> (accessed 25 July 2018).

Self-management

One of the best ways to effectively manage mild to moderate kidney disease is to empower patients with knowledge of their condition and likely outcomes. Most people with CKD spend the majority of time managing their own condition, supported by healthcare professionals, for only a few hours each year. Both primary and secondary care nurses are well placed to facilitate opportunities for self-management. Key messages include:

- urine test: a reminder to come for urine tests (ACR) as required which will help identify if at risk of progressive CKD.
- blood test: a reminder to come for blood tests to monitor kidney function as required.
- blood pressure control: to explain the importance of BP tablets not only for blood pressure control but also to delay progression of CKD. Explain the need to report side effects, as high blood pressure is a key factor in the progression of CKD.
- blood pressure monitoring: to monitor their blood pressure at home, but they will need advice on which machine to buy and training on how to do this.
- smoking cessation.
- diet: avoid processed, high-salt, and high-fat foods.

- medicine management:
 - give advice on buying tablets over the counter (particularly anti-inflammatory drugs);
 - patients should tell the pharmacist that they have CKD.
- lifestyle modification: taking exercise and keeping to ideal weight.

Self-management packages

One quality-improvement project (Thomas and Loud 2012) aimed to reduce inconsistencies in CKD care and improve self-management opportunities for patients. At the end of the project a 'Package of Innovation (POI) for Managing Kidney Disease in Primary Care' was developed. This package was developed by a team of practitioners and people with experiences of kidney disease and other chronic conditions, and aims to improve the quality of care of people with kidney disease in the community.

The package includes:

- details about how to validate a CKD register used in primary care;
- training packages for healthcare professionals on CKD management, quality improvement techniques, and self-management facilitation;
- a training package that can be delivered by patients or healthcare professionals to people in a group education session to educate about kidney disease and encourage both self-management and collaboratively working with healthcare professionals;
- an information booklet and a DVD to help patients to look after their kidneys.

All materials can be used as per the step-by-step guide detailed in the package, although each is also a stand-alone item. The majority of the resources are freely available to download from <https://www.kidneyresearchuk.org/packageofinnovation> (accessed 20 June 2018).

A more recent innovative resources pack has been developed by the East London Community Kidney Service (Thomas and Rainey 2018). The pack includes a 'conversation map' to be used in both one-on-one and group education sessions, a short and long booklet, plus films in different languages. All resources are freely downloadable at <https://bartshealth.nhs.uk/renal> (accessed 24 July 2018).

Cardiovascular risk management in CKD

Cardiovascular risk management is the main aim of care for people with stage 3 CKD, as both CKD and proteinuria are independent risk factors for CVD.

In summary, the following actions should be undertaken to reduce CVD risk:

- blood pressure control. The goal is to keep blood pressure below 140/90 mmHg or 130/80 mmHg (for those with diabetes and/or proteinuria [ACR of 70 mg mmol⁻¹ or more]). If the blood pressure target is not met on more than two occasions, it is recommended to prescribe a low dose of ACEI/ARB (e.g. ramipril 1.25 mg day⁻¹) and then monitor renal function and serum K⁺ after 5–10 days. Treatment can be increased progressively with monitoring, but a combination of renin–angiotensin system antagonists to people with CKD should not be offered (NICE 2014). It is important to monitor renal function in case of renal function decline. This can happen when glomerular filtration pressure is dependent on angiotensin II – driven efferent arteriole tone (as in volume depletion or renal artery stenosis).

- salt intake should be assessed and reduced to 4–6 g day⁻¹.
- follow the recommendations for lipid modification (NICE guideline CG181) for the use of statins in CKD and offer antiplatelet drugs to people with CKD for the secondary prevention of cardiovascular disease, but be aware of the increased risk of bleeding.

Medicines review

A medicines review should be undertaken in any newly identified patient with CKD. Patients with CKD should be asked about over-the-counter and herbal medicines, to ensure medications are indicated and safe for the individual to take. It is important to emphasise that some medications can affect the kidneys – for example, nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen – so advise patients it is best to check with a pharmacist before purchasing any over-the-counter tablets. Metformin is excreted by the kidneys and has the potential to cause lactic acidosis. Many clinicians prescribe metformin until eGFR is $<30 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$, when it should be stopped altogether, whilst the dose should be reduced when eGFR $30\text{--}45 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$. Special caution should be used when starting metformin in patients who are already on antihypertensive or diuretic therapy, or NSAIDs.

Referral

It is crucial to refer patients to a renal unit if eGFR <30 or if there is rapidly decreasing kidney function. Renal units require at least one year to prepare people for dialysis, and once people with diabetes and CKD have an eGFR <30 there may be a rapid decline in kidney function, especially if blood pressure and/or blood glucose are not well controlled.

The NICE (2014) guideline gives further details on referral to secondary care and a summary of indicators for referral is shown in Box 6.1. Always take into account the individual's wishes and comorbidities when considering referral.

BOX 6.1

Indicators for referral to secondary care

- GFR less than $30 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$ (GFR category G4 or G5), with or without diabetes.
- ACR 70 mg mmol^{-1} or more, unless known to be caused by diabetes and already appropriately treated.
- ACR 30 mg mmol^{-1} or more (ACR category A3), together with haematuria.
- sustained decrease in GFR of 25% or more, and a change in GFR category or sustained decrease in GFR of $15 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$ or more within 12 months.
- hypertension that remains poorly controlled despite the use of at least 4 antihypertensive drugs at therapeutic doses (see also Hypertension [NICE guideline CG127]).
- known or suspected rare or genetic causes of CKD.
- suspected renal artery stenosis.

Note: People with CKD and renal outflow obstruction should normally be referred to urological services, unless urgent medical intervention is required – for example, for the treatment of hyperkalaemia, severe uraemia, acidosis, or fluid overload.

Diabetes Mellitus

Good blood glucose control in individuals with type 1 diabetes mellitus has been shown some years ago to prevent or slow down the progression of renal disease (DCCT Research Group 1993). This landmark study demonstrated that a reduction in HbA1c (glycated haemoglobin) from 9.0 to 7.0% was associated with a 39% reduction in the occurrence of microalbuminuria and a 54% reduction in the occurrence of proteinuria over 6.5 years in patients with type 1 diabetes (DCCT Research Group 1993).

Early research in type 2 diabetes mellitus indicated that tight blood pressure control was also crucial (United Kingdom Prospective Diabetes Study Group 1998). More recent studies (cited in NICE guidance (2014) for CKD) reflect these findings. A summary of CKD management in people with diabetes is shown in Box 6.2.

Care and Management of Moderate to Severely Decreased Kidney Function (Stage 4)

The care and management of people with stage 4 CKD should be the same as in stage 3a/b but other considerations should also be taken into account. Once the eGFR drops to below $20 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$, the focus should start to be on preparation for RRT.

Optimal nutritional management

Management of nutrition, especially the controversial issue of reducing protein intake in CKD, is discussed in Chapter 13. All patients at CKD stage 4 should receive a dietary assessment and be screened for malnutrition.

Control of serum bicarbonate within normal levels

As an individual becomes more uraemic, the pH balance in the internal environment starts to become more acidic. The body's natural response to this is to produce bicarbonate, metabolised from the liver and activated by the kidney, which

BOX 6.2

Management of mild to moderate kidney disease in people with diabetes

- education and promotion of self-management.
- annual monitoring of eGFR.
- annual monitoring of microalbuminuria (ACR) (early morning urine sample recommended). An ACR $>3.0 \text{ mg mmol}^{-1}$ is clinically significant.
- systolic blood pressure control to $<130 \text{ mmHg}$.
- diastolic blood pressure control to $<80 \text{ mmHg}$.
- blood glucose control. A target HbA1c of $<48 \text{ mmol mol}^{-1}$ (6.5%) is often given although individualised targets are recommended. (Changes in the reporting of HbA1c values were introduced in the UK in 2009 and from June 2011 HbA1c is reported in mmol mol^{-1} , often alongside HbA1c%.)
- prescription of ACE inhibitors or ARBs once microalbuminuria is present.
- lifestyle changes (especially smoking cessation).
- referral if eGFR <30 , especially if there is progressive CKD.
- immunisation for influenza and pneumococcus advised.

acts as a buffer to return the pH to more neutral levels. However, if the kidney is defective, this process is thwarted, and supplementary bicarbonate may be administered. The nurse must be aware that administering bicarbonate may result in plasma volume expansion and hypertension, which should be reported. The safest way to control bicarbonate balance is with dialysis. Hence, if this condition is not adequately controlled then commencement of dialysis may be indicated.

Management of bone disease

Renal disease causes an abnormality of vitamin D metabolism, causing deficient calcium levels, skeletal damage, and bone pain. Refer to Chapter 2 for further information on the underlying physiological processes. The aim of care is to keep calcium and phosphate levels within normal ranges, preventing hyperparathyroidism. After correcting the acidosis, plasma phosphate and calcium levels can be controlled with oral phosphate binders, calcium supplements, and dietary changes. See Chapter 13 for more discussion.

Control of anaemia

An eGFR of less than $60\text{mlmin}^{-1}1.73\text{m}^{-2}$ should trigger an investigation into whether anaemia is due to CKD. Anaemia in CKD is usually normocytic and normochromic, and due to primary causes such as reduced production of erythropoietin production, uraemic toxins inhibiting erythropoiesis, and haemolysis due to uraemic changes to the red cell membrane.

The individual will become more anaemic as renal disease progresses, as three types of cells in the blood are affected:

- erythrocytes – causing anaemia;
- leukocytes – causing immunosuppression;
- platelets – causing bleeding tendencies.

Treatment with erythropoietic stimulating agents (ESAs) should be prescribed to people with anaemia of CKD who are likely to benefit in terms of quality of life and physical function. Blood transfusions should always be avoided in people with anaemia of CKD in whom kidney transplant is a treatment option, yet there might be a few situations where a transfusion is indicated clinically. In these cases, follow the relevant national guidance.

The National Institute for Health and Care Excellence guidance (2015) was updated from the 2011 guidance because of the need to review evidence in several areas that provide challenges for clinicians managing anaemia in CKD, namely people who consistently fail to respond to the ESAs and the role and management of iron deficiency.

The correction to *normal* levels of Hb with ESAs is not usually recommended in people with anaemia of CKD. The aspirational Hb range should be maintained between 100 and 120g l^{-1} for adults, young people, and children aged two years and older, and between 95 and 115g l^{-1} for children younger than two years of age, reflecting the lower normal range in that age group. To keep the Hb level within the aspirational range, do not wait until Hb levels are outside the aspirational range before adjusting treatment (for example, take action when Hb levels are within 5g l^{-1} of the range's limits).

It is also important to monitor iron status, and iron therapy should be offered to people receiving ESA maintenance therapy to keep:

- percentage of hypochromic red blood cells less than 6% (unless serum ferritin is greater than $800\mu\text{g l}^{-1}$)

- reticulocyte Hb count or equivalent tests above 29 pg (unless serum ferritin is greater than $800 \mu\text{g l}^{-1}$)
- transferrin saturation level above 20% and serum ferritin level above $100 \mu\text{g l}^{-1}$ (unless serum ferritin is greater than $800 \mu\text{g l}^{-1}$).

In people who are in the predialysis stage, levels of the above should be monitored every three months. If people have a normal full blood count there is little benefit in checking iron status. See National Institute for Health and Care Excellence guidance (2015) for further information on iron therapy for people who are iron deficient and are/are not receiving ESA therapy. In all cases discuss the results of the iron therapy with the patient or family and offer ESA therapy if needed.

Control of gastrointestinal disorders

These disorders are common in CKD, especially as the individual approaches the need for dialysis. The person may experience anorexia, nausea and vomiting, hiccups, a metallic taste in the mouth and, for those with diabetes, exacerbation of gut complications presenting as episodes of diarrhoea. Urea is excreted in the gut and broken down, releasing ammonia which acts as an irritant. Some medications may give unpleasant side effects, e.g. heartburn with phosphate binders and oral iron supplementation. Constipation can be common in established renal disease as fluid intake is reduced. Generally, the person with renal disease is less physically active due to the effects of a chronic illness causing lethargy and tiredness.

Treatment of dermatological disorders

Generalised uraemic pruritus (itching) is a distressing symptom in persons with CKD, with often little relief from drugs. Deposits of calcium and phosphorus in the skin and sweat glands excreting urea are thought to be the causative factors of pruritus, but dry skin and drug allergies must not be overlooked as causes. Platelet defects and capillary permeability, both complications of renal failure, can cause bleeding and bruising of the skin, especially if there is continued scratching. Many persons with advanced kidney disease have a yellow tinge to their skin that is a combined result of hypermelanosis and the deposition of pigments in the skin (urochrome and carotene) that are usually excreted by the kidneys. Although medications may be of some help (Rayner et al. 2013), commencement of dialysis may be the only long-term relief.

Control of volume disorders

During the progression of kidney disease some nephrons remain intact whilst others continue to be destroyed. The remaining undamaged nephrons hypertrophy and produce an increased volume of filtrate with increased tubular reabsorption, even though there is a reduction in the GFR. This process allows the kidney to continue to function until three-quarters of the nephrons are destroyed. In persons with CKD with blood urea levels above 40 mmol l^{-1} , the solute load becomes greater than can be reabsorbed, producing an osmotic diuresis accompanied by polyuria of up to 3 l in a 24-hour period. The urine is dilute as the kidney's concentration ability is lost and the person will have nocturia. As more nephrons are destroyed, oliguria with the retention of waste products is evident. The individual develops a wide range of biochemical, haematological, and endocrine disorders and the clinical features of fluid overload.

Changes in fluid allowance may be required in association with diuretics. Loop diuretics such as furosemide will increase sodium excretion from the kidney and so

prevent sodium retention. During episodes of polyuria, volume replacement should be administered to prevent further reduction in renal perfusion and worsening of kidney function. When volume overload is unresponsive to treatment the commencement of dialysis is indicated.

Control of potassium disorders

Excess potassium is normally removed by renal excretion, but as CKD progresses, excretion of urinary potassium decreases because of a reduced GFR caused by tubular defects in diseases such as diabetes mellitus, ultimately resulting in hyperkalaemia. Hyperkalaemia (indicated as a potassium level of above 6.0 mmol l^{-1}) can occur in CKD following episodes of acute illness, infection, or nonadherence to dietary restrictions. Chronic metabolic acidosis also causes potassium to shift out of the cells and into the extracellular fluid, giving rise to hyperkalaemia.

If metabolic acidosis is present this should be corrected first, and this will then help to reduce the serum potassium to within safe limits. If chronic hyperkalaemia is present, dietary advice may be indicated, so high-potassium foods are avoided (see Chapter 13).

Potassium-sparing diuretics should usually be discontinued as these drugs block the distal potassium transfer so that potassium is retained. If hyperkalaemia persists, this should be monitored very closely and managed in one of two ways – either conservatively or with dialysis. Conservative management of hyperkalaemia may involve the use of exchange resins (e.g. calcium resonium). Oral resins are not absorbed but exchange potassium for calcium or sodium from the gastrointestinal tract. The choice of calcium or sodium depends on the level of hypercalcaemia or fluid overload in the individual.

Control of acid–base balance

In normal health, acid–base balance is maintained by the excretion into the renal tubules of excess acid (hydrogen or H^+ ions) where the following processes then take place:

- filtered bicarbonate is reabsorbed.
- there is increased production of ammonia that combines with H^+ ions and is then excreted in the form of ammonium salts.
- a titratable acid is formed.
- tubular fluid pH is reduced.

In CKD, a mild metabolic acidosis may be present as normal renal tissue is not sufficient to perform the above functions efficiently. Metabolic acidosis may also be worse in persons who have renal tubular acidosis.

The individual will present with:

- a blood pH of less than 7.35;
- hyperkalaemia, as metabolic acidosis shifts potassium from the cells into the extracellular fluid;
- signs of renal bone disease, as metabolic acidosis reduces the bone carbonate buffers, allowing calcium to be lost from the bones: calcium is more soluble in an acid environment;
- gasping for breath caused by acidosis as the person attempts to breathe off the excess acid through expired carbon dioxide.

Intravenous sodium bicarbonate may correct acidosis but the sodium may cause hypernatraemia, leading to fluid retention and hypertension. Essentially, metabolic

acidosis indicates kidney failure and the most efficient and safest way to treat it is with dialysis.

Disorders of the central nervous system

In CKD, nervous system dysfunction can cause numerous mental disabilities such as poor memory function, loss of concentration, and slower mental ability. Physical disabilities result in peripheral neuropathies affecting the legs and feet and may result in 'restless legs' and paraesthesia. More serious neurological problems are rarely seen these days, where there is fluid overload and hypertension in advanced kidney disease, in the form of convulsions and cerebral oedema. A 'uraemic flap' may be seen in very toxic patients, where the hands involuntarily flap from the wrists. Other electrolyte disorders (such as hyper- or hypocalcaemia) also cause shaking, or an involuntary reflex, when nerve points are stimulated. All these symptoms and complications can be avoided with the introduction of timely dialysis.

Sexual function

In women, the loss of sexual function may take the form of infertility due to amenorrhoea and other menstrual abnormalities. Loss of libido may be present. There is also risk to the mother's health as it is possible that progression to ESKD will accelerate because of the extra workload on damaged kidneys.

In men, the incidence of infertility and impotence increases with age and the advancement of CKD. There are multiple causes of impotence, which include poor nutrition, anxiety, side effects of antihypertensive drugs, and reduced plasma testosterone. The individual and partner should be given ample opportunity to express fears and talk about symptoms that are causes for concern.

With the wider use of erythropoietin to correct anaemia, fewer women with decreased renal function are experiencing loss of fertility and amenorrhoea. Successful pregnancy for couples where at least one partner has a degree of kidney disease is becoming more common, although requires careful planning and monitoring for a successful outcome (Davison and Lindheimer 2011). Piccoli et al. (2018) in their editorial for World Kidney Day 2018 raised interesting questions about pregnancy in CKD. They asserted that as the presence of any degree of CKD has a negative effect on pregnancy, plus there is an increase in risk of CKD progression post-partum, ethical issues around conception, and maintenance of pregnancies are raised for the healthcare team and the patient.

Education in the Predialysis Phase

The need for good education and preparation of the individual and the family at all stages of CKD, potentially heading towards ESKD, cannot be underestimated (Harwood and Clarke 2011). The psychological aspects of dealing with this chronic illness have been dealt with in Chapter 4, but it is worth reiterating the importance of education and information as part of the preparation process. It is essential that the person and renal staff work in collaboration, not only to ensure the best care possible for the person, but also for the renal team to understand the patient and family perspective. For some, it is very important to be able to continue in their present employment, and so education about RRT modalities must include consideration of how dialysis is to be performed. For example, peritoneal dialysis that people can perform for themselves, or some form of home dialysis programme, is key to maintaining employment status.

Shared decision making during the predialysis stage is crucial and this involves not just clear, understandable information about the condition and the treatment or support options, but also prompts to help them think about what the different options might mean for them (Coulter and Collins 2011). These prompts are called patient decision aids (PDAs) and are designed to help clinicians to actively engage patients in the decision-making process. Decision aids include several components with relevant information that help patients to remember facts and make deliberate choices between two or more treatment options. Decision aids for people with kidney disease have been developed (for example YoDDA <http://www.yodda.leeds.ac.uk/Survey/Information> [accessed 24 July 2018]) but NICE (2018) guidance has suggested that further research into PDAs is needed. One of the research recommendations from the NICE (2018) guidelines asks what is the clinical effectiveness and cost effectiveness of using decision aids in the context of RRT. For some, the thought of attempting to understand any aspect of the RRT process is daunting and overwhelming. This may be due to the immediacy of the circumstances in which they commenced RRT, or indeed their sense of control and unique personal characteristics, which mean the understanding healthcare professionals should take the lead in directing care. This in no way means that the individual absolves responsibility or plays no part in any of the decision-making processes about care and treatment.

For predialysis preparation to be effective, influences on learning such as cultural and religious beliefs about the context of CKD have to be taken into consideration. Indeed misunderstanding and misinterpretation by the individual and their family may have more to do with the way information is presented (e.g. jargon used) by healthcare professionals. For many patients the cultural and religious contexts of health are crucial in shaping how far healthcare advice is accepted. The renal unit is a confusing place where the individual has to make sense of their symptoms and proposed treatment plan. Patients also have to work through the stages of grief of losing an old life, and also have to realign the new (renal) life with personal ideology and life goals.

The ultimate skill that any renal healthcare professional can hope to achieve in the care of those approaching RRT is to be able to gain an understanding of each individual. That person is unique as regards personal hopes and aspirations for the future, the ability to understand the care and treatment strategies that lie ahead, and how the individual wishes to be involved in that care delivery. All too often, renal professionals of all kinds can be very focused on the pathological and technical aspects that dominate their understanding of their role as a renal practitioner. For the individual approaching RRT, the priorities may be quite different, so it is important to start providing information very early on, at least one year before dialysis is required.

Combes et al. (2017) support this view. A qualitative study with 96 staff and 93 patients concluded that all staff, irrespective of their role, need to be trained about all treatment options so that informal conversations with patients are not biased. The study argues for a more individualised approach to PDE (predialysis education) which is more like counselling than education and demands a higher level of skill and training for specialist PDE staff. The study concludes that even if these improvements are made to PDE, not all patients will benefit, because some find decision-making in the predialysis period too complex or are unable to engage with education due to illness or emotional distress. A co-produced study (Thomas et al. 2016) in two NHS Trusts also supported the assertion that predialysis education programmes (PDEPs) improve on the quality of the information provided, especially how daily living can be affected by dialysis.

It is also important to always be aware that there may be those for whom initiation of dialysis may not be feasible or preferable. The option of not commencing dialysis at all is discussed in detail in Chapter 11.

Predialysis education programmes

There are many benefits to running a structured PDEP. Many units run group education sessions for patients, and content of the programmes may include introductions to HD (haemodialysis), PD (peritoneal dialysis), and transplantation, plus other issues such as nutrition and social/psychological support available. PDEPs should enable patients to make informed choices about dialysis, and indeed Goovaerts et al. (2005) found that a high percentage of patients exposed to a structured PDEP often choose a self-care modality such as home HD.

NICE (2018) guidelines recommend the importance of educational programmes to enable patients to make informed choices of treatment options. A good overview of how to set up and implement education programmes for CKD has been written by Goovaerts et al. (2015). The overview describes how experts brainstormed and discussed quality standards for RRT option education: standards for the education team, processes, content/topics, media/material/funding, and quality measurements. Critical points include the requirements for the education of nurses who are involved in education; for example they need training in the principles of adult education, communication skills, motivational interviewing, and how to avoid bias.

The authors also make useful suggestions on the decisions that patients and their families need to consider before deciding on a treatment modality:

- should I have active treatment or opt for conservative care?
- should I have dialysis and/or a (pre-emptive) transplant?
- should I have dialysis at home, at a self-care facility or in the unit?
- should I have HD or PD?
- what type of HD (standard, nocturnal, short frequent) or PD (continuous ambulatory PD [CAPD], automated PD [APD]) should I have?

A summary of the content (Box 6.3) and recommendations for implementing PDEPs identified in this handbook is shown in Box 6.4.

The content of any education programme or session should always be individualised for each patient and their family but Box 6.5 summarises the information priorities that were identified by and important to patients with CKD (modified from Ormandy et al. (2007)). Goovaerts et al. (2015) has identified the questions that nurses should ask when assessing the quality and suitability of a material/resource:

- will I feel comfortable using it?
- will it enhance the understanding of disease and treatment?
- will it present the consequences of the patient's decision?
- will it encourage the patient to use their own reasoning?
- will it help the patient to develop realistic expectations?
- will it supplement rather than replace the information provided by the educator?

When Should Dialysis Commence?

The optimal time at which the individual concerned can benefit most from commencing RRT continues to be controversial. It is important to bear in mind that pre-emptive transplantation is the gold standard, where possible. What is not disputed is that timely referral to the renal team is beneficial as late referral often results in poorer outcome in terms of mortality and morbidity rates and quality of life experienced during this period (Chan et al. 2007). There is also evidence that

BOX 6.3**Suggested content for predialysis education programmes from NICE (2018) guidelines for renal replacement therapy and conservative management**

Information about treatments and how they may affect lifestyle (NICE 2018)

- information about treatments*
 - what they involve, for example, availability of assistance, time that treatment takes place, and number of sessions per day/week
- potential benefits
 - the benefits of adherence to treatment regimens and the potential consequences of nonadherence
- potential adverse effects, their severity and how they may be managed
 - the likely prognosis on dialysis, after transplant, or with conservative management
- the transplant listing process (when appropriate)
- switching the modality of RRT and the possible consequences (that is, the impact on the person's life or how this may affect future treatment or outcomes)
- reviewing treatment decisions
- stopping treatment and planning end-of-life care
- information about how treatments may affect lifestyle
- the person or carer's ability to carry out and adjust the treatment themselves
- the possible impact of dietary management and management of fluid allowance
- how treatment may fit in with daily activities such as work, school, hobbies, family commitments, and travel for work or leisure
- how treatment may affect sexual function, fertility, and family planning
- opportunities to maintain social interaction
- how treatment may affect body image
- how treatment may affect physical activity (for example, whether contact sports should be avoided after transplantation, whether swimming should be avoided with peritoneal dialysis)
- whether a person's home will need to be modified to accommodate treatment
- how much time and travel treatment or training will involve
- the availability of transport
- the flexibility of the treatment regimen
- whether any additional support or services might be needed

* Treatments include RRT, conservative management, and dietary intervention.

BOX 6.4**How to set up and implement education programmes**

- **ASSESS.** Assess learning style (activist, reflector, theorist, pragmatist) (Honey and Mumford 1986). Assess barriers to learning.
- **PLAN.** Develop a learning plan in partnership with the patient, e.g. aim of learning; how much information is wanted; how to learn the information.
- **IMPLEMENT.** Implement either one-to-one or group education session individualised to level of literacy, language, age, and stage of disease. Consider different learning resources tailored to individual preference and learning style (face-to-face; books, DVDs; online resources; apps; talking with other patients)
- **EVALUATE.** Evaluate how far the aims of the educational session/programme were achieved. Evaluate the nurse's expertise in facilitation of learning (peer review).

BOX 6.5**Suggested content of a predialysis education programme**

- information on CKD – cause, progression and the future.
- information on how disease may affect the patient, recognition of symptoms and what to expect.
- information about different treatment options.
- information about practicalities of starting or changing treatment options and preparation for treatment chosen (e.g. fistula).
- information about complications or side effects of treatment chosen or medication.
- information about managing or influencing patient's own condition.
- information on effects of CKD on daily life, work, finance, and social activities.
- information from other patients regarding living with CKD and various treatment options.
- information on adjusting and coping with CKD and where to find support.

early referral may result in the rate of decreasing renal function being slowed and the prevalence of cardiovascular disease can be twice as high in persons who were referred less than six months before starting RRT than in those who benefit from effective nephrological care for more than three years in the predialysis period.

Although, in principle, early referral appears beneficial, this is not always easy to achieve in practice, especially as many people with stage 4 CKD will not progress to dialysis, and also predicting rate of progression can sometimes be challenging.

How early is early? National guidance (NICE 2018) recommends to consider starting dialysis when indicated, by the impact of symptoms of uraemia on daily living, or biochemical measures or uncontrollable fluid overload, or at an estimated glomerular filtration rate (eGFR) of around 5 to 7 ml/min⁻¹/1.73 m⁻² if there are no symptoms.

Conclusion

Having reviewed the guidelines and strategies for supporting the individual with CKD it can be seen there has been an evolution in this area of care, especially concerning patient decision making.

Primary care practitioners and nonspecialist healthcare professionals are now increasingly expected and encouraged to be involved in CKD care delivery. There have been developments in the management of eGFR, anaemia, nutrition, and patient education, and new clinical guidelines for managing CKD are still evolving.

Future development of approaches to CKD needs to include cultural and religious considerations when these areas of a person's life clearly impact on the presenting biomedical symptoms, as well as psychological adaptation and coping strategies. Nurses in particular have many professional skills that could be harnessed within guidelines to address these issues.

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Resources

- Kidney Care UK educational resources <https://www.kidneycareuk.org/about-kidney-health/newly-diagnosed> (accessed 24 July 2018).
- Kidney Research UK educational resources <https://www.kidneyresearchuk.org/health-information/resources> (accessed 24 July 2018).
- NHS Choices web page on CKD <https://www.nhs.uk/conditions/kidney-disease> (accessed 24 July 2018).

CHAPTER 7

Investigations in Kidney Disease

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Learning Outcomes

- to explain the procedures commonly undertaken in the diagnosis of acute kidney injury (AKI) and chronic kidney disease.
- to evaluate the nurse's role in post-procedure care.
- to gain knowledge and understanding of the investigations required in the diagnosis of renal impairment.
- to provide a rationale for the use of these investigations and procedures.

Introduction

Patients referred to a nephrologist are subjected to a bewildering array of diagnostic tests and procedures. Nurses working in this area should familiarise themselves with these investigations, in order to be able to completely explain them to the patient; consent can then be truly 'informed'. The tests covered in this chapter include those involving blood and urine, radiological tests, invasive investigations, and methods of evaluating glomerular filtration rate (GFR). Investigations that are carried out prior to initiating anaemia treatments, such as erythropoietin stimulating agents (ESAs), are discussed, as well as those used in cases of diminished response to ESAs.

Some patients who have progressive kidney disease show no specific signs or symptoms and do not feel unwell until the disease is advanced. Abnormal results of blood and urine tests carried out at routine medical examinations, whether they be pre-employment, pre-life insurance, or preoperative, or during visits to a general practitioner for other reasons, may warrant referral. Patients with AKI from whatever cause also come under the remit of a nephrologist, and urgent diagnosis and treatment in this potentially life-threatening situation are vital (see Chapter 5). Sometimes only a large number of investigations will help make the diagnosis.

Nurses are responsible for correctly undertaking many of the investigations, so an understanding of the nature of these tests is vital, as is the ability to recognise abnormal results.

An individual with end-stage kidney disease (ESKD) is subjected to constant investigations to monitor the effectiveness of renal replacement therapy (RRT), with the objective of giving the patient maximum benefit from treatment with the minimum of side effects, in order to maintain a reasonable quality of life.

Phlebotomy

The World Health Organization (2010) published guidelines on best phlebotomy practices, recommending standards for quality care that include laboratory sampling and the maintenance of quality control. Nurses must complete the necessary training before carrying out a new role, such as venepuncture (NMC 2015). Prior to embarking on the collection of blood samples there are several factors that should be considered:

- the safety of healthcare personnel;
- the safety and comfort of the patient;
- planning ahead, for example availability of the correct collection system and, for some samples, that the lab is ready to receive the sample.

Safety of healthcare personnel

European Council Directive 2010/32/EU, the sharps directive, is a framework aimed at the prevention of sharps-related injuries in the health sector. Preventative measures include the use of protective equipment such as disposable gloves (also aprons and eye shields in some situations), attention being paid to proper hand washing before and after procedures, and the use of safety devices such as closed blood-collection systems, shielded and retractable needles, safety lancets, blunt needles, and needle-free systems. Occupational exposures to a blood-borne virus (BBV) that were reported to Public Health England increased among healthcare workers from 373 in 2004 to 496 in 2013. Over this 10-year period, approximately 30% of exposures involved a source patient infected with human immunodeficiency virus (HIV); 54% involved hepatitis C (HCV), and 9%, hepatitis B (HBV). Hepatitis B, C, and HIV are among the dangerous blood-borne pathogens that can be transmitted via contaminated needles (Woode Owusu et al. 2014). Local protocol may demand that samples from patients known to be infected with HIV or hepatitis B or C and other contagious organisms should be identified with internationally recognised yellow biohazard labels and be processed at the end of a laboratory run.

The Health and Safety Executive (Sharps Instruments in Healthcare) Regulations 2013 for effective safe management of sharps advise:

- avoid the unnecessary use of sharps where it is reasonably practical.
- use of safer sharps (incorporating a protection mechanism) – safety devices – for example, closed systems to avoid the need to transfer blood from syringe to laboratory sample tube, as the blood collection device fulfils both functions. Not decanting blood from syringe to blood tube unless absolutely necessary.
- prevent the recapping of needles – the correct disposal of sharps – on completion of the procedure; no attempt should be made to resheathe the needle.
- sharps should immediately be discarded at the point of use in a suitable secure sharps container.

Choice of vein in those with CKD

When carrying out venepuncture, great care must be taken to preserve veins that may be needed in the future for vascular access. In stages 4 and 5 CKD the forearm and upper arm veins should be avoided; in particular the non-dominant arm should be prohibited to preserve the forearm cephalic, antecubital, and upper arm veins for future vascular access (Mitra and Reid 2015). The dorsal veins in the hands are sometimes preferable; however, this can be painful (Figure 7.1). If the arm veins need to be used, the sites should be rotated and the antecubital fossa preferred. Patients and healthcare professionals should be provided with education on access preservation (Mitra and Reid 2015). Arteriovenous fistulae sites should not be cannulated except for dialysis purposes, to avoid the risk of infection or haematoma which may render the fistula unsuitable for dialysis in either the short or long term.

The correct collection procedure

Before attempting venepuncture, the correct method of collection according to local policy should be ascertained and all necessary equipment assembled. There are many designated tubes available; if blood is sent to the laboratory in the wrong tube it cannot be processed, time and money are wasted, and unnecessary discomfort is caused to the patient in repeating the procedure. Check unfamiliar tests with the laboratory before commencing.

If difficulties arise in collecting a blood sample from a patient it is advisable that only two attempts should be made before calling for assistance from a more experienced member of staff. Factors that can cause difficulties locating a vein include dehydration, hypotension, obesity, and fragile veins.

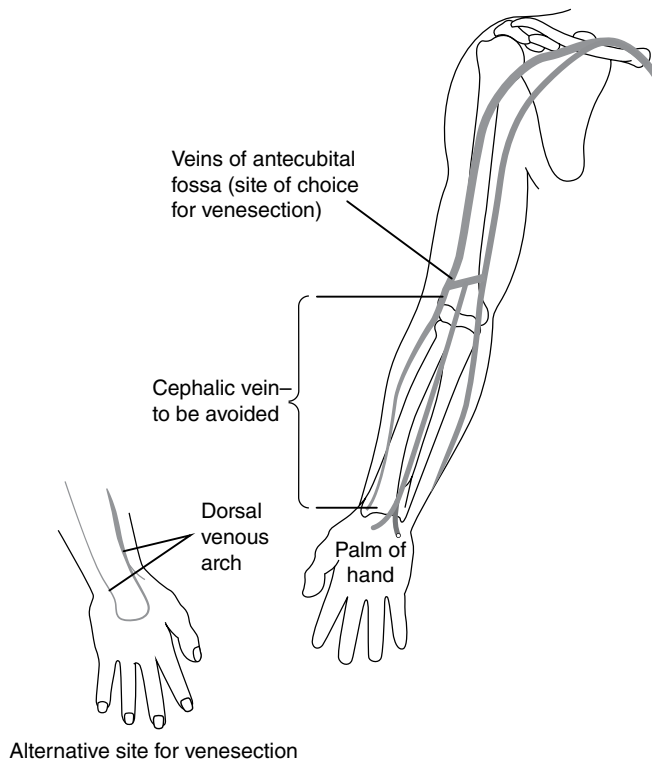


Figure 7.1 Veins of the arm.

Points for consideration

If difficulty is encountered in locating a suitable vein:

- the vein should be visible without a tourniquet.
- gently tap the chosen site and then re-disinfect with 70% alcohol and allow to dry preventing contamination. Alcohol is preferred to iodine which can give false readings of high potassium, phosphate, or uric acid.
- ask the patient to open and close their fist several times.
- inflate a sphygmomanometer cuff to a pressure between the patient's systolic and diastolic blood pressure proximal to the venepuncture site.
- hang the arm down towards the floor for a few minutes.
- in cold weather, keep clothing intact until the last moment, or apply a heat pack to the site to encourage peripheral circulation.
- do not bend arm after needle removed as may cause haematoma.
- haematoma formation can be prevented by applying adequate pressure to the puncture site until clotting occurs.

Blood samples from dialysis access needles or lines must be free of saline and anticoagulants (for example, heparin), be free of clotted material, be blood taken directly from the patient and not the machine, and must not be recirculated blood. Blood for any clotting tests should be taken pre-dialysis from another site such as the dorsum of the hand or antecubital fossa, as any heparin contamination will falsify the result. Haemodialysis samples should all have 'pre-, mid-, or post-dialysis sample' clearly marked on the request form to avoid confusion.

Key points

- check the tourniquet is clean prior to use as they are a potential methicillin-resistant *Staphylococcus aureus* (MRSA) source.
- always check that the correct collection tube and request form are to hand.
- know whether the sample has to be delivered immediately to the laboratory, or can be stored at room temperature, in a fridge or on ice.
- check whether the patient should be fasting.
- release the tourniquet before removing the needle; some suggest releasing tourniquet once blood flow is achieved.
- place blood into collection tube that has no additives initially to prevent contamination.
- ensure the sample is correctly labelled.
- do not use peripheral venous access as it will provide erroneous results
- use biohazard labels for known contaminated samples (as per local protocol). However, all samples should be treated as potentially hazardous.
- a haemolysed sample may occur if:
 - an incorrect size of needle for the vein is used;
 - skin disinfectant is not allowed to dry;
 - blood is sampled from an IV cannula or central venous catheter;
 - the blood sample tube is underfilled;
 - too much pressure is used with a tourniquet, this can also cause bruising;
 - too much force is used drawing back or to mix the sample;
 - overnight storage such as an electrolyte sample (WHO 2010).

Biochemical Blood Tests

Normal values are listed in Table 7.1. These may vary locally and may be expressed in alternative units of measurement. Paediatric normal values should always be

Table 7.1 Analysis of a normal blood sample.

Urea (blood urea nitrogen)	Adult 2.5–6.4 mmol l ⁻¹ Child 1.1–6.4 mmol l ⁻¹
Creatinine	Adult 70–120 µmol l ⁻¹ Child (increasing with age) 27–88 µmol l ⁻¹
Sodium	135–147 mmol l ⁻¹
Potassium	3.5–5 mmol l ⁻¹
Calcium	2.2–2.65 mmol l ⁻¹
Phosphate	0.8–1.5 mmol l ⁻¹
Bicarbonate	22–30 mmol l ⁻¹
Cholesterol	3.5–5.2 mmol l ⁻¹
Total protein	60–80 g l ⁻¹
Albumin	35–55 g l ⁻¹
Glucose (fasting)	3.9–5.5 mmol l ⁻¹

checked (see Chapter 12). Monitoring the blood biochemistry of patients with CKD is central to their diagnosis and ongoing care as this reflects the kidneys' function in excreting the waste products of metabolism. Serum or heparinised plasma samples are suitable for most biochemistry investigations.

Blood to be separated for serum samples is collected in a plain clotting tube (no additives) or in a tube containing beads treated with a clotting activator.

Blood to be separated for plasma samples is collected in a tube containing lithium heparin or beads treated with lithium heparin. The beads form a layer between the blood clot and serum or plasma after centrifugation, which allows serum to be withdrawn by pipette for the appropriate analysis. Some tubes contain a gel for the same purpose to act as a barrier between cells and plasma or serum.

Renal profile

The following tests (urea, creatinine, sodium, potassium, corrected calcium, phosphate, bicarbonate, and albumin) are often requested together. The result is generated from one 5 ml blood sample in a plain or lithium heparin tube. Some centres may include other tests under this profile.

Urea

Urea (normal range 2.5–6.4 mmol l⁻¹) is one of the principal end-products of protein metabolism. Urea is formed in the liver, carried by the blood, and excreted by the kidneys in the urine. Raised blood urea indicates failure of the kidneys and usually increases in tandem with serum creatinine levels in CKD and ESKD. However, serum urea levels may remain within normal limits whilst serum creatinine levels increase.

Urea can rise dramatically in previously healthy individuals who experience overwhelming infection or major crush injuries and are admitted to hospital with AKI. A slight rise in urea may be seen if a very high-protein diet is consumed, and in low-protein diets a lower level of blood urea may be observed. Certain drugs, such as corticosteroids and tetracycline, can cause a sudden rise in blood urea, especially if the patient already has CKD.

Nonrenal causes of increased urea levels

- high-protein diet.
- chronic malnutrition – increased protein metabolism.
- gastrointestinal bleeds – increased protein absorption.
- dehydration – increased urea reabsorption.

A normal or low urea level is not necessarily indicative of adequate dialysis if a patient is malnourished with a low protein intake.

Creatinine

Creatinine (normal range $70\text{--}120\mu\text{mol l}^{-1}$) is produced by the breakdown of creatine phosphate in muscle by catabolism and is excreted by the kidney. Patients should not eat cooked meat at least 12 hours prior to a serum creatinine test. Creatinine levels may not show a significant increase until there is a 50% loss of kidney function. Therefore, serum creatinine is not a sensitive test for early kidney disease. Estimated glomerular filtration rate (eGFR) is now recommended by NICE Clinical Guideline (2014) (see Chapter 6). A higher level of serum creatinine may be expected with large muscle mass, in males, and in those of African-Caribbean ethnicity (see Chapter 6 for use of a correction factor for people of African-Caribbean descent). A lower level may be seen in those with a low muscle mass (for example, the elderly, those with an amputation, and women), hyperthyroidism, those who are malnourished, and/or with the use of some drugs such as trimethoprim, testosterone therapy, corticosteroids, and vitamin D metabolites and amiloride.

In advanced kidney disease, creatinine levels may eventually rise to a level where it is considered expedient to commence dialysis. This may be in the region of $500\text{--}1000\mu\text{mol l}^{-1}$ but varies with the individual and the symptoms experienced. Those with diabetes are usually commenced on dialysis earlier, sometimes with serum creatinine levels of $300\text{--}500\mu\text{mol l}^{-1}$.

Sodium

Sodium, Na^+ (normal range $135\text{--}147\text{mmol l}^{-1}$), is the principal electrolyte of the extracellular fluid of the blood, maintaining osmotic pressure, and is involved in acid–base balance and the transmission of nerve impulses. Sodium is taken into the body with the diet and is conserved or excreted by the kidneys. Hyponatraemia ($<135\text{mmol l}^{-1}$) can be an indication of excess body fluid, and is also often present in burns, diarrhoea, vomiting, nephritis, neoplasms, and diabetic acidosis.

Hypernatraemia ($>148\text{mmol l}^{-1}$) can be an indication of dehydration and insufficient water intake, multiple myeloma, diabetes insipidus, metabolic acidosis, or excessive intravenous isotonic fluids in advanced kidney disease. Patients may be proportionally hypernatraemic or hyponatraemic without an altered fluid state.

Potassium

Potassium, K^+ (normal range $3.5\text{--}5\text{mmol l}^{-1}$), is the principal electrolyte of the intracellular fluid, with only low concentrations (2%) circulating in the extracellular fluid. Potassium is provided by the diet and excreted mainly by the kidneys, where regulation of the body potassium content occurs – a small amount is also lost in the faeces. Potassium is necessary to maintain nerve conduction and plays a major role in control of cardiac output. Potassium levels usually remain normal if a urine output in excess of 1500ml day^{-1} can be maintained. Hypokalaemia ($<3.5\text{mmol l}^{-1}$) may be found in cases of diarrhoea, vomiting, renal tubular acidosis,

diuretic usage, intravenous fluid administration without added potassium, and when excess insulin causes an increase in the cellular uptake of potassium. Hypokalaemia can cause cardiac arrhythmias.

Hyperkalaemia ($>5.5 \text{ mmol l}^{-1}$ but sometimes defined as $>6.0 \text{ mmol l}^{-1}$ for those on haemodialysis) may be seen in advanced kidney disease, burns, insulin deficiency, post-traumatic conditions (including surgery), disseminated intravascular coagulation, or when potassium-sparing diuretics are used with Slow-K, and in any condition where cell damage has occurred causing leakage of intracellular potassium into the extracellular fluid. In CKD a potassium level $>6.5 \text{ mmol l}^{-1}$ may be a medical emergency requiring immediate instigation of dialysis or other treatments. If left untreated, it may result in cardiac arrest caused by the arrhythmic effect of potassium build-up. Blood samples for accurate potassium analysis should be delivered swiftly to the laboratory or, if this is impossible, separated and stored, to prevent leaching of intracellular potassium into the serum, which results in a falsely raised level.

Mineral and bone disorder tests

Calcium, phosphate, alkaline phosphatase (ALP), parathyroid hormone (PTH), and calcidol ($25 (\text{OH})\text{D}_3$) are routinely monitored in people with CKD or undergoing dialysis.

Calcium

Calcium, Ca^{2+} (normal range total Ca^{2+} $2.2\text{--}2.6 \text{ mmol l}^{-1}$) is provided by the diet, and is excreted by the kidneys. Most body calcium is found in the skeleton but a small proportion is circulated in the blood. About 50% of serum calcium is protein-bound and 50% is ionised. Ionised serum calcium is responsible for muscle contraction, cardiac function, and blood clotting. Corrected calcium estimates the total concentration of calcium as if the albumin concentration was normal, i.e. estimates the free calcium, and is calculated as follows:

$$\begin{aligned} \text{Corrected calcium (mmol/l)} \\ = \text{Ca}^{2+} + (40 - \text{albumin (g/l)}) \times 0.02. \end{aligned}$$

It is the corrected calcium value that is reported by the laboratory.

In the healthy individual, calcium homeostasis is controlled by PTH, vitamin D, and the hormone calcitonin. Hypocalcaemia is found in CKD where phosphate retention is present. Chronic hypocalcaemia causes an excess of PTH to be excreted into the bloodstream which in turn releases calcium from the bone, resulting in the mineral bone disorder often seen with vitamin D deficiency in CKD. In nephrotic syndrome low levels of calcium will be found due to albumin leaking into the urine, taking bound calcium with it. In the patient with nephrotic syndrome, the ratio of protein-bound and ionised calcium will remain the same. The acidosis of CKD is an added cause of loss of bone calcium. Hypercalcaemia may be an indication of hyperparathyroidism, sarcoidosis, or malignancy. High levels of calcium can cause kidney stones and renal tubular disease.

Phosphate

Phosphorus is found in the diet. Phosphate, PO_4^{3-} (normal range $0.8\text{--}1.5 \text{ mmol l}^{-1}$), is mainly combined with calcium in the skeletal bone. It is controlled, with calcium, by PTH, and apart from its skeletal function has a part in the metabolism of

glucose and lipids. Phosphates are excreted by the kidney. When phosphate is increased, calcium is lowered and vice versa.

Hypophosphataemia may be found in the patient with renal tubular disease who loses phosphate, possibly leading to osteomalacia. Hyperphosphataemia will often be found in conjunction with hypocalcaemia.

Parathyroid hormone

Normal values of PTH vary according to the local assay method being used. PTH is a hormone produced in the parathyroid gland and is involved with the regulation of extracellular calcium. This test is useful in establishing whether hypercalcaemia is due to an overactive parathyroid. Increased PTH is common in stage 3 CKD, vitamin D deficiency, and osteomalacia. Hyperparathyroidism has been implicated in reduced response to anaemia treatments and possibly due to the effect on endogenous erythropoietin synthesis, bone marrow progenitors, red cell survival, or as a result of indirectly causing bone marrow fibrosis (NICE 2015). Blood for PTH analysis should be delivered immediately to the laboratory for analysis or, if this is impossible, kept on ice for a maximum of 30 minutes.

Calcitrol (calcidol, 25(OH)D)

The Renal Association (Steddon et al. 2015) has suggested routine monitoring in stages 3–5 CKD and for those patients on dialysis. Calcitrol (normal value: 30–74 ng ml⁻¹) is the most active metabolite of vitamin D and is mainly synthesised in the kidneys. Low levels are associated with osteoporosis, CKD, phosphate retention, malabsorption, and obesity (Steddon and Sharples 2015).

Other biochemical blood tests

Uric acid

Uric acid (normal range female 200–350 µmol l⁻¹ male 260–500 µmol l⁻¹) is an end-product of purine metabolism and is excreted mainly by the kidney, but in part by the bowel. In gout, excess uric acid crystallises in joints. In CKD there is an impaired ability to excrete uric acid and a high serum level may be found in association with raised urea and creatinine. Increased serum uric acid is also found in pre-eclampsia of pregnancy, leukaemia, multiple myeloma, various cancers, and in acute shock.

Bicarbonate

The normal range of HCO₃⁻ is 22–30 mmol l⁻¹. Low plasma HCO₃⁻ indicates metabolic acidosis caused by CKD with an inability to excrete hydrogen ions adequately.

Measuring glucose

The normal range of fasting serum glucose is 3.9–5.5 mmol l⁻¹. Blood glucose levels are maintained by the liver, which absorbs and stores glucose as glycogen and releases it into the circulation in response to the demands of the body. Glucose is regulated by insulin which is synthesised by the beta cells in the islets of Langerhans in the pancreas.

Glycosylated haemoglobin

Glycosylated haemoglobin, more commonly known as HbA1c, indicates the amount of glucose carried by red blood cells in the body and is a more accurate measure of long-term glucose control in people with diabetes. The target HbA1c in Type 2 diabetes is <48 mmol mol⁻¹ (6.5%), or a higher target if the person is at risk

of hypoglycaemia ($<5.3 \text{ mmol mol}^{-1}$ (7.0%) (NICE 2017). HbA1c provides an average blood glucose level over a 12-week period (the average life of a red blood cell), however it may underestimate blood glucose control in advanced kidney disease or conditions where the red blood cell lifespan is reduced, for example sickle-cell disease, with the use of ESAs. Higher results can also be found in uraemia. Other tests may be required to give a more accurate glucose level, which include:

- fructosamine estimation;
- quality controlled blood glucose profiles;
- total glycated haemoglobin estimation of abnormal haemoglobins.

Serum protein electrophoresis

Serum protein electrophoresis uses an electrical field to separate out the proteins in the serum and helps to diagnose certain diseases such as multiple myeloma.

Lipids

Cardiovascular disease is a major cause of morbidity and mortality in patients with kidney disease (Jun et al. 2011) and one of the main risk factors for this is dyslipidaemia. A full lipid profile should include measurement of total cholesterol, HDL cholesterol, non-HDL cholesterol, and triglyceride concentrations. A fasting sample is not needed. A normal value for non-HDL cholesterol is $<4 \text{ mmol l}^{-1}$ and total cholesterol $\leq 5.0 \text{ mmol l}^{-1}$ and for those at high risk of cardiovascular disease (CVD) $\leq 4 \text{ mmol l}^{-1}$ (NICE 2016). Atorvastatin (20 mg) for the primary or secondary prevention of cardiovascular disease should be offered to people with CKD. The dose should be increased if a greater than 40% reduction in non-HDL cholesterol is not achieved and eGFR is $30 \text{ ml min}^{-1}/1.73 \text{ m}^2$ or more.

Liver function tests (LFTs)

This is a collection of tests that include serum albumin levels, total plasma protein, ALP, alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma glutamyl-transpeptidase (GGT), bilirubin levels, and clotting to assess liver function.

Albumin

The normal range of albumin is $35\text{--}55 \text{ g l}^{-1}$. Albumin levels can be elevated in patients with dehydration. Low albumin levels are common in CKD due to protein loss through peritoneal dialysate, poor dietary intake, and nephrotic syndrome. Other causes of low albumin levels are decreased absorption in liver disease and increased breakdown in malignancy.

Plasma total protein

The normal range of plasma total proteins is $60\text{--}80 \text{ g l}^{-1}$. Hypoproteinaemia associated with low albumin (normal value $35\text{--}55 \text{ g l}^{-1}$) levels may be found in the many conditions associated with nephrotic syndrome where protein leakage occurs from the kidney into the urine. Also, decreased total protein in conjunction with low albumin may be found in liver disease, burns, and haemorrhage. Hyperproteinaemia (increase of total plasma protein) with a normal albumin/globulin ratio may occur in dehydration. If total protein increases with a falling albumin/globulin ratio (i.e. a raised globulin), this may indicate autoimmune disease such as systemic lupus erythematosus (SLE), shock, chronic infection, or myeloma.

ALP is a protein involved in cellular metabolism which is mainly produced in the bones and bile ducts of the liver, though some is produced in the kidneys and intestines. An elevated ALP is seen in mineral bone disorders, liver damage, and pregnancy.

ALT and AST are enzymes found in high concentrations in the heart, liver, and skeletal muscle. Increased levels most commonly indicate liver disease, for example hepatitis.

GGT is an hepatic enzyme; elevated levels may be seen with liver disease, heart failure, and with alcohol use and with some medications.

Bilirubin (normal range $3\text{--}17\mu\text{mol l}^{-1}$) is a bile pigment produced by the breakdown of haem and reduction of biliverdin. Unconjugated bilirubin is insoluble in plasma unless bound to protein, mainly albumin. Salicylates, sulphonamides, non-esterified fatty acids, and reduced pH levels result in decreased protein-binding of unconjugated bilirubin. Normally, 95% of the circulating bilirubin is unconjugated. Raised levels occur with increased production, for example in haemolysis or in hepatobiliary disease or obstruction. Jaundice or icterus describes the yellow staining of the tissues due to an excess of bilirubin – unconjugated or conjugated. Jaundice becomes clinically detectable at levels $>40\mu\text{mol l}^{-1}$.

Serology

Serological tests are frequently required as renal impairment is often a manifestation of a systemic disease. Many kidney disorders arise from immune dysfunction and serology will often, therefore, provide an exact diagnosis. A positive anti-neutrophil cytoplasmic antibody (ANCA) test is found in diseases such as systemic and renal vasculitis. Anti-glomerular basement membrane (anti-GBM) is detected in Goodpasture's syndrome. The presence of other immunoglobulins may indicate other autoimmune diseases, e.g. antinuclear antibodies may be found in SLE.

Complement

The most common complement studies performed are for C3 and C4. These levels rise during an acute inflammatory state. However, there are many other specialised complement studies that can be undertaken in order to diagnose a particular disease process.

Creatine kinase

An enzyme present in heart and skeletal muscle which is elevated in myocardial infarction and rhabdomyolysis.

Immunoglobulins

Immunoglobulins (five groups – IgD, IgE, IgG, IgM, and IgA) are proteins present in both circulating blood and in the cells which function as antibodies defending the body against infection. Elevated levels may be seen in autoimmune disease, cancers, and allergic reactions, for example IgA nephropathy and multiple myeloma. Cryoglobulins are abnormal immunoglobulins that are found in diseases such as multiple myeloma, autoimmune disease, such as systemic lupus nephritis, and infections such as hepatitis.

Viral serology

Screening for hepatitis B, C, and HIV is required for at-risk groups and those requiring RRT. HIV and Hepatitis B and C can also be a primary cause of kidney disease.

Haematology

Haematological tests give information about anaemia, haematological malignancies, and clotting disorders. Infections, inflammatory disease, and other conditions

Table 7.2 Normal values – haematological tests.

Haemoglobin	Male 135–180 g l ⁻¹ Female 115–165 g l ⁻¹
Haematocrit	Male 40–55% Female 35–45%
Platelets	150–450 × 10 ⁹ l ⁻¹
Leukocytes (white bloodcells)	4.5–10 g l ⁻¹

can be indicated by changes in total and differential white cell counts. Normal values are shown in Table 7.2 (there may be slight local variations, especially in the paediatric normal range).

Full blood count

This test includes haemoglobin, haematocrit, red blood cell count, white blood-cell count and differential, platelet count, and blood film, which often provide evidence of renal anaemia in CKD. It may be appropriate to investigate further those values falling outside normal parameters.

Haemoglobin

Haemoglobin (Hb) should be checked to ensure that anaemia is not present. Haemoglobin varies with age, gender, and ethnicity. The level at which it is considered that an ESA should be initiated varies from one centre to another, but the current recommendation is for an aspirational haemoglobin range of 100–120 g l⁻¹ for adults, young people, and children (2 years and older) and investigations for anaemia should be undertaken if Hb < 110 g l⁻¹ (NICE 2015). Normocytic erythrocytes are typical in the patient with renal anaemia. However, in the case of iron-deficiency anaemia, microcytic and hypochromic red blood cells will be seen.

Haematocrit

Haematocrit (HCT) is the percentage of red blood cells in the whole blood volume, which will be low in the patient with renal anaemia, running in parallel with the low level of haemoglobin. When the patient responds to the effect of erythropoietin, a rise in HCT will be seen in conjunction with a rise in haemoglobin and red blood cells.

Red cell count

Red cell count (RCC) and mean corpuscular volume (MCV) reflect the size, and mean corpuscular haemoglobin (MCH) and mean corpuscular haemoglobin concentration (MCHC) reflect the haemoglobin concentration, of individual cells. These red blood cell indices are useful in the diagnosis of types of anaemia.

Anaemias are classified on the basis of cell size MCV as microcytic, normocytic, or macrocytic, and on the basis of the amount of haemoglobin MCH as hypochromic, normochromic, or hyperchromic. They can therefore be classified as follows:

- normocytic/normochromic anaemia – from acute blood loss, prosthetic heart valves, sepsis, tumour, or aplastic anaemia.

- microcytic/hypochromic anaemia – from chronic blood loss, iron deficiency, lead poisoning, or thalassaemia.
- microcytic/normochromic anaemia – erythropoietin deficiency in CKD.
- macrocytic/normochromic anaemia – from chemotherapy, folate deficiency, or vitamin B-12 deficiency.

White blood cell count and differential

White blood cells are the cells in the body that fight against infections and allergies. There are five types of white blood cells, which can be split into two groups – granulocytes and agranulocytes. The granulocytes include neutrophils, eosinophils, and basophils and have granules in their cell cytoplasm, they also have a multi-lobed nucleus. Agranulocyte white blood cells, lymphocytes, and monocytes do not have granules and have nonlobular nuclei. They are sometimes referred to as mononuclear leukocytes.

The normal range for total white blood cell count is $4\text{--}11 \times 10^9 \text{ l}^{-1}$. A low white cell count is referred to as leukopenia and a high white cell count as leukocytosis. Leukocytosis is usually due to an increase in one of the five types of white blood cells and is given the name of the cell that shows the primary increase (i.e. neutrophilia, eosinophilia, basophilia, lymphocytosis, and monocytosis). Leukocytosis may be indicative of an infection, inflammation, or a haematologic malignancy and leukopenia may be due to bone suppression or replacement, hypersplenism, or deficiencies of cobalamin or folate.

Differential (or relative value)

This is a count of the five different types of white blood cells and is often expressed as a percentage of the total white cell count (rather than their absolute value).

- neutrophils: 50–70% relative value. An increase may indicate infection and is called neutrophilia. A decrease is called neutropenia and may be due to chemotherapy.
- eosinophils: 1–3% relative value. An increase may indicate infections or allergies.
- basophils: 0.4–1% relative value. Basophilia is an uncommon cause of leukocytosis but can be caused by infections or inflammatory conditions such as inflammatory bowel disease or chronic airway inflammation.
- lymphocytes: 25–35% relative value. Absolute lymphocytosis may be caused by acute infections (cytomegalovirus infection, Epstein–Barr virus infection, pertussis, hepatitis, toxoplasmosis); or chronic infections (tuberculosis, brucellosis); or lymphoid malignancies (chronic lymphocytic leukaemia). Relative lymphocytosis is seen in the acute phase of several viral illnesses, in connective tissue diseases, thyrotoxicosis, Addison's disease, and splenomegaly with splenic sequestration.
- monocytes: 4–6% relative value. Monocytosis may be due to either chronic infection, chronic inflammatory disorders such as Crohn's Disease, or carcinoma. However a transient monocytosis can be seen with the resolution of an infection. A monocytosis may also be seen in the myelodysplastic conditions.

Coagulation

In circulating blood a series of factors are present that provide the means for clot formation as appropriate when damage to a vessel occurs. Prior to many kidney procedures, such as kidney biopsy, it is standard practice to ascertain that the patient has normal clotting function to avoid the risk of haemorrhage. Those with uraemia are more prone to bleeding as urea affects the clotting cascade.

Included in this group of tests are platelets (normally, $150\text{--}450 \times 10^9 \text{ l}^{-1}$ included in the full blood count [FBC]). Platelets adhere to each other and initiate the clotting cascade when damaged endothelium is encountered. Platelet deficiency (thrombocytopenia) is a common cause of prolonged bleeding.

Other coagulation studies likely to be encountered in kidney investigations include the bleeding time (normal <10 minutes); partial thromboplastin time (PTT); activated partial thromboplastin time (APTT); fibrinogen and international normalised ratio (INR). Most methods in current use require a very precise amount of blood in coagulation tests; the blood sample should exactly reach the marked line. Blood for coagulation studies during or immediately post-haemodialysis or from heparinised lines (for example, temporary or permanent dialysis catheters) should not be taken from a central line as the result will be inaccurate – it is recommended to use a vein instead.

Further investigations for renal anaemia

Anaemia is a major complication of CKD and a contributory factor to cardiovascular disease in patients needing dialysis. The major cause is the lack of production of the hormone erythropoietin which is produced by the kidney. There are clinical benefits associated with correcting renal anaemia, including improved cardiac function, quality of life, and reducing the decline in kidney function in the early stages of CKD.

Symptoms of anaemia

These include lethargy, dyspnoea, headache, dizziness, palpitations and pallor, and decline in exercise tolerance, sexual function, and cognitive function.

Prior to the commencement of treatment, some basic investigations must be completed in order to correct any deficiencies which may prevent an adequate response to this very expensive therapy. It is also important to exclude or treat (if possible) underlying causes such as:

- iron deficiency;
- blood loss;
- infection or inflammatory disease;
- hyperparathyroidism;
- aluminium toxicity;
- vitamin B₁₂ and folate deficiency;
- haemolysis;
- haemoglobinopathies.

Other anaemia investigations

Having ascertained that the patient has renal anaemia, the next step is to carry out certain investigations to check that there is no condition present which may prevent or reduce the effect of anaemia treatment. There are currently research clinical trials into other treatments, with a view to reducing the need for ESA therapy and IV iron such as hypoxia inducible factor (HIF) stabilisers, however they are not currently recommended and this chapter will refer to ESA therapy (Locatelli et al. 2017). These tests should be repeated if diminished or nonresponse to ESAs occurs at a later date.

Haematinics

In order to maintain the haem component of the healthy red blood cell, an adequate amount of available and stored iron must be present. There are several tests which can be carried out to determine this very important factor – the main cause

of nonresponse to ESAs has been found to be low available iron. Iron-deficiency anaemia is either absolute or functional.

Ferritin

The normal range in health is 30–200 $\mu\text{g l}^{-1}$. Iron deficiency anaemia in CKD is indicated if ferritin is less than 100 $\mu\text{g l}^{-1}$ and should be reviewed if $>500\mu\text{g l}^{-1}$ and not be allowed to exceed 800 $\mu\text{g l}^{-1}$ (Mikhail et al. 2017; NICE Guideline 2015). Ferritin is the main form of stored iron found in all tissues, but especially in the liver, spleen, and bone marrow. Ferritin found in the serum relates to the amount of stored iron, but is not necessarily an accurate assessment of available iron. Unless ferritin levels are at least 100 $\mu\text{g l}^{-1}$ before commencing treatment with ESAs therapy, the response will be short lived. A false high level can be seen in infection and inflammatory states, indicated by an elevated CRP.

Transferrin saturation rate

Iron is transported by the specific plasma protein transferrin (or siderophilin). A useful test of available iron for red cell production is the transferrin saturation rate. Transferrin saturation indicates how much iron is circulating in the plasma relative to total iron-binding capacity. Less than 20% is indicative of iron deficiency anaemia, however it is not a reliable test and requires sequential readings to determine an average. Ferritin and transferrin saturation rates should not be used alone to monitor iron deficiency (NICE Guideline 8, 2015).

Serum iron

Serum iron (standard reference range varies between laboratories) in those with CKD is of no great significance (except in iron overload) but is necessary for calculating transferrin saturation rate.

Red-cell folate

Folic acid is a water-soluble vitamin in the B-complex group that is absorbed from the duodenum and jejunum. Folic acid works along with vitamin B₁₂ and vitamin C to help the body digest and utilise proteins and to synthesise new proteins when they are needed. It is necessary for the production of red blood cells and for the normal DNA synthesis, and affects erythrocyte precursors. Folic acid also helps with tissue growth and cell function. Low levels can cause macrocytic anaemia. Stores of this vitamin last only a few months.

Vitamin B₁₂

Vitamin B₁₂ (normal range 150–1000 ng l^{-1}) is a water-soluble vitamin that is part of the vitamin B complex. It is absorbed in the ileum. The uptake is dependent on the production of acid and intrinsic factor in the stomach, adequate oral intake, and production of transcobalamin (transport protein). Vitamin B₁₂, like the other B vitamins, is important for metabolism, and helps in the formation of red blood cells and in the maintenance of the central nervous system. Although the body stores can last several years without oral intake, low levels (e.g. in pernicious anaemia) can cause a macrocytic anaemia.

As folic acid and vitamin B₁₂ are water soluble they are both lost during haemodialysis, which can lead to dialysis-induced deficiency.

Other tests

C-Reactive Protein

C-reactive protein (CRP) is a globulin that is synthesised by the liver and is present in small amounts in a normal individual. An elevated CRP is indicative of infection,

inflammation, or malignancy. The most important role of CRP is its interaction with the complement system, which is one of the body's immunologic defence mechanisms. It is normally present in the plasma at a concentration of less than 5 mg l^{-1} .

CRP increases in virtually all conditions associated with tissue damage and may double its concentration every six hours. It is better than ESR for monitoring fast changes as it does not depend on fibrinogen or immunoglobulin levels, and is not affected by red blood cell numbers and shape.

Haptoglobins

Haptoglobin is an acute-phase protein, rising in concentration during acute inflammation. Classically, a low haptoglobin concentration is indicative of intravascular haemolysis. It may also occur in extravascular haemolysis – some free haemoglobin leaks from the phagocytic cells of the spleen, chronic liver disease, metastatic malignancy, and sepsis.

Coombs' test

The Coombs' test is used in the investigation of haemolytic anaemia. A positive Coombs' test is found in cases of autoimmune haemolysis due to the presence of immunoglobulin G (IgG), complement or both, on the surface of the red cells. A positive result may be found in a haemolytic transfusion reaction or autoimmune haemolysis, including drug-induced haemolysis.

Lactate dehydrogenase (LDH)

This is an enzyme that is found throughout the body in the tissues with low levels found in the circulating blood. Elevated levels occur when there is damage to the tissue as the enzyme is released from body tissue into the bloodstream. It is used to assess acute and chronic liver damage, monitor progressive diseases, for example liver, kidney, and malignancy, and to diagnose haemolytic anaemia.

Occult blood

A faecal occult blood test (FOBT) is a noninvasive test that detects the presence of hidden (occult) blood in the stool. Such blood may arise from anywhere along the digestive tract. Hidden blood in stool is often the first, and in many cases the only, warning sign that a person has colorectal disease, including colon cancer. A positive test result requires further investigation of the gastrointestinal tract, usually with a colonoscopy in the first instance.

Reticulocytes

Reticulocytes (normal range in men 0.5–1.5%, in women 0.5–2.5%) are immature red blood cells that have been newly released from the bone marrow, and can be recognised as such for about 48 hours before reaching a mature state. Patients with renal anaemia have a depressed reticulocyte count before ESA therapy and a rise should be seen when stimulation of erythrocyte production occurs as a response to ESAs. If no response occurs, further investigation should be considered. Measurement as recommended by NICE Guideline (2015) to diagnose iron deficiency and determine potential responsiveness to iron therapy is to use

- percentage of hypochromic red blood cells, %HRC > 6% – assesses how much iron is being incorporated into the red blood cell. This test can only be used if the sample can be processed within six hours.
- if this is not possible, then the use of reticulocyte Hb content CHr < 29 pg or a reticulocyte equivalent test. This test is a more sensitive test and shows the content of young reticulocytes as well, so it gives a picture of the availability in a few days.

Transferrin saturation and serum ferritin should be used if these tests are not available or the person has thalassaemia or thalassaemia trait.

Poor response to ESA therapy

Low or non-response to ESA therapy, other than when caused by reduced haematinic levels, requires investigation to assess concordance to treatment regimen and to exclude other causes such as iron deficiency anaemia, infection or inflammation, occult malignancy, bone marrow disorders, hyperparathyroidism, inadequate dialysis, ACEI and immunosuppressive drugs, aluminium toxicity, carnitine deficiency, chloramine toxicity in haemodialysis patients only, chronic blood loss (for example, haemorrhoids, menorrhagia, gastrointestinal bleeding), and pure red cell aplasia (PRCA). Tests to confirm PRCA are the presence of anti-erythropoietin antibodies along with a lack of pro-erythroid progenitor cells in the bone marrow (NICE 2015).

Urine investigations

Urinalysis plays an important part in the assessment of kidney disease, as kidney damage may allow increased concentrations of various chemicals through to the urine, together with other signs of disease such as haematuria or proteinuria. This includes visual assessment, urinary dipstick, and microscopic examination. The quantity of urine passed during the day together with its specific gravity also gives an indication of kidney function. Table 7.3 lists the normal volumes of urine passed per day.

Urine is composed of about 95% water and 5% solids, mainly urea and sodium chloride, it is slightly acidic (pH 6.0), and it has a specific gravity of 1.010–1.030 (specific gravity of water = 1.000).

Urinalysis

Low urinary pH can be associated with eating acidic fruits, respiratory or metabolic acidosis, high protein diet, diabetes, diarrhoea, or anorexia.

High urinary pH can be associated with a low carbohydrate diet, renal calculi, respiratory or metabolic alkalosis, or UTI.

Measurement of specific gravity can be unreliable in the presence of water and electrolyte imbalance, low-protein diets, chronic liver disease, and pregnancy.

Appearance

Urine can vary in colour from pale straw to dark amber.

- pale urine is dilute because of:
 - heavy fluid intake;
 - polyuria due to kidney disease where the tubules fail to reabsorb water;
 - diabetes insipidus or diabetes mellitus.

Table 7.3 Normal volumes of urine.

Healthy adult	1–1.5 l day ⁻¹
Newborn baby	50–300 ml day ⁻¹
Infant	350–550 ml day ⁻¹
Child	500–1000 ml day ⁻¹
Adolescent	700–1400 ml day ⁻¹

- dark urine may indicate:
 - concentration due to fluid depletion
 - presence of bile.
- haematuria can vary in appearance from 'smoky' to 'tea' to red, either bright or dark.
- coloured urine can be caused by blackberries, beetroot in the diet and other vegetable food dyes, porphyria, and some medications, for example, orange-coloured urine is caused by rifampicin or senna, bright yellow can be caused by vitamins or bilirubin.
- frothy urine indicates heavy proteinuria or presence of glucose; however may occur with an old urine sample.
- smoky urine may indicate the presence of bleeding from the kidney.
- deposits or cloudy/turbid urine, which occurs when the urine sample is left to stand, may be crystals of phosphate, oxalate or urates, or due to pus in the presence of infection.
- pink to black/brown (coca cola) urine may indicate the presence of myoglobin, dark brown may indicate iron supplementation, urobilin.

Dipstick tests

Dipstick tests can be carried out in the clinic or ward situation as well as in the laboratory. Dipsticks are available that accurately show the presence of a variety of substances which may occur in the urine (for example, protein, glucose, ketones, blood, leucocytes, and nitrites) as well as giving the pH of the urine sample. The stick should be briefly dipped into a fresh sample of urine and read after one minute or according to the manufacturer's instructions. The results are then compared with those supplied on the instruction sheet. These kits are very reliable providing that the container is always kept dry and capped between use, the strips are only briefly dipped into the urine sample, and the expiry date is not exceeded.

Osmolality

Osmolality (normal 500–800 mOsmolkg⁻¹) measurement indicates the kidney's ability in concentration and dilution and is considered more reliable than measuring the specific gravity, and requires collection of an early-morning urine sample.

Glucose

The presence of glucose may indicate diabetes mellitus, proximal tubular dysfunction, Fanconi's syndrome, glomerulonephritis, or nephrotic syndrome.

Blood

The presence of blood in the urine is either microscopic – invisible – or macroscopic – visible to the naked eye. Microscopic haematuria is often an incidental finding and requires further investigation to assess for kidney disease or malignancy if >+1. Two to three positive results are indicative of persistent invisible haematuria on two or three separate occasions. Reagent strip testing is recommended and not the use of microscopy. It is also important to establish the cause is not related to a urinary tract infection, and rule out other causes such as menstruation, sexual intercourse, trauma, e.g. urinary catheter, too much exercise, or an old sample (lysis of red blood cells).

Protein

Although protein is a normal urinary constituent, the average daily excretion is <150mgday⁻¹. Albumin accounts for approximately 15% of normal daily excretion,

with the other 85% made up of plasma proteins and Tamm-Horsfall protein. Proteinuria is either transient or persistent in nature.

Causes of proteinuria

- glomerular (most common): includes primary and secondary glomerulonephritis (e.g. diabetes, SLE).
- tubular: includes tubulointerstitial nephritis (e.g. nephrotoxic medications such as tetracycline) and lead.
- overflow: includes multiple myeloma, myoglobinuria, haemoglobinuria.
- secretory: includes inflammatory such as UTI, urinary tract tumours.
- transient episodes: include intercurrent illness, excessive exercise, acute metabolic crisis, congestive cardiac failure.
- orthostatic or postural.

Measurement and quantification of proteinuria is an important diagnostic tool and useful in the early detection of kidney disease. Proteinuria is an independent risk factor of CVD, death, and ESKD in the general population and in CKD patients, and there is a higher mortality rate in critically ill patients.

If proteinuria is not treated, it will lead to loss of kidney function. Protein cannot be measured on dipstick unless it is sensitive to very low levels of albumin. Nephrotic syndrome is diagnosed when proteinuria is ≥ 350 mg day⁻¹. It is important to rule out a urinary tract infection or orthostatic hypotension.

Microalbuminuria

This is defined as persistent small amounts of albumin not determined by the usual dipstick test. It is used to categorise CKD (see Chapter 6).

Albumin : creatinine ratio

The NICE Guideline (2017) recommends the use of albumin : creatinine ratio (ACR) in preference to protein : creatinine ratio (PCR) as it cannot detect low levels of albumin, i.e. <15 mg mmol⁻¹. ACR is an effective diagnostic investigation for the early detection of kidney disease and if not treated can lead to deterioration of kidney function. It is also a strong predictor of CVD and death. An ACR measures the concentration of albumin and creatinine, has a greater sensitivity in detecting low levels of proteinuria, and should always be used in diabetes (see Chapter 6 for interpretation of results).

- normal range: ACR < 3 mg mmol⁻¹.
- ACR 3–70 mg mmol⁻¹, a repeat early-morning sample should be taken.
- if ACR ≥ 70 mg mmol⁻¹, no repeat test required.

Ideally an early-morning urine sample should be used, although a 'spot urine' can be taken, then repeated with an EMU if positive. The urine should be kept refrigerated following the collection period to minimise bacterial growth. Twenty-four hour urine collections are no longer required for quantification of protein, however they may be required for other tests.

Bence Jones protein

This test consists of a sample of urine from the first specimen of the day. In the laboratory the urine is heated; if this protein is present, it will precipitate on heating and dissolve at 100°C; on cooling the protein will precipitate again. This test is now performed by electrophoresis and immunoelectrophoresis. It is most commonly (70–80% of positive results) found in multiple myeloma due to the proliferation of paraprotein-producing bone marrow. It is also occasionally seen in amyloidosis, cryoglobulinaemia, and hyperparathyroidism.

Myoglobin levels

Myoglobinuria may occur due to conditions such as rhabdomyolysis where there is a breakdown of muscle tissue, causing the release of myoglobin into the bloodstream. This may occur due to trauma or crush injury, seizures, immobility, or severe exercise. The kidneys filter the blood and excrete the myoglobin in the urine. Myoglobin is nephrotoxic and large amounts of this protein can cause the occlusion of the renal tubules, leading to acute tubular necrosis and AKI. This can be diagnosed by a sample of urine – usually the first sample of the day.

Urine microscopy and culture

Microscopy will reveal information from the sediment found in urine – casts, crystals, blood cells, and bacteria. The site of origin of casts can often be determined, indicating the type and extent of damage to the kidney. It is normal to find red blood cells in urine at approximately <2 hpf (high power field) and these normally originate from the renal pelvis, ureter, or bladder and are uniform in shape and size. Leukocytes are also present at approximately <2 hpf but the presence of eosinophils can be indicative of an allergic interstitial nephritis.

Points for consideration

- ensure patient/healthcare professional clean external genitalia to prevent contamination.
- should be a midstream collection.
- sample should be stored in the fridge if not processed within two hours.
- samples taken from urinary catheters should not be taken from the bag, but from the catheter directly.

Casts

Different types of casts found in the urine may indicate underlying conditions. Hyaline casts, known as Tamm–Horsfall proteins, originate from the renal tubules. They may be present due to the use of diuretics, fever, and exercise; however, they may also be present in kidney disease (for example, pyelonephritis). Granular or cellular casts may be seen in renal parenchymal disease. Red cell casts indicate bleeding and white cell casts indicate pyelonephritis or renal parenchymal disease.

If micro-organisms are found to be present in the urine specimen – usually determined by the Gram staining method – the laboratory will provide information as to which antibiotic is most appropriate. The presence of multiple organisms may indicate contamination of the sample. It is important that the urine sample is collected before a broad-spectrum antibiotic is taken – this may be given in the interim period before specific sensitivity is ascertained.

A positive microscopy sample shows at least $>10^5$ cfu ml⁻¹ and organisms 1–10 hpf; below this figure is not considered significant. However, with very dilute urine, a false-negative result may occur despite infection being present.

Kidney Function Tests

In CKD, a regular assessment of kidney function can be useful in monitoring the decline in kidney function and in predicting the time when RRT is likely to be needed. GFR tends to decrease in a linear fashion over time in progressive kidney disease and so, by extrapolation, predictions can be made as to when ESKD may occur. Measuring GFR provides details of the filtration rate of the functioning nephrons.

Knowledge of the amount of nephron damage is useful in assisting in making the choice of suitable drug regime. When there is more than 30% of nephron loss, certain drugs should be avoided or used with caution because of the slow excretion of the drug or its metabolites. GFR often declines with age (as much as 1 ml min^{-1} each year), starting at the fourth decade.

- increased GFR can occur with:
 - increased protein intake;
 - diurnal variation;
 - pregnancy.
- decreased GFR can occur with:
 - exercise;
 - age;
 - low-protein diet;
 - liver disease.

Many research studies and clinical trials of pharmaceuticals depend on regular GFR calculations to monitor the effect of treatments with regard to kidney function. Kidney function investigations discussed here include creatinine clearance, the ^{51}Cr ethylenediaminetetraacetic acid GFR, (^{51}Cr EDTA GFR), and eGFR.

Estimated glomerular filtration rate

The eGFR (calculated from serum creatinine results) provides the best overall assessment of the level of kidney function. However, creatinine clearance estimation (using 24-hour urine collection) can be helpful in the following situations:

- estimation of GFR in individuals with exceptional dietary intake (vegetarian diet, creatine supplements) or decreased muscle mass (amputation, malnutrition, muscle wasting).
- assessment of diet and nutritional status.

Kidney function in adults should be evaluated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine equation, using laboratory values standardised to isotope dilution mass spectrometry (IDMS), which is validated and now the recommended eGFR formula (NICE 2014), superseding the Modification of Renal Diet (MDRD) equation. This equation takes into account the serum creatinine concentration and the following variables: age, gender, and race. However, caution is required in interpreting the results in those people with muscle wasting disorders and body builders respectively, due to the problem of overestimation and underestimation:

CKD-EPI equation

$$141 \times \min(S_{\text{Cr}/k,1}) \propto \times \max(S_{\text{Cr}/k,1})^{-1.209} \\ \times 0.993^{\text{Age}} \times 1.018 \text{ (if female)} \times 1.159 \text{ (if black)}$$

- K is 0.7 females and 0.9 in males
- $\propto$ is -0.329 for females and -0.411 for males

- min indicates the min $S_{Cr/k, 1}$
- no weight is required as normalised to 1.73m² body surface area (BSA)

eGFR Cystatin C

The eGFR Cystatin C diagnostic calculation was developed in 2012 and estimates GFR from serum cystatin C, age, and sex. It is less affected by age, sex, and ethnicity.

NICE guidance (2014) has recommended using eGFRcystatinC at initial diagnosis to confirm or rule out CKD in people with:

- an eGFRcreatinine of 45–59 ml⁻¹ min⁻¹/1.73m², sustained for at least 90 days and
- no proteinuria (ACR less than 3 mgmmol⁻¹) or other marker of kidney disease.

In AKI, the use of serum creatinine, rather than eGFR, is recommended. eGFR should not be used in those <18 and >90 years or in pregnancy (NICE 2014). Prior to measuring eGFR patients should be advised to not eat meat for 12 hours before the test and for the most accurate results, the test should be processed within 12 hours.

Measurement of protein excretion

Twenty-four hour protein estimations are no longer recommended. The total daily protein excretion (in mg) can be estimated simply by multiplying the total protein-creatinine ratio (TPCR) (from a spot urine sample, preferably early morning, measured in mg mmol⁻¹) by a factor of 10. For example: Urine protein = 750 mg l⁻¹, urine creatinine = 7.5 mmol l⁻¹. So, TPCR = 750/7.5 = 100 mg mmol⁻¹. Therefore, daily protein excretion = 100 × 10 = 1000 mg, or 1 g

Creatinine clearance

Note: this test is not recommended to estimate kidney function, however may still be requested by the medical staff. The principle of clearance is that an estimation of a known substance in the plasma is compared with the amount in the urine. This substance must only be excreted in the urine. The calculation by which the clearance of the substance occurs can be measured is thus:

$$\frac{\text{urine concentration of substance (U)} \times \text{volume of urine in 24 h (V)}}{\text{Plasma concentration of substance (P)}}$$

Because creatinine is believed to be manufactured at a fairly constant rate by the muscle mass, is circulating in the bloodstream, and is filtered by the glomeruli (although a very small amount is excreted by the tubules), this is the usual substance measured. When used in the above example, this is known as creatinine clearance.

About 50% of nephrons will have lost their function before an appreciable alteration occurs in the result of the creatinine clearance test. The normal value of creatinine clearance should be between 70 and 125 ml min⁻¹; the function lessens with age. A creatinine clearance result of less than 10 ml min⁻¹ is often an indication to start RRT.

Procedure

A 24-hour urine collection is made which will provide the urinary creatinine content (U) and volume (V). A blood sample should be taken to indicate the plasma creatinine (P).

Patient information for 24-hour urine collection

The reason for the test should be explained to patients and they should be told what is expected of them. One (or more) 2l collection bottles containing no additives or preservatives should be given to the patient. Whilst male patients can usually void straight into the bottle, female patients should be provided with a suitable receptacle in which they can catch the urine. The patient must be instructed to discard the first urine of the day (on day 1) into the lavatory and then collect all urine passed for the next 24 hours into the bottle provided. On the following morning (day 2), patients should empty their bladders precisely 24 hours after the initial sample and then the collection is complete. The completed urine collection should be labelled with the date and time of start and completion of the collection as well as the usual details such as name, identity number, and date of birth.

The urine collection and the blood sample should be delivered to the laboratory with the request form, which should specify creatinine clearance test. The above formula is then applied and the creatinine clearance calculated.

CKD ^{51}Cr EDTA GFR

A more accurate method of assessing kidney function than the creatinine clearance test is the ^{51}Cr EDTA GFR. As with the creatinine clearance test, the normal range is a clearance of 70–125 ml min⁻¹.

Patient preparation

The patient should be informed of the reason for this test, the fact that a small dose of a radioisotope will be injected, and the necessity of a series of blood samples over a four-hour period, and consent should be sought.

Procedure

The radio-labelled substance is given by intravenous injection. The patient's weight and height must also be recorded to enable the result to be normalised for the individual patient's body surface area.

Over the four hours following the injection the usual procedure is for four blood samples to be drawn from the opposite arm to the injection of the radioisotope. This is to avoid contamination from any activity still lingering around the injection site, which will falsify the result.

Kidney Biopsy

Patients who are referred to the nephrology outpatient clinic with proteinuria, haematuria, or renal impairment with no obvious cause may require a kidney biopsy in order that the nephrologist can make a diagnosis and commence appropriate treatment. Whilst in experienced hands kidney biopsy is a fairly safe procedure, there are risks which should be taken into consideration. Risks of kidney biopsy, which are greater in AKI, are perirenal haematoma, prolonged and severe bleeding necessitating blood transfusion and possible surgery, and, rarely,

irreparable damage to the kidney requiring a nephrectomy. Kidney biopsy is contraindicated in the following:

- small kidneys;
- a single kidney;
- cystic kidney or hydronephrosis;
- UTI, acute pyelonephritis;
- gross obesity;
- uncontrolled hypertension;
- non-adherent patient;
- obvious diagnosis;
- severe anaemia;
- uncontrolled coagulopathy.

Patient preparation

Information regarding the benefits and risks attached to this procedure should be given to the patient, who should be allowed the opportunity to ask questions and time to consider the implications before consenting to the biopsy. Children under 16 years usually need written parental consent.

Patients are usually admitted to the ward on the day planned for biopsy and a further explanation of the exact procedure and what is expected of the patient should be given prior to signature of a consent form. Children are fasted for four hours before the biopsy as they will be sedated with a preparation such as midazolam following a mild premedication. In order to gain full compliance, whilst still in the ward, it is helpful to ask the patient to practise deep breathing and breath holding. Unless the patient can cooperate with breath holding on demand, the procedure should not be attempted, as the danger of malplacement of the sharp biopsy needle causing laceration or haemorrhage becomes a possibility.

Investigations include baseline urinalysis to exclude the presence of urinary tract infection and haemodynamic observations – the BP should be $<140/90$ mmHg. Blood samples are required for FBC, group and save, and clotting profile ($\text{Hb} > 10 \text{ g dl}^{-1}$, $\text{INR} > 1.2$, bleeding time > 10 minutes, platelets $> 100 \times 10^9 \text{ l}^{-1}$) as the highly vascular kidney can haemorrhage even when clotting times are within normal limits. It is also important to check if the patient is currently on any anticoagulant therapy (e.g. warfarin, heparin, clopidogrel), which should have been ceased five to seven days prior to the procedure and that they are not taking any non-steroidal anti-inflammatories or aspirin.

Some patients may require DDAVP (desmopressin), a synthetic version of the antidiuretic hormone vasopressin which improves haemostasis and is beneficial in uraemia platelet dysfunction, usually given via IV injection, one hour prior to procedure. A blood transfusion may be required in the case of urea $\geq 20 \text{ mmol l}^{-1}$ or creatinine $\geq 300 \text{ mmol l}^{-1}$ or for abnormal clotting times. Check the patient is not allergic to iodine if to be used as antiseptic preparation solution.

Procedure

Patients will be asked to empty their bladders before the procedure. Percutaneous kidney biopsy may be performed on the ward or X-ray department, under local anaesthetic. The patient lies in a prone position, with a pillow under the upper abdomen to isolate the kidney, perhaps supported with sandbags to prevent movement. The kidney (usually left) is identified by real-time ultrasound (US) as to position and depth and the skin is marked as to where the needle should be inserted. After cleaning the US gel from the skin, using a full aseptic technique, the area is cleaned, the area infiltrated with lidocaine as a local anaesthetic, and a needle is

inserted into the lumbar muscle layer until the needle (14–18G) is noted to swing with the patient's respirations. The patient should be asked to hold the breath whilst the needle is advanced 5 mm at a time, leaving the needle to swing free when the patient breathes in and out. When the needle has located the kidney, more local anaesthetic should be injected.

The needle is then withdrawn and a small incision is made at the needle exit site. An automated biopsy gun is inserted along the same pathway, making advances as the patient holds their breath (Brachemi and Bollee 2014). When the kidney is again located, the biopsy is taken with the patient holding a breath. The biopsy gun is withdrawn and the specimen obtained is immediately placed on a slide and viewed under a dissecting microscope to ascertain that the cortex which has been obtained is large enough (about 5 mm length) to divide into three samples. If not enough cortex has been obtained, the biopsy gun will have to be inserted again until a suitable strip of cortex containing sufficient glomeruli has been identified. Samples are sent to the laboratory for histology (in a 10% formalin pot), for immunofluorescence (in sterile normal saline), and electron microscopy (in specific glutaraldehyde fixative, kept cold). These samples should be delivered immediately (within minutes, not hours) to the laboratory, which must have had advance warning of the biopsy.

Finally, after the biopsy gun has been withdrawn, a pressure dressing is applied and the patient is asked to remain flat in bed. The patient will need much encouragement and reassurance during the kidney biopsy procedure as it can be painful, despite local anaesthetic. A friendly hand to hold and quiet encouragement to cooperate with breathing requirements from the attending nurse can be very reassuring.

Patient care following kidney biopsy

It is usual practice to keep patients in lying flat for two to six hours and bed rest will be dependent on unit policy, but it is common to be performed as a day case unless there is any frank haematuria which will require overnight observation. Haemorrhage and haematoma are the main complications following kidney biopsy; the wound site should be frequently checked for surface bleeding and blood pressure and pulse observations should be carried out until stable, for example on the time scale of every 15 minutes for 2 hours, then every 30 minutes for 2 hours, and then hourly for 4 hours. The signs and symptoms giving an indication of internal bleeding are a rise or fall in blood pressure and dull aching pain in the abdomen, back, or shoulder. The most common complication is transient haematuria, so the patient should be advised that some degree of haematuria will occur initially, but only persisting or heavy haematuria is of significance (1% require blood transfusions). Small urine samples from each void should be retained in transparent specimen containers for observation of diminishing haematuria and dipstick testing. The patient should be advised not to do any strenuous activity for four weeks, no playing contact sports for one week, to check the puncture site for signs of swelling, bleeding, and redness, and contact the renal unit if they have any back pain, fever, dizziness, or haematuria, passing blood clots in urine post-biopsy.

Kidney biopsy in the transplant recipient

Closed percutaneous biopsies of the transplanted kidney are undertaken to support evidence of rejection and also to confirm suspicion of recurrent or primary glomerular disease (see Chapter 10). The procedure is similar to the biopsy of the native kidney but more straightforward due to the superficial position of the transplanted kidney. The patient will be placed in a supine position with a pillow beneath

the transplant side to move the intraabdominal contents away from the site. The amount of tissue required in a transplant biopsy will be less than in a native kidney biopsy as fewer tests will be performed. The patient should remain resting in bed for four to six hours and usually discharged home the same day, though it is important to ensure the patient has passed urine and a dipstick test has been performed to check for blood.

Radiographic Investigations

Investigations using various radiographic methods are often employed to assist diagnosis and to assess progression of kidney disease and its attendant side effects. The most common techniques are discussed here.

Patients should have received adequate explanations before entering the department in order to allay any fears they may have on finding themselves in a department full of strange machinery, hazard warnings, and unfamiliar staff. If they are aware of the reasons for the investigation and what will be expected of them, the likelihood of an accurate result of the examination will be enhanced. The patient will be asked to sign a consent form for some invasive tests and early information will be of help for understanding the procedure.

All investigations involving X-rays must be performed according to the safety regulations in using a potentially hazardous substance, and these techniques must not be used unless the risk to the patient is outweighed by the benefit. It is important that women of child-bearing years are asked specifically if there is any possibility of pregnancy prior to carrying out the test. The foetus is most vulnerable to ionising radiation in the first trimester and the woman may not know that she is pregnant, so if there is any possibility it should be discussed with the referring doctor.

Plain abdominal X-ray

Plain abdominal X-rays incorporating the kidneys, ureters, and bladder (KUB) indicate the size, shape, position, and the presence or absence of one or both kidneys, and may be taken before other more complicated radiological procedures in order to provide an overall background picture. Most calculi may be seen as they are usually composed of radiopaque material. KUB X-rays are usually taken from the anterior aspect. A combination of KUB and US often forms the basic routine screening in those with kidney disease.

Bone density scan

Also known as dual-energy X-ray absorptiometry (DEXA) scan the bone density scan measures the mineral density of bones using a low-dose noninvasive X-ray technique. The X-ray beam has two energy peaks, one aimed at the bones and the other the tissue, then the tissue amount is subtracted, providing a bone mineral density amount which indicates the strength of the bones.

Skeletal X-rays

Skeletal X-rays are not commonly performed as superseded by bone density scans, but may be taken in patients on dialysis. This is to detect osteodystrophy, which may become apparent in association with impaired glomerular filtration and associated

disturbed metabolism of calcium and phosphate. Those bones most likely to show the characteristic abnormalities are the phalanges, skull, pelvis, and vertebrae. Pain and deformity will ultimately develop unless imbalances of calcium and phosphate can be corrected and inadequate metabolism of vitamin D can be halted (see Chapter 13).

Intravenous urogram

This procedure is also known as the intravenous pyelogram (IVP). This examination indicates the size and position of the kidneys and the anatomy of the calyces and pelvis. The ureters are also outlined by the progression of the dye containing urine to the bladder and the subsequent use of sequential X-rays, enabling any deformities in these organs to be demonstrated. The intravenous urogram (IVU) gives little useful information in advanced CKD and consequently is not the investigation of choice if more than 50% of nephron loss is suspected. If impaired kidney function is known and an IVU is indicated, a greater dose than usual of the radiopaque contrast medium may need to be given – this in itself is nephrotoxic and may exacerbate CKD, at least temporarily.

Patient preparation

The patient should be told that the investigation will take about an hour to complete – longer if there is renal impairment. If the patient is taking metformin it must be stopped 24 hours prior to prevent the risk of lactic acidosis. After an explanation of the procedure with adequate time to ask questions, the patient may be asked to sign a consent form and be checked for any allergies to iodine or shellfish. Caution should be observed with asthmatics and others who have allergic conditions, as the contrast medium is iodine based. Therefore, it is standard procedure that injections of adrenaline (epinephrine) 0.5–1 mg (0.5–1 ml of 1 : 1000 solution = 1 mg ml⁻¹) i.m., antihistamine (e.g. chlorphenamine [chlorpheniramine] 10–20 mg i.v.), and hydrocortisone should be immediately available to treat anaphylaxis should it occur. Some patients may require prophylactic corticosteroids if there is a history of asthma.

Bowel preparation will be dependent on local policy and, if used, should be carried out two days prior to the procedure to clear the bowel to enable a clear view of the urinary system. It may not be used in older patients as there is a risk of dehydration, which could lead to reduced kidney perfusion. Adult patients should fast for four to six hours, but limited clear fluid is usually allowed until one hour before the IVU. Emptying the bladder beforehand is important, or the contrast will become overdilute on reaching a full bladder and a poor picture will result. A fluid restriction of 500 ml in 24 hours may be requested if the patient has normal kidney function for better images as a result of concentrated contrast media.

Post procedure, kidney function should be checked in known CKD and urinalysis checked for any sign of haematuria. Haemodynamic observations should check for signs of infection or bleeding and allergic reaction to the contrast agent. Symptoms of mild to moderate allergy include pruritus, urticaria, and vomiting, and can be treated with an antihistamine. Symptoms of severe anaphylaxis (a medical emergency) include bronchospasm, hypotension, and shock. Any reaction should be noted in the medical file for any further procedures. The patients should be encouraged to drink fluids if not contraindicated, to aid clearance of the contrast media. Nurses should be aware that there is a possibility of AKI following this investigation, so urinary output should be monitored. Prior to restarting metformin, a check creatinine level is required 48 hours post procedure.

Retrograde pyelogram

In this examination, radiopaque dye is injected directly into the upper urinary tract via a catheter inserted through a cystoscope into the ureter. A series of X-rays are performed on one or both kidneys. This test is useful in outlining stones, calyceal defects, and masses in the ureter or renal pelvis and in defining deformities such as hydronephrosis or hydroureter. This investigation is sometimes performed after an IVU or US has demonstrated a hydronephrosis and more clarification is needed for a diagnosis. After the procedure the urine should be observed for haematuria and patients should be watched for signs and symptoms of infection. Post-procedure care is as for IVU. Patients should be encouraged to drink copiously to help avoid infection, unless contraindicated due to reduced fluid allowance (antibiotics may be given as a prophylaxis).

Computed axial tomography or computed tomography (CAT/CT) scan

CT scanning is used to evaluate renal cysts and masses, to stage renal tumours, assess urethral obstruction not detected on US, and also in the diagnosis of renal calculi disease and in the diagnosis of renal vein thrombosis. CT is an X-ray technique that uses a computer to reconstruct cross-sectional images of 1 cm slices of the organ targeted. The dose of radiation is about the same as that for an IVU. A clear bowel is necessary so a suitable laxative may be given two days before the scan. A light diet should be taken for two days before the scan and nothing on the day of examination apart from clear fluids. Patients must be able to follow instructions such as when to hold the breath, to be able to lie motionless, and not to talk. Contrast agents may be used to assess the renal cortex better, so check for any allergy to contrast media or history of asthma.

Nuclear magnetic resonance or magnetic resonance imaging

This form of scanning involves application of a strong external magnetic field along with a radiofrequency signal that produces a current in a receiving coil proportional to the density of protons in the body organ being scanned. This signal is processed by computer to create a tomographic slice of the organ similar to a CT scan. Magnetic resonance imaging (MRI) is used to evaluate renal masses such as renal cell carcinoma as it can differentiate between solid and cystic masses. It can also be used to diagnose renal vein thrombosis. Magnetic resonance angiography can be used to evaluate patients with possible renovascular hypertension.

The advantage of MRI over CT imaging is that no ionising radiation is used. A non-nephrotic contrast agent may be used and many planes can be visualised. Caution is required with the use of gadolinium as it has been associated with nephrogenic systemic fibrosis and kidney function should be checked prior to use. Older patients are more at risk and high-risk gadolinium should not be used in severe kidney disease (European Medicines Agency 2010).

It is important that the patient is not wearing any magnetic metal object, and it must be ascertained that no internal metal objects are present such as aneurysm clips, screws, pacemakers, or shrapnel.

Ultrasound

US investigations have replaced some x-ray procedures (especially the IVU) to a large degree, and because this procedure does not carry the hazards associated with radiation this method can be used in women without consideration of the possibility

of pregnancy. This is a noninvasive procedure where a transducer (sonar probe) is moved in close contact with the skin over the area of investigation and it can be repeated frequently if necessary, unlike X-ray. US is especially useful in examinations of the abdominal and pelvic organs. It is widely used to determine the size and shape of the kidney, its presence and position, and the composition of cysts or neoplasms if present, and also in the diagnosis of polycystic kidney disease. However, it is less useful in providing information about the ureters. US is also used to guide the operator in procedures such as kidney biopsy.

Patients who are to have kidney US scans are usually asked to fast for six to eight hours (in order to keep pockets of air in the gut to a minimum) except for drinks of clear fluids.

US in kidney transplantation

The most important and common cause of early transplant dysfunction is acute rejection, which occurs in 10–20% of all patients. This is accompanied by inflammation, which leads to swelling of the kidney and an increase in pressure inside the organ. US can visualise any changes to the kidney and can be undertaken daily; two size increases on consecutive days would be strongly indicative of acute rejection. However, dysfunction attributed to other causes must be excluded. Infection may be associated with an increase in the kidney size, but this is easily diagnosed by routine testing of midstream specimens of urine.

Renal vein thrombosis is a serious complication and will cause a rapid increase in size, possibly resulting in a tear of the kidney substance. If this condition is quickly diagnosed with US, rapid surgical intervention is possible and the graft may be rescued. Renal artery thrombosis may be diagnosed ultrasonically by the observation of lack of vessel pulsation. For greater accuracy, duplex scanning using a combination of imaging and frequency waveform analysis is available.

Early complications following transplantation include urine leaks, usually from the site of the ureteric anastomosis. These are seen ultrasonically as a fluid collection around the graft site. Later complications are obstructive lesions, which are often insidious in onset and lead to deteriorating kidney function. Routine scanning of outpatients is a simple and easy method of detecting dilatation and stenoses of the urinary tract, which are then treated surgically.

Needle core biopsy of the transplanted kidney remains the best method of detecting rejection and determining the degree of interstitial fibrosis and acute inflammation. Using US guidance of the biopsy needle, a good core of the renal cortex may be safely obtained, carefully avoiding the structures of the renal medulla and damage to the graft. US is therefore a valuable tool in the detection and diagnosis of kidney allograft dysfunction, allowing intervention and early treatment of problems.

Renal Doppler studies

A noninvasive US test to assess vascular flow to the kidney, for example renal vein thrombosis, acute tubular necrosis, renal infarction, renal artery stenosis, and evaluate transplanted kidneys for urine outflow obstruction and acute rejection. CT and MRI scans are however more reliable to diagnosis these conditions.

Renograms

An injection of intravenous radioisotope, which is excreted via the kidneys, and a series of x-rays are taken over a two to four hours period, which enables the assessment

of kidney function and tubular secretion and can indicate the position of an obstruction – no radioisotope is seen if there is a reduction in blood supply to the kidney or in the obstructed area. This investigation can be used in place of IVU if the patient is allergic to iodine contrast medium, and it is also used in transplanted patients. In renal artery stenosis, a renogram (using either DPTA or MAG 3) may be performed and then repeated, incorporating an injection of captopril as a test dose to outline any response induced – i.e. a reduction in renal blood flow in the presence of a blockage. Check with medical staff if the patient on antihypertensive treatment as he/she may need to stop or adjust dose. Blood pressure should be monitored after the procedure for two hours.

Renal scans

There are three types of radioisotope scans that can be performed to provide quantitative data on the function of the kidneys.

Firstly, the isotope, ^{99m}Tc technetium-labelled diethylenetriaminepentaacetic acid (^{99m}Tc DTPA), is rapidly excreted by the kidney and shows the blood flow through the kidneys, identifies obstructions, for example renal artery stenosis, and provides valuable information about the function and excretion capacity of the kidney. A diuretic may also be given intravenously and the patient should be well hydrated. It is not as effective if creatinine $>200\mu\text{mol l}^{-1}$.

The second isotope is ^{99m}Tc Technetium-labelled dimercaptosuccinic acid (^{99m}Tc DMSA), which is retained by the cells in the proximal tubules and parenchyma and enables the identification of areas of cortical scarring, contusions and solid lesions. This will provide quantification of relative kidney function between kidneys and within a kidney.

The third is known as MAG 3, which uses the isotope ^{99m}Tc technetium-labelled benzoyl-captoacetyl triglycerine and is a dynamic imaging scan as the isotope is rapidly excreted by the kidney via glomerular filtration or a combination of filtration and tubular secretion. The test enables visualisation of the aorta and renal perfusion. Quantification of renal blood flow can be calculated and it identifies the overall kidney function and presence of obstruction, thrombus, emboli, and stenosis. When patients undergo radioisotopic scans they should empty their bladders immediately before scanning. Patients should be advised that they are radioactive for 24 hours and nursing staff should ensure universal precautions when managing waste disposal.

Renal angiogram

This is performed through a catheter inserted via the femoral vein (however the brachial artery may also be used if required) and fed to the renal artery. Radiopaque contrast dye is injected and a series of fluoroscopic X-rays performed. It identifies tumours, emboli, thrombosis, trauma, and stenosis of vessels, and can be used for transplant donor assessment and identification of bleeding site post-kidney biopsy. Caution should be taken with patients who have some degree of renal insufficiency as the dye is nephrotoxic. If patients are able then they should drink plenty of fluids to flush through the contrast.

The most common complication of a femoral angiogram is bruising, false aneurysm, haemorrhage, infection, reaction to the contrast agent, and haematoma. Consent is required.

The patient should fast four hours for food and two hours for clear fluids prior to the procedure and must be checked for any allergies to iodine and shellfish. It is important to ensure that hydration is adequate, especially if there is decreased kidney

function and low urine output, which may require the use of a nephroprotective agent or IV 0.9% normal saline or 1.26% sodium bicarbonate over a four-hour period prior. Other agents used include N-acetylcysteine (NAC) for low urine output and impaired kidney function. Anticoagulants may be required (if INR < 1.7) and possibly heparin. Metformin should be stopped preprocedure to prevent lactic acidosis. Baseline neurovascular observations should be recorded. Bloods samples should be taken for FBC, U&Es, and clotting profile.

After the procedure, the frequency of observations of the puncture site, neurovascular and haemodynamic observations are dependent on the unit policy, but as a guide should be performed every 15 minutes for 1 hour, then half-hourly for 2 hours for signs of bleeding whilst the patient is lying flat or at 45° for 1–2 hours and bed rest for up to 24 hours, which is dependent on unit policy. Increase oral intake where possible to flush contrast media. Kidney function should be checked if known renal impairment and serum creatinine checked 48 hours post-recommencement of metformin. Anticoagulants should be recommenced, usually the evening post-procedure.

Patients should be advised not to do any strenuous exercise for 48–72 hours or have a bath/shower for 24 hours. The puncture site should be patted dry and slight pressure placed over the site initially if the patient coughs or sneezes.

Conclusion

The investigations which have been discussed above are by no means exhaustive. Since those with kidney disease usually have multifactorial disease processes, many other specific investigations may be indicated, especially cardiovascular tests such as electrocardiography and echocardiography. The gastrointestinal tracts in patients with kidney disease are frequently investigated for bleeding problems using techniques involving endoscopy (e.g. gastroscopy, colonoscopy).

Such is the commercial pressure to exploit the latest technology, it is inevitable that new methods and procedures will enter the renal field in the near future, condemning some present-day tests to redundancy. However, it is hoped that if nurses understand something of the current techniques used in renal investigations, they will be able to inform and reassure their patients reliably.

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CHAPTER 8

Haemodialysis

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Learning Outcomes

- to define haemodialysis and how it replaces the functions of the kidney.
- to examine the components of the haemodialysis prescription and when this may need adjustment.
- to explore vascular access options for haemodialysis treatments and how to care for these, minimising complications.
- to explain the nursing care required to look after patients during haemodialysis, including recognition of complications.
- to explore the patient's experience of haemodialysis.

Introduction

Dialysis is a life-sustaining treatment for patients who have advanced kidney disease. Dialysis is a renal replacement therapy, replacing some functions of the kidneys when they fail. It prevents life-threatening complications from the build-up of fluid, electrolytes, and the waste products of metabolism including urea, creatinine and acid, that would normally be prevented through excretion from the kidneys.

What Is Haemodialysis?

Haemodialysis is a form of dialysis that performs the functions of dialysis directly via the bloodstream. It is an extracorporeal therapy, meaning the procedure is performed outside of the body. A simple summation of haemodialysis is that it removes the blood from the body to perform the dialysis process and then returns the blood to the body.

What does haemodialysis do?

Haemodialysis does not replace all the functions of the kidneys, but prevents the life-threatening complications of kidney failure. There are some important considerations to this therapy:

- fluid removal needs to be accurate and safe.
 - at the end of haemodialysis the patient needs to be euvolaemic, so not dehydrated and not overloaded, with minimal side effects for patients.
- electrolyte removal needs to be balanced to ensure the therapy leaves behind exactly what the body needs without leaving an excess or deficit. This involves:
 - removing the correct amount of the correct electrolytes, e.g. potassium;
 - leaving behind the correct amount of electrolytes;
 - ensuring that other useful molecules in the body, such as glucose and medications, are not removed.
- the removal of the waste products of metabolism needs to be maximised, whilst minimising complications from rapid removal of these waste products. The waste products that haemodialysis normally focusses on removing is urea and creatinine. However, other waste products may also be removed via haemodialysis, some of which are not even known. These can include beta-2-microglobulin, cytokines, and uraemic toxins (Kirsch et al. 2016; Santoro and Guadagni 2010).
- the metabolic acidosis that builds up from kidney disease is easily corrected. This is completed in two ways – administration of bicarbonate to buffer the blood pH and removal of excess acid.

When you start to examine what haemodialysis does and how it does this, you realise that the kidneys perform a phenomenal role in maintaining homeostasis in the body. Replicating this in an artificial therapy and ensuring individual conditions are maintained within a body is challenging.

To add to this challenge, haemodialysis is an intermittent therapy, normally undertaken three times a week, although current trends aim to increase this frequency. Therefore, haemodialysis is not undertaken simply to maintain the status quo, but also correct imbalances that have accumulated in between haemodialysis sessions. Haemodialysis provides rapid corrections of the build-up of fluid, electrolytes, and waste products of metabolism and acid, which can also be challenging for the body to tolerate.

A combination of all these considerations makes haemodialysis a complex therapy to perform with potentially damaging effects on the body. Throughout this chapter this complexity will be explored alongside how to optimise the therapy to minimise adverse effects and maximise outcomes for patients.

What is needed to perform haemodialysis safely?

To perform haemodialysis, the most essential components are the dialyser and dialysate fluid. These are the elements that perform the dialysis process, providing the medium and conditions to remove the waste and excess products normally removed by the kidneys.

The **dialyser** uses a membrane to separate two compartments – one for the blood and one for the dialysate fluid. Current dialysers use a ‘hollow fibre’ approach where the membrane is structured into tubes. The blood flows through the middle of the tubes and the dialysate fluid flows in the space around the tubes (Figure 8.1). The blood and dialysis fluid flow in opposite directions.

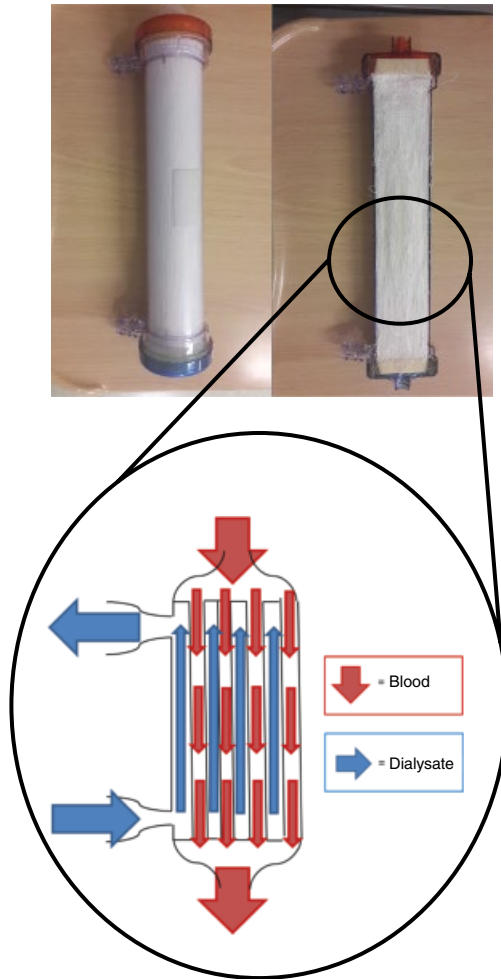


Figure 8.1 Image of a dialyser.

The **dialysate fluid** is constructed to have the right components to draw excess electrolytes, waste products, and excess fluid out of the blood, across the membrane, and into the dialysate fluid. This dialysate fluid containing removed products, then exits the dialyser and is disposed of via the waste system and replaced with fresh dialysate fluid (Figure 8.2). The dialyser and dialysate fluid are individualised according to patient need. See 'Haemodialysis Prescription' section.

The **extracorporeal circuit** is a circuit of plastic tubes that runs to and from the dialyser. It incorporates many of the elements used to keep the dialysis process safe. The extracorporeal circuit includes:

- anticoagulation to prevent clotting in the extracorporeal circuit;
- pressure monitoring for both the circuit and vascular access;
- bubble traps to prevent air entering the patient;
- saline infusion that can administered in an emergency;
- monitoring functions for the machine and patient.

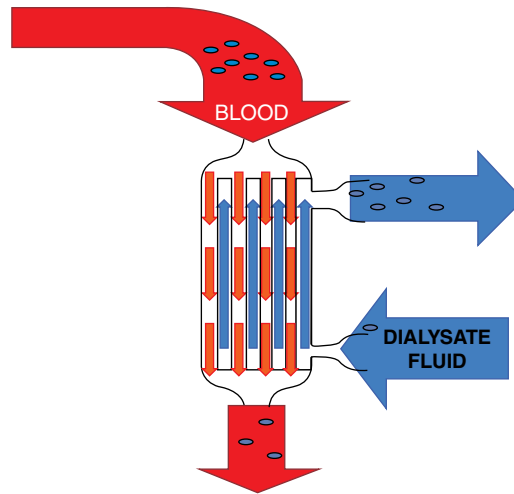


Figure 8.2 How the dialyser works.

Correct handling of the extracorporeal circuit is essential to:

- prevent contamination from bacteria, leading to infections in haemodialysis patients.
- ensure air is not administered into the patient's circulation, causing an air embolism. Priming, secure connections, and clamping of lines is essential to prevent air entering the circuit at any point.
- ensure red blood cells are not damaged through excess pressure, leading to haemolysis.

Haemodialysis machinery

The haemodialysis machine provides the structure for the extracorporeal circuit to be mounted on (Figure 8.3). The machine provides three essential functions:

- creation and monitoring of the dialysate fluid.
 - the dialysate fluid is created in a circuit within the machine, often known as the dialysate pathway. Sensors and pumps within this dialysate pathway ensure the dialysate fluid is of the correct composition. The dialysate pathway also removes waste dialysate.
- monitoring of the extracorporeal circuit and machine functions, to ensure the haemodialysis treatment is administered safely.
- provision of the haemodialysis prescription, providing a platform for this to be programmed, monitored, and translated into reality in the extracorporeal circuit.

Haemodialysis involves complex medical devices that bring about rapid correction of haemostasis through an extracorporeal circuit and vascular access. This is required for the correct dialysis prescription to be administered to the patient. The vascular access and extracorporeal circuit delivers the blood to the dialyser safely and then returns the blood to the patient. The haemodialysis machine provides a monitoring function to ensure safe administration of the haemodialysis prescription.

However, patients' needs vary. Haemodialysis nurses need to assess what the patient needs from haemodialysis and their response to the prescribed treatment,



Figure 8.3 Image of an extracorporeal circuit and haemodialysis machine.

allowing prompt adjustment as patients' needs change. Despite good assessment and advances in technology, complications still occur in haemodialysis, some frequently, due to the complexity of the treatment (Fielding et al. 2016a; Saha and Allon 2016). Haemodialysis nurses need to be able to detect complications and know how to correct these, minimising harm to patients.

The whole process of maintaining a safe haemodialysis treatment and monitoring patients' response to the therapy requires skilled and knowledgeable haemodialysis nurses. Haemodialysis nurses need an understanding of:

- what the haemodialysis treatment is doing and how it is doing it;
- how to detect the patient's changing prescription needs and respond;
- what can go wrong in the treatment, how to prevent this, and how to respond when it occurs.

Vascular access

To remove and return the blood to the patient during haemodialysis requires access to the circulation. This is achieved through special vascular access, which normally comprises of two access points:

- one to remove the blood (often known as the arterial access) and
- one to return the blood (often known as the venous access).

Special vascular access is required as normal veins will not provide sustained support for haemodialysis. The vascular access provides the high blood flow rate (BFR)

required for haemodialysis. It also needs to be robust, allowing repetitive use with the minimum amount of complications.

There are three types of vascular access normally used for haemodialysis:

- arteriovenous fistula (AVF);
- arteriovenous graft (AVG);
- central venous catheter (CVC).

How Does Haemodialysis Work?

Haemodialysis works under a number of principles, which occur within the dialyser. These principles dictate how solutes and fluid are removed. The three main principles of haemodialysis are:

- diffusion
- ultrafiltration (UF)
- convection.

Whilst the effects of other principles, like adsorption and concentration polarisation are often considered in dialysis membrane technology – diffusion, UF, and convection are the principles of clinical significance.

Diffusion

Diffusion is a principle of nature that applies to solute removal in haemodialysis. It relates to the concentration difference between two solutions.

For diffusion to occur, the following are required:

- a semipermeable membrane – this is a permanent barrier with pores ('holes') that separates two solutions. The pores allow some molecules to move across but not all.
- two solutions containing molecules of different concentrations – these two solutions are separated by the semipermeable membrane. The molecules are called solutes which are molecules dissolved in a fluid medium.

Diffusion states that when you have two solutions separated by a semi-permeable membrane, solutes will move from a high-concentration solution to a low-concentration solution (see Figure 8.4). What diffusion is attempting to do is equalise the concentration on either side of the membrane to create equilibrium.

Diffusion works through concentration differences, which are known as concentration gradients. The larger the concentration gradient, the more of the solute moves across the membrane or in the case of haemodialysis moves into the dialysate fluid. In haemodialysis, diffusion is used to manipulate what is removed and what is left behind. The dialysate fluid concentration is altered to diffuse out the molecules that need to be removed. For example, dialysate fluid contains no urea because as much urea as possible needs to be removed from the blood. However, whilst potassium also needs to be removed, the correct amount of potassium needs to remain in the blood. Therefore, some potassium is found in the dialysate fluid and the specific amount of potassium in the dialysate can be titrated to ensure that a safe level of potassium remains in the blood.

Diffusion is also affected by the properties of the membrane and the size of the molecules you want to remove. The size of the pores in the membrane, in comparison

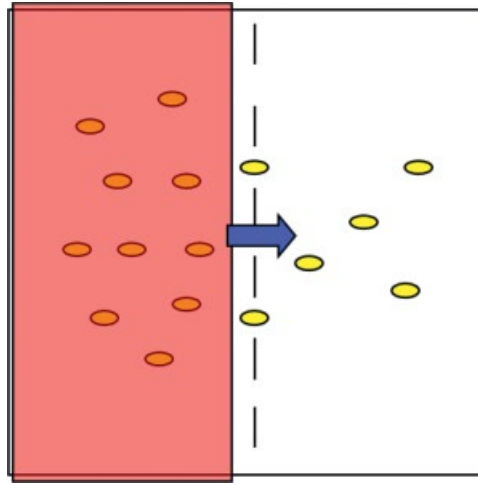


Figure 8.4 Diffusion.

to the molecule size, can affect whether a molecule is able to move across the membrane. For example, the pores in the dialyser are made small enough not to allow red blood cells to move across.

Diffusion selects the type of solute removed based on these characteristics of dialysate concentration and membrane properties. However, sometimes molecules that need to be retained are lost, for example medications. Whilst diffusion allows haemodialysis to be selective about what molecules it removes, it is still not perfect. Over a number of years, renal research has worked towards manipulating the dialyser to assist in removal of what needs to be removed without removal of what should not (Clark and Gao 2002; Clark et al. 1999; Humes et al. 2006; Kirsch et al. 2016; Santoro and Guadagni 2010).

Convection

Convection is a principle of physics and is often referred to in relation to heat movement. If the general principles of convection were explored in detail, it might be that it is explained in different ways from those explained in the context of dialysis. The following explanation will focus on how convection happens in haemodialysis.

Within the dialyser, convection occurs when fluid moves across the haemodialysis membrane. Convection is not how this fluid moves, but what happens when this fluid moves across the haemodialysis membrane and is about the movement of solutes. A simple explanation of convection is that as the fluid moves across the membrane it pulls solutes with it (Figure 8.5). Hence why convection is often known in haemodialysis as ‘solute drag’.

Small, middle, and large molecules

It is important to discuss molecule size in relation to haemodialysis. Small molecules are molecules like potassium, phosphate, and urea, which need to be removed by dialysis. Middle molecules are molecules such as beta-2-microglobulin, cytokines, and protein-bound uraemic toxins (Santoro and Guadagni 2010), which often need to be removed. Larger molecules are molecules like blood cells and complex hormones. Usually these do not need to be removed by dialysis, although some uraemic toxins may fit into this category (Santoro and Guadagni 2010).

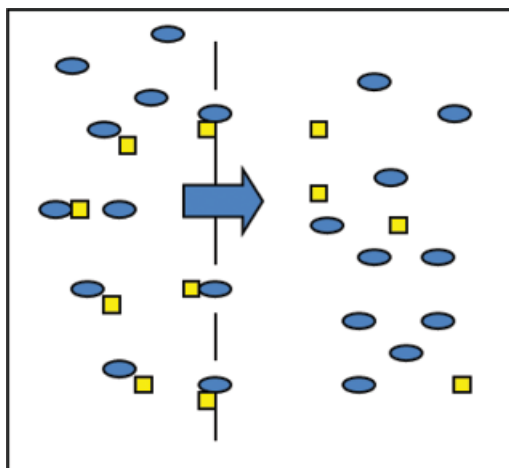


Figure 8.5 Diagram of convection.

Diffusion is effective at removing small molecules, but not so effective at removing middle molecules. Convection is more effective at removing middle molecules (Santoro and Guadagni 2010). However, as little convection occurs in traditional low flux haemodialysis, it is considered to have little effect on solute removal. Haemodiafiltration (HDF) produces more convection as the fluid exchange promotes fluid movement across the membrane. However, high flux dialysers are also considered to promote convection through ‘back-filtration’ (Santoro and Guadagni 2010).

Research into dialysers and maximising the removal of the correct molecules continues. Recent studies have started to demonstrate how adsorption properties of membrane materials could assist in removal of other ‘large molecule’ uraemic toxins (Aucella et al. 2013; Kirsch et al. 2016; Santoro and Guadagni 2010).

Ultrafiltration

Diffusion describes the process of molecule removal, and UF describes the process of water removal. Fluid removal in haemodialysis is called UF. In haemodialysis, UF is driven by a pressure difference. UF creates a pressure difference or pressure gradient across the dialyser membrane. It achieves this by creating a negative pressure in the dialysate fluid that ‘sucks’ fluid across. This is driven by pumps in the dialysate pathway, with the ‘out’ pump running faster than the ‘in’ pump and drawing water across the membrane and into the dialysate fluid (as shown in Figure 8.6).

Current haemodialysis machines are volumetric, which means that the required fluid removal can be programmed into the machine and the machine will titrate the dialysate fluid pumps to remove the correct amount of fluid in a linear manner.

Summary of the principles of haemodialysis

Whilst the three principles of haemodialysis are simple to describe, applying them to the practical removal of solutes and fluids in the dialyser to ensure the correct things are removed from the blood is complex. However, haemodialysis nurses should persevere to achieve understanding of this. These principles and their understanding allow the haemodialysis treatment to be tailored to individual need. Haemodialysis is often described using a ‘cup of tea’. Whilst not physically accurate, this can allow nurses to visualise and understand these principles. This is outlined in Box 8.1.

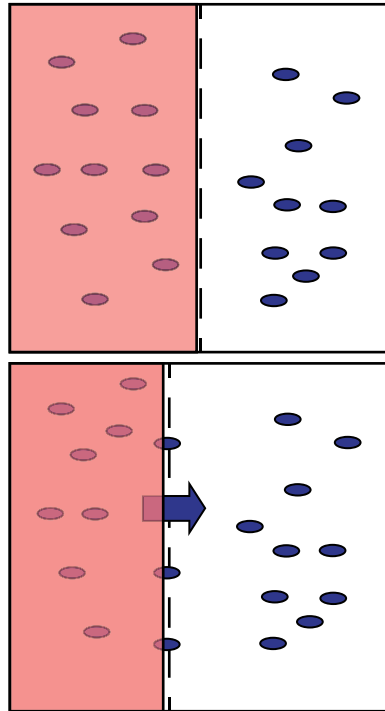


Figure 8.6 Creation of ultrafiltration (UF) in the dialysate circuit.

BOX 8.1

The 'not very accurate' cup of tea analogy to describe the principles of haemodialysis

Step 1 – Diffusion

When making a cup of tea, hot water is poured over the tea bag in the mug. As the tea bag then sits in the water, the water gradually turns brown as the tea 'diffuses' out of the tea bag and into the water.

- the tea bag is a membrane separating the water and the tea.
- there is no tea in the water and lots of tea in the tea bag.
- the tea molecule is small enough to move through the membrane of the tea bag.
- tea moves out of the tea bag and into the water.
- tea leaves are too large to move through the membrane so stay inside the tea bag.

Step 2 – Ultrafiltration

Once the tea is brewed, a spoon is used to squeeze the water out of the tea bag before it is removed. This squeezing motion, whilst a crude form of UF, is using pressure to remove water from the tea bag as UF would. In reality, the dialyser is not able to squeeze the blood, so uses a negative pressure to 'suck' fluid out of the blood.

Step 3 – Convection

Milk is added to the tea and a spoon used to distribute the milk evenly through the tea. The stirring motion moves the water molecules which then drag the milk molecules with it.

NB: This analogy should not be taken as accurate or correct. However, it allows a demonstration of how diffusion, UF, and convection could work.

Mortality and Haemodialysis

The UK Renal Registry report (Steenkamp et al. 2016) shows that survival on dialysis is improving. However, patients undergoing dialysis still have a higher mortality rate than patients of a similar age who are not dialysing, with the gap widening for younger patients (Steenkamp et al. 2016). The UK Renal Registry report does not distinguish between haemodialysis and peritoneal dialysis mortality rates, due to confounding issues with respect to dialysis choice. However, dialysis outcomes continue to vary across the UK (Steenkamp et al. 2016). 'Kidney Health: Delivering Excellence' (Loud and Gallagher 2013) highlights the need to reduce this variation, ensuring all patients undergoing dialysis receive optimal care. Dialysis is a challenging therapy, associated with many complications and lifestyle changes for patients (Loud and Gallagher 2013). The UK Renal Research strategy highlights one important area of focus is improving outcomes for patients on dialysis (Karet Frankl et al. 2016).

As well as quality improvement and research initiatives, haemodialysis nurses can ensure patients receive the best haemodialysis treatment that current evidence dictates. One way to achieve this is to tailor the haemodialysis prescription to patient's individual needs. This requires continuous and on-going monitoring and assessment of the effect of this prescription on the individual patient – a key role of nurses.

Haemodialysis Prescription

The haemodialysis prescription includes various aspects that can be tailored to individual patient needs. Different aspects of the haemodialysis treatment can vary, which is normally dictated by availability of different equipment; the ability of the haemodialysis machine to alter parameters; the results of blood tests; patient symptoms and stability during and after haemodialysis; and patient choice.

Aspects that are normally altered come under the general areas:

- the type of dialysis often known as 'modality';
- the dialysate fluid;
- the dialyser;
- aspects that affect the Kt/V and Urea Reduction Ratio (URR);
- fluid removal;
- anticoagulation.

Dialysis modality

Dialysis modality includes peritoneal dialysis or haemodialysis, but also the different types of haemodialysis such as whether the therapy is being undertaken at home. This section is going to explore the different modalities that come under the definition of haemodialysis, such as the frequency and length of haemodialysis treatments, use of HDF, and the location of the haemodialysis treatment.

The standard minimum haemodialysis modality currently is considered thrice weekly in-centre haemodialysis, with each treatment as a minimum of four hours using a high flux dialyser. The UK Renal Association standards for haemodialysis (Mactier et al. 2009) recommend this is the minimum amount of haemodialysis a patient should receive.

One challenge of haemodialysis is the intermittent nature of the treatment, which leads to two significant issues:

- the correction of fluid, electrolytes, and acidosis alongside the removal of waste products of metabolism needs to be performed rapidly. This rapid removal can be difficult to tolerate.
- fluid, electrolytes, and waste products of metabolism start to build up within the body once the haemodialysis session is completed. The time between haemodialysis sessions (sometimes three days) causes some of the long-term complications that haemodialysis patients experience.

This intermittent therapy causes peaks and troughs in the body. Removal of waste products occurs rapidly in haemodialysis, but then accumulates in-between haemodialysis sessions. For example, glucose removal in haemodialysis can make diabetes very difficult to manage in haemodialysis patients (Allen and Fielding 2011; JBDS-IP 2016). Figure 8.7 demonstrates this peak and trough effect.

Outcomes from the DOPPS (Dialysis Outcomes and Practice Patterns Study) indicate that three times a week, four hours, haemodialysis does not lead to the best outcomes for patients, despite it being the main modality used in the UK and worldwide (Canaud et al. 2006; Saran et al. 2006).

Haemodiafiltration

HDF is one modality that may lead to better outcomes than standard haemodialysis. The difference between haemodialysis and HDF is that HDF incorporates a fluid exchange. This is where 'extra' fluid is removed in the dialyser via UF. This 'extra' fluid is in excess of the programmed fluid loss required from the patient. As 'extra' fluid is removed, this also has to be replaced. This occurs through an infusion into the circuit. This removal and replacement of 'extra' fluid is the fluid exchange. The advantage of the fluid exchange is the 'extra' fluid removal, which leads to 'extra' fluid moving across the membrane in the dialysis. This triggers more convection in the treatment. HDF is often referred to as a 'convective' therapy.

Previously, large bags of infusate were attached to the circuit to replace the 'extra' fluid removed, but current technology allows dialysate to be used as the infusate. This is often known as on-line HDF. This advancement in technology to on-line HDF has allowed an increase in the volume of exchanges performed. HDF machines have an essential role in balancing the 'extra' fluid removed with that replaced, to ensure the fluid exchange does not interfere with the patient's fluid balance.

HDF was originally designed as combination of haemodialysis and haemofiltration, which at the time, was associated with removal of large as well as small

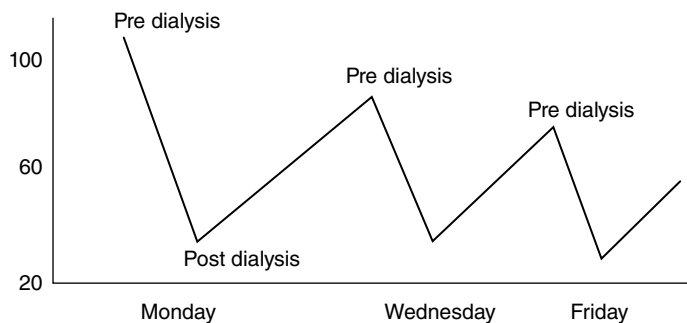


Figure 8.7 Peak and trough effect of haemodialysis.

molecules (Cioni et al. 1984; Kohlne et al. 1979). Early studies demonstrate the rationale for HDF was to promote better removal of middle molecules and large molecules like beta-2-microglobulin and uraemic toxins (Cioni et al. 1984; Henderson et al. 1975; Kohlne et al. 1979). Following an initial study, Henderson et al. (1975) stated that the solute clearance pattern of HDF was very similar to the human kidney and this was in sharp contrast to standard haemodialysis.

However, with the advent of high flux haemodialysis, more recent studies have struggled to identify the benefits of HDF on patient outcomes. The DOPPS examined outcomes for patients on HDF (Canaud et al. 2006). They identified that HDF with high exchange volumes was associated with lower mortality than both high flux and low flux haemodialysis (Canaud et al. 2006). However, the improvement in mortality was not significant with low volume of exchanges with HDF (Canaud et al. 2006). Since then, randomised control trials have struggled to identify a benefit to HDF over high flux haemodialysis (Smith et al. 2017; Vilar et al. 2009). Nistor et al. (2015) updated a Cochrane review and were unable to identify a benefit to convective therapies, due to the limitation and bias in current studies. The benefit of HDF may lie in the high volume of the fluid exchange, which is not always achieved (Chapdelaine et al. 2014). However, NICE (2018) recommended to “consider HDF rather than HD if in centre (hospital or satellite unit).” Until a large randomised trial is completed, the debate will continue. The H4RT trial which is currently recruiting within the UK is hoping to achieve this (www.bristol.ac.uk/population-health-sciences/projects/h4rt-trial).

More frequent and longer haemodialysis

Another way to reduce the intermittent effect of haemodialysis is to perform haemodialysis more frequently. The rationale is that fluid, waste products of metabolism, and electrolytes have less opportunity to build up in between sessions and more frequent sessions can thus be shorter, as there is less abnormality to correct. As the body system is being corrected less and more frequently, leading to fewer ‘peaks and troughs’, it can be hypothesised that this leads to better outcomes for patients (Twardowski and Misra 2010).

This rationale has recently been proven in research studies. In particular, the Frequent Hemodialysis Network (FHN) in the United States has performed a number of studies into frequent haemodialysis versus normal thrice weekly haemodialysis. They have identified that six times weekly haemodialysis in-centre leads to:

- reduces mortality, improved heart function, and improved blood pressure and phosphate control (The FHN Trial Group 2010).
- reduces extracellular water (Kaysen et al. 2012), indicating better fluid status control.
- improves self-reported physical health and function (Hall et al. 2012).
- improves mental health (Unruh et al. 2013).

Jefferies et al. (2011) also identified that more frequent haemodialysis was associated with less cardiac injury, possibly as this is related with lower ultrafiltration rates (UFRs).

Studies have also examined the adverse effects of more frequent haemodialysis. Notably, albumin loss and nutritional status do not appear to be affected by more frequent haemodialysis (Kaysen et al. 2012; The FHN Trial Group 2010). Studies examining vascular access complications have conflicting results. The FHN Trial group (2010; Suri et al. 2013) identified more vascular access complications with more frequent haemodialysis; however, Achinger et al. (2013) performed a longer study and identified no effect of more frequent haemodialysis on vascular access outcomes.

More frequent haemodialysis appears to be associated with improved outcomes. There is agreement within the renal community that this promotes more normal function for the body. However, current provision of haemodialysis for the majority of patients remains at thrice weekly haemodialysis. Whether this is driven by patient choice and culture or the availability of haemodialysis capacity is unknown.

Longer haemodialysis is also considered to improve outcomes for patients. This was first demonstrated in Tassin, France. This unit has always performed haemodialysis for eight hours, thrice weekly for all their patients. They consequently have improved survival (Innes et al. 1999), probably through improved blood pressure control without the use of anti-hypertensives (Charra et al. 1992; Innes et al. 1999). The DOPPS also identified that longer haemodialysis treatments, with lower UFRs, led to reduced mortality (Saran et al. 2006). However, since then the use of this regime of haemodialysis has not been explored, possibly due to the emergence of nocturnal haemodialysis and poor patient tolerance of longer treatment time.

Nocturnal dialysis

Nocturnal haemodialysis combines the benefits of frequent and longer, slower haemodialysis. Nocturnal dialysis normally involves dialysing for six to eight hours a night, using a slower dialysate flow rate and BFR to slow the dialysis process. Patients normally dialyse for up to six nights a week, adding the benefit of more frequent haemodialysis.

The FHN performed a trial examining the effect of nocturnal six times a week haemodialysis compared with three times a week haemodialysis. However, they were unable to identify any benefit to nocturnal haemodialysis, but identified this could be due to small patient numbers (Rocco et al. 2011). However, other studies have found a benefit to nocturnal haemodialysis, including:

- improved survival (Bridge and Holt 2015; Lockridge and Kjellstrand 2011);
- improved anaemia control (Poon et al. 2015; Tang et al. 2011);
- improved cardiac markers (Thomson et al. 2014) including decreased left ventricular mass (Friesen et al. 2015; Tang et al. 2011) and reduced arterial stiffness (Bridge and Holt 2015; Demirci et al. 2012);
- improved phosphate control (Tang et al. 2011);
- improved blood pressure control (Tang et al. 2011; Xi et al. 2013);
- improved clearance (Poon et al. 2015; Tang et al. 2011);
- improved quality of life (Tang et al. 2011; Xi et al. 2013).

The majority of these studies are observational, sometimes with small patient numbers, so no true comparison via a randomised trial has been performed. Initially there was concern about the burden of this treatment regime. However, studies have indicated that nocturnal haemodialysis could be associated with less burden of treatment and improved mental health, especially when used in the correct patient and family context (Rioux et al. 2012; Xi et al. 2013). The results for nocturnal haemodialysis do indicate a benefit, at least in patients that it suits as a modality.

Home haemodialysis

Since NICE recommendations on home haemodialysis (2002) were published, there has been an emphasis on improving home haemodialysis rates. NICE (2002) recommended that all patients who are suitable should be offered home haemodialysis as a modality of choice. Home haemodialysis improves clinical outcomes, in a similar manner to those discussed with more frequent and longer and nocturnal haemodialysis. NICE (2002) also identified home haemodialysis as economically

efficient when compared with in-centre haemodialysis. The NICE (2002) recommendations are still considered relevant despite their age. The UK Renal Association standards recommend all patients should be encouraged to do home therapies, whether this is peritoneal dialysis or home haemodialysis (Warwick et al. 2013).

One main benefit of home haemodialysis provides is the flexibility of the treatment regime. This allows options of longer, more frequent haemodialysis, including nocturnal haemodialysis. Currently, four hours of haemodialysis thrice weekly remains the main in-centre modality, with the home setting use for other modality choices.

Home haemodialysis can have advantages for patients feeling they have regained control of their life and decisions about their health, as well as developing a 'healthy' self-identity rather than taking on the sick role (Walker et al. 2015; Xi et al. 2013). However, home haemodialysis can also cause patients and carers concern including feelings of vulnerability, especially in relation to potential complications; social isolation and disconnection from medical personnel, plus there is a potential burden on carers to support the home treatment (Walker et al. 2015).

Many initiatives are in development to increase the number of patients accessing home therapies and home haemodialysis. The Kidney Quality Improvement Partnership (KQIP) is developing a national project to improve the uptake of home therapies (www.thinkkidneys.nhs.uk/kquip/about-us/kquip-national-projects). SHARE-HD is a Health Foundation funded project (www.shareddialysis-care.org.uk/sharehd) to encourage patients to become more involved in their care and also to encourage more independent haemodialysis (Fotherington et al. 2017).

There are numerous ways of performing haemodialysis that can be individualised to patients' clinical, psychological, and social needs. Whilst certain modalities have benefits, these benefits are only proven for those patients where the modality works for them. In reality, modality choice needs to be a balance between what is proven to have the best clinical outcomes, considered alongside what will suit that individual patient's lifestyle and concerns.

The dialysate

The dialysate comprises three components (Figure 8.8):

- electrolyte solution, often call acetate or 'acid';
- sodium bicarbonate;
- ultra-pure water.

In online HDF treatments, the dialysate fluid is also used as the replacement fluid for the fluid exchange (Figure 8.9). Therefore, the dialysate is infused directly into the patient and contains all the constituents of normal dialysate. For this reason, it becomes even more important in HDF that the dialysate fluid is of the correct composition and does not contain undesired elements.

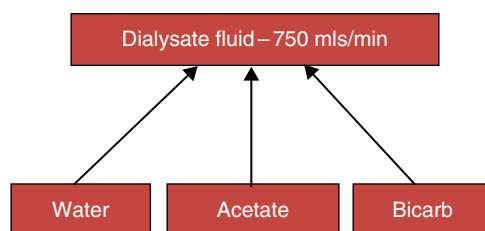


Figure 8.8 Composition of the dialysate fluid.

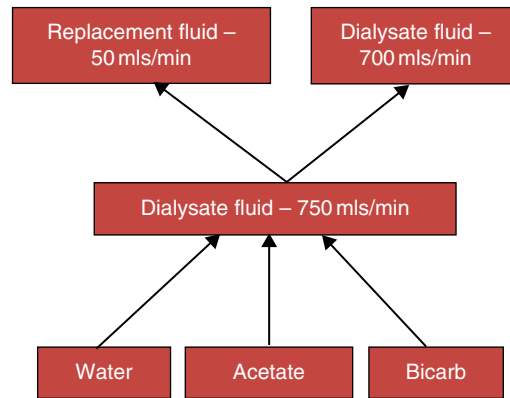


Figure 8.9 Dialysate use in haemodiafiltration (HDF).

The three components of the dialysate will now be examined, alongside how they may vary during individual haemodialysis prescription.

Acetate

The main electrolytes included in normal acetate are:

- potassium – acetate solutions can vary from 1 to 4 mmol⁻¹. This is usually prescribed by the nephrologist and determined from monthly blood potassium levels. However, the latest results from the DOPPS indicate that altering the potassium in the dialysate has less effect on pre-dialysis potassium levels than other interventions to manage potassium (Karaboyas et al. 2017).
- calcium – dialysate concentration can vary from 1 to 1.75 mmol⁻¹. Varying the calcium concentrations in dialysate is uncommon, but may be used when deranged serum phosphate levels alter the control of serum calcium. Higher calcium dialysate concentrations (1.5 or 1.75 mmol⁻¹) may be used post-parathyroidectomy, when patients often initially have low serum calcium levels, until physiological control is stabilised.
- glucose – this is normally set at 90 mg dl⁻¹ or 1 g l⁻¹ depending on the make of acetate. Low levels of glucose in the dialysate can lead to hypoglycaemia (Burmeister et al. 2012; JBDS-IP 2016). Use of 1 g l⁻¹ glucose in dialysate is now recommended for patients with and without diabetes to prevent hypoglycaemia balanced with inflammation created by glucose in the dialysate (Allen and Fielding 2011).

Other electrolytes in the acetate include magnesium, chloride, acetic acid and sodium. These are rarely altered within the clinical environment. Whilst research has examined altering of these levels, especially magnesium, or addition of vitamins to the dialysate to prevent vitamin loss, none of this research has changed clinical practice.

Bicarbonate and sodium

Sodium bicarbonate is another component of dialysis fluid, which supplies both bicarbonate and sodium to the dialysate. Bicarbonate normally comes in one concentration, but haemodialysis machines can then vary the levels of sodium and bicarbonate through the prescription programmed into the machine. Bicarbonate levels are set physiologically and normally within individual centres there is little variation in patient prescriptions. As a general rule, the bicarbonate level in the dialysate is set to correct the metabolic acidosis that develops in between haemodialysis sessions. Patients

normally arrive with low bicarbonate levels, bicarbonate diffuses into the blood during treatment and then patients leave with higher bicarbonate levels.

Sodium levels of the dialysate are an area of debate. Sodium has previously been used in high levels in the dialysate to make fluid removal more tolerable for patients (Davenport 2009a). This occurred via 'sodium profiling'. However, this often led to high sodium blood levels which increased the patient's blood pressure and made them thirsty, increasing inter-dialytic weight gains (IDWG) (McCausland and Waiker 2014). Current thinking recommends setting the sodium dialysate close to the individual patient's normal levels and aim for this to be lower rather than higher. Reducing sodium levels in the dialysate can help reduce IDWG (Penne et al. 2010). However, this is an area for debate, with a Cochrane review in progress (Dunlop et al. 2014).

Ultra-pure water

To ensure the acetate and sodium bicarbonate are mixed to the correct concentrations, ultra-pure water is used to dilute these concentrates. This allows efficiency of the volume of concentrate attached to the haemodialysis machine. As mentioned earlier, the process of diffusion in the dialyser is not selective. Therefore, anything that is in the water in the dialysate that is not present in the patient's blood, or present in lower concentrations, will diffuse into the blood. Coupled with the volume of water exposed to the blood in a single haemodialysis treatment (90–120l), this allows contaminants to enter the blood in large volumes.

Normal drinking water contains copper, fluoride, aluminium, calcium, magnesium, bacteria, and endotoxins. If present in the dialysate water, these could all diffuse into the bloodstream causing ill health in patients. In particular, haemolysis can occur from bleach contamination of water dialysate (Davenport 2006; Rylance 2014). The UK Renal Association has produced their own guidelines on water quality standards for haemodialysis in the UK (Hoenich et al. 2016).

The dialyser

The dialyser can vary in three ways:

- the size of the membrane of the dialyser.
This is expressed in surface area. It works through a very simple principle – the larger the surface area of the dialyser, the more diffusion can occur in the dialyser, which then allows more solutes to be removed. Often the level of clearance required, indicated by the Kt/V , dictates the size of the dialyser.
- the flux of the membrane.
Dialysers can either be low flux or high flux. This relates to the size of the pores in the membrane. High flux dialysers have larger pores and are designed to allow middle molecules as well as small molecules to be removed. Low flux dialysers only allow removal of small molecules. High flux dialysers are now the recommended standard for haemodialysis, to allow this middle molecule removal (Mactier et al. 2009). High flux dialysers are also required for HDF, to allow the volume of fluid to pass over the membrane that is required for the fluid exchange.
- biocompatibility.
Membrane biocompatibility is considered the ability of the membrane to minimise the complement activation caused by the artificial nature of the membrane (Clark et al. 1999). In simpler terms, it is the ability of the membrane to minimise the reaction to the artificial membrane. In the last few decades, work has been focussed on reducing complement activation from the membrane whilst also reducing thrombogenicity (ability to promote clotting), as described by Clark et al. (1999).

Whilst the latest Renal Association Guidelines (Mactier et al. 2009) promote the use of modified cellulose and synthetic membranes, current practice has moved to the use of synthetic membranes. Currently, these include AN69 ST, polysulfone, and polyamide membranes. The majority of membranes have a similar level of biocompatibility, although if reaction to one membrane is suspected then movement to another membrane is recommended. There have been case studies demonstrating the successful use of the AN69 ST membrane following reactions to other membranes (e.g. Coentrão et al. 2010), indicating this is a more biocompatible membrane. Due the rarity of a dialyser reaction, this has never been tested further than individual case studies.

Haemodialysis clearance

There are many aspects of the haemodialysis prescription that can be altered. One focus of the haemodialysis prescription is to achieve the level of clearance of solutes that the individual requires. This was previously known as adequacy, but adequacy has become a more inclusive term to encompass all aspects of haemodialysis. Now the term adequacy has been replaced by the term clearance and describes how much effective haemodialysis is achieved. This section will examine how to best measure the clearance, and how to control or maximise this clearance to achieve the best outcomes for patients.

Kt/V and Urea reduction ratio

Haemodialysis clearance can be measured in two ways – Kt/V or URR. Both methods are currently in use within the UK and both have advantages and disadvantages. Both Kt/V and URR measure urea clearance during a haemodialysis treatment but contextualise and express this in different ways.

Kt/V is an equation. It produces a ratio to describe urea clearance in a haemodialysis treatment. The equation is expressed as follows:

$$\frac{\text{Urea Clearance (K) (in mls / min)} \times \text{Time (t) (in mins)}}{\text{Distribution volume (V) (mls)}}$$

The distribution volume is the volume of body water in the body and is included in Kt/V to allow for the fact that urea is stored in all water within the body and not just within the blood.

URR measures the percentage reduction of urea during a haemodialysis treatment. Kt/V and URR both gained significance in the early 1990s, when large multicentre studies within the US demonstrated that achieving a significant level of Kt/V or URR led to improved survival for haemodialysis patients (Held et al. 1996; Parker et al. 1994). UK Renal Association guidelines (Mactier et al. 2009) recommend that patients dialysing thrice weekly should have a Kt/V greater than 1.2 and an URR greater than 65%.

These levels have been associated with the best patient outcomes, although there is some debate whether achieving higher clearance levels than this will lead to better outcomes. The UK Renal Registry report (Davenport et al. 2017) compares URR achievement between units within the UK, but does not report Kt/V.

Measurement of URR and Kt/V

Kt/V or URR are normally measured by taking a urea level before and after dialysis, thus identifying how much urea is removed during treatment. Whilst this seems a simple procedure, the post-dialysis sample requires consideration. Following haemodialysis, solute levels within the blood experience a phenomenon known as

BOX 8.2**Urea rebound**

During haemodialysis, solutes are removed from the blood. However, solutes are also stored outside of blood, in water in other compartments in the body (i.e. interstitial fluid, intracellular fluid)

In haemodialysis:

- urea is removed from the blood during haemodialysis
- the urea level in the blood is then lower than the urea level in the interstitial and intracellular fluids
- diffusion pulls urea from the interstitial and intracellular fluid into the blood.

Following haemodialysis:

- the urea level in the blood is lower than the urea level in the interstitial and intracellular fluid
- therefore, urea is pulled from these fluids and into the blood for one to two hours after haemodialysis until the level is equal in all three fluids.

This means the blood urea level directly after haemodialysis is falsely low and will 'rebound' up in the first two hours after haemodialysis.

'rebound', which is described in Box 8.2. This means the urea level post-haemodialysis is falsely low and will overestimate the URR or Kt/V.

To compensate for urea rebound various post-haemodialysis sampling techniques have been developed. These involve either slowing the blood pump speed prior to disconnection from haemodialysis or stopping the dialysate flow before taking the post-dialysis sample (Mactier et al. 2009). Individual unit policy can vary and there is no one single recommended method for taking the post-dialysis blood sample.

Kt/V can also be measured through an online clearance monitor present on the majority haemodialysis machines. These come in a variety of forms, but have the advantages including:

- provision of a real-time measurement of Kt/V – this makes it easier to relate actions in the treatment to the Kt/V result. For example, the effect of increasing BFRs during treatment can be directly observed, providing valuable feedback to the nursing staff running the haemodialysis session.
- provision of a reading at every haemodialysis session. McIntyre et al. (2003) found that Kt/V readings vary from adequate to inadequate over a four-week period in 55% of patients. This indicates that a monthly assessment of Kt/V via blood samples does not provide a true reflection of the haemodialysis dose the patient has received over the month.

Improving clearance

Regardless of whether Kt/V or URR is measured, the general theme is that haemodialysis clearance needs to be optimised for individual patients. The optimisation should occur within a minimum haemodialysis regime of four hours of thrice weekly haemodialysis (Mactier et al. 2009).

Within a single haemodialysis treatment there are a number of factors that can affect the clearance and be altered to improve clearance:

Dialyser size Increasing the dialyser size can serve to increase the clearance.

Blood flow rate BFR affects clearance through a very simple principle that the faster the BFR, the more blood is processed in the haemodialysis treatment. This

means more blood is exposed to the dialyser membrane in the treatment time and clearance improves. BFR is considered the factor that can have the most effect on clearance. Lambie et al. (2004) found that higher BFR lead to a better clearance. Borzou et al.'s (2009) study demonstrates that a relatively small increase in BFR from 200 to 250 ml min⁻¹ had a significant effect on improving both URR and Kt/V. There has also been a direct link between BFR and mortality, where BFRs lower than 250 ml min⁻¹ have been associated with higher mortality rates (Chang et al. 2016).

However, the relationship between BFR and clearance is not linear, with the benefits of increasing BFR reducing as higher BFR are achieved. This could be related to a number of hypotheses:

- the blood requires time in the dialyser for diffusion. The faster the blood moves through the dialyser, the less time is available for diffusion, so there may be a point where higher BFR does not lead to more diffusion.
- higher flow rates are associated with higher arterial pressures. Higher flow rates and arterial pressures can increase vascular access recirculation, ultimately reducing the clearance.

There is often an optimal BFR that obtains the best clearance. Within the UK, adequate BFRs can vary between 200 and 500 ml min⁻¹. However, there is significant variation in unit policy. Haemodialysis nurses can be reticent to increase BFRs due to concerns of pressure alarms and effect on patient stability which is often unfounded (Lambie et al. 2004). With the advent of online clearance monitors, it is now easy for haemodialysis nurses to assess the effect of changes in BFR on the clearance during the haemodialysis session. Currently this is rarely used in practice, but could be used to identify the optimal BFR to obtain the optimum clearance. Haemodialysis nurses need to consider what is the best BFR for individual patients, that maximises clearance, rather than adhering to rigid policies.

Dialysate flow rate Dialysate flow rates can also be used to improve clearance. The higher the dialysate flow rate the better the clearance (Hauk et al. 2000). Currently haemodialysis machines can vary the dialysate flow rate from 300 to 800 ml min⁻¹. Higher dialysate flow rates can be used to improve clearance and lower dialysate flow rates used to slow clearance, for example in nocturnal haemodialysis.

Vascular access recirculation Zeraati et al. (2013) define vascular access recirculation as 'some of the dialysed blood leaving the dialyser through the venous needle, re-enters the dialyser through the arterial side'. This reduces clearance as previously dialysed blood enters the dialyser again. In reality, an element of recirculation happens in all haemodialysis treatments, but the aim is to minimise this. Vascular access recirculation is often expressed as a percentage of the total blood dialysed.

Factors that affect vascular access recirculation include:

- vascular access type – recirculation happens to a higher extent with CVC due to the proximity of arterial and venous lumens in the same vein.
- position of needles within AVF/AVG (Zeraati et al. 2013). The arterial and venous needle should be at least 2 inches apart to minimise recirculation between the two needles.
- presence of venous stenosis promotes back flow in the AVF/AVG increasing recirculation (Zeraati et al. 2013).
- inadequate flow in the AVF/AVG that is lower than the blood pump speed (Zeraati et al. 2013).

Many of these factors are related to vascular access function. Recognition of poor vascular access function can allow referral to improve this.

Single-needle or double-needle dialysis Single-needle dialysis uses one point of access into the circulation for haemodialysis. This could be one needle or a single-lumen CVC. Consequently, double-needle dialysis is when two points of access are used either via two needles or a dual-lumen CVC. Single-needle dialysis will usually lead to poorer clearance than double-needle dialysis, for two reasons:

- vascular access recirculation is increased in single-needle dialysis, as only one lumen is used to return and remove the blood.
- BFRs are lower due to the configuration of single-needle dialysis to minimise access recirculation.

Single-needle dialysis should only be used temporarily for haemodialysis treatments, as this does not provide adequate clearance for long-term treatments.

Clotting in the dialyser Adequate anticoagulation of the dialyser is essential to maintain clearance throughout the haemodialysis treatment. Clots that form on the membrane of the dialyser serve to block diffusion. Therefore, the anticoagulation regime is essential to maintain the function of the dialyser through the treatment. Priming of the dialyser is also essential. Air pockets in the dialyser during haemodialysis promote clot formation on the membrane and reduce clearance. The priming process needs to ensure all air is removed from the dialyser prior to commencing haemodialysis.

The renal nurse's role in maintaining an optimal haemodialysis prescription

Elements of the haemodialysis prescription that will change over long periods of time and are often assessed monthly have been discussed in previous sections. The variations discussed so far are often made following assessment of U&E results, plus URR and Kt/V. Changes to the prescription can then be made to the equipment used for haemodialysis and the prescription programmed into the machine. These elements are often managed by consultant nephrologists and/or senior haemodialysis nurses. The role of the junior haemodialysis nurse in this situation is to have awareness of what may need to change, refer to more senior colleagues for advice, and understand how to implement changes and why they may be necessary.

Many aspects of the haemodialysis prescription may change on a day-to-day basis. Due to more frequent variation, assessment, and decisions to change these aspects is within the role of all haemodialysis nurses.

Fluid removal

Assessment of correct fluid removal for haemodialysis is an essential role of haemodialysis nursing staff. The amount of fluid removed during each haemodialysis session can fluctuate in between sessions, alongside how well patients tolerate the fluid removal. For each session, haemodialysis nurses need to determine how much fluid to remove and how to do this in a safe manner for the patient. The dry weight (also known as target weight or ideal weight) is normally used to determine the amount of fluid to remove.

The challenge of fluid removal

Most instability during haemodialysis is caused by fluid removal. Unless another cause is known, low blood pressure during haemodialysis (intra-dialytic hypotension

[IDH]) is normally attributed to poor tolerance of fluid removal and is the most frequent adverse event during haemodialysis (Davenport 2009a). An audit of adverse events during haemodialysis identified that hypotension was the most common adverse event during haemodialysis and accounted for 29.3% of all adverse events during haemodialysis treatments (Fielding et al. 2016a).

Ensuring stability during haemodialysis requires management of multiple aspects. IDH can be related to UFR, which is dictated by the amount of fluid to be removed, and the accuracy of the dry weight, which ensures the correct amount of fluid is removed (Davenport 2006). The patient needs to be monitored through treatment for signs of IDH and poor tolerance of fluid removal. IDH should always be treated promptly with reduction in UFR to minimum levels, saline bolus of 100–200 ml, and reclining the patient (Davenport 2009a).

Dry weight assessment

Fluid removal during haemodialysis is normally dictated by the dry weight. Patients' weight prior to haemodialysis treatments and how much they are over their dry weight indicates how much excess fluid is present, which needs to be removed. 1 g of body weight is equivalent to 1 ml of fluid (1 kg of body weight is equivalent to 1 l of fluid).

To ensure fluid removal programming is accurate, the dry weight needs to be accurate. The dry weight indicates the weight the patient should be at euvolaemia, without any excess fluid present and without any dehydration. However, dry weight can fluctuate as patients gain and lose body mass, through muscle and fat changes, so the dry weight requires frequent assessment. Indications that dry weight requires adjustment are summarised in Figure 8.10.

Dry weight assessment can be complex. Other comorbidities can affect the dry weight assessment, including cardiac disease which is common in patients with kidney disease. Symptoms during haemodialysis can also be caused by high UFR rather than a need to adjust dry weight. Haemodialysis nurses need to gain the

Factor	Indication	Related Signs and Symptoms
Blood pressure	Low usually indicates need to increase dry weight	• Dizziness • Vomiting • Unresponsive / fainting • Instability on haemodialysis
	High indicates need to decrease dry weight	• Headache
Oedema	Ankle oedema or pulmonary oedema indicates need to decrease dry weight	• Ankle swelling with pitting oedema • Shortness of breath • Cough with white frothy sputum • Inability to lie flat
Appetite	Reduction indicates need to decrease dry weight	Patient reported change in appetite
	Increase indicates need to increase dry weight	
Changing fluid status	Decreasing fluid gains indicate need to decrease dry weight	Patient reports no change in fluid intake
	Increasing fluid gains indicate need to increase dry weight	
Cramps	Cramps indicate need to increase dry weight	Muscle cramps during haemodialysis in the absence of high ultrafiltration rates

Figure 8.10 Indicators that dry weight requires adjustment.

skills of dry weight assessment and identify any changes in dry weight promptly, to prevent IDH from inaccurate fluid removal. In particular, nurses need to learn to consider all pertinent factors that can affect the assessment of dry weight, including the trends of change, rather than overly relying on assessment of one factor.

Accurate dry weight assessment is crucial for haemodialysis. IDH is frequent, but also harmful to patients' long-term outcomes. McIntyre (2010) describes how improving stability of haemodialysis reduces damage to the heart during haemodialysis. IDH also causes distressing symptoms, discomfort, and anxiety for patients. However, the effects of fluid overload also need to be limited. As patients are usually unable to excrete excess fluid, even if post-haemodialysis treatment euvolaemia is achieved, once the patient drinks or eats again they become fluid overloaded. This fluid stays in their system until the next haemodialysis treatment. Patients are often prone to left ventricular hypertrophy due to a number of reasons, one of which is the stress from fluid overload. Cardiac disease continues to be the leading cause of death in patients undergoing dialysis, although the rate is reducing (Methven et al. 2017). However, ensuring accurate dry weight will reduce the stress and damage caused to the heart during haemodialysis and in between haemodialysis sessions.

Technology may be developing to assist in the assessment of dry weight. Bioimpedance technology works using electrical currents to estimate the volume of extracellular water. This assessment indicates whether a patient is over- or under-loaded with fluid and can estimate by how much. Initial studies have shown that bioimpedance measurements are objective and accurate in assessing dry weight (Moissl et al. 2013; Onofriescu et al. 2012; Wabel et al. 2009). Within the UK the BISTRO clinical trial is evaluating the use of bioimpedance to assess dry weight (www.keele.ac.uk/bistro) on a larger scale.

Managing fluid loss

Prior to each haemodialysis session, the nurse needs to determine the correct fluid to remove from the patient. Whilst the dry weight can be used to determine what should be removed, the haemodialysis nurse also needs to assess whether the patient will tolerate the volume of fluid to be removed in the treatment time. Haemodialysis can only remove fluid from the blood, as not all fluid within the body is stored in the vascular space. Fluid is also stored in the cells (intracellular space) and around the cells (interstitial space) (Figure 8.11). As excess fluid builds in the body, fluid distributes between these three spaces. As fluid is removed from the vascular space, the blood becomes more concentrated and pulls fluid from the interstitial and intracellular spaces by osmosis. This process is known as 'refilling' (Figure 8.12).

To be able to remove all the excess fluid from each compartment, refilling needs to occur (Davenport 2009a). The best way to describe this process in haemodialysis is to explore what happens in the three fluid compartments (see Figure 8.11).

Prior to haemodialysis, excess fluid equilibrates across all 3 fluid compartments. Once haemodialysis is commenced, fluid is removed from the vascular compartment reducing the volume in this compartment. As fluid is removed from the vascular space, this fluid becomes more concentrated so draws fluid from the ICF and IF compartments. This reduces the volume in the ICF and IF compartments. At the end of haemodialysis, the excess fluid has been removed from all three compartments.

In Figure 8.12, ICF represents the volume in the intracellular compartment, IF represents the volume in the interstitial compartment, and V represents the volume in the vascular compartment.

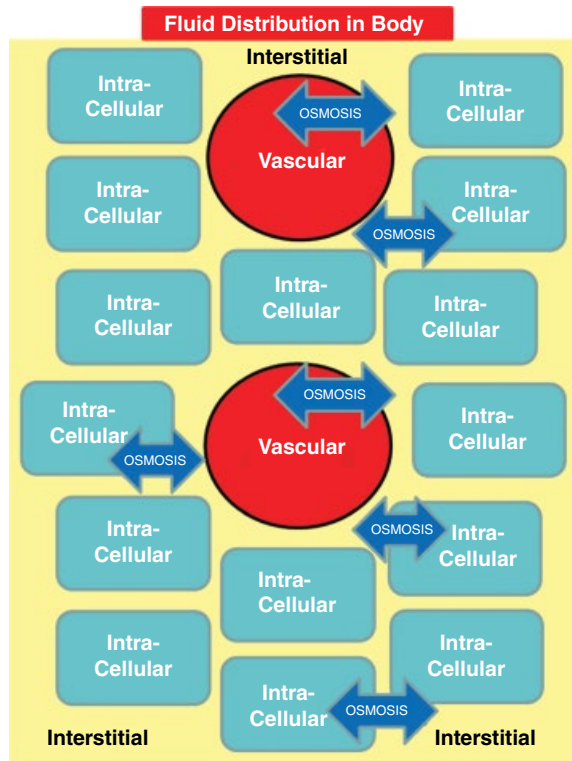


Figure 8.11 Fluid distribution in the body.

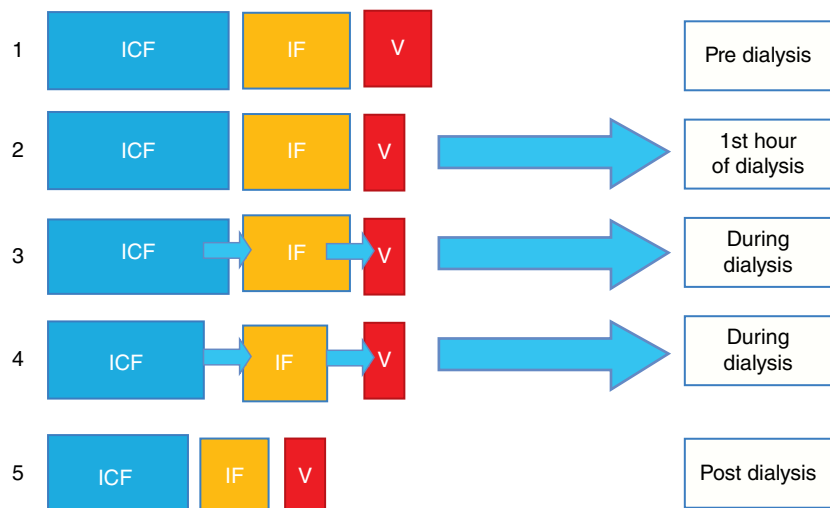


Figure 8.12 Refilling during haemodialysis.

Ideally this process should happen in a manner that ensures the volume in the vascular compartment is maintained, preventing IDH. When UFR exceeds the refilling rate, the volume in the vascular space reduces through treatment, making it harder to maintain the blood pressure (Figure 8.13). Post-haemodialysis the volume in the vascular compartment will return as refilling catches up with the fluid removal, but then each compartment has excess fluid present.

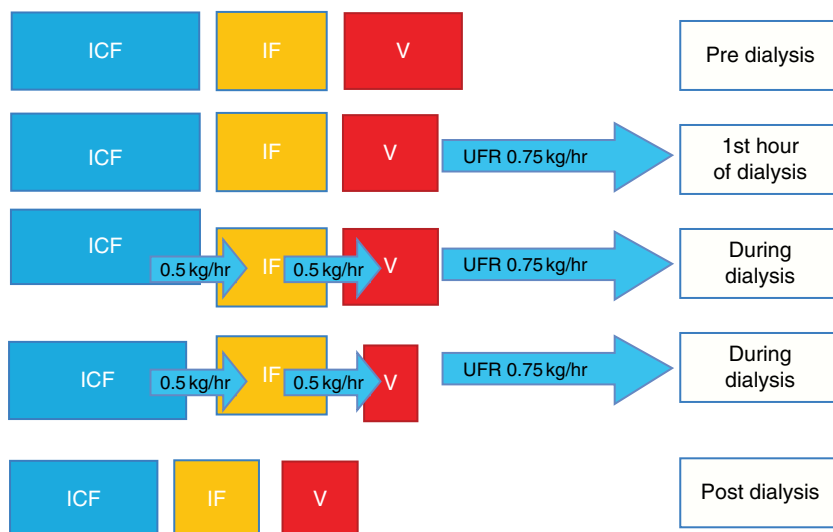


Figure 8.13 What happens when the refilling rate is lower than the ultrafiltration rate (UFR).

It is important to manage the UFR and refilling rate to maintain stability through haemodialysis (Davenport 2009a). Not only does this ensure stability through haemodialysis, but lower UFRs are associated with reduced mortality (Saran et al. 2006) and less cardiac damage (Jefferies et al. 2011) for haemodialysis patients.

Managing the UFR

There are a number of things that can be done to help minimise the UFR. These include:

- managing IDWG – the less fluid the patient has to lose in the prescribed dialysis time, the lower the UFR will be. Patients are often advised on fluid allowances to manage IDWG. These allowances vary between 500 and 1000 ml in 24 hours, plus whatever their 24-hour normal urine output is. However, a low fluid allowance can be difficult for patients to adhere to, so advice about thirst management is critical.

Thirst can be managed by:

- reducing the sodium in the dialysate;
- reducing the sodium in the diet through reduction of salt (Davenport 2009a; Penne et al. 2010);
- ensuring good blood sugar control in patients with diabetes (Davenport 2009a; JBDS-IP 2016);
- reviewing diet for hidden fluid;
- using ice cubes, smaller cups, etc. to assist patients in managing their fluid intake;
- advising use of a jug to hold the total fluid allowance for that day, and then removing the equivalent amount of fluid as each drink is consumed.
- increasing the treatment time – the longer the treatment time, the lower the UFR required to remove the fluid.
- reducing the fluid removal gradually – this means that patients complete haemodialysis with extra fluid still present. This approach can achieve improved fluid removal over a longer period of time and reduces the risk of instability in the short term (which can necessitate a fluid bolus and minimal UFR). Also, IDH

can trigger the thirst mechanism leading to larger IDWGs. Maintaining stability not only improves clinical outcomes, but also assists in managing IDWG and ensures the planned fluid removal happens accurately.

Managing refilling

As well as managing the UFR to minimise IDH, actions can be taken during haemodialysis to encourage refilling. These actions are:

- recline the patient and raise legs – as well as reducing the effect of gravity on the blood supply to the head and central core, reclining the patient also promotes refilling.
- use of isolated UF – this also promotes refilling during isolated UF and the effect can prolong into haemodialysis. Isolated UF is the process of only removing fluid in the dialyser. UF only occurs in the dialyser, so no dialysate or diffusion is utilised. Solutes are left behind in the blood and not removed. This leads to haemoconcentration within the blood which triggers the refilling process more rapidly. This allows greater volumes of fluid to be removed more rapidly and tolerated better by patients. Often isolated UF is used at the start of haemodialysis treatments to remove fluid rapidly. The use of isolated UF should come with two cautionary notes:
 - no diffusion occurs during isolated UF, so this should not be included as part of the haemodialysis time and does not contribute to the Kt/V .
 - solutes become more concentrated in the blood with isolated UF, so hyperkalaemia is a risk. Isolated UF should never be used initially with patients with high potassium. Haemodialysis, with diffusion, is the priority.
- maintaining an adequate albumin and haemoglobin – albumin and haemoglobin help promote refilling. They create osmotic potential in the plasma to encourage refilling. Haemodialysis nurses should be aware that when these levels are low, patients are less likely to tolerate fluid removal.

Dialysate temperature

The dialysate temperature can also be used to reduce IDH. This is the temperature that the dialysate is warmed to before it enters the dialyser. It fulfils the purpose of maintaining body temperature within the blood in the extracorporeal circuit, thus preventing hypothermia from cold blood re-entering the patient. Traditionally the dialysate temperature has been set at 37°C. However recent studies have indicated this is not best option for the majority of patients (Roumelioti and Unruh 2015). Setting the standard dialysate temperature at 37°C is above the majority of people's core temperature. This then means the patient is warmed, causing vasodilation and exacerbating IDH (Davenport 2009a). Studies have examined what is the best dialysate temperature to use. Van der Sande et al. (2009) found that cooling the dialysate temperature 0.5°C below body temperature reduces IDH in patients with a history of hypotension. Selby et al. (2006a) found that using a dialysate temperature of 35°C reduced hypotensive episodes, improved blood pressure, and reduced cardiac stunning during haemodialysis. A systematic review identified similar results (Selby and McIntyre 2006).

However, the case for cooling the dialysate or running it below 37°C is not as clear cut as this. There have been concerns that reducing the dialysate temperature will alter kinetics in the dialyser and reduce the movement and clearance of molecules. It has been identified that cooler dialysate does not affect the clearance of small molecules (Selby and McIntyre 2006b). However, the effect on middle molecule

clearance is not known and under investigation by Maheshwari et al. (2015). Van der Sande et al. (2009) also found that cooling the dialysate could lead to shivering and cold symptoms during haemodialysis, making patients feel uncomfortable. Tsujimoto et al. (2017) are undertaking a Cochrane systematic review to identify the benefits and harm of cooling the dialysate.

Current opinion suggests that cooling the dialysate is an intervention that can be used to manage frequent IDH events (Davenport 2006; Roumelioti and Unruh 2015). However, whether this practice should be applied routinely is still unknown.

Blood volume monitoring

Blood volume monitoring has been promoted as a tool to predict IDH. It monitors the concentration of the blood, providing a blood volume reading which is tracked over the period of the haemodialysis treatment. It works under the assumption that if the blood is becoming more concentrated then there is less volume on the vascular compartment. It can be used to identify how well refilling keeps up with the UFR. If it becomes too negative, then this indicates the patient could drop their blood pressure. However, the value of blood volume readings is in question. Booth et al. (2011) identified little correlation between the blood volume reading and blood pressure. Often much emphasis is placed on the blood volume reading, when in reality, it is only one tool that adds to the nursing assessment of the patient.

Summary of managing fluid removal during haemodialysis

Managing fluid loss in haemodialysis is more complex than calculating differences between dry and pre-dialysis weight. Haemodialysis nurses need to assess the correct amount and method of fluid removal for patients and ensure the target weight is accurate. Whilst changes in fluid status will occur slowly over time, haemodialysis nurses need to be vigilant to indications that the dry weight is changing. Poor management of fluid removal in haemodialysis can lead to rapid instability in haemodialysis, so it is critical that haemodialysis nurses manage this well.

Anticoagulation

The final aspect of the haemodialysis prescription to be examined is anticoagulation. During haemodialysis a number of mechanisms trigger the clotting cascade and fibrin formation in the extracorporeal circuit. The mechanism for triggering the clotting cascade is complex, with causes including contact with foreign plastics in the circuit, sheer stress caused by vascular access use and the blood pump action (Davenport 2009b), cooling in the extracorporeal circuit, and stasis during blood pump stoppages and chambers. To counteract clotting within the circuit, heparin is normally administered into the arterial side of the circuit, either in the form of unfractionated heparin or low-molecular weight heparin (LMWH). Whilst both are valid ways of preventing clotting in the extracorporeal circuit, the latter has simplified this. However, the renal nurse has an essential role to protect patients from the risks associated with anticoagulation administration alongside balancing the prevention of clotting within the circuit. This next section will examine:

- what is challenging about managing clotting within the extracorporeal circuit;
- how nurses monitor and manage clotting;
- what else can be used to minimise clotting.

Managing clotting within the circuit is a balancing process between minimising clotting in the circuit whilst not creating or exacerbating a bleeding risk in patients. Clotting can have many detrimental effects during a haemodialysis treatment, including:

- blockage of the circuit from clots, preventing flow through the circuit.
- exacerbation of anaemia, caused by blood loss in the circuit either when:
 - The circuit becomes completely blocked preventing washback;
 - Clots left behind during washback which contain vital haemoglobin.
- frequent alarms and blood pump stoppages due to pressure in the circuit. This will exacerbate clotting further and is also distressing for patients attached the circuit.
- reduction in clearance.
- reduction in vascular access function due to fibrin formation in vascular access. CVC are vulnerable to loss of function due to inadequate anticoagulation of the extracorporeal circuit.

As can be seen, clotting is more than just an inconvenience during haemodialysis treatments, but also affects the efficacy of the treatment, exacerbates anaemia and vascular access problems, and is distressing for the patient.

Managing clotting within the extracorporeal circuit

Managing clotting can be through the administration of heparin, whether it be unfractionated heparin or LMWH. Heparin requirements can be assessed in a number of ways:

- assessment of clotting directly in the circuit through:
 - inspection following washback – ideally the circuit should be clear, with minimal clotting in chambers and minimal streaking in the dialyser;
 - inspection during treatment for signs of clotting (Davenport 2009b).
- pressure monitoring during treatment, as pressures will rise with increased clotting. This is often a late sign of clotting and difficult to rectify.
- decline in online clearance readings during treatment – this is normally due to clotting.
- excessive bleeding following needle removal, which indicates too much heparin was administered (Davenport 2009b).
- use of clotting times through lab tests or bedside clotting block – these tests are only effective with unfractionated heparin but allow real-time adjustments through treatment (Mactier et al. 2009).
- using the patient's weight in conjunction with assessment of the circuit, which can be used to dose LMWH (Davenport 2009b).
- using a standard dose, as recommended with tinzaparin use (Davenport 2009b).

Prevention of clotting is essential to maintain the haemodialysis treatment, but using anticoagulation to do this needs to be balanced with the bleeding risk this introduces, as highlighted by Davenport (2006). In the majority of patients this requires the use of the minimum amount of heparin needed to prevent clotting.

Anticoagulation interrupts clot formation, which is used to prevent clot formation in the extracorporeal circuit. However, the anticoagulation will enter the patient's systemic circulation via the extracorporeal circuit, so will also anticoagulate the patient. The risk is minor, but whilst the patient is anticoagulated, bleeding will be harder to stop. UK Renal Association Guidelines recommend that unfractionated

heparin or LMWH can be used for patients without increased bleeding risk, but these should be avoided in patients with a high risk of bleeding or heparin-induced thrombocytopenia (HIT) (Mactier et al. 2009). Therefore, haemodialysis nurses need to ensure that anticoagulation is only administered to patients with no known bleeding risk.

Sometimes bleeding is not evident, so haemodialysis nurses need to be aware of the situations where patient may be deemed to have a high bleeding risk, so heparin can be avoided. Signs of a high bleeding risk without observed bleeding can include:

- head injury or altered mental neurological status;
- coffee ground vomit;
- melaena or black faeces;
- liver failure;
- raised INR or low platelet level;
- unexplained bruising;
- fractures or after falls;
- post-surgery or post-procedure.

If heparin cannot be administered to patients then high BFR and boluses of saline directly into the arterial side of the extracorporeal circuit can be used to minimise clotting in the circuit (Mactier et al. 2009). The volume of saline administered can be added to the fluid removal during haemodialysis. However, high BFRs are not always possible, especially if the vascular access will not allow this or the patient has a risk of disequilibrium syndrome. Sometimes these actions will not prevent clotting of the circuit and the circuit needs to be changed mid-treatment. Ideally the circuit should be changed before the washback is lost, to prevent blood loss from the haemodialysis patient.

Citrate anticoagulation has been suggested as an alternative to heparin use in the patient with a high bleeding risk (Mactier et al. 2009), especially as it is easy to reverse the effects through a calcium infusion (Davenport 2006). Citrate anticoagulation reduces calcium levels and creates a risk of cardiac arrhythmias due to hypocalcaemia. Whilst this can be managed with calcium infusions, this is difficult to do well in a non-critical care environment (Clark et al. 2008).

Unfractionated v. LMWH

There has been debate as to whether unfractionated heparin or LMWH is the best heparin to use to manage clotting in haemodialysis treatments. There are many advantages and disadvantages, which are summarised in Figure 8.14. LMWH has less detrimental effects than unfractionated heparin, but is more expensive and systemically present in the circulation for longer, in theory creating a bleeding risk. Various studies have been performed to compare LMWH to unfractionated heparin and have found LMWH does not lead to a higher bleeding risk and can compare in cost (Berneih et al. 2009; Bramham et al. 2008; Hoy et al. 2010). One study also identifies that with high flux membranes, LMWH is removed through treatment reducing the systemic affect post haemodialysis (Sombolos et al. 2009).

Heparin-induced thrombocytopenia (HIT)

Occasionally, haemodialysis patients can develop HIT from heparin use (Davenport 2009b). Although rare, nurses need to be aware how to manage these patients. HIT is normally an immunological condition where the body has created antibodies against heparin (Chong 2003). Whilst thrombosis and acute

Unfractionated Heparin	Low-Molecular Weight Heparin
Short half-life, so removed systematically promptly (Davenport, 2009b)	Longer half-life, so stay active systematically for longer (Davenport, 2009b)
Require continuous infusion throughout treatment	One-off bolus at start of treatment
Dosing can be changed through treatment in response to clotting	Dosing can only be changed in between treatment in response to clotting
Protamine is more effective as an antidote, to reverse the effects of anticoagulation (Davenport, 2009b)	Protamine is less effective with LMWH (Davenport, 2009b)
Higher interference with lipid metabolism, worsening lipid profiles (Davenport, 2009b)	Less interference with lipid metabolism, leading to improved lipid profiles (Davenport, 2009b)
Increase in osteoporosis (Davenport, 2009b) NB. Only proven in pregnant women	Less incidence of osteoporosis (Davenport, 2009b)
Slightly higher frequency of HIT (Davenport, 2009b)	HIT is less frequent (Davenport, 2009b)
Lower cost (Davenport, 2009b)	Higher cost (Davenport, 2009b)
Less convenient to dose and administer (Mactier et al, 2009)	More convenient to dose and administer (Mactier et al, 2009)

Figure 8.14 Unfractionated heparin v. LMWH.

systemic sensitivity reactions are often mentioned as signs of HIT, patients often present with a low platelet count or a purpuric (non-blanching) rash. Heparin administration should stop immediately as this can escalate to anaphylactic-type reactions to the heparin (Chong 2003). HIT is a reaction to all heparin, so HIT developed from unfractionated heparin is also likely to escalate if the patient is then transferred onto LMWH (Mactier et al. 2009). Alternative anticoagulants that can be used in the presence of HIT include lepirudin or danaparoid (Chong 2003; Mactier et al. 2009).

Whilst anticoagulation management is often seen as the remit of medical staff, as it is a prescribed drug, haemodialysis nurses are often the personnel that monitor the effect of anticoagulation on haemodialysis. Nurses have a responsibility to dispense medications in the context of treatments and other healthcare needs (Nursing and Midwifery Council 2015). For haemodialysis nurses this means managing anticoagulation to minimise clotting in the circuit, avoiding heparin use due to an identified, often transient, bleeding risk, and managing clotting with alternatives to heparin. Haemodialysis nurses need to be aware of all these factors to ensure patients receive haemodialysis where the actions to minimise clotting are considered against the bleeding risk introduced to patients.

Vascular Access for Haemodialysis

Vascular access is a large and important aspect of haemodialysis. Vascular access provides the means to remove and return the blood in and out of the circulation. Vascular access is often referred to as the cornerstone of haemodialysis, as without it haemodialysis cannot be performed. However, vascular access continues to be a

point of vulnerability in haemodialysis care. UK Renal Association guidelines on vascular access summarise this challenge:

Vascular access should be easy to use, reliable and have minimal risk to the individual receiving haemodialysis. However, the provision of good quality access, whilst it is a fundamental aspect of the treatment of haemodialysis patients, remains difficult to achieve. (Kumwenda et al. 2015)

There are three types of vascular access used for haemodialysis: AVF, AVG, and tunnelled CVCs. The types of vascular access are summarised in Box 8.3. However, no type of vascular access is perfect with different complications associated with each type of vascular access. Figure 8.17 summarises the complications associated with each type of vascular access.

AVF is considered the best option for haemodialysis, as it is associated with the lowest mortality rate, the least complications, and has the best longevity (Almasri et al. 2016; Kumwenda et al. 2015; Ng et al. 2011). AVG is the second-best option, as mortality, complications, and longevity are worse than AVF but better than a tunnelled CVC (Almasri et al. 2016; Kumwenda et al. 2015; Ng et al. 2011). However, whilst AVG may be associated with slightly worse outcomes than AVF, AVGs are used when an AVF is not feasible, so selection bias tends to confound studies comparing outcomes from AVF and AVG (Almasri et al. 2016). A tunnelled CVC is the third-best option but is associated with highest rate of mortality, complications, and the worst longevity (Almasri et al. 2016; Kumwenda et al. 2015; Ng et al. 2011). In particular, the use of tunnelled CVCs for haemodialysis is associated with much higher risk of infection and higher hospitalisation rate (Ng et al. 2011).

The UK Renal Association standards recommend that 80% of the dialysis population should dialyse via definitive access, which includes AVF, AVG, and Tenckhoff catheters (for peritoneal dialysis). Sixty percent of new patients should dialyse via an AVF or AVG (Kumwenda et al. 2015). However, the latest figures from the UK from 2015 demonstrate that many units are not meeting these standards and there is large variation in vascular access provision across the UK (Hole et al. 2017). A similar variation in practice is demonstrated internationally between countries in the DOPPS (Port et al. 2017). Japan and Russia maintain a high rate of AVF use of over 90%, whilst countries like Canada struggle to maintain AVF use above 50% (Port et al. 2017). Interestingly the DOPPS data provide an AVF and AVG rate in the UK of 84%, whereas the UK Renal Registry data estimate this at approximately 69%. The DOPPS only used a selection of UK units to collect data. As there is significant variation across the UK in AVF rates, the difference could be accounted for through the selection of units for the DOPPS data collection (Rao et al. 2016). Due to the strength of evidence that demonstrates better outcomes for patients who use an AVF for haemodialysis, there is much focus on improving AVF rates within the haemodialysis population.

BOX 8.3

Types of vascular access used for haemodialysis

Arteriovenous fistula

This is a surgical joining of an artery to a vein. This allows diversion of the blood supply from the artery to the vein, with strong high flow arterial blood supply in the vein. The vein becomes arterialisised with a higher flow and pressure than is normal for a vein, a larger vein diameter, and thickening of the vein wall. This creates a vessel that provides the high flows required for haemodialysis as well as robust enough to cope with repetitive cannulation for each haemodialysis session over periods of years.

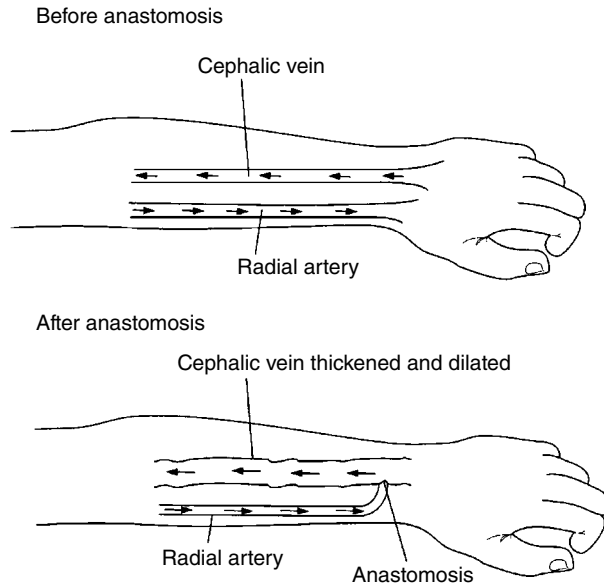


Figure 8.15 Arteriovenous fistula.

Figure 8.15 demonstrates the anatomy of a radiocephalic AVF, attaching the radial artery to the cephalic vein to use the cephalic vein for cannulation. The join between the artery and vein is known as the anastomosis. Other common AVF are brachiocephalic (using the brachial artery connected to the cephalic vein at the elbow) and brachio basilic (using brachial artery connected to the basilic vein). The latter often require superficialisation to raise the basilic vein closer to the skin surface for cannulation.

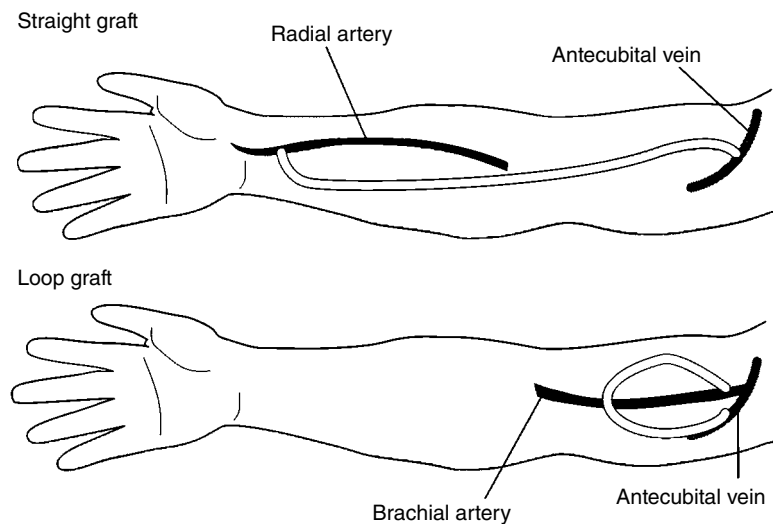


Figure 8.16 Arteriovenous graft.

Arteriovenous graft

This is insertion of a plastic tube between the artery and the vein. PTFE is the common material used, although new plastics are regularly being tested and launched to reduce complications related to AVG use. The latest developments include biosynthetic grafts that use ovine (sheep) collagen (Koens et al. 2015) and early cannulation grafts (Al Shakarchi et al. 2015). Figure 8.16

(Continued)

BOX 8.3 (Continued)

provides an example of a forearm AVG. AVGs can be placed anywhere anatomy can support this (Kumwenda et al. 2015). Leg AVGs are common practice and necklace AVGs can be used where vascular access options are limited. Once inserted AVG care is similar to AVF, with cannulation into the plastic tubing for each haemodialysis session.

Central venous catheter

CVCs are wide bore catheters that sit in a central vein. Common veins used are internal jugular vein and femoral vein. The subclavian vein is normally avoided due to the high risk of developing a central venous stenosis (Kumwenda et al. 2015). CVCs can be tunnelled central venous catheters (TCVC) or non-tunnelled central venous catheters (NTCVC). NTCVC are not recommended for long-term use due to the high infection risk (Kumwenda et al. 2015). TCVCs sit in a subcutaneous tunnel underneath the skin before entering the circulation and include a cuff within the tunnel to maintain the position of the TCVC.

AVF	AVG	TCVC
Infection – lowest rate (Almasri et al, 2016)	Infection (Almasri et al, 2016)	Infection – highest rate (Almasri et al, 2016)
Failure to mature, leading to a high primary failure rate before AVF is cannulated (Al-Jaishi et al, 2016)	Bleeding from degradation of AVG material	Poor flow rate/catheter dysfunction (Kumwenda et al, 2015)
Cannulation complications • Inability to cannulate (van Loon et al, 2009) • Missed cannulation (van Loon et al, 2009) • Pain and associated cannulation anxiety (Figueiredo et al, 2008) • Infiltration and associated bruising / haematoma (van Loon et al, 2009) • Damage to surrounding structures including nerves and arteries		Insertion complications • Damage to surrounding arteries • Air embolism • Cardiac arrhythmias • Pneumothorax • Bleeding and bruising
Aneurysm and stenosis formation from repetitive cannulation (Al-Jaishi et al, 2016)	Aneurysm and stenosis formation from repetitive cannulation (Kumwenda et al, 2015)	Central venous stenosis (Nicholas et al, 2017)
Thrombosis leading to failure – lowest rate (Al-Jaishi et al, 2016)	Thrombosis leading to failure – highest rate (Kumwenda et al, 2015)	Fibrin build up in lumens and fibrin sheath
Steal syndrome causing peripheral limb ischaemia (Al-Jaishi et al, 2016)	Steal syndrome causing peripheral limb ischaemia (Kumwenda et al, 2015)	

Figure 8.17 Complications of the three vascular access types.

Achieving definitive access provision

As the figures tend to indicate, achieving definitive access provision is challenging. The many factors that impact this include:

- patient choice
Patients often make decisions based on the experience of others. McCarthy et al. (2015) identified that vicarious learning from other patient experiences often affects modality choice and the same could be extrapolated for vascular access choice. Similarly, concern then develops that poor experience of cannulation and AVF/AVG use will dissuade patients from having an AVF/AVG. Cavanaugh et al.

(2009) identified that patients with more knowledge about dialysis were more likely to choose an AVF for haemodialysis use. Attention needs to be given as to how patients are prepared to make choices about their vascular access.

- preparation for haemodialysis

As AVF and AVG use requires prior planning, patients who start haemodialysis in an unplanned manner are more likely to use a TCVC for haemodialysis (Hole et al. 2017) and are more likely to remain on a TCVC.

- service structure to ensure timely vascular access provision.

Much work has been done on this in the UK. Oliver et al. (2015) performed an appraisal of vascular access in Scotland, particularly focussing on what led to success. Keys to success include having:

- proper patient support and education about vascular access.
- clear pathways for access formation in a timely manner with allocated surgical and radiological time.
- a co-ordinator to prioritise the correct patients for vascular access surgery.
- regular vascular access MDT meetings.
- adequate assessment and surveillance of AVF/AVG.
- access to radiological support to salvage of failing vascular access.

The British Renal Society's Vascular Access Special Interest Group (BRS VA) performed a survey into vascular access services within the UK (Kumwenda et al. 2017). They identified that much of the required structure is present in renal units across the UK, despite the variation in vascular access provision. This may mean we haven't yet identified what leads to success or that this structure takes time to have an effect on vascular access provision rates.

- well-trained staff to form and care for vascular access

The DOPPS identified that surgical training that included AVF formation led to surgeons who had more successful AVF formation procedures (Goodkin et al. 2010). The DOPPS also identified that vascular access type was associated with centre preference rather than any other factors (Port et al. 2017), indicating staff preference highly dictates vascular access provision. However, vascular access provision is not just about formation but also how you care for the vascular access once in place. In particular, optimum cannulation of an AVF and AVG is widely accepted to affect survival of the AVF/AVG, but cannulation practice continues to vary across the UK (Fielding et al. 2016b). Knowledgeable haemodialysis nurses in the assessment and care of vascular access is essential to maintain good outcomes and longevity of AVF/AVG (Fielding et al. 2016b; Oliver et al. 2015).

- surveillance programmes to detect failing vascular access

The repetitive use of AVF/AVG affects the function of the AVF/AVG, ultimately leading to failure. Surveillance of AVF/AVG is essential to ensure failing access is detected and corrected, before AVF/AVG function is lost completely (Kumwenda et al. 2015; Oliver et al. 2015). An ACCESS algorithm to assist with assessment and surveillance of AVF/AVG has been created (Figure 8.18). This includes basic nursing assessment pre-cannulation through to more complex surveillance measurements that assesses flows through the AVF/AVG and detects stenosis development, allowing pre-emptive correction.

There are many factors that affect the prevalence of AVF and AVG use. These include having adequate formation of AVF/AVG in a timely way in preparation for haemodialysis use, but also preserving the function of the AVF/AVG once in use. Regardless of vascular type used, the complications associated with all vascular access needs to be minimised. Figure 8.19 summarises the many facets associated with promoting AVF/AVG use.

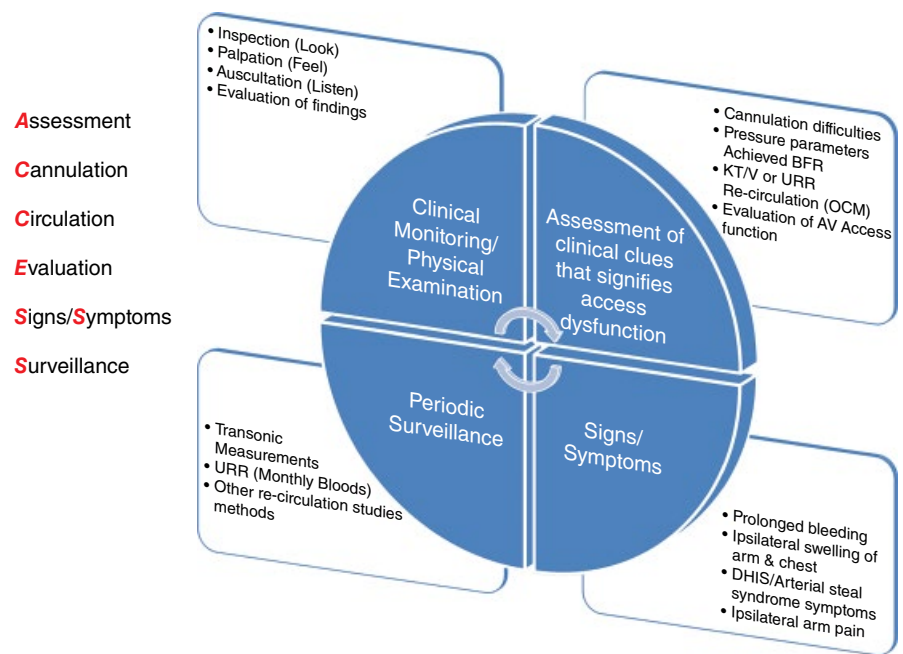


Figure 8.18 ACCESS for assessment and surveillance of AVF/AVG. Source: Reproduced with kind permission from Kristine Paule.

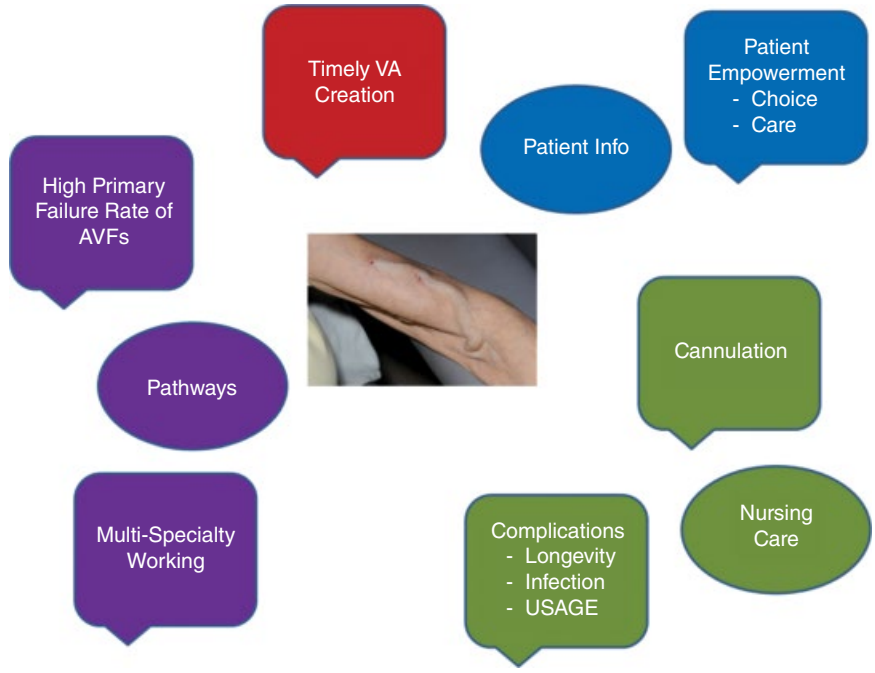


Figure 8.19 Multi-faceted approach to promote AVF/AVG use.

Care of AVF and AVG

Post-operative care

The post-operative care of an AVF/AVG is similar to most post-operative care. The wound from the anastomosis formation needs to remain clean and dry, with a dressing intact until it has healed. This prevents infection at the wound and promotes healing. Often the wound will be stitched either with soluble stitches or non-soluble stitches that need to be removed once the wound has healed. A brachio basilic (upper arm) AVF and AVG may involve more complex wounds, but the principles remain the same. As with any operation, whilst a wound is present there is a bleeding risk from the wound. Consideration needs to be given to management of anticoagulation and clotting of the circuit, and anti-thrombolytic use to treat TCVC dysfunction needs to be avoided at all costs.

There are also more specific considerations when caring for an AVF/AVG post-formation. Firstly, a good blood supply to a newly formed AVF/AVG will help prevent failure from thrombosis and promote maturation of the AVF. Hypotension during or post-haemodialysis can bring about thrombosis of the new and vulnerable AVF/AVG. The dry weight can be increased by 0.5–1 kg for two to four weeks post-AVF/AVG formation to prevent thrombosis of the newly formed access. Also, increased anticoagulation of the haemodialysis circuit may prevent thrombosis of the new AVF/AVG. The haemodialysis nurse needs to use clinical judgement as to which is a priority, preventing bleeding from the wound or minimising clotting in the haemodialysis circuit, which may promote thrombosis of the new AVF/AVG.

Secondly, if the patient has not had an AVF/AVG before, they need to be taught how to care for the AVF/AVG. They need to be shown how to check it is working, by checking the thrill, plus the importance of keeping the wound dry and how to care for their AVF/AVG to avoid failure. Patients should be advised to avoid tight clothing, heavy lifting, BP measurements, and non-haemodialysis related venepuncture or cannulation on their AVF/AVG limb. Once the wounds have healed, the patient can also exercise the AVF to promote maturation of the vein. This involves engorging the AVF vein three to four times a day, using a tourniquet applied lightly, and squeezing their hand for two to three minutes. Often squeeze balls are provided for the patient to do these exercises. This exercise should continue until the AVF is fully mature. AVGs do not need to mature in the same way as AVFs so this exercise is not required.

Cannulation of the AVF/AVG

Once mature, the AVF/AVG will be ready to cannulate for use. Cannulation is critical to the success of AVF and AVG use:

- cannulation needs to be successful to allow use for haemodialysis and obtain optimal flows.
- cannulation damages the AVF/AVG vessel, ultimately leading to failure of the AVF/AVG.
- cannulation affects the patient's experience of haemodialysis.

Cannulation techniques to preserve AVF/AVG function

It is well known that the repetitive nature of cannulation for haemodialysis leads to stenosis and aneurysm formation in the AVF and AVG. Stenosis formation is the main cause of AVF thrombosis as it slows blood flow through the vessel (Fulker et al. 2017). In particular, mechanisms for stenosis development include development

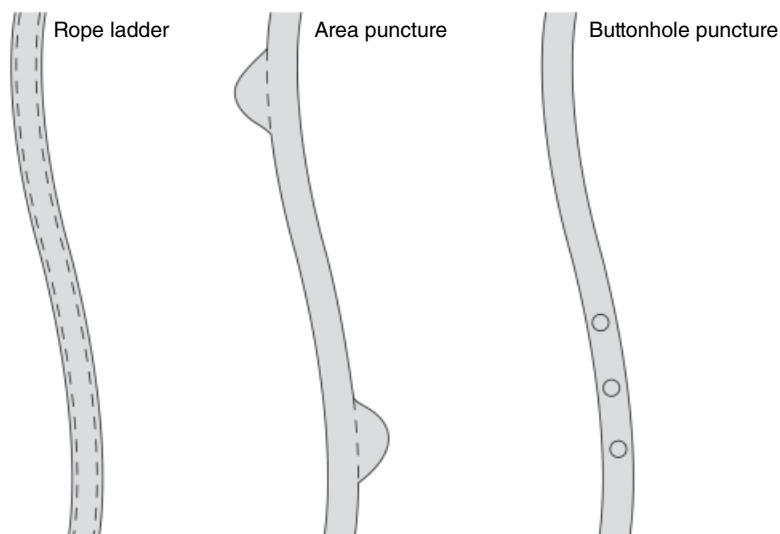


Figure 8.20 Cannulation techniques, as described by Kronung (1984).

of intimal hyperplasia from scarring, inflammation, and turbulent flow in the vessel (Fulker et al. 2017). Aneurysms develop from weakening of the vessel wall from repetitive cannulation and can exacerbate in the presence of an outflow stenosis (Kronung 1984).

Kronung first described three cannulation techniques that either promote or minimise stenosis and aneurysm development (Figure 8.20). These are Rope Ladder, Buttonhole, and Area Puncture. Kronung's (1984) work was based on the presumption that aneurysms and stenoses can be minimised by either maximising the length of the fistula or graft used for cannulation, which he describes as minimising 'punctures per unit area', or by using the same cannulation site each time. This minimises aneurysm and stenosis development. Therefore, Kronung (1984) recommended rope ladder or buttonhole cannulation and avoidance of area puncture. The three techniques are described in the next sections.

Buttonhole technique

The buttonhole technique was first introduced by Twardowski and Kubara (1979). It involves needling each cannulation site in the same manner each time. The needle enters the same hole in the skin, travels the same route to the vein both in depth and direction and then enters the vein at the same point (Fielding et al. 2016b; Pergolotti et al. 2011). This insertion of the needle into the same point develops a track of scar tissue and weak point on the vein wall (Fielding et al. 2016b) (Figure 8.21). The technique involves:

- removal of the scab from the previous needle insertion
- a track development phase where 1–3 of the same nurses cannulate the AVF in the same manner each time
- after 6–12 cannulations, conversion to blunt / dull needles allowing multiple cannulators (British Renal Society Vascular Access Special Interest Group 2016a; Fielding et al. 2016b)

Whilst each site is cannulated in the same manner each time, the buttonhole technique can involve two to four different sites (BRS VASIG 2016b; Twardowski and Kunara 1979). This allows resting of sites for some haemodialysis sessions,

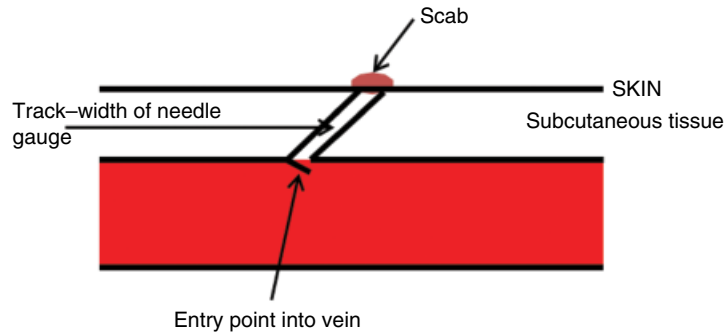


Figure 8.21 Buttonhole site.

which is particularly necessary when patients have haemodialysis more frequently than thrice weekly.

The buttonhole technique has been associated with a higher infection risk leading to some units avoiding this technique (Grudzinski et al. 2013; MacRae et al. 2012; O'Brien et al. 2012). However, some units have been able to use this technique without problems with infection (Vaux et al. 2013) or have overcome infections to identify better practice (Ball 2010; Labriola et al. 2011; Nesrallah et al. 2010; van Loon et al. 2010). The BRS VA and Vascular Access Society of Britain and Ireland (BRS VA and VASBI) (2018a) (Fielding et al. 2016b) have produced clinical practice recommendations on how to perform buttonhole and minimise infections. This technique is currently recommended for AVF only (BRS VA and VASBI, 2018a).

Rope ladder technique

The rope ladder technique was originally described as 'equal distribution of punctures along the whole length of the fistula vein'. This has led to rope ladder being described as cannulation that moves up the vein and then down again. However, this definition has often led to claims that rope ladder is being performed, when really this is area puncture with associated aneurysm and stenosis development (Fielding et al. 2016b; Vaux et al. 2013). BRS VA and VASBI (2018a) have further defined rope ladder to delineate it from area puncture:

- each cannulation occurs 0.5–1 cm above the previous site
- each cannulation moves up the vein in systematic manner and once the top of the vein is reached, cannulation starts at the bottom again
- cannulation can move side to side in veins wider than 9 mm diameter, but this needs to still be done in a systematic manner (Figure 8.22)
- cannulation sites should cover a minimum distance of:
 - 8 cm when both arterial and venous needle sites are on the same segment of vein
 - 5 cm for each site, when cannulation sites are on different segments of vein (BRS VA and VASBI, 2018a).

The rope ladder technique has been considered the default technique within the UK. However, the rope ladder technique has been poorly investigated, with a majority of research studies based on various definitions of rope ladder and study methods only comparing rope ladder with buttonhole technique. Rope ladder technique can lead to a harder needle insertion than buttonhole, with higher frequency of haematoma and cannulation problems (Twardowski and Kunara 1979; van Loon et al. 2010; Vaux et al. 2013). Whilst some studies have proven the opposite (Chow et al. 2011; Smyth et al. 2013), the reality is that studies are often poorly

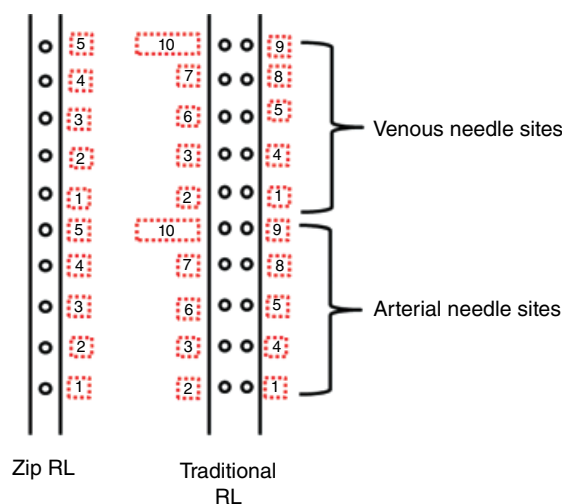


Figure 8.22 Site rotation in rope ladder.

designed to draw accurate conclusions (Grudzinski et al. 2013). Rope ladder can be used on both AVF and AVG and is the recommended technique for AVG (BRS VA and VASBI, 2018a).

Area puncture

Area puncture is cannulating in the same area each time, but not in a planned or systematic manner. The description of area puncture is also vague. BRS VA and VASBI (2018a) have defined area puncture as cannulation that covers smaller areas than those defined by the rope ladder definition. Area puncture is not recommended for use, as it leads to aneurysm development and earlier AVF/AVG failure. Despite this, area puncture is prevalent, with an estimation of area puncture use at 65.8% in an international study that included the UK (Parissotto et al. 2014).

The debate as to whether rope ladder or buttonhole is better continues, with variation in practice across the UK. Regardless of the outcome of this debate, haemodialysis nurses need to strive to not use area puncture.

Good cannulation technique

Needle insertion can be a painful and anxiety-provoking procedure for patients (Casey et al. 2014; Taylor et al. 2016). There is a strong need for haemodialysis nurses to perform needle insertion well. Techniques that may promote good needle insertion are not well evidenced, with some research evidence from Canada (Harwood et al. 2016).

Good assessment of the vessel prior to cannulation leads to more successful cannulation (Harwood et al. 2016). The look, listen, feel assessment is used pre-cannulation to identify complications and determine where and how to insert the needle. The look part involves visual assessment of the vessel and limb; the feel part involves palpation of both the vessel and thrill; the listen part involves auscultation of the bruit (Fielding et al. 2018; BRS VA and VASBI, 2018a). This can also involve gathering a history about previous cannulations (Harwood et al. 2016). This prepares the cannulator (the person inserting the needle) in determining where to insert the needle and performing the cannulation in a considered and accurate manner. Needles should never be inserted 'blind' without an idea of where the vessel is.

Planning cannulation

Much has been discussed in the literature about the need to plan buttonhole track development, using only one to three nurses to cannulate the sites. However, in reality all cannulation needs planning and communication (BRS VA and VASBI, 2018a). Rope ladder technique also needs to be planned to be able to undertake this in a systematic manner. Planning not only allows communication of how to cannulate the vessel, but also dissemination of experience. It is recognised that cannulation skill develops with experience and that individual cannulators sometimes develop better skills than others. Good cannulation practice within a unit requires experienced cannulators to support less experienced cannulators, especially when cannulating difficult AVF/AVGs (Harwood et al. 2016). This can be completed through physical presence and support during individual cannulations (Harwood et al. 2016). Nursing teams need to consider how they can communicate the plan of cannulation, to allow knowledge of individual cannulations to be transferred between staff. This may involve facilitating patient involvement in the cannulation, so the patient can provide guidance (Harwood et al. 2016), but also requires support through documentation.

Self-awareness of the cannulator

Cannulation is an emotive subject that is stressful for both the patient, but also the cannulators, especially if the cannulation is difficult. Cannulators need to be aware that there may be times when they are unsuccessful with cannulation and need to ask for help from others, even if they have been successful with that AVF/AVG previously (Harwood et al. 2016). It is recommended that nurses only attempt cannulation twice before getting assistance from others (BRS VA and VASBI, 2018a).

Gentleness and sensitivity throughout the cannulation

If it is recognised that cannulation can be difficult for both patients and cannulators, then cannulators need to approach this in a sensitive manner. They need to recognise patients' anxiety and give this time (which is often in short supply), respect, and consideration (Harwood et al. 2016). Harwood et al. (2016) identify that cannulators need good communication skills to deal with this element of cannulation. The cannulation procedure also requires an element of pragmatism, as regardless of anxiety, haemodialysis and the related cannulation is a life-sustaining procedure that is necessary. Cannulators need skill to balance empathy with an anxious patient and pragmatism to perform the needling procedure (BRS VA and VASBI, 2018a). This should be reflected in the actual needle insertion procedure, with the insertion performed with a gentle and consistent movement that occurs in a timely manner.

Correct placement of the needles

The aim of cannulation is get the needle into the centre of the vessel. Assessment of the vessel should allow cannulators to determine what angle and direction of needle insertion is required to achieve this. The technique (buttonhole or rope ladder) will help determine where to place the needle on the vessel length. However, there are certain areas that should always be avoided:

- needles should never be inserted at the anastomosis and ideally placed at least 2in. away from this.
- needles should not be placed too far away from the anastomosis. Ideally there should be an audible bruit at both needling sites.
- sites with an indication of complications should be avoided. This may be bruising, redness, inflammation, or signs of poor skin integrity.
- divisions on the veins should be avoided, as cannulation at this site often leads to infiltration and bruising/haematomas.

Tourniquet use

Tourniquet use with an AVF during needle insertion makes the vein firmer and plumper to needle, making the centre of the vein easier to determine. BRS VA and VASBI (2018a) and Ball (2010) recommends a tourniquet should always be used with AVF cannulation. A tourniquet is not necessary with an AVG, as it will not alter the firmness or diameter of the vessel.

Experienced and well-trained nurses

Harwood et al. (2016) identified that training and experience of staff when learning how to cannulate is critical. Cannulation skill develops over time and with experience, but new cannulators also need good training and mentorship to develop their cannulation skills. Fielding et al. (2016b) has identified that cannulation requires well-trained staff to be successful, but also requires monitoring of cannulation practice to ensure procedures are adhered to.

These points provide some guidance on the skills needed to insert a needle well into AVF/AVG. It should be noted that AVG cannulation often feels different as the vessel wall is tougher to insert a needle through. Cannulators often describe a double 'pop' sensation when inserting a needle into the AVG, where it feels as if you passed through the wall twice as you pass through the multiple layers of the AVG wall. This leads to inexperienced cannulators inserting needles into the AVG that are too shallow, especially as a flashback of blood may be seen before the needle passes completely into the vessel lumen.

Despite the importance of good cannulation technique, there is very little exploration of this area of practice. Further research is required to identify what is good cannulation practice and reduce variation in cannulation practices.

Tunnelled central venous catheter care

As TCVCs should ideally be avoided, there has been less attention paid to TCVC care. Much current practice development focusses on how to improve AVF and AVG rates. However, the care of TCVC is essential to minimise the complications associated with their use. There are two main complications that need to be prevented and managed on a day-to-day basis – infection and flow problems.

Prevention of Infection in TCVC

The biggest concern with a TCVC is the risk of infection. Ravani et al. (2013) identified that TCVCs have a much higher risk of mortality and infection than AVFs and AVGs. There are a number of strategies that can be used to prevent infections when using a TCVC, including:

- screening of patients for MSSA and MRSA with appropriate decolonisation (Nicholas et al. 2017).
- use of sterile gloves and sterile equipment to access a TCVC.
- use of a two-person procedure to connect patients to haemodialysis, allowing one person with sterile gloves to access and handle the TCVC and a second person to operate the non-sterile haemodialysis machine.
- use of a non-touch technique to handle TCVC connections and disconnections (Nicholas et al. 2017).
- use of antibiotic or antimicrobial locks (Jaffer et al. 2008; Kumwenda et al. 2015; Yon and Low 2013).
- use of chlorhexidine (or povidone iodine if allergic to chlorhexidine) to clean the exit site (Kumwenda et al. 2015; Loveday et al. 2014).

- use of a sterile, transparent, semi-permeable dressing on the exit site (Loveday et al. 2014). Recently, chlorhexidine dressings have been adopted for use in haemodialysis catheters (Nicholas et al. 2017) after successes in critical care settings (Timsit et al. 2012). NICE (2015) now recommends that the Tegaderm CHG (2% chlorhexidine gluconate) dressing, which includes a chlorhexidine patch, should be used on all CVCs (NICE 2015).
- the exit site should be examined at each dialysis session for signs of infection (Kumwenda et al. 2015; Loveday et al. 2014; Nicholas et al. 2017).
- prompt treatment of identified infections with intravenous antibiotics to minimise serious infectious complications associated with TCVC infection (Kumwenda et al. 2015). Serious infectious complications can include endocarditis, osteomyelitis, spinal abscesses, and septic arthritis (Kumwenda et al. 2015).

Prevention of infection is not just important to prevent morbidity and mortality, but also appears to be associated with central venous stenosis development (Nicholas et al. 2017). Central venous stenosis can affect the existing and future success of vascular access (Nicholas et al. 2017), causing flow problems in TCVCs and future upper-body AVFs and AVGs.

Prevention of flow problems

TCVCs can regularly experience reduced flow rates during haemodialysis, leading to frequent pressure alarms throughout haemodialysis and an inability to dialyse effectively (Kumwenda et al. 2015). Causes of flow problems can include thrombosis or fibrin in the lumen or at the catheter tip, build-up of a fibrin sheath, catheter malposition, pinch-off syndrome (kinked or twisted catheter), the catheter sitting close to the wall of the vein (Godelieve 2015), or migration of the catheter out of the vessel. The latter four complications are mechanical and often require manipulation of the catheter position by the medical team. However, thrombi and fibrin build-up are regular problems with TCVCs often because of long-term use.

Flushing and locking of the TCVC can affect fibrin and thrombi build-up (Godelieve 2015). Pulsatile flushing, where insertion of the flush stops and starts, builds turbulence in the lumen, clearing it more effectively (Ferroni et al. 2014). Insertion of the lock using positive pressure locking, where the catheter lumen is clamped before releasing pressure on the end of the syringe, is thought to create a positive pressure on the end of lumen preventing the back flow of blood into the lumen (Godelieve 2015). Both these techniques can be used with a TCVC to prevent flow problems, through prevention of thrombi and fibrin in the lumen. If flow problems do develop, anti-thrombolytic agents like urokinase (Godelieve 2015) and alteplase (Zacharias et al. 2003) can be used to dissolve fibrin build-up (Kumwenda et al. 2015).

Again, these strategies are not just important to prevent TCVC dysfunction, but also help minimise infection through prevention of biofilm build-up (Godelieve 2015; Ferroni et al. 2014). It is also important that training and education of staff is undertaken to ensure they are aware of good TCVC care.

Summary of vascular access

Vascular access care is critical for the success of haemodialysis and minimising morbidity and mortality for haemodialysis patients. Whilst AVF and AVG provision is an essential part of good vascular access care, the way haemodialysis nurses care and cannulate AVFs and AVGs is critical for the longevity of the vessel, and good TCVC care can minimise complications and associated morbidity and mortality. Haemodialysis nurses have an essential role in provision of care for vascular

access and promoting good outcomes for patients. A repetitive theme throughout this chapter is the good training of haemodialysis nurses to be able to provide haemodialysis well, which includes good vascular access care. Potentially this is an area to highlight due to poor provision and lack of respect for the necessity of good education of haemodialysis nurses. The evidence base for much vascular access care is poor or medicalised through interest from the medical profession. Whilst the latter should not be criticised, haemodialysis nurses are the true experts of vascular care and need to fill the void of research evidence in this area.

Assessment and Monitoring During Haemodialysis

Monitoring the patient through the haemodialysis treatment is a significant part of the haemodialysis nurses' role. Whilst haemodialysis machines provide a monitoring function, the monitoring on the haemodialysis machine needs interpretation and application to the individual situation.

Common complications during haemodialysis

Monitoring of the patient requires knowledge of potential complications that can occur in haemodialysis. If haemodialysis nurses are aware of potential complications and how to prevent these, then adverse events can either be avoided or at least minimised. There have been a number of recent studies that have examined adverse incidents in haemodialysis.

Fielding et al. (2016a) used a trigger tool approach to monitor adverse incidents during haemodialysis. This identified frequent adverse events during 566 haemodialysis treatments. These included:

- symptomatic hypotension;
- high UFR;
- more than one attempt to insert a needle into an AVF/AVG (multiple cannulation attempts);
- prolonged bleeding post-haemodialysis;
- other vascular access problems including problematic flows and haematoma;
- hypoglycaemia;
- delayed start to treatment (i.e. late on treatment);
- machine failure during treatment;
- error programming the dialysis prescription.

Many of these frequent complications have already been discussed through the chapter – patients should always be monitored for development of these complications.

Haemodialysis nurses also require knowledge and vigilance that haemodialysis machines can go wrong and humans can make errors when preparing the machine. This requires adequate training of haemodialysis staff to minimise error and an awareness of what can go wrong in haemodialysis treatments (Rylance and Fielding 2014). Rylance and Fielding's (2014) work also highlighted that whilst rare, critical incidents are of concern, common adverse incidents are also of concern, as well as more generic adverse incidents that renal patients are vulnerable to, e.g. falls; pressure ulcers. Rylance and Fielding (2014) highlight the following concerns:

- bleeding and haemorrhage from vascular access, requiring a proper assessment for risk by nursing staff at each haemodialysis treatment;
- venous needle dislodgement (VND);

- infection;
- failure of equipment and disposables for haemodialysis;
- error in use of haemodialysis equipment;
- medication errors.

Bleeding from vascular access, especially from an AVF/AVG, has also been the focus of work in the British Renal Society and VASBI, with the production of recommendations focussed on prevention of life-threatening bleeds for AVF and AVG and management when the bleed occurs (BRS VA and VASBI (2018b); Gagan et al. 2018).

Prabhakar et al. (2015) performed a retrospective case note analysis to identify intra-dialytic complications on haemodialysis and identified the following incidence of complications:

- hypotension (26.1% of treatments);
- fever and chills (14.4%), mainly due to vascular access infection;
- nausea and vomiting (14.2%);
- chest and back pain (13%);
- hypertension (10.4%);
- headache (10.4%);
- cramps (3%);
- haematoma (0.64%).

The authors highlight that incidence of complications has changed as dialysis technology has improved (Prabhakar et al. 2015). Awareness of these complications and proper prevention allows better management of these complications (Prabhakar et al. 2015).

Bray et al. (2013) performed an analysis of deaths of patients on renal replacement therapy in Scotland. This included haemodialysis, peritoneal dialysis, and transplant patients. They identified five areas of concern for patients undergoing renal replacement therapy:

- prompt recognition and management of hyperkalaemia;
- safe prescribing of medication;
- out-of-hours care for haemodialysis patients who are often cared for by non-renal services if they have an emergency in this time period;
- prevention and management of infection;
- haemodialysis vascular access.

They highlighted that many of these risks occur away from the haemodialysis machine, but should still be of concern for haemodialysis patients.

Haemodialysis continues to be a high-risk treatment, with adverse events for patients quite common. Of concern include the effects of fluid removal including hypotension; vascular access problems including infection, bleeding, and problems with flows during treatment; hypoglycaemia and the problems with managing diabetes in the context of haemodialysis; machine failure and human error using this equipment; safe prescribing and administration of medications in the context of haemodialysis; out-of-hours care for haemodialysis patients with very specific needs and management of electrolyte imbalances caused either by haemodialysis or CKD. Whilst clotting of the extracorporeal circuit and associated blood loss is not highlighted as an issue, Fielding et al. (2016a) did detect some instances. Potentially this is highlighted as less of a problem, as it is monitored and managed well. However, haemodialysis nurses need to continue to monitor for this.

Less Common Complications of Haemodialysis

Whilst more frequent complications are important to prevent, it is still essential that the haemodialysis nurse understands the risks of rarer complications. In particular, there are a few rare complications that have catastrophic consequences for patients, but awareness can ensure they are prevented. Complications that fall into this category are haemolysis, disequilibrium syndrome, air embolism, and VND. Each complication is defined in the next sections. Figure 8.23 summarises the causes, symptoms, and management of each complication.

	Causes	Signs and Symptoms	Prevention and Management
Haemolysis	Contamination of water supplies for haemodialysis with chloramine, copper, zinc, or nitrate (Saha and Allon, 2016; Rylance, 2014) Kinking of haemodialysis tubing (Rylance, 2014) Excessively negative pressure in the extracorporeal circuit, greater than -250 mmHg Exposure of the blood to high temperatures e.g. overheated dialysate fluid (Saha and Allon, 2016)	Bright, red, frothy blood Chest pain Hyperkalaemia Anaemia Pancreatitis (Rylance, 2014)	Prevention Appropriate water systems and testing (Hoenich et al, 2016) Care when lining to prevent kinking Ensure pressure gates always active and never extended beyond -250 mmHg Haemodialysis machine monitoring of dialysate temperature Management Discontinue haemodialysis – do not washback blood Cardiac monitoring Medical review Treatment of hyperkalaemia and anaemia
Disequilibrium Syndrome	Rapid reduction of urea or rapid correction of metabolic acidosis (Saha and Allon, 2016; Yee et al, 2016; Regeti et al, 2015; Donegan and Kashani, 2014) Normally evident in acute kidney injury or new patients to haemodialysis	Nausea Vomiting Headache Disorientation Restlessness Hypertension Dizziness Seizures Coma (Saha and Allon, 2016; Regeti et al, 2015; Donegan and Kashani, 2014)	Prevention Low doses of haemodialysis limited by time and blood flow rate Slow Low Efficiency Dialysis (SLED) or haemofiltration for high-risk patients, rather than haemodialysis (Saha and Allon, 2016; Yee et al, 2016; Regeti et al, 2015) Management Discontinue haemodialysis Mannitol Critical care support for cerebral oedema (Donegan and Kashani, 2014)
Air Embolism	Inadequate priming of the	Chest pain Dysnoea	Prevention Secure connection of the

Figure 8.23 The rare complications of haemodialysis.

	extracorporeal circuit (Saha and Allon, 2016) Loose connections on the extracorporeal circuit (Saha and Allon, 2016) Disconnection from open jugular central venous catheter.	Altered mental status Seizures Hypotension Tachycardia (Saha and Allon, 2016)	extracorporeal circuit Completion of proper priming of the extracorporeal circuit Haemodialysis machine with air detectors on the venous line Management Lie the patient head down on left-hand side Apply 100% oxygen The air embolism will either disperse over time or aspiration can be attempted (Saha and Allon, 2016)
Venous Needle Dislodgement	Inadequate taping of venous needle Insecure lines attached to the access Patient agitation (Saha and Allon, 2016)	Blood loss onto the floor Hypovolaemia Hypotension Tachycardia Anaemia	Prevention Use of butterfly taping method Visible venous access Venous pressure gates that are near to the venous pressure measurements (Saha and Allon, 2016) Blood leakage detectors placed around access (Saha and Allon, 2016) Management Replacement of lost volume of blood through blood transfusions and normal saline infusion.

Figure 8.23 (Continued)

Haemolysis

Haemolysis is the destruction of red blood cells. This can be a particular problem on haemodialysis as causes of this can lead to mass breakdown of red blood cells. This leads to severe anaemia and hyperkalaemia, as potassium is released from destroyed red blood cells. This can be life threatening and has been known to lead to death (Rylance 2014).

Dialysis disequilibrium syndrome

Dialysis disequilibrium syndrome (DDS) is a phenomenon that occurs in the presence of a high urea that is decreased rapidly by dialysis (Saha and Allon 2016). The rapid reduction in urea creates an osmotic difference between the blood and brain cells, leading to fluid moving into the brain cells causing cerebral oedema (Saha and Allon 2016). However, the risk seems to be higher in the presence of metabolic acidosis, infection, and smaller body weight (Donegan and Kashani 2014; Regetia et al. 2015; Yee et al. 2016). DDS is a rare complication, but as published case studies demonstrate (Donegan and Kashani 2014; Regetia et al. 2015; Yee et al. 2016), it is still a catastrophic complication of haemodialysis.

Air embolism

Air embolism occurs when a significant amount of air enters the circulation. As a wide bore extracorporeal circuit is utilised in haemodialysis, the risk of a life-threatening air embolism is high, although it is not known exactly what volume of

air is life threatening (Saha and Allon 2016). Current haemodialysis machines have sensitive air detectors on the venous line, to prevent infusion of air into the patient's circulation. However, there are still potential ports of entry for air on the venous line beyond the air detector and between the connection to the arterial access and circuit. Due to the location of these areas of weakness, CVCs have a higher risk of air embolism. Arteriovenous access is more likely to exert a positive pressure through connections, preventing air entering any loose connections, but this is not the case with a CVC.

Venous needle dislodgement

VND is a life-threatening risk to the haemodialysis patient if undetected (Rylance 2014; Rylance and Fielding 2014; Saha and Allon 2016). Dislodgement of the venous needle does not always lead to a change in venous pressure on the machine. This means it does not trigger an alarm and the blood pump continues removing blood from the arterial needle, which is then not returned to the patient as the venous access is no longer in place.

Recently there has been discussion about the use of blood leakage detectors to detect VND. EDTNA/ERCA has produced advice about how to prevent VND and when to use these detectors. Advice can be accessed at <http://www.edtnaerca.org/pages/erb/venousneedle.php>

Monitoring for complications during haemodialysis

To detect and prevent common complications during haemodialysis, the following should be monitored regularly through treatment:

- blood pressure, pulse, and signs of intolerance of fluid removal;
- pressure monitoring to detect vascular access flow problems and clotting within the extracorporeal circuit;
- monitoring of machine functions including fluid removal to ensure this is completed accurately;
- checking the correct programming of the haemodialysis prescription;
- monitoring for signs of infection and vascular access disconnection;
- signs and symptoms of less common complications of haemodialysis.

Vascular access should be assessed at each haemodialysis session for signs of infection and also issues indicating a risk of life-threatening bleed. U&E and FBC blood tests are normally performed and haemodialysis nurses should be aware of current results for individual patients.

On completion of treatment, haemodialysis nurses also need to ensure the patient is well enough to return home. They should ensure the patient has adequate blood pressure, is void of symptoms related to haemodialysis, the vascular access is healthy with any bleeding ceased, and haemodialysis has been completed adequately, to ensure correct correction of blood chemistry and fluid status.

Management of diabetes in the context of haemodialysis

Diabetes is a common cause of CKD requiring dialysis (MacNeill and Ford 2017) and the management of diabetes in the context of haemodialysis is complex (Allen and Fielding 2011; JBDS-IP 2016). For this reason, mortality in patients with diabetes on haemodialysis, compared with those patients without diabetes on

haemodialysis, is higher (Methven et al. 2017). These patients require complex care due to a number of factors:

- the risk of hypoglycaemia in the patient with diabetes on haemodialysis (Allen and Fielding 2011; JBDS-IP 2016).
- the removal of glucose during haemodialysis and the intermittent nature of haemodialysis; interference of CKD and haemodialysis on glucose metabolism, insulin resistance, renal gluconeogenesis, and hypoglycaemia regulation. This makes the use of antidiabetic therapy complex (JBDS-IP 2016).
- the higher risk of complications from diabetes that haemodialysis patients experience, for example diabetic foot disease (Allen and Fielding 2011; JBDS-IP 2016).
- the effect of anaemia management for end-stage renal disease on HbA1c results (JBDS-IP 2016).
- complex dietary needs in the context of both renal and diabetes diets (JBDS-IP 2016).
- increased thirst due to poor glycaemic control leading to larger fluids gain in between haemodialysis sessions (JBDS-IP 2016).
- the burden of hospital and primary care appointments for the patient with diabetes managing haemodialysis thrice weekly (Allen and Fielding 2011; JBDS-IP 2016).
- management of comorbidities across multiple specialties (Allen and Fielding 2011; JBDS-IP 2016).

Recently, to address this complexity, the Joint British Diabetes Societies for Inpatient care (JBDS-IP) have produced guidelines on managing patients with diabetes on haemodialysis (2016). These guidelines provide guidance on all aspects of management of the patient with diabetes on haemodialysis including monitoring, risks and complications, pharmacological management, prevention, and management of diabetic foot disease and dietary management. They are endorsed by the UK Renal Association and can be accessed via the Renal Association website. Guidelines within this document which are particularly relevant to haemodialysis nurses include:

- all patients with diabetes should have pre- and post-blood glucose reading
- patients should be educated about the risk of hypoglycaemia and be aware they are less likely to show symptoms of this
- patients may require different regimes to manage their diabetes on haemodialysis days
- patients should be encouraged to self-monitor their blood glucose levels
- an awareness that HbA1C results are affected by anaemia control and recent transfusions and are likely to underestimate average blood glucose
- there should be referral pathways for haemodialysis units to refer diabetic emergencies in glycaemia control, eye problems, foot problems or cardiovascular disorders to the appropriate team for management
- each haemodialysis unit should have a link nurse role to the diabetes team. This link nurse should co-ordinate foot checks and escalates issues to the diabetes nurse specialist.
- haemodialysis nursing staff should perform foot checks weekly on their patients with diabetes
- haemodialysis patients with diabetes with hot swollen feet should be referred to diabetes team immediately (JBDS-IP 2016).

Allen and Fielding (2011) recommend a similar, less-structured approach. In particular they highlight the need to manage both diabetes and renal as one disease, with joint diabetes and haemodialysis out-patient clinics and close working links

between the two specialties. Given the challenges that patients with diabetes on haemodialysis experience, this approach is critical to improve the outcomes of these vulnerable patients (Allen and Fielding 2011).

Patient's Perspective of Haemodialysis

One aspect not yet considered in this chapter is the patient's experience of haemodialysis. Whilst nurses aim to maintain the patient's lifestyle to be as healthy as possible, the burden of haemodialysis for patients and the effect on their lifestyle also needs to be considered. Whilst a lengthy life is important, it is also the quality of that life that is critical.

One study that examined patient priorities for haemodialysis is the Standardised Outcomes for Nephrology (SONG) group. This international study aims to standardise outcomes for nephrology research to allow more cohesive research that is meaningful to both patients and healthcare professionals (Tong et al. 2015). Through their approach to this work, which includes clarification of priorities from qualitative nominal groups, interviews, and Delphi technique surveys with patients, carers, and healthcare professionals (Tong et al. 2015) they have produced work that identifies what is important for haemodialysis patients and carers. The nominal group technique with patients and carers identified that their highest priorities were those aspects that affected their ability to live a normal life (Urquhart-Second et al. 2016). Patients and carers ranked fatigue, resilience and coping, ability to travel, dialysis free time, the impact on their family, and the ability to work as important factors to them (Urquhart-Second et al. 2016). Complications were deemed as important when they had a severe or debilitating impact on their life (Urquhart-Second et al. 2016), when they affected how they lived day-to-day life through symptoms. Morton et al. (2011) identified similar findings with patient and carers' priorities around living day-to-day life and having freedom.

Whilst this perspective is understandable, healthcare professionals continue to focus on clinical outcomes over and above these priorities. The full SONG-HD study which combines patients and caregiver priorities with healthcare professionals, the highest priorities for haemodialysis research were vascular access problems, dialysis adequacy, fatigue, cardiovascular disease, and mortality (Evangelidis et al. 2017). SONG have since removed dialysis adequacy from this list and focussed on four core domains (<http://songinitiative.org/projects/song-hd>).

Within the UK, the Transforming Participation in Chronic Kidney Disease (TP-CKD) programme has developed a Patient Reported Outcome Measure (PROM) and Patient Reported Experience Measure (PREM) that was used for the first time in 2016. The PROM showed that patients suffered from a number of symptoms. Top symptoms included weakness/lack of energy, poor mobility, pain, trouble sleeping, and shortness of breath. This survey concluded that patients have a heavy symptom burden (Gair and Steenkamp 2016). The Patient Activation Measure also identified that patients often feel overwhelmed by their chronic kidney disease which makes decision making difficult (Gair and Steenkamp 2016). The PREM identified that whilst experience was generally rated high patients had poor experience of transport for haemodialysis and sharing decisions with healthcare professionals varied between centres, as did the environment (UK Renal Registry and British Kidney Patients Association 2016). These initial results again reiterate that clinical outcomes are not the only priority to good haemodialysis care.

Some studies have also examined patients' experience of vascular access. Casey et al. (2014) performed a systematic review of qualitative studies that included patients' experience of vascular access. They identified six themes to summarise the

patient's experience of vascular access including heightened vulnerability caused by the vascular access and related procedures; disfigurement from the vascular access; mechanisation of the body; impinging on life; using self-preservation and ownership to cope with their vascular access and related procedures; and confronting decisions as vascular access made haemodialysis real (Casey et al. 2014). Many of the studies they examined explored patient's experience of haemodialysis, a large part of which was influenced by experiences of vascular access. Casey et al. (2014) also identified that cannulation of fistulae was an issue of concern for patients. They found patients develop a fear of needling, a dread of needling complications, worry about unfamiliar staff needling them, and describe needling as an 'agonizing invasion' of their body (Casey et al. 2014). However needling is necessary and experiences of AVFs are still better than TCVCs (Kosa et al. 2015). This highlights the importance of good cannulation skills in haemodialysis nurses. Taylor et al. (2016) found similar experiences of AVFs and state:

Patients with vascular access rely on a precarious lifeline, which is confronting, intrusive and burdensome.

Haemodialysis nurses need to consider what will make patients' experience of haemodialysis better and what will reduce symptom burden. Nurses need to have empathy for the burden that patients experience. Whilst haemodialysis is necessary to maintain life, the burden of haemodialysis treatment and associated complications and symptoms should not be underestimated. Improving clinical outcomes will reduce this burden by reducing symptoms and complications, however we also need to consider what will make haemodialysis better for patients and their families.

Conclusion

The chapter commenced by examining the technical aspects of what haemodialysis is and how it works. This understanding allows considered clinical decision making to allow haemodialysis to be tailored to the individual patient. There are many aspects of the haemodialysis treatment that can be adjusted to suit the individual. Haemodialysis nurses need to use their clinical and pragmatic viewpoint, to evaluate the findings of research, and implement those which are accurate and relevant to their patients. The nurses' role in monitoring the patient through treatment and preventing complications has been demonstrated – not just to optimise clinical outcomes but also minimise the burden that patients experience due to their chronic kidney disease and also that caused by the haemodialysis itself. Skilled and knowledgeable haemodialysis nurses are essential to optimise the patient's haemodialysis treatment improving individual patient's outcomes, symptoms, and experience to relieve the burden of haemodialysis.

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CHAPTER 9

Peritoneal Dialysis

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Learning Outcomes

- to recognise the importance of individualised care for those receiving peritoneal dialysis (PD).
- to review the anatomy and physiology of the peritoneum.
- to identify best practice for the care of the PD catheter and exit site.
- to understand the best use of each PD therapy option.
- to understand the criteria for good patient selection for PD.
- to review all factors required to adequately dialyse a patient with PD.
- to review the complications of PD.
- to understand the importance of good ongoing education for those receiving PD.

Introduction

PD as a treatment for end-stage kidney disease (ESKD) is a relatively simple and very effective technique. From its introduction in the late 1970s, PD has been refined and developed into a flexible and adaptable therapy that is the treatment of choice for many patients. It has been found to be most effective if performed as a continuous treatment, either by the patient during the day (continuous ambulatory peritoneal dialysis or CAPD) or by a machine, whilst the patient sleeps (automated peritoneal dialysis [APD]). Owing to its continuous nature, patients who are treated by this therapy tend to have a more stable biochemical and fluid profile. Its flexible nature makes it suitable for almost all patients with ESKD. PD used in the context of an integrated dialysis programme is associated with good clinical outcomes, certainly comparable to haemodialysis (HD) in the medium term and potentially better in the first two years of dialysis (Woodrow et al. 2017).

This chapter discusses the importance of having an individualised treatment for each patient, which is structured around both clinical and lifestyle needs. The chapter starts with an overview of the anatomy and physiology of the

peritoneum and practical aspects of the therapy, and different therapy options on PD; complications and patient education and training are also discussed. As the therapy is predominately performed by the patients themselves, in the community, the main focus is on providing patients with not only an individualised treatment, but also adequate psychological and nursing care which are essential elements for the successful treatment of those needing PD and their families. The advent of assisted PD (whereby another person, who is not the patient, performs the exchanges) is now available in many centres.

Physiology of Peritoneal Dialysis

The peritoneal membrane, so called because it covers the abdominal cavity and is derived from the Greek word *peritonaion*, meaning 'to stretch around', has a surface area of up to 2 m². The peritoneal cavity is the potential space between the parietal membrane (which lines the abdominal cavity) and the visceral membrane (the inner layer which closely covers the organs and includes the mesenteries). Under normal circumstances this cavity contains between 50 and 100 ml of fluid which acts as a lubricant (Figure 9.1).

During PD, physiological solution or dialysis fluid is instilled into the peritoneal cavity. Uraemic toxins and solutes move across the membrane by the process of diffusion, from the bloodstream into the dialysis fluid, or vice versa, depending on the concentration gradient. The composition of the dialysis fluid is near to that of normal extracellular fluid.

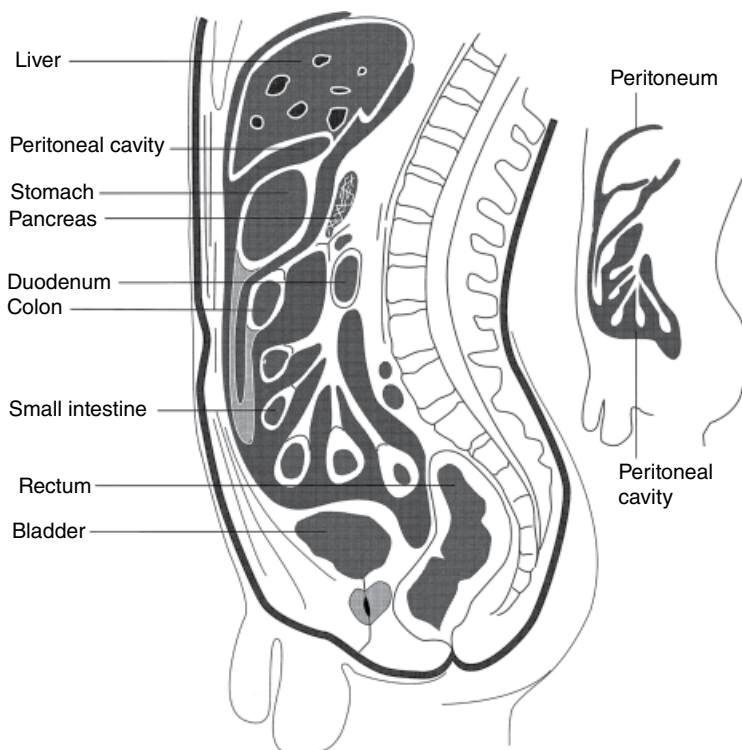


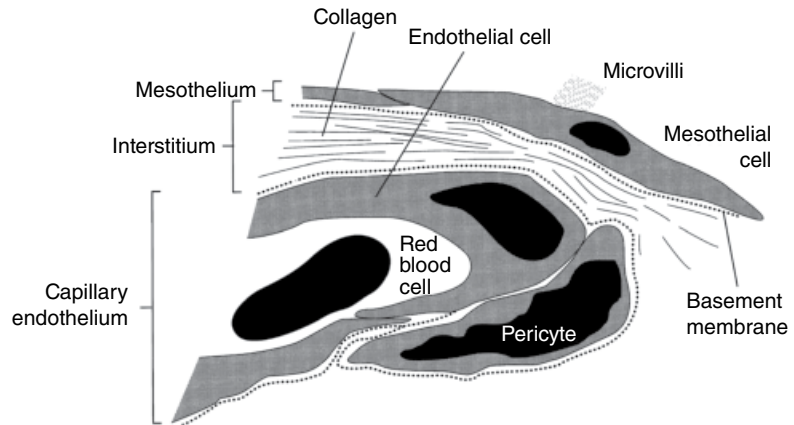
Figure 9.1 Location of the peritoneal cavity.

Fluid removal takes place by osmosis. The dialysis fluid is made hypertonic to plasma by the addition of osmotic agent, usually glucose. Other osmotic solutions are discussed later in this chapter.

The membrane is made up of three layers (Figure 9.2a):

- the mesothelium. Underneath this lies the connective tissue. The luminal side of the mesothelium is covered with numerous microvilli that are believed to increase the surface area of the peritoneum to up to 40m² in a healthy individual (Figure 9.2b).
- the peritoneal interstitium. This is composed of fibres and bundles of collagen.
- the capillary endothelium. This forms a complex branching system.

(a)



(b)

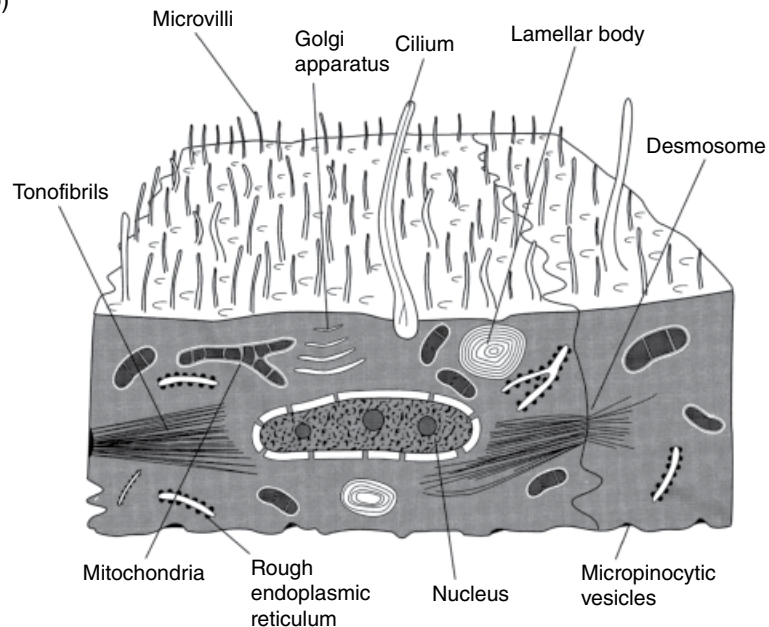


Figure 9.2 (a) The three layers of the peritoneal membrane. (b) Diagrammatic representation of a normal mesothelial cell.

Blood supply

The visceral peritoneum is supplied by the superior mesenteric artery. The parietal peritoneum is supplied by the intercostal, epigastric, and lumbar arteries. Venous return from the visceral peritoneum is to the portal circulation, whereas that from the parietal peritoneum goes into the caval circulation. This is important because it means that any drugs administered via the peritoneum will be transported to the liver, the normal route.

Lymphatic drainage

Lymphatic drainage from the peritoneal cavity returns excess fluid and proteins into the systemic circulation. Its other function is to remove foreign bodies from the peritoneal cavity. Lymphatic drainage is a one-way system, the flow rate of which may be affected by respiratory rate, intraperitoneal (IP) hydrostatic pressure, posture, or peritonitis.

Peritoneal membrane transport characteristics

The peritoneal membrane is semipermeable and allows the passage of both water and solutes. During PD three processes are involved in removing fluid and wastes from the bloodstream and balancing electrolytes. These are osmosis, diffusion, and convection.

Osmosis

This is the movement of water through a semipermeable membrane from a solution of low concentration into a solution with a higher concentration. The solution into which the water moves in PD contains an osmotic agent, usually glucose (other osmotic agents are discussed later in this chapter). The higher the glucose concentration, the greater the osmotic effect will be, so removing more water from the patient's bloodstream (Figure 9.3).

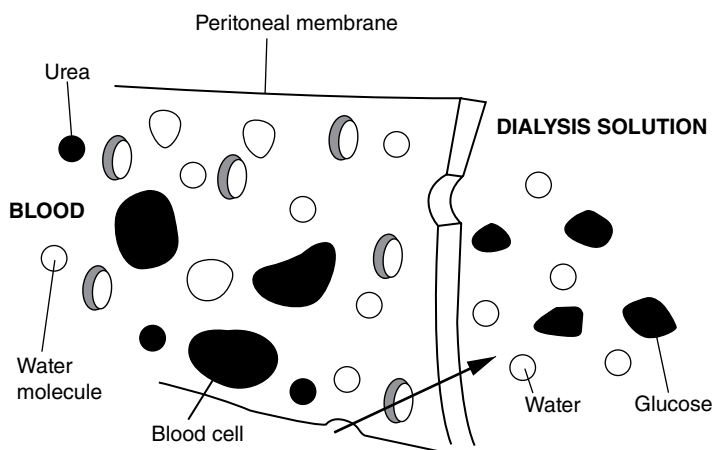


Figure 9.3 Osmotic ultrafiltration across the peritoneal membrane with a glucose dialysis solution in the peritoneal cavity.

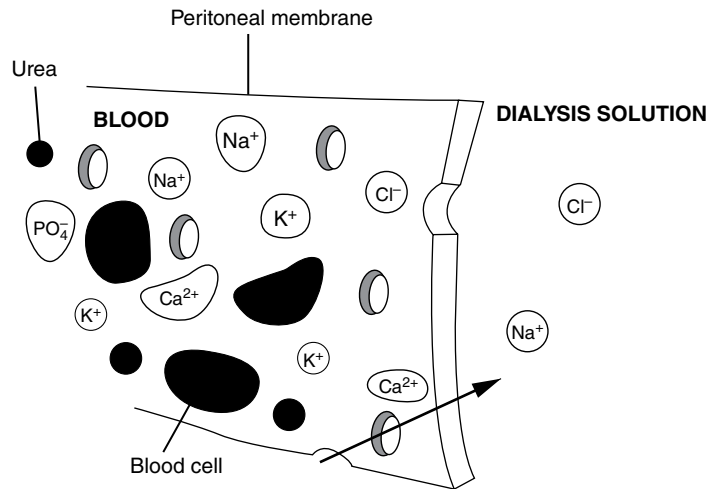


Figure 9.4 The peritoneum acts as a semipermeable membrane, allowing small solutes and water to diffuse through, but retaining large particles such as blood cells.

Diffusion

This is solute exchange between two solutions, usually separated by a semipermeable membrane. The solutes will travel in either direction across the membrane until equilibrium is achieved. The direction and speed at which the solutes flow depend on the concentration gradient. Solutes will flow from the stronger solution into the weaker solution (Figure 9.4). Therefore, solutes can pass in either direction across the peritoneal membrane. Other factors that affect diffusion rate are molecular weight and membrane resistance.

Molecular weight

Diffusion is a spontaneous process whereby solutes move randomly. Lighter, smaller molecules will move quicker than larger, heavier molecules. Urea (which has a molecular weight of 60Da) diffuses from blood to dialysate more rapidly than creatinine (molecular weight 113Da) or vitamin B₁₂ (molecular weight 1352Da). Unlike HD, where the membrane pore size is controlled, the peritoneal membrane allows transport of large molecules and even proteins. Protein transport into the dialysate is unfortunate as this is an essential nutrient, particularly in dialysis patients who may be catabolic.

Membrane resistance

The permeability of the individual's membrane is an important factor controlling diffusion of solutes. Measurement of this is discussed later in this section.

A patient's peritoneal permeability may be changed during illness. Acute episodes of peritonitis appear to greatly increase the membrane permeability to both solutes and water. However, fibrotic thickening of the membrane may lead to a severe reduction in its permeability. Further reading on the functional structure of the peritoneum can be found in Gotloib (2009).

Convection

Owing to the large amount of osmotic ultrafiltration (UF) that takes place during PD, convective flow transports or 'drags' water and solutes across the membrane. This occurs at a much faster rate than that which may be accounted for by diffusion alone.

The ability of glucose to exert an effective osmotic pressure depends on its ability to stay in solution in the dialysate. If the peritoneal membrane were perfectly semipermeable (i.e. only permeable to water), the osmotic pressure would be maximised. However, the peritoneum is permeable to solutes as well as water, and therefore allows the glucose through. The osmotic gradient is therefore maximum at the beginning of the exchange. The UF will decrease during the dwell time as glucose is absorbed into the bloodstream. It is estimated that UF is maximised at the beginning of the PD fluid exchange when the concentration gradient is highest. The total dialysate and ultrafiltrate volume continues to decrease after this point due to lymphatic absorption (Lokesh and Arun Kumar 2013).

Measurement of peritoneal permeability

The characteristics, pore size, and dimensions of the peritoneal membrane do not come printed on the side of a packet as they do in HD. It's therefore important to determine the characteristics of the patient's peritoneal membrane before an appropriate prescription can be written. A number of methods have been described, including standardised peritoneal assessment (SPA), the Peritoneal Equilibrium Test (PET) including Fast or mini PET, Personal Dialysis Capacity (PDC) test, and more recently double mini PETs. The PET is the most commonly used.

The PET was described in 1987 by Twardowski et al. and determines solute transport rates over time and the UF capacity of the membrane. The results of the test can therefore be used to determine the optimum length of time that PD fluid should be left inside the peritoneal cavity to gain maximum fluid and solute removal. It also alerts the practitioner to any changes in membrane function that could affect patient's dialysis adequacy and outcomes. A review of evaluation methods of peritoneal membrane characteristics has been written (Van Biesen et al. 2010).

Performing a PET

The PET test was traditionally carried out by an experienced PD nurse in a clinic environment, however with the adoption of the 'fast' PET where blood samples are taken at four hours only (Akdam et al. 2014) this can now be performed at home, allowing for greater flexibility. Prior to performing the test, the patient's PD catheter function should be checked so that poor drainage due to mechanical problems with the catheter (such as constipation) are not attributed to membrane function. In addition, patients should be normally hydrated, and patients with diabetes should have serum glucose levels within normal limits. This enables the results of the test to be interpreted accurately.

To enable accurate reproduction of the test according to Twardowski's original work, the following is the original protocol, which is the basis for all tests and should be used if there is any doubt over the reliability of the 'fast' or modified PET.

1. The patient attends the clinic with a 2.27% bag, which has dwelled in the peritoneum for between 8 and 12 hours. This is drained out, the volume and dwell time recorded, and a sample taken.
2. The patient is then instilled with another bag of 2.27%. The volume should be the same as the overnight bag but ideally no smaller than 2000ml.
3. This is drained in over 10 minutes with the patient in a supine position, rolling from side to side to ensure mixing whilst the fluid is infused.
4. Dialysate samples are taken at zero, two, and four hours with a serum sample at two hours.
5. It is essential to record the drain-out time and the drained-out volume at four hours to assess the UF capacity of the membrane.

6. Finally, the patient's usual PD solution is instilled before they are able to go home.
7. The samples are then sent for analysis of glucose and creatinine levels as soon as possible.

Calculating results

In order to determine the patient's membrane solute transport characteristics, the level of creatinine that is in the PD fluid at zero, two, and four hours is compared with the level of creatinine in the patient's plasma (D/P ratio). This gives a ratio of between 0 and 1. The closer the dialysate-to-plasma ratio is to 1, the faster solutes equilibrate across the membrane. Glucose absorption, from the PD solution into the patient's serum, is calculated in the same way. The level of glucose in the PD fluid at zero, two, and four hours is compared with the level in the patient's serum (D/P ratio). The closer the ratio is to 1, the faster glucose crosses the membrane. Patients who equilibrate solutes fast will therefore have good solute removal during PD; however, as glucose will also be absorbed quicker, the glucose concentration gradient will not be sustained. Thus, fluid removal will be poor. The results can be plotted to determine the transporter status of the peritoneum.

Analysis of results

When the patient's transport characteristics have been identified, it is easy to tailor the treatment to suit the membrane. The patient's peritoneal membrane is categorised into one of the four membrane classifications. Each membrane classification has specific characteristics that guide the clinician in tailoring the patient's prescription (see Table 9.1)

Patients who have high transport membranes should have rapid exchanges of fluid, usually achieved by using APD. Patients who transport glucose and solutes more slowly are better suited to receiving CAPD where the fluid remains in the peritoneal cavity for longer periods. Any prescription modification should be accompanied by an assessment of the patient's lifestyle to ensure that the treatment is achievable within work and social constraints. By performing this test regularly, it is possible to monitor peritoneal membrane function over time and therefore diagnose acute membrane injury, inadequate UF, and poor solute clearance.

Table 9.1 Classification of membrane type.

Percentage of patients	Membrane type	4 hours D/P creatinine	Characteristics
10	High	0.82–1.03	Very efficient membrane Transports solutes easily Increased glucose absorption May have difficulty achieving ultrafiltration At risk of low albumin
53	High Average	0.65–0.81	Efficient membrane Transports solutes well Ultrafilters well
31	Low Average	0.50–0.64	Less efficient membrane Transports solutes slowly Ultrafilters well
6	Low	0.34–0.49	Inefficient membrane Transports solutes slowly Ultrafilters well

The UK Renal Association (Woodrow et al. 2017) has recommended that repeat PET tests should be routinely performed six weeks after commencing PD and at least annually or when clinically indicated, for example if problems arise such as an apparent loss of UF or if there is a change in therapy such as transfer from CAPD to APD. Changes over time in the test results can then be related to clinical performance and treatment regimens may be altered accordingly.

Peritoneal Dialysis Access and Exit Site Care

Despite PD catheter insertion being a relatively simple procedure, the implications of getting it wrong can be catastrophic for the patient at a most vulnerable time – when they are new to PD. Not only can poor insertion technique lead to a malfunctioning catheter, it can also be responsible for infections and the failure of PD in about 20% of patients (Flannigan and Gokal 2005), which can be devastating for a patient who has chosen this therapy. Unsuccessful PD catheter insertion also has cost implications and can adversely affect the management of a renal unit. There are many facets to successful PD access:

- choosing the right catheter type and length;
- good insertion technique;
- meticulous preoperative and postoperative care.

However, what is fundamental is effective teamwork from the multidisciplinary team, in particular the medical and nursing staff.

Types of catheters

The perfect PD catheter is one that provides reliable and rapid inflow and outflow from the peritoneal cavity without leaks or infections. Catheters should be designed to stay in the pelvic cavity and be easy to insert.

PD catheters generally have three portions (Figure 9.5):

- the outer segment, which connects via an adapter to the solution transfer set.
- the intramural segment. This has Dacron cuffs, spaced about 8 cm apart. By creating an inflammatory response, fibrous tissue fixes the catheter into position,

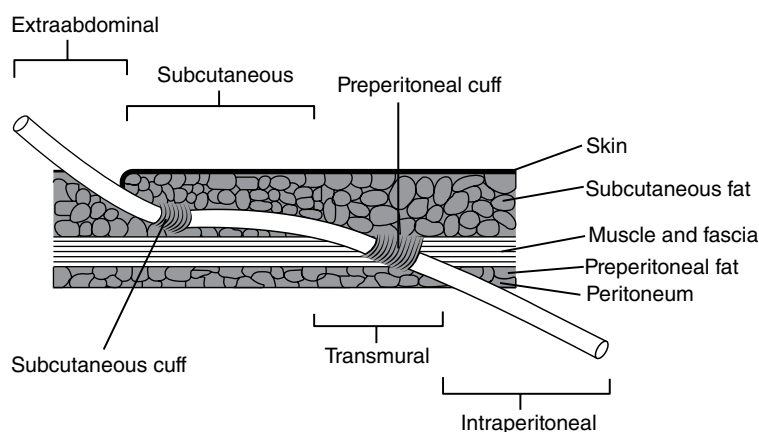


Figure 9.5 Functional parts of the peritoneal catheter.

thereby minimising leakage of dialysate and preventing bacteria entering the catheter 'tunnel' and intraperitoneal segment.

- the IP part, which has many small holes up the side, is situated inside the peritoneal cavity for the in- and outflow of the solution.

Variations in the design of catheters include the number of cuffs (one versus two), the design of the intramural segment (permanently bent versus straight), and the IP portion (straight versus curled). Despite the number of types of catheters available the most widely used are the straight (Figure 9.6) and curled (Figure 9.7) Tenckhoff catheters. They are easily inserted under local or general anaesthetic and choice of catheter will usually depend on local preference.

The Swan-neck (Figure 9.8), and Toronto Western (Figure 9.9) catheters were both developed to aid outflow of the dialysate.

Swan-neck

With two downward-pointing segments, migration of this type of catheter is rare thereby serving to aid outflow. It is also thought to prevent infections at the exit site as this segment of the catheter also points downwards, thus preventing accumulation of sweat and pus.

Toronto Western

This has two discs at the IP segment helping to prevent migration. This catheter also has a Dacron flange and bead at the deep cuff, which is sewn in position by a pursestring suture, helping to reduce leaks at the exit site.

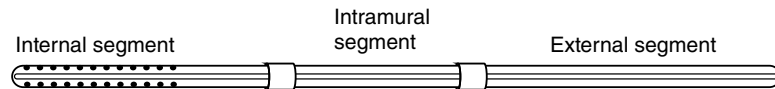


Figure 9.6 Straight Tenckhoff catheter.

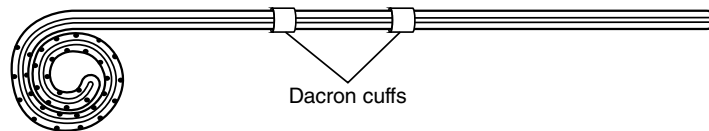


Figure 9.7 Curled Tenckhoff catheter.

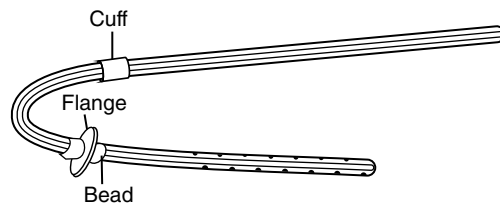


Figure 9.8 Swan-neck catheter.

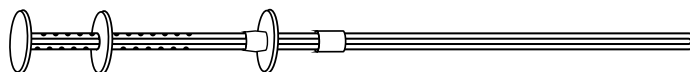


Figure 9.9 Toronto Western catheter.

Literature shows that there is little difference between risk of infection for the various types of catheters, however one study showed that there was increased catheter survival in the coiled catheter when compared to the straight (36% vs. 77% $p = 0.01$; Nielson et al. 1995). If properly placed, dual-cuff Tenckhoff catheters have a lower incidence of infection and a longer lifespan than single-cuff catheters (Ash 2003). Overall there seems to be no superior catheter to the standard straight Tenckhoff catheter.

Preinsertion preparation of the patient

A full preoperative assessment of the patient is essential to identify existing or potential hernias. If present these can be repaired during the catheter insertion. The catheter exit site should be determined before the catheter is inserted. The preferred site should first be discussed with the patient to help promote participation in and an understanding of the therapy. The following points should be followed when determining the exit site of the patient's catheter:

- the site should be determined whilst the patient is in a relaxed sitting or standing position;
- it should be either above or below the belt line, whichever the patient prefers;
- skin folds and abdominal scars should be avoided;
- the catheter exit site should be located where the patient can effectively carry out exit-site care;
- once the exit site has been determined, it should be marked clearly with a permanent skin marker.

The patient's lifestyle, work, and hobbies should be taken into consideration when placing the catheter.

Preoperative care of the patient

On the morning of the operation, the patient should bathe or have a shower. If necessary, abdominal hair should be clipped. A major cause of catheter failure, particularly at the start of PD, is constipation, and it is therefore recommended that a powerful aperient such as PicoLax is given the day before catheter insertion. It is also important that the patient has an empty bladder before the insertion procedure takes place. Other usual preoperative practices should also be followed.

***Staphylococcus aureus* screening**

There is evidence (Piraino et al. 2005) that patients who have nasal carriage of *S. aureus* have an increased risk of exit site infection and peritonitis, and that the use of Mupirocin cream or ointment at the exit site is recommended to reduce the incidence of infection. It is therefore advisable to screen all patients for *S. aureus* prior to catheter insertion and treat accordingly.

Prophylactic antibiotics

There is evidence that prophylactic antibiotics prevent catheter infections and peritonitis (Galallah et al. 2000). Recently published guidelines recommend that prophylactic antibiotics should be administered at the time of catheter insertion (Piraino et al. 2005).

Psychological preparation of the patient

This is of absolute importance for someone who is new to PD and this is discussed in detail in Chapter 4.

Insertion techniques

PD is a life-maintaining therapy. Access to the peritoneal cavity, via the PD catheter, is therefore particularly important in ensuring its success (see Figure 9.10 for the correct position of the catheter in the abdomen). The insertion technique should be treated as a skill acquired by experienced surgeons, physicians, and specialist nurses, rather like implantation of a pacemaker or similar device. A team approach is essential and nurse involvement is most important. The nurse's role in insertion of PD catheters starts with the preoperative preparation described in the previous section, all of which can be carried out by the nurse. In many centres the PD nurse accompanies the patient to the operating theatre or procedures room to ensure correct procedures are carried out and that the catheter is functioning well before final wound closure is made.

The four most frequently performed methods of catheter insertion include:

- surgical placement by dissection;
- blind placement using Tenckhoff trocar;
- blind placement using guidewire;
- minitrocar placement using peritoneoscopy.

(Wilkie et al. 2008)

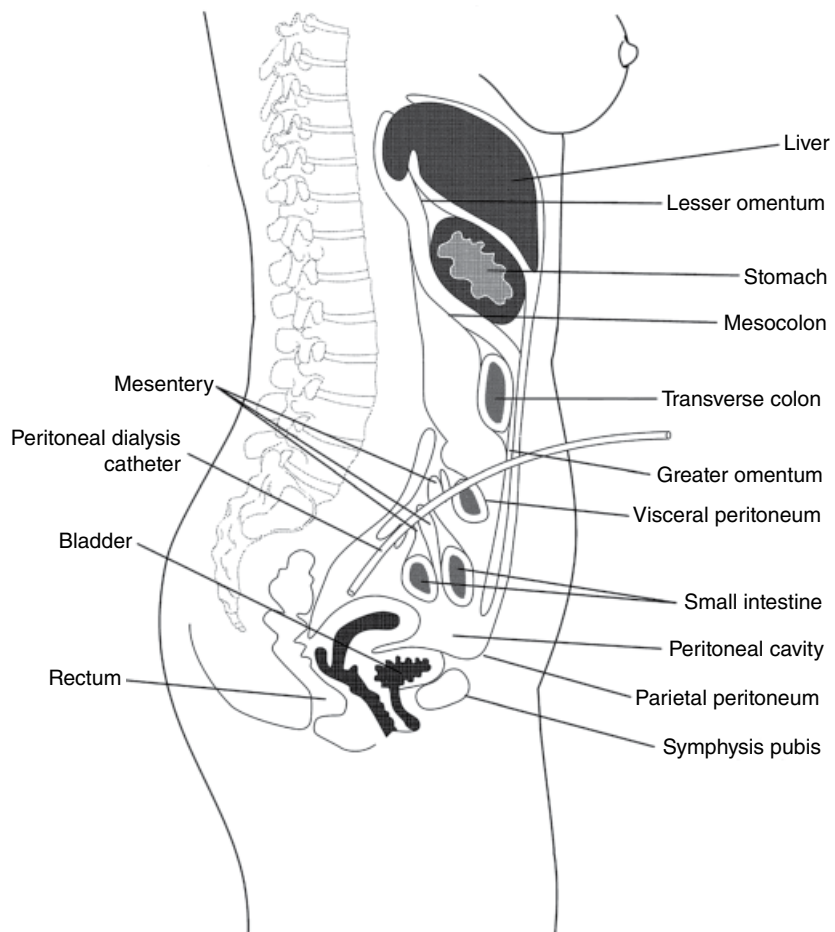


Figure 9.10 The position of a peritoneal dialysis catheter in the abdomen.

An alternative method of catheter insertion is performed by radiologists using a percutaneous modified Seldinger technique under fluoroscopic guidance and has been shown to be a clinically noninferior and cost-effective alternative to surgical laparoscopic insertion (Voss et al. 2012).

There is no evidence (with randomised controlled trials) to support one method of insertion over another; however, the method needs to be determined by patient characteristics. For more complicated patients, including those with previous significant abdominal surgery, a technique that involves direct vision is necessary, such as laparoscopic or open insertion (Figueiredo et al. 2010).

Perioperative care of the patient

For management of the catheter in the perioperative period, and catheter-related problems including leak (internal and external), poor flow, obstruction, and hernias, the guidelines developed by the International Society of Peritoneal Dialysis should be followed: www.ispd.org (accessed 30 June 2018). Catheter problems such as leaks, hernias, and prolapse are an important medical indication for the use of APD either temporarily or permanently; poor flow or catheter-related flow pain should be treated with tidal APD. In the majority of cases where surgical repair for mechanical complications is required (e.g. catheter replacement, hernia repair) it is possible to avoid the need for temporary HD. In many PD patients, remaining residual renal function (RRF) may permit an adequate period post-surgery before dialysis needs to be recommenced. Where PD does need to start soon after surgery, in many cases this may be safely achieved by initial use of APD with small volume exchanges and avoiding a day dwell in ambulant patients (Woodrow et al. 2017).

Postoperative care of the patient

The goals of postoperative catheter care are to:

- minimise any bacterial colonisation of the exit and tunnel during the early healing period;
- prevent trauma to the exit site and traction on the cuffs by immobilisation of the catheter;
- minimise intra-abdominal pressure to prevent leakage.

Ideally, the exit site should be undisturbed for 7–10 days following insertion of the catheter. The patient may be discharged home during this period. If, during the first 10 days, the dressing becomes soiled, it should be redressed by a nurse. If it merely becomes dislodged, it should simply be replaced with a fresh sterile dressing. During this period, the catheter tubing must be immobilised by securely taping it to the patient's abdomen. Local unit policies will be in place and should be followed.

Before discharge from hospital, during this resting of the patient's catheter, clear instructions must be given as to the correct procedures for caring for the catheter at home. It may be appropriate to involve the community district nursing team if no specific community PD nurse is available. In this case, adequate training and support must be provided for the nursing team.

Directly following insertion of the catheter, it may be flushed with 500–1500 ml of PD fluid to check patency. It may then be 'capped off' using a small locking cap on the catheter adapter (this adapter is available in titanium metal or plastic) and left covered until PD commences. Ideally, PD should not be started until healing of the exit site and tissue ingrowth into the catheter's Dacron cuffs have taken place, usually after 10 days. If dialysis is necessary before this time, automated PD would

be the preferred method. This is because this treatment will help to minimise the risk of leakage of PD fluid by allowing the patient to be treated using small fill volumes of fluid in a supine position. It is worth noting that patient-healing mechanisms may be altered in those patients who are uraemic or who have diabetes mellitus.

Long-term care of the exit site

As with any wound, care is aimed at keeping the site clear of exudate or debris that could encourage bacterial growth. A method of exit-site care that best fits in with the patient's lifestyle is most likely to encourage full participation in the treatment, and therefore reduce the risk of complications. A number of studies have been undertaken to attempt to ascertain which particular method of exit-site care is preferred. Various protocols do exist – for example cleansing with soap and water or cleaning with povidone-iodine; however, there is to date no consensus on which method will reduce the incidence of infection (Twardowski and Nichols 2009).

Whichever solution is chosen, the following points should be considered:

- harsh solutions should be avoided as they have the potential to cause skin damage, which may predispose to bacterial colonisation.
- different agents may be preferred in different circumstances. In an immunosuppressed patient the normal skin flora may represent an infection risk; in this case an antiseptic solution may be preferred.
- whichever method is used, it is important to ensure that the exit site is carefully dried to avoid skin maceration, which could predispose the site to bacterial colonisation.

There is also some debate as to whether it is necessary to keep the catheter exit site covered. The use of no dressing and a simple exit-site care routine for a well-healed exit site would appeal to many; however, most centres do use some kind of cover (Piraino 2008).

Catheter immobilisation

From the moment the catheter is inserted, it should always be securely anchored to the patient's skin to avoid torque movements at the exit site. This has been shown to reduce the risk of exit-site infection (Mushahar et al. 2016) and can be achieved by using tape or a commercially available immobilisation device or tube holder.

Swimming and bathing

Swimming and bathing can be discussed with patients once the exit site is fully healed and ideally free from infection, with the following recommendations:

- a waterproof or occlusive dressing should be applied (there are specialist products available) and the exit site should be cleaned and new dressing applied immediately after immersion in water using normal technique.
- it is not recommended to immerse the exit site in water without a waterproof dressing, particularly hot tubs, jacuzzis, and so forth. Diving should be avoided as this may put tension on the catheter at the exit site (Wild and Ansell 2010).

Indications for catheter removal

A PD catheter is designed to be a permanent access device, and its removal should not be routine. However, catheters may have to be removed under the following conditions:

- if they are no longer needed;
- in recurrent peritonitis without an identifiable cause;

- in peritonitis due to an exit-site and/or tunnel infection;
- with an unusual causative organism of peritonitis, for example fungus, tuberculosis;
- in bowel perforation accompanied by peritonitis;
- with persistent and severe pain due either to the catheter impinging on internal organs or during solution inflow;
- when there is Dacron cuff erosion and infection.

ISPD guidelines (Figueiredo et al. 2010) recommend the following audit standards for catheter-related complications:

- bowel perforation: <1%
- significant haemorrhage: <1%
- exit-site infection within two weeks of catheter insertion: <5%
- peritonitis within two weeks of catheter insertion: <5%
- functional catheter problem requiring manipulation or replacement or leading to technique failure: <20%

Peritoneal Dialysis Therapy Options

Dialysis should be prescribed according to each individual patient's clinical and lifestyle needs. The dose of PD can be increased or decreased by adjusting any one of the following parameters:

- dialysis fluid fill volume per exchange;
- number of dialysis fluid exchanges;
- length of dialysis fluid dwell time;
- osmotic strength or type of dialysis fluid.

By using the PET each patient's membrane characteristics can be determined, therefore allowing optimisation of the therapy. There are two general methods of performing PD: CAPD and APD.

Continuous ambulatory peritoneal dialysis

CAPD (Figure 9.11) is carried out during the daytime, manually by patients themselves or sometimes by a carer. Dialysis fluid is infused into the peritoneal cavity and left to dwell for between 3 and 10 hours. After this time the dialysate is drained from the cavity, fresh solution is infused, and the whole process starts again. Patients usually perform four exchanges of PD fluid each day, fitting them in as appropriately as possible with their normal lifestyle. For example, exchanges may be performed at breakfast, lunch, and supper time with the last exchange of the day being carried out at bedtime. Each exchange takes about 20–30 minutes to complete.

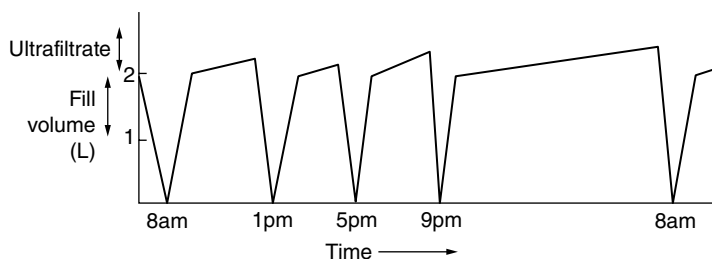


Figure 9.11 Continuous ambulatory peritoneal dialysis (CAPD).

CAPD is most suited to those patients whose membranes transport solutes at an average rate (i.e. low, low-average, and high-average ‘transporters’) as it provides the opportunity for longer dwell times. This long dwell period is best achieved during the nighttime whilst the patient sleeps. Those patients whose membranes transport solutes quickly (‘high transporters’) may need to use an icodextrin solution for the longest dwell overnight. This will avoid dialysate fluid absorption which could occur in these patients during long dwell periods.

Automated peritoneal dialysis

APD is carried out by a machine, which performs the dialysis fluid exchanges at night whilst the patient sleeps. An APD machine automatically controls the fill volume, dwell time, and length of treatment the patient receives. The dose of dialysis can easily be increased during APD as it is easy and convenient to alter the parameters of the treatment. Dialysis fluid fill volumes can be more safely increased due to the reduction in intra-abdominal pressure achieved whilst the patient is supine. This not only decreases the risk of problems associated with high intra-abdominal pressure such as leaks around the catheter exit site, abdominal hernias, and back pain, but it also increases the amount of dialysis the patient can achieve.

The length of the dwell time and the number of exchanges can effectively be altered without disruption to the patient’s lifestyle. This is a major advantage to ‘high transporters’. Performing frequent exchanges is essential for these patients to achieve adequate dialysis but this can be inconvenient if the patient is on CAPD. APD provides an effective and convenient alternative by enabling rapid exchanges of dialysis fluid whilst the patient sleeps. This increases the clearances of solutes whilst maintaining maximum UF. As with CAPD, the osmotic strength of the fluid can be altered according to each patient’s need.

APD is particularly suitable for those patients needing to be free during the daytime. Patients who work or who are studying can benefit from this treatment, as the preparation time for the treatment is short and the dialysis takes place whilst they sleep, leaving them free during the day. APD is also suitable for those patients who rely on a carer to perform their dialysis, for example children, older people, or those with disabilities. The carer simply prepares the machine, connects the patient to the machine at bedtime, and disconnects them the following morning. APD is therefore an effective therapy option for those patients who require more dialysis and/or freedom during the daytime. However, in order to achieve adequate dialysis, many patients will also need to perform an exchange in the early evening.

Some APD machines have the facility to store information regarding the patient’s therapy on a data card that is fitted inside the machine. This data card also stores the patient’s individual prescription, enabling the prescription to be altered by a healthcare professional, without the need for the patient’s intervention.

There are three different types of APD:

- continuous cycling peritoneal dialysis (CCPD);
- tidal peritoneal dialysis (TPD);
- optimised cycling peritoneal dialysis (OCPD).

Continuous cycling peritoneal dialysis

The ‘continuous’ part of the acronym is derived from the fact that the patient has dialysis fluid in constant contact with the peritoneal membrane (Figure 9.12). There are typically between five and seven exchanges of fluid with relatively short dwell periods, so maximising the UF and clearance capabilities of those patients whose

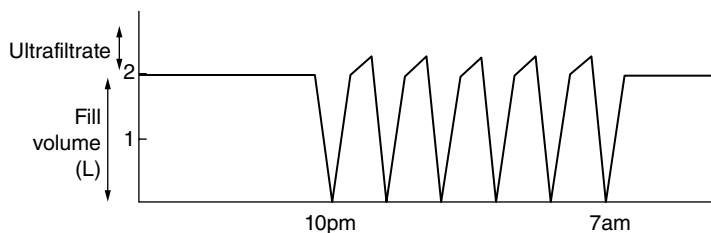


Figure 9.12 Continuous cycling peritoneal dialysis (CCPD).

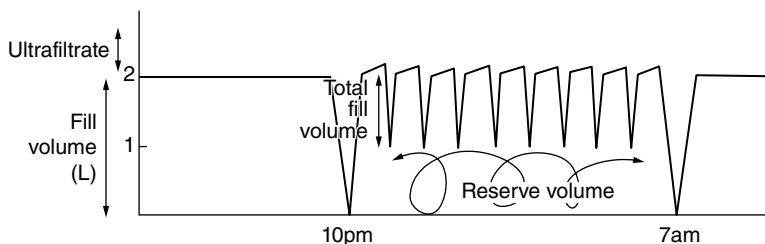


Figure 9.13 Tidal peritoneal dialysis (TPD).

membrane transports solutes quickly. The treatment regime can be programmed to end with a 'fill', giving the patient a 'wet day' (the fluid would be left inside the peritoneal cavity during the day and drained when the patient next starts treatment on the machine at bedtime). Icodextrin solution, designed for long dwells, should preferably be used in these circumstances.

Rarely, the treatment ends following the 'drain', giving the patient a 'dry day'. This may help to prevent absorption of the PD fluid in 'high transporters'. It should be noted, though, that utilising a 'dry day' will result in severely reduced clearances and possibly underdialysis.

Tidal peritoneal dialysis

Tidal PD is a form of APD where the dialysis fluid fill volume is not fully drained after each cycle (Figure 9.13). It is typically used for patients who experience pain at the end of each drain phase, particularly new or acute patients getting used to the sensation of fluid in the peritoneal cavity. By leaving a small 'sump' volume of about 10% of the dialysis fill volume in the patient's peritoneal cavity at the end of each drain phase, pain is minimised. A full drain takes place at the end of the therapy during the final drain. It is important to remember to check the minimum drain volume parameters to avoid IIPV (increased intraperitoneal volumes) and associated risks.

Optimised cycling peritoneal dialysis

This method of APD enables the delivery of more dialysis as the patient's RRF declines (Figure 9.14). During OCPD the patient performs overnight CCPD or TPD as well as adding a daytime exchange of PD fluid. Some APD machines are designed so that the patient can perform both the night and day exchanges using the same disposable equipment and solution bags. The longer dwell of fluid during the daytime will optimise clearance opportunities and the shorter dwells of the nighttime dialysis will help to achieve UF goals.

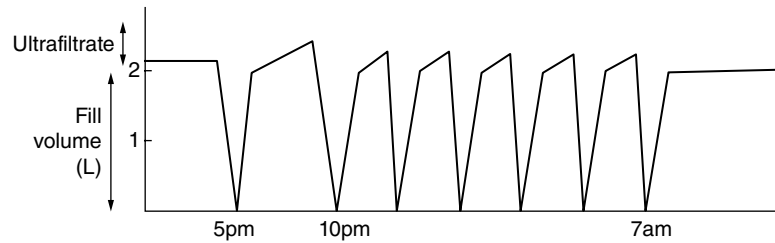


Figure 9.14 Optimised cycling peritoneal dialysis (OCPD).

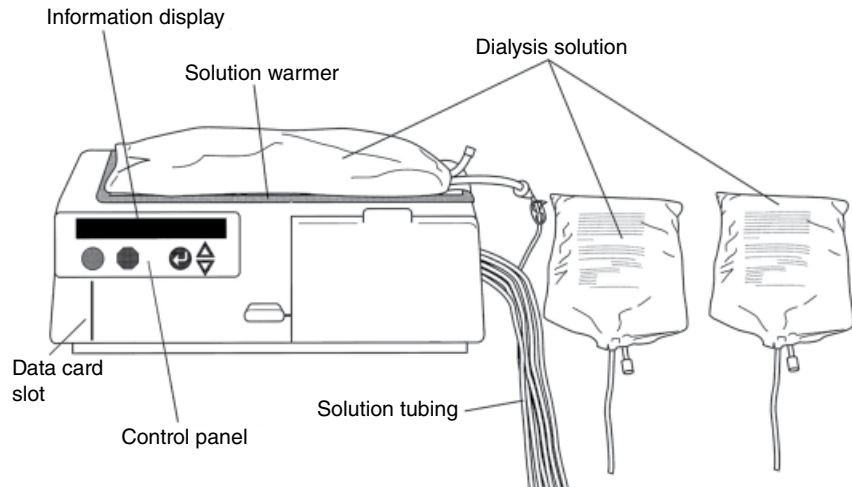


Figure 9.15 Baxter Healthcare Ltd. HomeChoice Pro automated peritoneal dialysis (APD) machine. Source: Used with kind permission from Baxter Healthcare Ltd.

Whichever method of PD is chosen for the patient at any particular time, it should provide a balance between clinical and lifestyle needs. Figure 9.15 shows an example of an APD machine.

Patient Selection

An important consideration when developing a successful PD programme is good patient selection. Treating the most appropriate patients with PD will avoid the patient being subjected to increased risk of morbidity and mortality. In the early years of PD, selection was mainly based on the patient's inability to have HD – for example, those patients with poor or no vascular access, poor biochemical control on HD with high predialysis serum levels of creatinine, those patients with poorly controlled hypertension, and those with excessive fluid gain between dialysis sessions. Positive selection criteria are now preferred as PD has proven to be a successful viable alternative to HD as a treatment for chronic renal disease.

The National Institute for Health and Care Excellence (2011) guidelines recommend that PD should be first-line treatment for patients without significant comorbidity and those with RRF, although later guidance (NICE 2018) recommended a choice of dialysis modalities informed by clinical and patient preferences. In 2011, Molnar published a paper reporting that PD pre-transplantation had a positive effect on survival post-transplant. As there are two different therapy modes within the broad title of PD (i.e. CAPD and APD), the selection criteria for each are

Table 9.2 Patients who are most suited to continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal dialysis (APD).

Suited to CAPD	Suited to either CAPD or APD	Suited to APD
Patients whose membranes transport solutes slowly or at an average speed.	Those who prefer a home-based therapy.	Patients who seek daytime freedom to attend work or school.
	Patients with complicating cardiovascular disease.	Patients at risk of complications associated with raised intra-abdominal pressure.
	Children with small body size.	Patients who require a carer to perform their dialysis.
	Patients with poor vascular access.	Patients with chronic backache.
	Patients with diabetes mellitus.	Patients who require enhanced dialysis, i.e. those without residual renal function (RRF).
	Patients with severe hypertension.	
	Patients with anaemia.	
	Patients who wish to travel.	

Table 9.3 Patients who could be unsuitable for continuous ambulatory peritoneal dialysis (CAPD) or automated peritoneal dialysis (APD).

Unsuitable for CAPD	Unsuitable for either CAPD or APD
Patients with chronic back pain.	Patients with chronic obstructive lung disease.
Patients at risk of complications associated with raised intra-abdominal pressure.	Patients with diverticular disease.
	Patients who are unable to care for themselves and do not have the assistance of a full-time carer.

seen to be slightly different with many overlaps. Tables 9.2 and 9.3 indicate which patients are more suited to APD and those who are more suited to CAPD.

Peritoneal Dialysis for Those with Diabetes

Diabetic nephropathy is the leading cause of end-stage renal disease worldwide (Atkins and Zimmet 2010). Although death rates of patients with diabetes on HD and PD have decreased substantially, they remain higher than rates in nondiabetics on both modalities. PD offers equal survival compared with HD for younger patients with diabetes during early years of dialysis. Mehrotra et al. (2011) describes the benefit of preserving vascular access in patients who often have poor vasculature.

Blood glucose control

A patient using only glucose-based solutions will absorb between 100 and 150 g of glucose per day from the dialysis fluid. This can lead to problems, such as hyperinsulinaemia and premature arteriosclerosis. Alternative solutions offer benefits for

those with diabetes. Glucose-free solutions (Icodextrin and amino-acid solutions) provide an excellent solution for people with diabetes, as the use of these fluids significantly reduces the amount of glucose absorbed by the patient.

In a study by Li et al. (2013) where both icodextrin and amino acid PD dialysis fluids were compared with usual glucose solutions, there was a 0.5% reduction in glycated haemoglobin in the icodextrin/amino acid group. However, as there was an increase in adverse events and deaths in this group, including events related to extracellular fluid expansion, it is critical that this approach with use of low-glucose solutions is accompanied by careful monitoring of hydration and glucose levels (Woodrow et al. 2017).

There are a number of methods of blood sugar control for patients with diabetes on PD. These include subcutaneous or IP insulin, oral agents, or dietary control. Any combination of these methods can be used. No single method has been shown to be more suitable than another for all patients as there appear to be no studies that compare the effectiveness of different methods of insulin administration; however, all methods appear to be effective in achieving metabolic control of blood sugar. Poor glycaemic control appears to be associated with higher mortality in patients on PD (Duong et al. 2011). It is very important to be aware of the danger of using inappropriate point-of-care glucose meters in patients using icodextrin dialysate (Perera et al. 2011).

IP Insulin

There are many benefits to adding insulin via the IP route. Insulin administered by the IP route crosses the peritoneal membrane by passive diffusion and is predominantly delivered to the liver via the portal circulation before reaching the systemic circulation. Following IP administration, the concentration of peripheral-free insulin is lower when compared to the peripheral-free insulin concentration achieved following subcutaneous dosing. A proposed advantage of IP insulin administration is that insulin is delivered to the liver without creating hyperinsulinaemia, a situation thought to be potentially atherogenic.

Absorption of insulin from the peritoneal cavity is concentration dependent. Insulin administered into an empty peritoneal cavity will be absorbed more rapidly and completely than if the insulin is administered in a large volume of dialysis solution. Direct injection of multiple daily doses of insulin into the peritoneum may be impractical for most patients. Therefore, IP insulin is usually administered via the routine dialysis fluid exchange. Conversion from a stable subcutaneous insulin dose to IP insulin dosing at initiation of PD usually requires a 2.5–3.5-fold increase in the insulin dose. This increase is needed because of the incomplete absorption during the dialysate dwell period, an increased insulin requirement due to the hypertonic dextrose-containing dialysate, and possible adsorption (binding) of the insulin to the polyvinyl chloride surface of the dialysis bags. Approximately 10–20% of the administered dose may bind to the surface of the PD bag and tubing. Regular (short-acting) insulin should be used for IP dosing.

For patients using CAPD, the total daily insulin dose should be divided amongst the exchanges according to anticipated calorie intake from food and dialysate dextrose. Additional amounts of insulin may need to be added to exchanges containing more hypertonic dextrose concentrations. The exact amount varies between patients but may be assessed at onset by using a sliding scale of insulin with capillary blood glucose monitoring. Dose stabilisation may require several days. Insulin requirements often increase during episodes of peritonitis.

There are a few issues that should be taken into consideration when deciding to use this method of administration: Patients who have dexterity and/or visual

problems may experience difficulties injecting insulin into the medication port and the potential exists for contamination of the sterile dialysate solution when adding any medicine via the IP route. Patients also require frequent blood glucose monitoring when attempting to regulate IP insulin initially.

Insulin should be added to the bag of dialysis fluid before it is connected to the patient. In this way, the bag may be discarded if accidentally contaminated or punctured by the needle. Strict aseptic technique must be followed when adding the insulin, which is usually done through the specially designed medication port. All bags should be inverted several times before the fluid is drained into the patient to ensure thorough mixing of the insulin. There is no evidence to suggest that IP insulin administration increases the risk of peritonitis (Williams et al. 2000).

A recent meta-analysis of subcutaneous versus IP insulin for patients with diabetes mellitus on CAPD found that use of IP insulin provides adequate glycaemic control, which appears superior to that seen following treatment with conventional SC insulin. However, the authors reported that research data are limited and further studies are needed to assess for the long-term safety of this approach (Almalki et al. 2012).

There is also the option of continuous IP insulin infusion using an implantable pump. This is a treatment option for patients with type 1 diabetes mellitus. Dijk et al. (2014) described the long-term course of glycaemic control, complications, health-related quality of life, and treatment satisfaction amongst patients with type 1 DM treated with continuous infusion of insulin. Results showed that a continuous infusion can decrease the number of hypoglycaemic episodes compared with bolus injections.

Solution Formulation

PD solution is presented in sterile plastic bags with a protective over-pouch in volumes of 500, 750, 1000, 1500, 2000, and 2500 ml. Bags of 5000 ml are available for use with APD machines. The electrolyte concentration of dialysis fluid is similar to that of normal serum, with lactate acting as a bicarbonate-generating agent to combat metabolic acidosis, which is common amongst patients. Electrolyte composition of the dialysis fluid has been changed several times over the years. A major challenge when treating patients with kidney disease has been effective phosphate control. Consequently, dialysis fluid does not contain any phosphate, and patients are given oral phosphate-binding agents to help eliminate dietary phosphate intake from the body. Calcium is an effective phosphate binder given in the form of calcium carbonate or calcium acetate. These binders can lead to raised serum calcium levels, particularly if the patient is also having vitamin D therapy. This led to the manufacture of a dialysis fluid containing physiological levels of ionised calcium and this solution (a) is compared with the original solution (b) in Table 9.4.

Table 9.4 Comparison of dialysis fluid containing ionised calcium (a) with original solution (b).

	a (mmol l ⁻¹)	b (mmol l ⁻¹)
Sodium (Na)	132	132
Chloride (Cl)	95	95
Lactate	40	35
Magnesium (Mg)	0.25	0.75
Calcium (Ca)	1.25	1.75

Glucose-based solutions

Up until the early 1990s, the most commonly prescribed and the most widely available osmotic agent used in PD was glucose. Glucose-based dialysis fluid comes in three strengths (1.36, 2.27, and 3.86% monohydrate glucose). The strong (hypertonic) solutions provide the greater osmotic strength. Patients should use 1.36% glucose most often whilst their weight is within 0.5 kg of their 'dry' or 'target' weight. Hypertonic solutions should be used when the patient has fluid overload. Most patients ultrafiltrate an extra 200–600 ml by using a 2000 ml medium (2.27%) glucose solution bag and an extra 400–1000 ml by using a 2000 ml strong (3.86%) glucose solution bag. Patients should be taught to record their body weight on a daily basis and choose the appropriate solution strengths for that day.

UF by hypertonic solutions is maintained for approximately eight hours in most patients. After this time some reabsorption of fluid may occur. In those patients whose membranes transport solutes quickly (high transporters), reabsorption may occur sooner than eight hours, giving rise to the need to use an icodextrin fluid exchange for the longer dwell times (i.e. the overnight dwell in CAPD or the day-time dwell in APD).

Icodextrin peritoneal dialysis solution

There are problems associated with the use of glucose as an osmotic agent, such as hyperglycaemia and hyperlipidaemia. Patients who have poor UF provide the greatest challenge in this area. Worsening fluid balance results in reduced technique and patient survival. Icodextrin solution is known to improve UF in the long dwell during PD (Silver et al. 2014).

Icodextrin 7.5% is a formulation of a large molecular-weight glucose polymer, which is a more biocompatible solution as it is approximately iso-osmolar with serum. The use of this larger molecule means that less glucose is available for absorption through the peritoneal membrane. Its long-acting UF performance (up to 12 hours) is combined with low carbohydrate absorption. Icodextrin reduces the exposure of the peritoneal membrane to glucose for more than 50% of the dialysis time if used for the long dwell and improves fluid balance and BP control compared with 2.27% glucose (Lin et al. 2009).

Paniagua et al. (2002) demonstrated that patients using Icodextrin had significantly reduced glucose exposure and this was, in turn, associated with stabilisation of weight in patients with diabetes.

UK Renal Association standards (Woodrow et al. 2017) recommend that specialised solutions such as glucose polymers (Icodextrin) are preferable for patients with high or high-average solute transport.

Bicarbonate/lactate-based peritoneal dialysis solutions

Bicarbonate/lactate solutions were developed following extensive research to identify the most suitable alternative formulation to the traditional lactate buffered solutions. The commercially available solution comes in a double-chambered bag because some of the compounds of the bicarbonate/lactate solution are not stable during the steam sterilisation process. Glucose needs to be in acidic conditions (low pH) in order to prevent caramelisation. Since the bicarbonate/lactate solution is neutral, the glucose has to be separated from the other compounds. The glucose sits in the upper, smaller chamber, together with calcium and magnesium salts, under acidic conditions. The bicarbonate, lactate, and sodium salt sit in the lower, larger

chamber. The two solutions are mixed just before infusion (usually whilst the patient is draining the used fluid during CAPD or during the setup of the APD machine).

This solution, with a combination of bicarbonate 25 mmol and lactate 15 mmol as the buffer, is intended for all exchanges. The solution has a physiological buffer system, with a physiological pH of 7.4, and reduced glucose degradation product levels. It allows a significant reduction of inflow pain and/or discomfort in sensitive patients and has a high potential for improved long-term preservation of the peritoneal membrane (Han et al. 2009).

The composition of a bicarbonate/lactate-based solution is:

- glucose monohydrate: 1.36, 2.27, or 3.86%;
- sodium chloride: 5.38 g l⁻¹;
- calcium chloride: 0.184 g l⁻¹;
- magnesium chloride hexahydrate: 0.051 g l⁻¹;
- sodium bicarbonate: 2.10 g l⁻¹;
- sodium lactate: 1.68 g l⁻¹.

They have several advantages as a buffer for PD solutions:

- physiological pH and bicarbonate concentration;
- reduced pain on infusion;
- improved membrane preservation;
- retrospective studies have suggested that biocompatible PD solutions may reduce the rates of peritonitis, although a long-term follow-up study did not detect any clinically significant advantages in terms of technique survival or peritonitis (Srivastava et al. 2011);
- preservation of RRF (Johnson et al. 2012).

Physiological pH and bicarbonate concentration

Bicarbonate is the natural buffer of the body. As a result of the metabolism of ingested foods, our body produces hydrogen ions (protons). This acid must be excreted or neutralised in order to maintain the body's acid–base balance. The kidneys play a key role in maintaining the acid–base balance. Not only do they excrete hydrogen ions, but they also regenerate bicarbonate. In people with renal failure this function is impaired or lost. It is important to replace the lost bicarbonate to maintain the acid–base balance and prevent the occurrence of acidosis. Using bicarbonate in the PD solution is the most natural way of restoring the bicarbonate level. Alternative buffers, like lactate, need some conversion (metabolism) before they result in bicarbonate.

The biocompatibility of a PD solution has been defined as the ability of a solution formulation to permit adequate long-term dialysis without a clinically significant undesirable host response (*Consensus Conference on Biocompatibility* 1994). These objectives will best be met by solutions whose composition is identical to the composition of extracellular fluid in the body, in particular to the composition of blood. Bicarbonate and lactate PD solution has been developed as an alternative buffer component.

Reduced pain on infusion

A clinical study on the treatment of pain on infusion (Cho et al. 2012) compared a bicarbonate/lactate solution and another experimental solution based on 38 mmol l⁻¹ of bicarbonate (without lactate). The experimental solution and the bicarbonate/lactate solution both reduced the infusion pain, but the bicarbonate/lactate mix appeared the most effective.

Table 9.5 The electrolyte formulation of intraperitoneal amino acid (IPAA) solution.

Sodium	132 mmol l ⁻¹
Chloride	95 mmol l ⁻¹
Lactate	40 mmol l ⁻¹
Magnesium	0.25 mmol l ⁻¹
Calcium	1.25 mmol l ⁻¹

Amino acid based peritoneal dialysis solution

Intraperitoneal amino acid (IPAA) solution contains 15 amino acids. Eight are essential amino acids, two are considered essential to patients with kidney disease, and five are nonessential. The electrolyte formulation is shown in Table 9.5. The osmotic agent glucose is replaced by 1.1% amino acids, which have the comparative UF capability of 1.36% glucose solution. After a four- to six-hour dwell, 65–95% of the amino acids are absorbed, the equivalent to about 18 g (from a 2000 ml bag containing 22 g of amino acids) or 0.3 g kg⁻¹ day⁻¹ in a 70 kg patient. This is approximately 25% of the daily protein requirement for a patient on PD.

IPAA is administered in the same way as other PD solutions. It is prescribed for one exchange per day, replacing one of the usual glucose dialysis solution bags or mixed with overnight glucose solutions during APD. If given during the day, it should be given either at a main meal or with a high-calorie snack, as this will ensure that the amino acids are used in the anabolic process to generate protein rather than being expended as an energy source. The use of 1.1% amino acid PD solution, when used instead of one glucose exchange, decreases both peritoneal membrane glucose exposure and systemic glucose absorption.

Patients will benefit from using a combination of all the available solution formulations, including amino acid, polyglucose, bicarbonate/lactate, and glucose. UK Renal Association Guidelines (Woodrow et al. 2017) offer advice on using different PD solutions, including the suggestion that biocompatible solutions (normal pH and/or low concentrations of glucose degradation products) be considered for preservation of residual kidney function. Currently there is insufficient evidence to recommend that all patients should be treated with biocompatible solutions, especially as this may have a significant cost implication.

Assessing Peritoneal Dialysis Adequacy

It is well documented that many patients survive well on dialysis and this is due to its ability to remove nitrogenous waste products, correct electrolyte and acid–base imbalance, and remove excess fluid. Patients feel unwell if they are inadequately dialysed; they eat less, become malnourished, and are therefore at increased risk of infection. Inadequate fluid removal causes hypervolaemia, which results in hypertension, fluid overload, and cardiac complications.

The goals of PD are to prolong life, reverse the symptoms of uraemia, maintain patients in positive nitrogen balance, have an adequate energy intake, and have their maximum level of quality of life in a way that is least disruptive to their lifestyle. A major benefit of a home-based therapy is promoting patients' control over their own condition and treatment, which can have positive physical and psychological effects (Mathers 2011). This can be summarised by saying that

well-dialysed patients feel well enough to eat a sufficient diet rich in protein and experience a minimum of complications to their treatment.

There are a number of ways in which dialysis adequacy can be measured and all parameters must be taken into consideration:

- creatinine clearance – a solute-removal test based on body surface area;
- Kt/V – a urea index relating urea clearance to the volume of urea distributed in the body;
- protein nutrition;
- general wellbeing.

Creatinine as a measure of dialysis adequacy

Creatinine is a metabolic product from the breakdown of muscle. Patients who have a larger muscle mass therefore tend to have higher serum creatinine levels. Creatinine, with a molecular weight of 113 Da, will equilibrate more slowly across the peritoneal membrane than urea (molecular weight 60 Da).

A normalised BSA of 1.73 m² is used to enable an assumption of the creatinine generation rate based on a patient's size, provided that the patient is infection free and in nitrogen balance.

Urea as a measure of dialysis adequacy

Urea is a metabolic product of the protein we eat. As more protein is eaten, more urea is generated. It therefore follows that when examining a patient's serum urea levels it is important to take into consideration recent protein intake. A low serum urea in a patient with ERF (established renal failure) may simply be due to a low protein intake, rather than adequate dialysis. A high serum urea on the other hand may indicate increased catabolism, a deterioration in RRF, or inadequate dialysis. Urea is a small molecule (molecular weight 60 Da), which is distributed in body water. It diffuses readily and is therefore easily removed from the blood.

The prescription index Kt/V was developed by Gotch et al. (1983) and Gotch and Sargent (1985) in the National Co-operative Dialysis Study of patients on HD. Kt/V is an index of urea removal, which is patient-specific as it looks at urea removal achieved over time ($K \propto t$) and measurement of urea in the body water (V) for each patient. Therefore: K = clearance; t = time; V = volume of body water in which urea is distributed.

The index does not account for dietary protein intake, protein catabolic rate, or urea generation rate. It is just as important to measure residual renal Kt/V as it is to measure dialysis Kt/V . The two should be added together to give a total weekly Kt/V value. Kt/V for both the patient's dialysis regime and RRF can be calculated using the worksheet shown in Figure 9.16.

Protein nutrition

Malnutrition has been shown to be a major risk factor in survival of patients on PD (Carrero 2009). See Chapter 13 for further details.

General wellbeing

Despite the efficacy of a combination of the above physical parameters for measuring adequacy of dialysis, there can be no doubt that the ultimate gauge of treatment success must increasingly become the overall quality of life of the patient. There is

Name patient:
Date:

Kt/V^*

1. Information required

a. Patient

Weight kg
Height cm

b. 24 hour urine

Volume l
Urea mmol/l
Creatinine mmol/l

c. 24 hour dialysate

Volume l
Urea mmol/l
Creatinine mmol/l
($\frac{\mu\text{mol/l}}{1000}$)

d. Serum

Urea mmol/l
Creatinine mmol/l
($\frac{\mu\text{mol/l}}{1000}$)

2. Kt/V calculation

a. Residual renal Kt/V

$$\begin{aligned} \text{Step 1: } & \frac{\text{..... mmol/l}}{\text{..... mmol/l}} \times \frac{\text{..... l} \times 1000}{\text{min. in 24 h}} = \text{..... ml/min} \\ & \text{Residual renal clearance} \\ \text{Step 2: } & \frac{\text{..... mmol/l} \times 1440 \times 7}{\text{..... kg} \times \begin{matrix} \text{♂ 0.6} \\ \text{♀ 0.55} \end{matrix} \times 1000} = \text{Weekly residual } Kt/V \end{aligned}$$

b. Dialysate Kt/V

$$\begin{aligned} & \frac{\text{..... mmol/l}}{\text{..... mmol/l}} \times \text{..... l} \times 7 \\ & \text{..... kg} \times \begin{matrix} \text{♂ 0.6} \\ \text{♀ 0.55} \end{matrix} = \text{Weekly dialysate } Kt/V \end{aligned}$$

3. Total kt/V

$$\text{Weekly residual } Kt/V + \text{Weekly dialysate } Kt/V = \text{Weekly total } Kt/V$$

4. Compare patient's weekly Kt/V with target

$$\text{Patient Weekly total } Kt/V \geq \text{..... Target}$$

* K = Urea clearance (l/week) $-t$ = Number of days per week the patient dialyses
 V = Volume of urea distribution

Figure 9.16 Kt/V worksheet.

now widespread agreement that in assessing the effects of a treatment it is essential to assess both the quality and quantity of life. Healthcare purchasers are increasingly under pressure to demonstrate cost-effective utilisation of the limited resources available to them. Quality-of-life assessment is a key outcome measure in determining this cost-effectiveness, but its multidimensional and subjective nature means that it is problematic to measure.

Preservation of RRF is an important goal for dialysis and patients treated with PD have been shown to have a 65% lower risk of RRF loss than those on HD (Moist et al. 2000). The direct mechanisms behind this are unknown but preservation of RRF is improved with better volume control, blood pressure management, and superior nutritional status (Blake et al. 2011). This should all be taken into consideration when measuring the adequacy of dialysis.

Clinical guidelines

UK Renal Association guidelines (Woodrow et al. 2017) recommend combined urinary and peritoneal small solute clearances of $Kt/V > 1.7 \text{ week}^{-1}$ or a creatinine clearance of $> 50 \text{ l week}^{-1} 1.73 \text{ m}^{-2}$ to be considered as minimum treatment doses and should be measured every six months in patients who are stable but more frequently if a patient's condition determines. The guidelines recommend that this is a minimum treatment dose and should be increased in patients experiencing symptoms, again reinforcing the importance of the patient's quality of life.

Various studies have explored increasing these clearances but have shown no survival benefit, and there is no clear evidence of this being affected by the patient's transport status (Blake et al. 2011).

A landmark study was conducted to demonstrate that PD can be a successful treatment for patients who do not pass urine (Brown et al. 2003). The European APD Outcome Study (EAPOS) was a two-year, prospective, multicentre study. A total of 177 patients were enrolled. The APD prescription was adjusted to aim for creatinine clearance (C_{crea}) of $60 \text{ l week}^{-1} 1.73 \text{ m}^{-2}$ and UF of $750 \text{ ml } 24 \text{ h}^{-1}$ during the first six months. Baseline solute transport status (D/P) was determined by peritoneal equilibration test. At one year, 78 and 74% of patients achieved C_{crea} and UF targets, respectively, with 50% of patients using icodextrin. The two-year patient survival was 78% and technique survival was 62%. This study showed that patients who do not pass urine can successfully use APD. Baseline UF, not C_{crea} or membrane permeability, is associated with patient survival.

There are a number of computer programs available on the market that will calculate the patient's Kt/V , creatinine clearance, and nutritional status. Some of these programs will also model the patient's treatment, allowing the nurse or physician to look at a wide range of PD therapy options for the optimal regime that meets the adequacy needs of each individual patient. This enables the clinician to eliminate the trial-and-error process of prescribing PD, takes away the need to perform manual calculations, and provides the renal unit with a database of their patients' quality of dialysis.

If patients are no longer achieving these adequacies the prescription can be increased, taking into account the patient's lifestyle and how these changes can be accommodated within reason. As this potentially becomes more difficult with the membrane beginning to deteriorate with the loss of RRF, the possible need for the change to HD should be explored to allow the patient time to rationalise this choice. The patient's reasons for choosing PD should be remembered and the implications of changing therapies on their lifestyle should be balanced with the patient's clinical condition to allow for a collaborative decision to be made.

Longitudinal Changes to the Peritoneal Membrane

The peritoneal membrane has proven to be remarkably resilient and there are a number of studies that have shown it to be stable over time (Selgas et al. 1998; Davies et al. 2001; Kendrick and Teitelbaum 2010).

Long-term changes, such as thickening of the peritoneal membrane, can cause a loss of UF (Davies et al. 2005). This may be associated with exposure of the membrane to the harmful effects of glucose-based solutions (such as glucose degradation products), peritonitis, or uraemic toxicity. In fact a marked thickening of the membrane is only seen in patients who experience more than two episodes of peritonitis but thickening was shown in patients who used hypertonic glucose solutions (Kendrick and Teitelbaum 2010).

It has been demonstrated that by avoiding the use of hypertonic glucose solutions, functional changes in the peritoneal membrane can be avoided for at least five years (Davies et al. 2001), but the catheter itself can cause membrane changes (Kendrick and Teitelbaum 2010).

It is worth noting also that thickening of the peritoneal membrane has been seen in patients with uraemia before the onset of dialysis (Plum et al. 2001) suggesting that uraemia itself may cause peritoneal membrane changes.

Encapsulating peritoneal sclerosis

Encapsulating peritoneal sclerosis (EPS) is a rare, but serious complication of long-term PD. It involves formation of an inflammatory, and later fibrotic, 'cocoon' surrounding the gastrointestinal tract which results in features of abdominal inflammation and intestinal obstruction (Johnson et al. 2010). Symptoms may include abdominal pain, nausea, vomiting, and blood in the peritoneum. EPS should be distinguished from the thickening of the peritoneal membrane that typically occurs with time on PD, but which is not associated with obstructive features. Changes in peritoneal membrane small-solute transport and UF capacity often occur, but are also common in long-term PD and not always present in EPS, so are not of diagnostic value for EPS.

One study found the rate of EPS to be 1.5%, which equated to an incidence of 4.9 per 1000 person-years (Brown et al. 2009). Radiology plays a key role in the diagnosis of EPS. Plain abdominal X-rays may show features of bowel obstruction, but are non-diagnostic, except in cases where peritoneal calcification is present as a feature suggestive of EPS. CT scanning is recommended as the definitive radiological investigation for the diagnosis of EPS (Woodrow et al. 2017). One study of 111 patients in the United Kingdom with EPS (one of the largest cohorts of patients with EPS in the literature) found that long-term survival occurred in over 50%, regardless of the various treatments strategies undertaken by various centres (Balasubramaniam et al. 2009).

It is important that patients are regularly monitored for loss of UF, changes to their membrane, and decreasing adequacy of dialysis. These patients need to be closely monitored and transition to alternative therapy discussed and planned carefully. Patients with suspected EPS should be referred or discussed early with units who have expertise in EPS surgery. Patients with EPS should have early dietetic referral and monitoring of nutritional status, with nutritional support by oral, enteral, or often parenteral supplementation usually required (see Chapter 13).

The National Institute of Health and Care Excellence (2018) guidelines do not recommend the routine switching of patients from PD to a different treatment modality in anticipation of potential future complications such as encapsulating peritoneal sclerosis. However, it is important to monitor risk factors, such as loss of ultrafiltration.

Fluid Management in Peritoneal Dialysis

During PD, hyperosmolar dialysis solution removes fluid by the process of osmosis. Water transport across the peritoneal membrane depends upon the concentration of glucose in the dialysis solution and the size of the pores in the peritoneal membrane. At the same time as fluid is being removed from the blood through osmosis, fluid is continually being reabsorbed through the lymphatic system. In addition, the osmotic gradient is continually reducing due to dilution of the PD solution (by the ultrafiltrate) and absorption of glucose into the blood. Therefore, there comes a point in time during the PD fluid exchange when fluid removal no longer takes place and fluid is reabsorbed back into the patient. This will occur before solute equilibrium.

Fluid removal and fluid balance can be enhanced in patients on PD by increasing the glucose concentration of the dialysate, increasing the volume of fluid used (although a substantial increase in intra-abdominal pressure may reduce UF due to the increased pressure), optimising the dwell time/using APD, reducing sodium intake, and by using Icodextrin solutions (Woodrow et al. 2017).

Sodium sieving

Most UF takes place during the first 30 minutes of an exchange (Venturoli and Rippe 2005). Due to the nature of the peritoneal membrane and the fact that the ultra-small pores are responsible for transporting water during the initial part of the exchange, no convection or diffusion takes place during this time. This results in a sieving process where no solutes are removed during the early stage of a PD exchange. It is important to take this into consideration when using rapid fluid exchanges such as in APD. The sieving effect, particularly of sodium, can have adverse effects on the patient. If rapid exchanges are continually used during the therapy, little sodium will be removed, giving rise to hypernatraemia and its possible effects such as hypertension in the longer term.

Problem Solving in Peritoneal Dialysis

Protein loss

Protein is lost through the peritoneal membrane at a rate of $6\text{--}12\text{ g day}^{-1}$ even in patients who are stable. To compensate for this loss, patients on PD need to eat between 1.0 and 1.2 g kg^{-1} of body weight/day of dietary protein.

This loss is increased during peritonitis, when a patient can lose up to 20 g day^{-1} . Both oral supplements and amino acid dialysate can successfully improve nutrition in PD. Amino acid dialysate therapy lowers the phosphorus load, and perhaps hyperparathyroidism, which offers the patient a benefit to reduce cardiovascular risk (Sozar et al. 2006).

Cardiovascular and lipid problems

Many patients reach ESKD with established left ventricular hypertrophy, coronary ischaemia, and vascular disease. However, despite the fact that there have been many advances in the technology and analysis of adequacy of dialysis, cardiovascular morbidity and mortality remain very high in patients on dialysis and this is the most common cause of death (Krediet and Balafa 2010).

Patients experience raised levels of cholesterol and triglycerides within the first year on PD. This is mainly due to the glucose absorbed from PD fluid. Several

studies have shown that these changes are not long-lasting and peak levels are usually reached within 3–12 months of starting dialysis.

Raised intra-abdominal pressure problems

Raised intra-abdominal pressure is caused by the pressure of high volumes of fluid in the peritoneal cavity. This pressure is further increased when the patient carries out strenuous exercise or suffers excessive coughing. Continuous raised intra-abdominal pressure can increase the risk of abdominal hernias such as inguinal, incisional, diaphragmatic, or umbilical, and of dialysate leakage around the catheter exit site.

Oedema of the labia in females and the scrotum and penis in males is a distressing complication caused by dialysate leakage through soft tissues. It is usually easily rectified by stopping PD for a short period (usually up to one week). Hernias and persistent leaks require surgical repair, while stopping PD for a time to allow the site to heal. If HD is not an alternative form of treatment for the patient during this temporary interruption to treatment, PD may be continued so long as the patient is lying down, therefore decreasing the intra-abdominal pressure (i.e. by using some form of APD).

In the event of dialysate leakage at the exit site, PD must be ceased immediately as the presence of a glucose-rich solution at a wound site gives rise to a markedly increased risk of infection. Leakage can be identified by using urine test sticks or blood glucose reagent strips at the exit site. The normal healing time for dialysate leakage is one week, but this may be increased in diabetes, severely uraemic, or malnourished patients.

Patients with previous vertebral disease may experience back pain due to the raised intra-abdominal pressure incurred in an upright position. In this situation APD may be the preferred therapy.

Drainage problems

These usually have a minor cause which, with proper patient training and education, can be rectified by the patients themselves at home. Reasons for poor inflow or outflow of dialysis fluid and their treatment are outlined in the next sections.

Kinks in the tubing

The most common cause of poor drainage or inflow of PD fluid is tubing kinks or closed clamps. Patients should be taught to check the tubing for kinks and closed clamps as a first line of action in the event of poor in- or outflow of dialysis fluid. Catheter kinks sometimes occur due to malpositioning during surgical insertion. This will become apparent shortly after insertion, if not during the insertion procedure, and can be confirmed by X-ray (the PD catheter has a radiopaque stripe along its length). This problem is usually rectified by surgical intervention; however, it can occasionally be improved if the patient has a bowel motion.

Constipation

Constipation should be avoided in patients on PD, not only because it causes problems with dialysate outflow but also because diverticulosis of the colon increases the risk of peritonitis. Constipation prevention is achieved by encouraging the patient to take a diet high in fibre along with a mild laxative if appropriate. Regular exercise is also recommended. If constipation does occur, treatment can be with

laxatives or glycerine suppositories. The use of phosphate-containing enemas should be avoided due to the absorption of phosphate through the bowel during their administration.

Fibrin formation

Fibrin strands or plugs (a protein formed from fibrinogen in blood plasma in the process of clotting) in dialysate effluent are a common cause of poor drainage. The blockage, usually in the catheter or tubing, can normally be removed by 'milking' the tubing. Heparin may be added to the dialysis fluid (200–500 units l⁻¹) as a prophylactic measure, as it prevents the formation of fibrin.

If 'milking' the tubing does not remove the obstruction a fibrolytic agent can be used. Both streptokinase (250 000 i.u.) and urokinase (5000 i.u.) in 2–3 ml sodium chloride 0.9% for IV (intravenous) injection are available and should be infused into the catheter under aseptic conditions; the catheter should then be clamped and the drug left to infuse for two hours. The catheter can then be checked for patency.

Malpositioned catheter

If catheter obstruction is not relieved by any of the above techniques, the problem may be due to obstruction caused by omentum attached to the catheter tip. The omental attachment usually causes the catheter to migrate out of the pelvic cavity. In such cases it often proves difficult to resolve this problem without surgery.

It is possible to remove omentum from the catheter whilst leaving it in place during surgical procedure. It is common for the surgeon to perform a local omentectomy at the same time to prevent further obstructions by omentum. If it proves impossible to rectify the obstruction or position of the catheter by surgical methods the final option is to remove the catheter completely and replace it with a new one.

Shoulder pain

Occasionally, patients complain of shoulder pain following the infusion of fresh dialysis solution. This is thought to be a referred pain caused by intra-abdominal pressure or air under the diaphragm. Although it usually resolves within 10–20 minutes from onset, the patient may find relief by taking a mild analgesia such as paracetamol 1 g.

Bloodstained effluent

This is a comparatively rare complication occurring most commonly in menstruating females. It may be due to endometriosis or retrograde bleeding through the fallopian tubes. The bleeding is usually mild and self-rectifies within a day or two without specific intervention.

More severe IP bleeding, causing darkly bloodstained fluid, can be caused by haemorrhage. This could be due to the patient straining whilst lifting a heavy object or suffering trauma to the abdomen and should be investigated.

Infectious Complications of Peritoneal Dialysis

Peritonitis is a common clinical problem that occurs in patients with ERF treated by PD. It contributes to the failure of PD and hospitalisation. Severe and prolonged peritonitis can lead to peritoneal membrane failure (Kam-Tao Li et al. 2017).

In the past, guidelines have focussed on the treatment of peritonitis, but more recent guidelines focus on the prevention of infection as this is one of the keys to success in PD.

Prevention of PD-related infections

PD programmes should carefully monitor the rate of infections – both peritonitis and exit-site infections. The cause of the infections should also be recorded as part of a continuous quality improvement programme. The incidence of relapsing peritonitis should be recorded and appropriate action taken for patients with recurrent infections. This might involve retraining or examining the PD catheter for signs of colonisation.

Rates of infection are expressed as episodes per patient month and are calculated by dividing the total number of episodes by the number of patients treated each month. For example if 100 patients were being treated with PD in January and four had an episode of peritonitis, the rate would be one episode in 25 or 1:25. Cumulative rates should be calculated over the course of a year. In this way interventions can be implemented if infection rates are rising to unacceptably high rates. The current recommended acceptable rate for peritonitis is 1:18 patient months (Kam-Tao Li et al. 2017).

The Advisory Committee for European Best Practice Guidelines (Kam-Tao Li et al. 2017) recommends the use of an assist device for all spiking procedures. The use of double-bag systems is preferred because they are more efficient in preventing peritonitis due to the flush-before-fill procedure.

The prevention of catheter exit-site infections is the primary goal of exit-site care. Once the catheter is placed, and until healing is completed, the dressing should be changed by a dialysis nurse using sterile technique. The exit site should be kept dry until well healed, which means that showers or baths should not be taken for this period, which can take up to two weeks. Once the exit site is well healed, the patient should be taught how to do routine exit-site care. Antibacterial soap and water are recommended by many centres. Use of an antiseptic to clean the exit site is preferred in some programmes (Kam-Tao Li et al. 2017).

In general, patients must be taught aseptic technique, with emphasis on proper handwashing techniques. If the water the patient uses is thought to have a high bacterial count, then use of an alcohol hand rub should be encouraged although this is used routinely in many centres. The hands must be completely dried using a clean towel after washing, before starting the exchange. The place where dialysis exchanges are carried out must be clean, free from animal hair, dust, and fans. All patients must be taught what contamination is and what to do in the event of contamination (they should go to their dialysis unit for a tubing set change if the end of the tubing is accidentally touched). The PD nurses are central to a successful PD programme that has low infection rates. Unfortunately, there are few if any studies on nurse-to-patient ratios that lead to the best outcomes. Overburdening the nurse with excessive numbers of patients will result in shortened training times and difficulty in retraining as needed. The Advisory Committee (Kam-Tao Li et al. 2017) recommends home visits. These may be very useful in detecting problems with exchange technique, but only can be carried out if the nurses have sufficient time to do such visits.

Causes of peritonitis

Most episodes of peritonitis are caused by organisms that are normal skin and nasal flora, for example *S. epidermidis* and *S. aureus*. Occasionally, water-borne organisms such as *Pseudomonas* may also cause this infection. There are five main routes of infection causing peritonitis, each one giving rise to common organisms.

Intraluminal (contamination at the solution bag and transfer set connection site)

This contamination occurs most frequently when poor techniques have been used to make the connection. Good patient training and education regarding bag exchange procedure techniques and handwashing are essential. The incidence of this cause of infection has reduced in recent years due to the use of disconnect systems.

Periluminal (infection introduced via the catheter tunnel from the exit site)

Bacteria present on the skin surface can enter the peritoneal cavity via the catheter tunnel. This infection can occur if there is infection present at the exit site or in the subcutaneous tunnel which has migrated into the peritoneal cavity. The most common organisms seen when periluminal contamination has occurred are *S. epidermidis*, *S. aureus*, *Pseudomonas*, *Proteus*, and yeast. *S. aureus* nasal carriage is known to cause an increased risk of *S. aureus* exit-site infections, tunnel infections, peritonitis, and catheter loss. Prophylaxis with intranasal mupirocin exit-site mupirocin or oral rifampin has been shown to be effective in reducing *S. aureus* exit-site infections. The use of mupirocin ointment at the exit site, however, should be avoided in patients with polyurethane catheters (Cruz catheters) as structural damage to the catheter has been reported. All patients at an increased risk for *S. aureus* infections, including *S. aureus* carriers, those with diabetes, and immunocompromised patients, should be provided with prophylaxis. A practical approach is to prescribe exit-site mupirocin for all at-risk patients and so routine nasal swab tests are therefore not necessarily required in these patients.

Transmural (infection through the gut wall)

There is an association between both severe constipation and enteritis and peritonitis due to enteric organisms (Piraino et al. 2011). The most common organism seen as a transmural cause of peritonitis is *Escherichia coli*, although multiple contamination with anaerobes and fungi may also be isolated.

Haematogenous (infection via the bloodstream)

This is a rare cause of peritonitis and it may be the peritonitis itself which causes septicaemia. The most common organisms associated with this cause of peritonitis are *Streptococcus* and *Mycobacterium*.

Vaginal (ascending through the vagina)

This is thought to be from bacteria entering the peritoneum via the fallopian tubes. The most common causative organisms seen here are *Candida* and *Pseudomonas*.

Diagnosis of peritonitis

Early diagnosis allowing prompt treatment of peritonitis is essential in minimising damage to the peritoneal membrane. Diagnosis is when two or more of the following conditions are present:

- cloudy PD effluent containing >100 white blood cells μl (more than 50% of which are neutrophils);
- abdominal pain and tenderness and pyrexia;
- identification of micro-organisms in the PD effluent by positive Gram stain or culture.

The process of diagnosis of peritonitis is summarised in Figure 9.17.

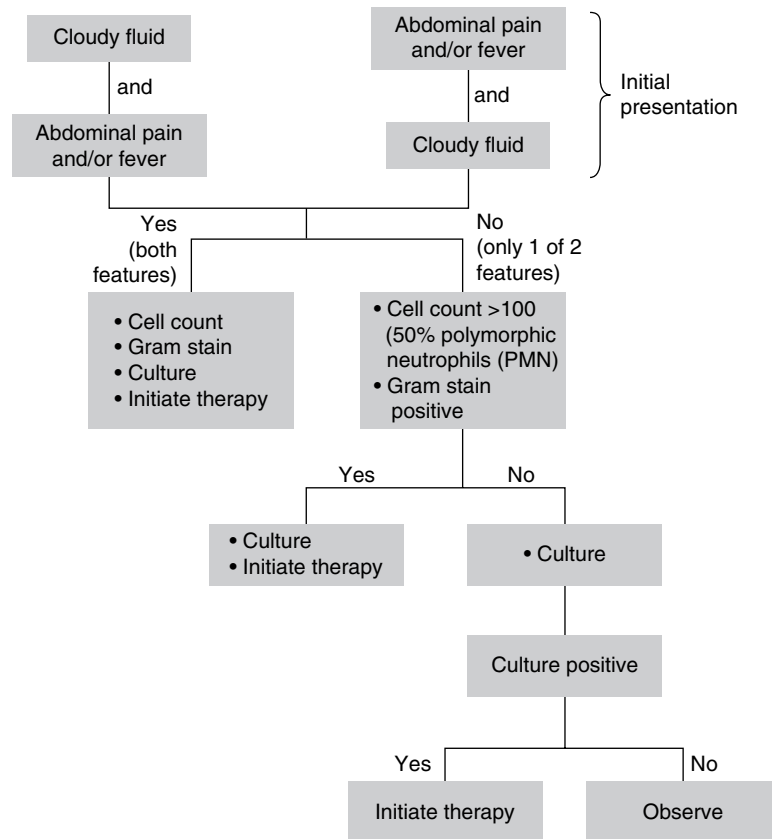


Figure 9.17 Initial clinical and laboratory assessment of a patient for peritonitis.

Obtaining a PD effluent specimen

Continuous ambulatory peritoneal dialysis

After disconnecting the drainage bag containing the effluent from the patient's transfer set, the bag should be inverted several times to mix the contents. Using strict aseptic technique, a sample is taken by sterile needle and syringe from the sample port on the bag.

Automated peritoneal dialysis

A sample may either be taken from the daytime dwell, if the patient utilises a 'wet day' (i.e. dialysate in the peritoneum during the day), by attaching a drainage set and bag to the patient's extension set. The sample is then taken in the same way as for CAPD. Alternatively, if the patient is usually 'dry' during the day (i.e. no dialysate in the peritoneum during the day), there are a number of options. Some APD machines have a sample bag that can be attached to the drainage tubing. Alternatively, the patient may be taught how to take a sample from the drainage solution containers. If this is not possible, the patient may be asked to detach the drainage solution container from the machine following treatment and take this into the unit.

There are many different protocols for the treatment of PD peritonitis. An ad hoc advisory committee has reviewed experiences reported in the literature and devised recommendations based upon these assessments. These recommendations were

published in *Peritoneal Dialysis International*, most recently updated in 2017 (Kam-Tao Li et al. 2017). Antibiotics have been administered IP, IV, or orally, and a number of different dosing regimens have been utilised. The ISPD recommendations (Kam-Tao Li et al. 2017) include advice on treating peritonitis due to the most common organisms such as coagulase-negative *Staphylococcus*, *Streptococcus*, *Enterococcus*, *Pseudomonas aeruginosa*, and also polymicrobial peritonitis, fungal peritonitis, mycobacteria, and culture-negative peritonitis. As always, individual clinical situations and variability in patient populations may necessitate modification of these recommendations. Table 9.5 in the ISPD recommendations provides an overview of IP antibiotic dosing recommendations for the treatment of peritonitis.

Many peritonitis episodes are mild and can be treated at home. Usually the incubation period from time of contamination for bacterial peritonitis is 24–48 hours. Any symptoms should resolve quickly following the initiation of therapy. If the infection shows either a slow response or no response to treatment, the choice of antibiotics could be inappropriate.

Those on PD should be taught how to recognise the signs and symptoms of peritonitis during their initial training period and at regular intervals. Ideally the patient, if on CAPD, should complete the bag exchange at home (the presence of PD fluid in the peritoneum may provide some pain relief from inflammation of the peritoneal membrane) and bring the bag of cloudy dialysate effluent into the clinic for sampling. Treatment can then be initiated immediately.

There is current debate as to the necessity to perform peritoneal lavage immediately after the diagnosis of peritonitis, as it is thought to reduce the number of phagocytes present in the peritoneum that are available to fight infection. Peritoneal lavage is therefore thought by some to be of benefit only to patients with purulent effluent and abdominal pain as a pain-relieving exercise. There is no evidence to suggest that a transfer set change performed at this time is of any benefit. On admission to the PD clinic the usual fill volume for the patient is medicated with antibiotics.

The patient or carer can be taught how to add the antibiotics to the dialysis fluid to facilitate self-care. Heparin (200–500 units l⁻¹) may also be added to the fluid to prevent the formation of fibrin, which is more likely in the presence of infection.

APD patients may receive antibiotics intraperitoneally by adding the antibiotics to the daytime dwell dialysis solution. Little is known about intermittent dosing requirements in patients treated with APD. In intermittent dosing, the antibiotic-containing dialysis solution must be allowed to dwell for at least six hours to allow adequate absorption of the antibiotic into the systemic circulation. Most antibiotics have significantly enhanced absorption during peritonitis (e.g. IP vancomycin is about 50% absorbed in the absence of peritonitis, but closer to 90% in the presence of peritonitis), which permits subsequent re-entry into the peritoneal cavity during subsequent fresh dialysis solution exchanges (Kam-Tao Li et al. 2017).

Peritonitis is monitored closely and dialysate effluent should be clear within 48 hours of commencing treatment. If the peritonitis resolves, antibiotics are discontinued 7–10 days after the start of therapy according to local protocol.

Absorption of antibiotics into the serum through the peritoneum from the dialysate is rapid. Therefore, in most cases, administration of IV antibiotics is unnecessary.

Permeability changes during peritonitis

The peritoneal membrane permeability tends to increase during episodes of peritonitis, perhaps due to increased blood flow through the peritoneum. Clearances of both large and small molecules increase, as does the absorption of glucose. This can result in marked increases in protein loss through the peritoneum and poor UF.

Patients need to be educated as to the need to increase dietary protein intake during episodes of peritonitis and to care for their fluid balance ensuring that, if they have no RRE, fluid intake is kept to a minimum. Rarely, patients are severely ill with peritonitis and need to be treated in hospital.

Culture-negative peritonitis

Occasionally (less than 20%), cultures may be negative for a variety of technical or clinical reasons. Duration of therapy should be two weeks. If, on the other hand, no clinical improvement occurs within 96 hours, repeat cultures should be taken with consideration of mycobacteria or fungi, and catheter replacement or removal should be considered.

Fungal peritonitis

The ISPD recommends anti-fungal prophylaxis when PD patients receive antibiotic courses to prevent fungal peritonitis. There should be immediate catheter removal when fungi are identified in the PD effluent. Irrespective of the choice of anti-fungal agent, observational studies suggest that prompt catheter removal probably improves outcome and reduces mortality. Anti-fungal agents should be continued after catheter removal for at least two weeks. A recent study suggested that around one-third of patients could return to PD (Nadeau-Fredette and Bargman 2015).

Relapsing peritonitis

Relapsing peritonitis is diagnosed as a recurrence of the same organism within four weeks of completion of the course of antibiotics. These infections should be treated in the same way as the initial peritonitis; however, the reason may be due to abscess formation, colonisation of the catheter, or subcutaneous catheter tunnel infection. If there is no response to the antibiotics within 96 hours, consideration should be given to catheter removal and replacement at a later date.

Exit-site and tunnel infection

Exit-site infection is defined as the presence of purulent discharge, with or without erythema of the skin at the catheter–epidermal interface. Tunnel infection is defined as the presence of clinical inflammation or ultrasonographic evidence of collection along the catheter tunnel (Kam-Tao Li et al. 2017). Updated peritoneal dialysis-related infection recommendations were published in 2017 by the ISPD (Kam-Tao Li et al. 2017) and can provide further details.

A culture of the drainage from around the exit site should be obtained. Antibiotic therapy may be initiated immediately if the infection looks severe, or delayed until the results of the culture are available. Therapy should be continued until the exit site appears completely normal. Prolonged antibiotics may be necessary. If three to four weeks of antibiotics fails to resolve the infection, the catheter may be replaced.

Redness and swelling around the catheter exit site without purulent drainage are sometimes an early indication of infection. If infection is suspected, then therapy should be initiated: this may be either intensified local care, a local antibiotic ointment, or an oral antibiotic that covers Gram-positive organisms. ISPD guidelines (2017) recommend empiric oral antibiotic treatment of exit-site infections with appropriate *S. aureus* cover such as a penicillinase-resistant penicillin (e.g. dicloxacillin or flucloxacillin) or first-generation cephalosporin. If the patient has had a prior history of infection or colonisation with methicillin-resistant *S. aureus*

(MRSA) or *Pseudomonas* species, they should receive a glycopeptide or clindamycin, or appropriate anti-pseudomonal antibiotic, respectively. Exit-site infection, except episodes caused by *Pseudomonas* species, should be treated with at least two weeks of effective antibiotics. Exit-site infection caused by *Pseudomonas* species should be treated with at least three weeks of effective antibiotics.

Simultaneous removal and reinsertion of the dialysis catheter with a new exit site under antibiotic coverage in patients with refractory exit-site or tunnel infection without peritonitis, defined as failure to respond after three weeks of effective antibiotic therapy, is recommended. Removal of the dialysis catheter in patients with exit-site infections that progress to, or occur simultaneously with, peritonitis is also recommended (Kam-Tao Li et al. 2017). In patients who have undergone dialysis catheter removal for simultaneous exit-site or tunnel infection and peritonitis, any reinsertion of a PD catheter should be performed at least two weeks after catheter removal and complete resolution of peritoneal symptoms (Kam-Tao Li et al. 2017).

Education and Training for Those on Peritoneal Dialysis

It is essential that effective education takes place before patients can be expected to treat themselves at home. Upwards of 90% of the care received by home dialysis patients is self-administered in the home. 'It is a common but erroneous belief that anyone can teach PD, but ... success depends upon the approach adopted' (Uttley and Prowant 2000). Finkelstein et al. (2011) described components of a successful CAPD education programme based on adult learning principles. The detailed recommended practice of PD training is covered in ISPD guidelines. Every PD programme should prepare the trainers according to this document and develop a specific curriculum for training. Unfortunately, high-level evidence guiding how, where, when, and by whom PD training should be performed is lacking (Zhang et al. 2016). Ideally, each patient should be trained by a dedicated nurse, whose time is totally focused on training the patient. However there are few published data on the optimal nurse-to-patient ratios or training protocols (Zhang et al. 2016).

Barriers to learning

People who are just about to start dialysis are often frightened – the prospect of dialysing oneself at home may not appeal. Many new patients have uraemia; symptoms may include nausea, vomiting, sleep disturbances, and confusion. Some patients feel so physically unwell by the time they are to commence dialysis that they lack the motivation to learn, feeling that they will never recover.

Teaching this group of patients can be made all the more difficult when other barriers to learning become apparent. A fundamental barrier is language. In the United Kingdom, for instance, there is a growing ethnic population, giving rise to a growing proportion of people who speak little English. There are limited resources available for translation and it is frequently the responsibility of a younger member of the family, often a son or daughter, to act as translator during training. It may thus be difficult to assess who is learning, and with no knowledge of the language that is being translated, the trainer finds it difficult to ascertain just who has grasped the concept or answered the question – the patient or the translator? Language may also become a barrier when speaking to patients with no previous medical knowledge. Jargon and clinical terminology can be frightening and confusing.

Many older patients have to learn PD and having to learn new concepts and procedures on which their life will depend may seem an overwhelming task. This sometimes makes learners feel vulnerable and inadequate, particularly if they are slow to

learn. Short-term memory loss is a problem suffered by many elderly patients and is a source of great frustration to both learner and trainer. These patients frequently have added physical barriers to learning, such as poor vision or lack of manual dexterity. Varying levels of deafness may also be a problem – the learner is trying not only to understand what has been said but is also straining to hear.

Literacy levels in England are poor, with 15% of the population between 16 and 65 years being below entry level (Entry level 3 is the level expected of an 11-year-old) (National Literacy Trust <https://literacytrust.org.uk> accessed 28 July 2018). If we consider this problem in relation to the concepts and procedures that need to be explained to patients receiving dialysis, it becomes apparent that the information given must be clear, unambiguous, and readily understood, particularly if the patient's literacy difficulty is paired with a second or even a third barrier to learning.

The learning environment

The PD training setting was discussed by Castro et al. (2012) who described increased patient, nurse, and physician satisfaction with home-administered PD training. The main objective of home training is to establish, early on, the patient's social environment and psychological status, and to assess how these influence aspects of learning and adapting to PD. When training was individualised to the patient, Davies et al. (2000) saw in-home patient training as more efficient than in-centre training as measured by time required to train.

Figueiredo et al. (2016) identified the lack of evidence in PD training, therefore the Nursing Liaison Committee of the International Society for Peritoneal Dialysis (ISPD) undertook a review of PD training programmes around the world in order to develop a syllabus for PD training. This syllabus was developed to help PD nurses train patients and caregivers based on a consensus of training program reviews, utilising current theories and principles of adult education. It is designed as a 5-day programme of about 3 h day⁻¹, but both duration and content may be adjusted based on the learner. After completion of the proposed PD training syllabus, the PD nurse will have provided education to a patient and/or caregiver such that the patient/caregiver has the required knowledge, skills, and abilities to perform PD at home safely and effectively. It is recommended that PD nurses review this syllabus prior to embarking on teaching patients and their families: <https://ispd.org/ispd-guidelines> (accessed 20 July 2018).

Recommendations for training within renal units

- set aside an area specifically for teaching purposes. The area should preferably be away from the ward, and be nonclinical and quiet. A television and DVD or PC can be used in this area for teaching.
- designate a team of nurses for training duties only. Establish some continuity of care by allocating each patient to a designated nurse.
- invite family members or partners to participate in the teaching programme.
- use a wide variety of training materials. Five points to good presentation of these materials:
 - teach the smallest amount possible for the job required;
 - make the point as vividly as possible;
 - review repeatedly;
 - have the learner restate and demonstrate material;
 - the subject matter should be relevant.
- any material should be presented in a way that is comprehensible to the learner.

- despite the fact that the readability of the material can be measured by the same formula, readers' skills may vary with their interest and background of experience in a particular topic area.
- training materials are most effective when presented in an interesting and appropriate manner. Both the language used and the material's degree of complexity need to be taken into account.
- the material should be presented in a memorable fashion. Any visual aids need vivid, simple messages which are easy for patients to remember.
- finally, but perhaps most importantly; it is essential that the patients want to learn what is being taught.

The training programme should be designed to prepare patients fully for return to the community. The aim of a training programme is to educate patients to a standard whereby they can confidently care for themselves and perform PD in the community. For some learners this may mean that they learn only how to perform PD, troubleshoot, and manage their renal diet. For others much more detail may be desired, for example, learning how dialysis works.

Group teaching is an excellent way for patients to learn. This not only enables patients to learn from each other, but also helps the teacher, as many patients can be taught the same subject at the same time. The bulk of the training programme should focus on the patients themselves, relating all they are learning to their disease, treatment and, ultimately, their lifestyle. Sessions should be designed to last for no longer than 20 minutes and visual aids such as flipcharts, acetates, and videos are used to make the material interesting and varied.

Online resources are a useful tool in the education of people with kidney disease. It provides many advantages in that the information is available 24 hours a day, 7 days a week. There are now many websites dedicated solely to the education of patients with ESKD. The following list proves a useful addition to any training programme:

- kidney Care UK <https://www.kidneycareuk.org/about-kidney-health> (accessed 29 July 2018)
- national Kidney Federation www.kidney.org.uk/help-and-info/medical-information-from-the-nkf- (accessed 29 July 2018)

What to teach patients

It is important that patients new to PD are discharged from the renal unit with enough knowledge to care for themselves safely on dialysis. Broadly speaking, when each patient is taught, priority should first be given to what they must know, then to what they should know, and finally to what they could know. However, all learning objectives should be patient centred.

The following topics should be included in a PD training programme:

- medication. The patient's own medicines can be used as the central focus for this session. The aim is to ensure that the patient knows how often and why each medicine is taken.
- normal functions of the kidney. This session can be given in groups using visual aids to explain in a simple way the basic functions of the kidney, relating these to the symptoms they suffer when kidneys fail.
- CAPD and APD procedures. These are most easily taught on a one-to-one basis. Demonstration techniques can be used to explain the procedure. A PD simulator (plastic torso with a PD catheter) is an excellent tool on which patients can practise their exchanges.

- catheter and catheter exit-site care. This can be taught to the patient on a one-to-one basis. The PD simulator can be used to practise exit-site dressing technique, as can getting the patient to practise the technique in front of a mirror. Photographs are useful to help explain visually the difference between a healthy and an infected exit site.
- how PD works. Osmosis and diffusion can be explained using simple experiments or diagrams.
- diet. Eating is an activity which most people enjoy and which therefore takes up a rather large part of our lives. Maybe it is for this reason that many patients focus on diet and want to know all there is to be taught. Plastic models of food can be used in training sessions to make the learning fun.
- infections. It has been well documented that peritonitis is a major complication of PD and it is therefore important that peritonitis is explained to patients well, using a purpose-printed flipchart.
- fluid balance. Fluid overload can be associated with excessive fluid intake and poor education. It is a common experience that one of the most difficult aspects of treatment to adhere to is the reduced fluid allowance. This subject can also be taught in groups using a purpose-printed flipchart. Weighing a jug of fluid can also be useful to demonstrate the difference between fluid weight and flesh weight.
- fertility and sexuality. It is important to discuss sexuality and body image with patients on PD. Having the PD catheter present in the abdomen may inhibit some people (either the patient or partner) and it is essential that any anxieties are discussed. Fertility should also be discussed with patients and partners where appropriate, as it is possible for PD patients to conceive.
- employment. Having dialysis is not a reason for giving up work. The training period is a good time to discuss work options with patients.
- ordering and delivery of PD supplies. The practicalities of ordering and delivery of the PD supplies to the patient's home prove a great worry for many patients and their families. This can often be compounded by the problem of where to store this large amount of equipment. Patients can be encouraged to talk amongst themselves to gain ideas from each other as well as utilising the experience of nurses.
- holidays and travel. It is possible to travel whilst being treated with PD and many patients go on holiday frequently. The practicalities of travel and holidays should be discussed during the training period and on an ongoing basis if appropriate.
- exercise. The nurse's role is to promote a healthy lifestyle for patients. The training period is an ideal opportunity to discuss which types of activities are best suited to that individual patient.

To complement the training programme, reading materials should be made available, along with posters and DVDs. Many training materials have been translated into other languages for use by those patients whose first language is not English.

Assessment of how much information the patient has retained is difficult to make accurately. Testing can be seen as a threatening procedure, even though it is essential. Games, therefore, make a valuable contribution to the task of assessing learning and can be used in a variety of forms. Simple homemade crosswords, word searches, and quizzes can be incorporated for patients and relatives to do at the end of their training.

Conclusion

There have been considerable advances in the delivery of PD, resulting in a cost-effective therapy, which now has equivalent – if not better – outcomes as compared with HD (Mehrotra et al. 2011). Technological advances (such as APD), the ability

to deliver adequate dialysis (both solute and fluid removal), and the minimisation of damage to the peritoneal membrane (biocompatible solutions, less peritonitis) will surely improve the outcome of patients in the future.

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Additional Resources

- ISPD teaching nurses to teach <https://ispd.org/teaching-nurses> (accessed 28 July 2018).
- ISPD Guidelines <https://ispd.org/ispd-guidelines> (accessed 20 June 2018).
- UK Renal Association Guidelines for PD <https://renal.org/wp-content/uploads/2017/06/final-peritoneal-dialysis-guideline667ba231181561659443ff000014d4d8.pdf> (accessed 20 June 2018).

CHAPTER 10

Renal Transplantation

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Learning Outcomes

- to analyse the risks and benefits of renal transplantation.
- to identify the contraindications to transplantation.
- to understand the importance of pretransplant assessment and the nursing role in the pretransplant clinical care pathway.
- to explore donor and recipient matching and its relevance to graft survival.
- to understand deceased and living donation.
- to evaluate critically the possible options to increase deceased donor supply.
- to outline the nursing care for the renal transplant recipient in the pre-, peri-, and postoperative stage.
- to explain the use of immunosuppressive regimens in individual recipients.

Introduction

Renal transplantation is now widely acknowledged as the treatment of choice for those with end-stage kidney disease (ESKD). Since the time of the first transplants in the 1950s, advances in antirejection therapies, surgical techniques, and tissue matching have enabled kidney transplantation to evolve from an experimental procedure to the treatment that can offer good quality of life and the most cost-effective care for patients with kidney disease.

A successful transplant offers freedom from the practical and psychological difficulties and restrictions of long-term dialysis; freedom from dependence upon a machine or fluid bag; freedom from fluid and dietary restrictions; a return of sexual functioning and fertility with the possibility of parenthood; and a return to an almost normal lifestyle.

Most research studies clearly show that for the majority, kidney transplantation has the greater rehabilitation potential and that the quality of life for patients with functioning grafts is superior to that which is usually achieved on dialysis (von der Lippe et al. 2014). Research into quality of life has received much criticism, and individual perception and assessment of quality of life is known to be

affected by a wide range of independent and personal variables. However, for many of those with renal failure, transplantation offers an improved quality of life, and may be the most significant factor for patients when considering transplantation.

Cost-effective care

Transplantation is the most cost-effective treatment option for ESKD. The cost of a year of haemodialysis or peritoneal dialysis is similar to that of a renal transplant in the first year. However, thereafter the cost of continuing care for a patient with a transplant is one-fifth of the cost of dialysis per year.

National waiting-list figures for kidney transplant

The improvement in quality of life and cost-effectiveness of transplantation support the suggestion that renal transplantation is the treatment of choice for the majority of patients. Unfortunately, such a goal is not possible at present because of the limited supply of deceased donor organs. The current UK waiting list for kidney transplantation stands at more than 5000 patients (Figure 10.1). 3042 renal transplants were performed in the UK in 2016–2017 (National Health Service NHS Blood and Transplant [NHSBT], 2017b).

We therefore need to explore ways of increasing donor numbers in order to offer all suitable patients the chance of a transplant.

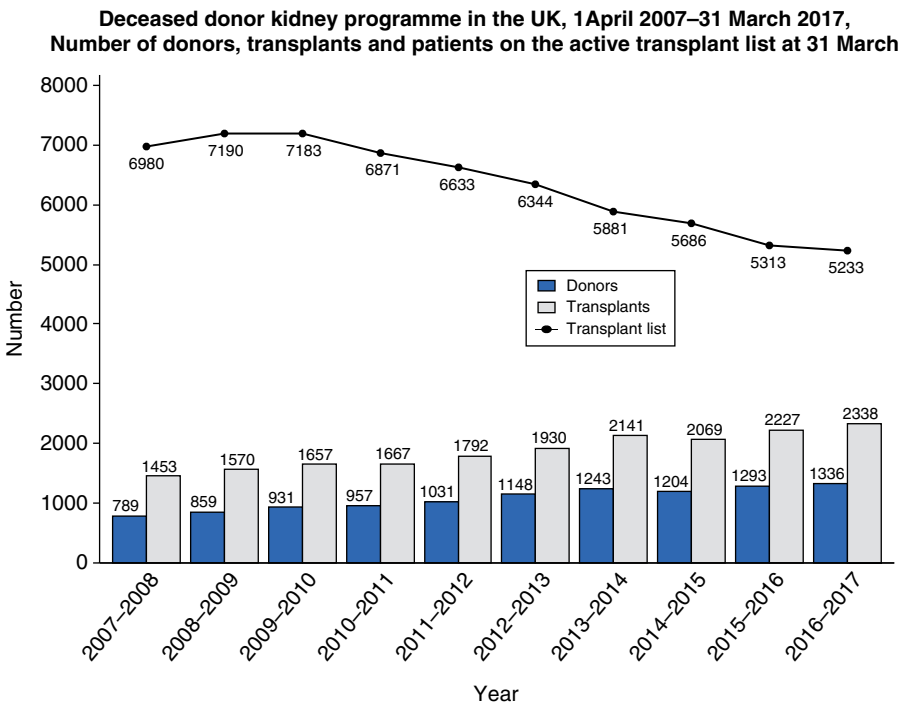


Figure 10.1 Deceased donor kidney programme in the United Kingdom, 1 April 2016–31 March 2017. Number of donors, transplants, and patients on the active transplant list at 31 March 2017. Source: from *Transplant Activity in the UK 2016–2017*, NHS Blood and Transplant.

Contraindications to Renal Transplantation

Although the majority of patients may request a transplant, transplantation may not be suitable for all those with ERF (established renal failure) because of possible medical complications.

Malignancy

Malignant disease must be excluded prior to transplantation as the immunosuppressive regime may cause accelerated growth of the malignancy and may encourage secondary spread. If the patient is known to have had cancer in the past, it is important to ascertain the type of malignancy, the stage of development, and the treatment received. Transplantation may still be possible provided that curative treatment has been given and sufficiently long follow-up has occurred to exclude recurrence. Current UK guidelines recommend a potential recipient be disease free for two years prior to listing for transplant (Dudley and Harden 2011). However, certain cancers, such as breast, colorectal, and melanoma carry a higher risk of recurrence and a disease-free period of five years may be required. The importance of time to transplant following treatment of a malignancy was shown by Penn's (1997) paper using data from the United States: in 1137 recipients who had been treated for a malignancy prior to transplantation, the recurrence rate was:

Treatment <2 years pretransplant 54%
 Treatment 2–5 years pretransplant 33%
 Treatment >5 years pretransplant 13%

Recent evidence however indicates the risk of recurrence may not be as high as previously thought. A meta-analysis of studies reporting cancer recurrence in all solid organ transplant recipients by Acuna et al. (2017) found cancer recurrence rates to be lower than previously reported. This analysis indicated that the recurrence risk was higher for kidney transplant recipients when compared to other solid organ transplant recipients and that the time from diagnosis of malignancy to transplantation was significant with more than five years offering a lower risk of recurrence. However, the authors conclude there is limited evidence available to support minimum cancer remission time to transplantation.

The risk of recurrence of cancer should be discussed fully with the recipient prior to listing for transplant. Guidance regarding specific malignancy and risk of recurrence can be obtained from the Israel Penn International Transplant Tumor Registry (<https://ipittr.uc.edu/about>).

Recurrent disease

It is important to consider the patient's primary renal disease, as in some cases the disease may recur and destroy the new kidney. Renal disorders with a high recurrence rate include primary focal segmental glomerulosclerosis (FSGS) (causing massive proteinuria and scarring of the glomeruli), mesangiocapillary glomerulonephritis (an immunological disorder of the glomeruli) and IgA nephropathy (IgAN). Studies variously report a recurrence rate post-transplant of between 20–40% in FSGS and 20–60% in IgAN (Canaud et al. 2012).

Transplantation can still be considered but only after counselling and explanation of the risks to the patient. Many centres would advise against living related donation in this situation, however it may still be possible providing both donor and recipient are fully aware of the risk of recurrence.

Other conditions, such as Goodpasture's syndrome and the other vasculitic illnesses need to have been fully treated before going ahead with transplantation because of the risk of damage in the new kidney in the presence of active disease. Twelve months is normally considered the earliest that transplantation would be considered following initial presentation of the disease. Several other diseases, such as diabetes, can cause microscopic changes in the kidney after many years, but rarely lead to graft loss.

Hepatitis virus and human immunodeficiency virus

Patients who are hepatitis B or hepatitis C positive may be at risk of progressive liver disease after transplantation due to the impact of the immunosuppressive therapy. Consultation with a hepatologist may be required and possibly liver biopsy in order to determine activity of the virus and presence of liver damage. Many patients who are hepatitis B or C positive have no disease or quiescent disease and are therefore suitable for transplantation. Careful monitoring in this group of patients is required after transplant to ensure early detection of increased viral activity and to ensure antiviral therapy is continued. Previously, infection with human immunodeficiency virus (HIV) was considered an absolute contraindication to transplantation, however the use of combination antiretroviral therapy (cART) and careful recipient selection has made transplantation possible in this group of patients. A recent UK study has shown outcomes in HIV positive patients that are comparable with non-HIV infected recipients with three-year patient and graft survival of 91.3 and 84.7% respectively (Gathogo et al. 2014).

Diabetes mellitus and cardiovascular disease

Diabetes is the second most common cause of ESKD in the UK and is more prevalent in those aged over 65; survival of those with diabetes is worse than those without diabetes when both are receiving RRT (renal replacement therapy) (MacNeill et al. 2016). Further to this, evidence in the literature suggests that outcomes for patients with diabetes after transplantation are worse than for others. ERBP (European Renal Best Practice) guidelines (2015) recognise that the patient with chronic kidney disease (CKD) and diabetes may require a longer period of assessment prior to transplant listing in order to ensure fitness and this is reflected in the guideline recommendation to refer at an earlier stage of CKD.

The death rate from cardiovascular disease is known to be approximately 15 times higher in patients receiving dialysis than those in the general population and is the leading cause of mortality in renal transplant recipients (Stoumpos et al. 2014).

Evaluation for Transplantation

Age

Morbidity and mortality after kidney transplantation tend to increase with age and therefore the age of the recipient must be classed as a risk factor. Age must also be considered within the context of other risk factors, such as advanced cardiovascular disease and diabetes mellitus. There is no age barrier for transplantation; health is assessed on an individual basis, and physiological rather than chronological age and the existence of other risk factors are seen as the important assessment issues. Many units have patients of 70 years and over who have progressed well following

BOX 10.1**Ethical discussion point on shortage of donor organs**

- renal transplants: demand far exceeds supply.
- younger patients are shown to gain greater life satisfaction after a transplant.
- older patients are at greater risk of complications.

Discussion

- should younger patients be given priority over the older group?

a kidney transplant. However, with demand far exceeding supply and studies reporting smaller changes in improvements in quality of life for the older age groups and a significantly increased risk of death within five years of transplantation for those over 60 years of age (Johnson et al. 2010), some may question the use of such a precious and scarce resource in this group (Box 10.1).

Polycystic kidney disease

This inherited kidney disease can result in several members of a family receiving ERF therapies. The native cystic kidneys may be very large, thus leaving little space for the transplant, and there may also be an increased risk of bleeding and infection. It may be necessary to perform a unilateral, or in severe cases a bilateral nephrectomy prior to listing for transplantation.

Urinary tract

It is important to assess that there are no problems with the bladder and urethra and that there will be no difficulties following transplantation; if it is felt that the bladder capacity is unacceptably low, surgical enlargement may be possible. In the presence of a history of repeated urinary tract infections with bilateral reflux, it may be necessary to undertake a bilateral nephrectomy prior to transplantation to reduce the risk of post-transplant infection.

Cardiac disease

Routine investigations such as an electrocardiogram (ECG) and echocardiogram and a cardiac history are essential for all patients undergoing assessment for transplantation. Those patients who are in the high-risk groups for cardiovascular disease (e.g. older patients and those with diabetes) should undergo more extensive assessment and may require referral to a cardiologist. There is no evidence at the present time that intervention in this high-risk group results in better outcomes following transplantation; cardiac screening may be most useful in identifying the high-risk patient in order to exclude them from the transplant waiting list (Dudley and Harden 2011).

Peptic ulceration

A history of indigestion and/or peptic ulceration must be noted and endoscopy undertaken if active ulceration is a possibility, as those with active ulceration risk bleeding after transplantation due to the action of the steroid therapy. Treatment with a proton pump inhibitor (PPI) in combination with antibiotics if required to eradicate *Helicobacter pylori* should be given prior to transplantation if active

disease is present. Many centres also use PPI as prophylaxis in all recipients during the first three to six postoperative months.

Respiratory disease

Pulmonary tuberculosis will require treatment before listing for transplantation. Patients with a history of tuberculosis and those who have visited or lived in high-risk areas will require prophylaxis with isoniazid for at least a year following transplantation.

Patients should also be strongly advised to stop smoking and should be offered information regarding smoking cessation strategies and support systems.

Obesity

Obesity may make the transplant surgery difficult and increases the risk of postoperative complications, however NICE guidance (2018) states that ‘people should not be excluded from receiving a kidney transplant based on BMI alone.’

Nutritional advice should be given before and after transplantation (see Chapter 13).

Oral hygiene

Dental hygiene and assessment of dental state are essential. Any gum infection or dental problems should be dealt with prior to transplantation. Calcineurin inhibitors (CNIs) can cause gum hypertrophy, which is made much worse in the presence of poor dental hygiene.

Pretransplantation Preparation

Patients may be referred for transplantation during different phases of the disease process; some may be in the predialysis stage, others may already be established on dialysis therapy. UK guidelines allow a patient to be listed on the deceased donor list once he/she is within approximately six months of requiring dialysis (eGFR of $<15 \text{ ml min}^{-1}$). A pre-emptive transplant gives a better outcome compared to having to spend time on dialysis. Evidence suggests that one year or less of RRT gave similar patient survival rates compared to pre-emptive transplantation but worse allograft survival (93% vs. 89%). However, more than one year of RRT prior to transplantation led to significantly worse outcomes for both patient (94% vs. 89%) and allograft survival (93% vs. 89%) (Jay et al. 2016).

A planned pre-emptive transplant from a living donor gives the best outcome in terms of graft success and recipient health. Early transplantation before the need for dialysis therapy is welcomed from a clinical perspective, but may prove difficult psychologically if emotional adjustments have not been successfully negotiated and the patient and family are still reeling from the impact of the disease. A structured approach to predialysis education and counselling should include discussion of suitability for transplantation, and the likelihood of any potential living donors being found. Suitable patients can then be seen for pretransplant education and assessment, and friends or relatives who are interested in living donation can be contacted at this early stage. An overview of the psychological support required prior to transplantation is outlined in Chapter 4.

Boxes 10.2–10.4 show useful checklists for the pretransplant stage. Pretransplant assessment is usually a multidisciplinary process, involving medical, surgical, and

BOX 10.2**Pretransplant information and assessment checklist used by the transplant nurse specialist: information and discussion**

1. Desire to receive a transplant.
2. Benefits of a renal transplant:
 - improved quality of life;
 - freedom from dialysis;
 - freedom from fluid and dietary restrictions;
 - freedom to travel (advise to wait until one year post transplant before travelling abroad);
 - employment;
 - improved fertility (majority) – contraception.
3. Risks/disadvantages of a renal transplant:
 - immunosuppression;
 - adherence with medication and healthcare advice, frequent clinic attendance;
 - drug side effects;
 - susceptible to infections and viruses;
 - lymphoma and cytomegalovirus (CMV) infection – risks and treatment;
 - risk of rejection/biopsies.
4. Practical information
 - Orientation
 - Waiting list
 - Planning for the transplant call
 - Transplant call
 - Contact numbers
 - Inpatient care
 - Pre- and postoperative care
 - Transplant nurse specialist
 - Tour of the transplant unit
 - How it works, how to manage waiting time
 - Arrange child/pet/others care
 - What to expect, transport arrangements
 - Holiday arrangements
 - What to expect, discharge arrangements, follow-up
 - Contact card – further contact

specialist nurse input. A systematic approach to assessing patients for suitability for transplantation should include those approaching ERF as well as those on dialysis. This is of particular importance when a suitable living donor may be found, thus allowing pre-emptive transplantation.

Specific Pretransplant Anxieties and Fears

Specific issues concerning body image are discussed in Chapter 4; other anxieties include acceptance of the transplant as part of the ‘self’ and guilt over benefiting from traumatic death. There are also very specific challenges relating to patients’ education and understanding of their immunosuppressive therapy.

It is vital that patients understand the need to continue with their antirejection therapy for as long as they have their transplant. Many patients believe that it will only be necessary to take the drugs until the kidney settles into the body. There are great challenges for the transplant team to ensure that patients are well informed about their medication.

BOX 10.3**Pretransplant information and assessment checklist used by the transplant nurse specialist: clinical information and investigations**

1. Blood group.
2. Tissue typing.
3. Biochemistry.
4. Haematology.
5. Liver function tests.
6. Lipid levels.
7. Virology screen:
 - Hepatitis B and C Virus;
 - CMV;
 - HIV;
 - Epstein–Barr Virus (EBV);
 - Varicella Zoster Virus (VZV).
 - Human T cell lymphotropic Virus (HTLV) 1 and 2
8. Infection screen:
 - Methicillin Resistant *Staphylococcus aureus* (MRSA)
 - *toxoplasma gondii*
 - *treponema pallidum* (Syphilis)
9. Midstream urine.
10. Further specific investigations as required.

Clinical information

- dental check: date of last check.
- female patients: last cervical smear; date of last smear and result.
- breast self-examination; date and results of last mammogram if applicable.
- weight.
- height.
- body mass index.

A systematic review (Belaiche et al. 2017) analysed 37 studies and found rates of non-adherence fluctuating from 1.6 to 96%. Assessment methods varied from one study to another, although self-reports were mainly used. It appears that age (≤ 50 years old), male, low social support, unemployment, low education, ≥ 3 months post graft, living donor, ≥ 6 comorbidities, ≥ 5 drugs d^{-1} , ≥ 2 intakes d^{-1} , negative beliefs, negative behaviour, depression, and anxiety were the factors significantly related to nonadherence. A variety of explanations have been given for these difficulties. These include the effects of immunosuppression on physical appearance, inability to accept the lifestyle limitations, misinformation given by one patient to another, poor education given by staff, and fear of long-term side effects. Sometimes, those who have had difficulty in accepting dialysis are exemplary transplant recipients because the post-transplant lifestyle is especially precious.

It is inappropriate to refuse transplantation to patients who are perceived as high risk for nonadherence. It is important to offer extensive pretransplant counselling to explore the reasons for not taking healthcare advice and to ensure additional post-transplant support is available to facilitate adherence to medication therapies. This may necessitate changing to an immunosuppression regime with a different side effect profile. Close monitoring of immunosuppressant levels and ensuring attendance at clinic visits are vital.

BOX 10.4**Pretransplant information and assessment proforma: checklist used by the physician/surgeon to evaluate clinical assessment and information****Clinical assessment*****Clinical history***

1. Renal disease and disease progression: dialysis status.
2. Previous medical history, noting previous blood transfusions, pregnancies, and previous transplants.
3. Previous surgery.
4. Current clinical status.
5. Social history, family status.
6. Smoking, alcohol, recreational drugs.
7. Current medications, allergies.
8. Immunological status, blood group.

Clinical assessment

1. Cardiac assessment, including baseline echocardiogram and ECG.
2. Respiratory assessment, tuberculosis risks/contacts.
3. Urological assessment.
4. Abdominal assessment – previous surgery, Tenckhoff site.
5. Vascular assessment – assess pulses.
6. Dentition.
7. Gynaecological status.

Information: discussion

1. Risks
 - surgical, anaesthetic, patient survival rates.
 - graft survival rates – deceased and living donor.
 - lymphoma.
 - CMV.
 - cardiovascular.
 - skin cancer.
2. Further investigations required.
3. Live donor possibility or deceased donor list.
4. Immunosuppression regimen required.
5. Decision.
 - on deceased donor transplant waiting list.
 - living donor programme.
 - await further investigations and/or referral.
 - patient undecided – does not want a transplant.
 - unsuitable for transplant due to ...

Transplant Waiting List

Once the pretransplant assessment has been completed satisfactorily and the tissue-typing and blood-group details are finalised, the name of the patient will be added to the national waiting list. Waiting time is impossible to predict but there are tools available that can estimate waiting times for patients based on factors such as blood group, human leukocyte antigen (HLA) type, etc. These are available for patients and clinicians at <http://www.odt.nhs.uk/transplantation/tools-policies-and-guidance/calculators> (accessed 20 June 2018).

It is important to explain to patients that the transplant waiting list is very different from other hospital waiting lists in that they do not simply have to wait

until their name reaches the top to receive a graft. The transplant list is essentially a pool of recipients, and each transplant is allocated on the basis of the closest match. Therefore, their name will join the recipient pool and they must wait for the best match for them. This is a difficult concept to understand and some patients become distressed if another patient, who has waited less time, is transplanted before them.

It is also important that patients do not sit by the phone all day waiting for 'the call', thus greatly restricting their lifestyle. Patients are encouraged to keep as active and as healthy as possible whilst waiting and to continue a normal lifestyle. Some patients may still feel ambivalent about a transplant at this time. Specific fears and anxieties may need to be explored and support given within the context that patients must be allowed the time to decide the best treatment for themselves. Ongoing contact with the transplant nurse specialist is vital during the waiting time and it is recommended that those who are waiting are contacted every 12 months and offered support and reassurance. Support is especially important at times of additional stress such as when a fellow dialysis patient receives or rejects a kidney.

Donor and Recipient Matching

Immune system: overview

The human body has a complex system of defences that can provide protection against infection and disease. This system has the ability to target, isolate, and destroy potentially harmful invaders. This destruction is achieved in three stages – first by the recognition of structures on the invader (antigens) which are not present in the host. Antibodies and T cells that can recognise the antigens as 'foreign' are then produced. These antibodies and T cells then attach to the invader and destroy it both directly and by recruiting other mechanisms of destruction. Exactly the same happens to a transplant unless it is from an identical twin. The 'foreign' antigens on the transplant induce antibodies and T cells. These target the transplanted organ and do their very best to destroy it. The term 'transplant antigens' is used to describe those antigens that are most important in this regard. Only two are really important: the HLA system and the ABO system (see below). In order to prevent rejection it is necessary to circumvent the immune system (by matching and cross-matching) and to suppress the immunological response.

Components of the immune system

Leukocytes (white blood cells)

These comprise the cells that produce the antibody (B lymphocytes), recognise the foreign antigens (T lymphocytes), directly destroy invaders (activated T lymphocytes), or can be called in to help with the destruction process (monocytes, polymorphs, and eosinophils). Thus, it can be seen that the lymphocytes play several roles and therefore have the major influence on graft acceptance.

Lymphocytes

These comprise 20% of the total white blood cell count and are made up of several groups of cells with specialised functions. The term 'orchestra' is often used to describe the mode of operation. Each section of the orchestra is made up of individuals with similar but not identical characteristics. The overall result of the orchestra playing is a result of each section performing in concert with the others.

Lymphocyte types

- T cells: these have antigen recognition structures fixed to their surface.
- B cells: these have antigen recognition structures that can be secreted (antibodies).

T cells and B cells can be naive or activated. T cells can be activated to various functions, namely helper, killer, or tolerant status. B cells can be activated to produce antibody or memory.

Each naive lymphocyte has an antigen recognition structure that is unique, for example different from other members of its section and thus capable of seeing a different antigen. In this way literally millions of 'foreign' antigens can be recognised. Each time a recognition event occurs, a naive cell becomes activated and divides. Thus, even if a single cell recognises an antigen as foreign it keeps dividing until it forms a significant number of identical cells (a clone), all capable of recognising the antigen.

Depending on influences from other sections, T cells can help B cells produce antibody (helper T cells), kill targets bearing the antigen directly (killer T cells), or become tolerant (i.e. capable of recognising the antigen but not producing a damaging response to it). B cells can produce antibody in around 8–10 days if they see it for the first time (naive B cells) or within 24 hours if they have seen it before (memory B cells). B cells produce much more antibody if they get help from the T cells, which can themselves see the same antigen.

One point about antibody production that is relevant to transplantation is that the process that produces it is long lived. This is very positive for vaccination programmes, where having antibody around for years and years is very beneficial, although negative of course for transplantation.

ABO blood groups

The ABO system of human blood groups was described by Landsteiner in 1902. Blood group is determined by A and B antigens on the surface of the red blood cells. Each individual has one of the four basic blood group types – O, A, B, or AB.

Each individual has antibodies to the blood group antigens that they do not express (Table 10.1). Antibodies against the blood group antigens can cause hyperacute rejection and therefore matching of blood group between donor and recipient is vital. Blood group O organs can be transplanted into all groups; O is classified as the universal donor. Blood group AB recipients can receive organs from all groups; AB is classified as the universal recipient. A small proportion of people with group A belong to a subgroup defined as A2, and have reduced expression of A antigen. These kidneys may be successfully transplanted into O or B, or A2B into AB, recipients with low anti-A titres (Bryan et al. 2007).

Recent advances in pretransplant care have allowed transplants to take place between a blood group incompatible (ABOi) donor and recipient. Such programmes are suitable only for living donor transplants due to the pretransplant

Table 10.1 The ABO blood group system.

Blood group	Percentage of population	Antigens expressed	Antibodies expressed	Acceptable donor blood group
O	47%	None	Anti-A, Anti-B	O
A	42%	A	Anti-B	O, A
B	8%	B	Anti-A	O, B
AB	3%	AB	None	O, A, B, AB

treatment required for the recipient. Antibodies can be removed from the recipient using various strategies, including plasmapheresis and immunoadsorption. More potent immunosuppressive medications may also be required. This strategy allows transplants to take place between donor and recipient pairs that would previously have been unsuitable, thus increasing the chance of transplantation for many recipients. The risk of rejection of the transplant, failure of the graft, and of serious side effects of immunosuppression are higher than with a blood group compatible transplant. It is important that recipients of this type of transplant are fully informed of the risks prior to undertaking this procedure.

Histocompatibility antigens

A further set of proteins that can trigger the B and T cell response are the transplantation antigens or the histocompatibility antigens. The histocompatibility antigens can be divided into two groups – major and minor.

Major histocompatibility complex

This system, first discovered in the mouse by Peter Gorer at Guy's Hospital in the late 1930s, is, as the name suggests, the most important system in transplantation and indeed in immunity to infection. The human system is termed HLA and was first identified in the 1960s. The sera from pregnant women were found to have antibodies that recognised lymphocytes from their partners and from some random blood donors. The reason for this is that pregnancy is in some ways like a transplant. Passage of blood from partner or child to mother results in T cells and antibody being produced to the foreign antigens on the blood cells. Since the most potent foreign antigens are those of the HLA system, most of the mother's response is directed against them and the long-lived antibody-producing cells remain in her blood. These antibodies can persist for over 40 years.

The HLA system is complex. There are four main series important for transplantation – A, B, C, and DR. There are over 30 antigens in each series. Each person can have two from each series (one from each parent). The permutation on 2/30 from A, 2/30 from B, 2/30 from C, and 2/30 from DR means that, outside a family, it is very rare for individuals to have identical HLA types. Luckily for matching in renal transplantation, DR is dominant. However, most of the antibody and T-cell response is produced to A, B, and C.

The rules for HLA and matching are not nearly so clear-cut as the rules for ABO, but there are several strong guidelines:

- transplantation of a kidney into someone who has antibodies directed to a foreign (mismatched) HLA antigen on that kidney will result in hyperacute rejection.
- transplantation of a kidney into someone who has strong memory to a foreign (mismatched) HLA antigen on that kidney will result in very rapid rejection.
- transplantation of a kidney with two mismatches at DR will have more rejection than one with no mismatch at DR. However, rejection episodes can be treated or mismatched patients given additional immunosuppression. The total number of mismatches has a bearing on long-term outcome (Figure 10.2).

Newer techniques allow organs to be transplanted where there is human leukocyte antigen incompatibility (HLAi) providing antibodies are removed or lowered to an acceptable level prior to transplantation. There are various techniques used to remove antibodies, for example plasmapheresis and immunoadsorption, in a similar strategy to that used in ABOi transplantation. This procedure is only suitable for living donation as the antibody removal must be carried out in the period

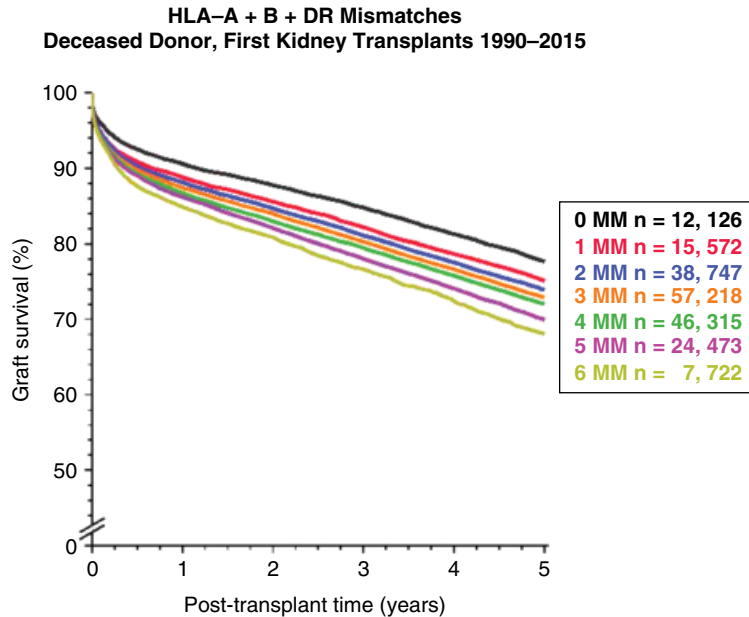


Figure 10.2 Influence of human leukocyte antigen (HLA) matching on renal allograft survival. Source: CTS (2017). MM = mismatch.

leading up to the transplant operation. The risks of transplant rejection, graft failure, and serious infection are twice as high as for antibody compatible transplants so patients contemplating this procedure must be fully aware of the risks before proceeding. Despite the risk this treatment may offer some patients their only chance of receiving a transplant, particularly as they may be unlikely to be offered a deceased donor kidney if highly sensitised, and many are willing to accept the risks involved.

Donor and recipient matching

The majority of organs for transplant come from deceased donors. It is essential to match for blood group and to achieve the best DR match possible. Since antibodies can be induced to pregnancies, transfusions, or previous transplants and can be boosted by infection, regular screening of patients on the waiting list is necessary to maintain knowledge of their current antibody status. Donors are avoided if they contain any mismatch to which the recipient has antibodies in current or recent serum.

Pretransplant cross-match

Immediately prior to transplant a cross-match test is performed in the tissue-typing laboratory. A recent blood sample and selected past samples from the recipient are checked against donor lymphocyte cells. If the donor cells react (die), the result is termed a positive cross-match; the recipient is adversely reacting to the donor antigens. In the presence of a positive cross-match, transplantation cannot proceed, as the transplant would be rejected.

Traditionally a cross-match was performed prior to deceased donor transplantation and the results were obtained before the transplant operation could proceed. Recognition of the significance of shorter cold ischaemic times (CIT) in improved

short-term graft success rates has led to the introduction of retrospective cross-matching. In this situation the transplant proceeds without waiting for the cross-match result to be available. This can only occur if the recipient has had regular blood samples sent to the laboratory for antibody testing and is known to be nonsensitised. Careful history should be taken at time of transplant to ensure the recipient has not received any recent blood transfusions that would affect antibody status.

Sensitisation

When there is a positive cross-match, the recipient is sensitised to that donor. The higher the level of sensitisation, the greater will be the difficulty in finding a transplant that will not reject.

Sensitisation can occur during pregnancy (to partner's antigens), during blood transfusion, and after transplantation. In order to reduce the risk of sensitisation it is important to minimise the giving of blood transfusions.

Some recipients may have a high level of sensitisation. The patient's serum is tested periodically against a representative panel of cells from many donors. If the patient does not react with the various donors tested then they are classified as unsensitised. If the blood reacts with 50% of donors (50% of the panel or 50% Panel Reactive Antibody [PRA]) they are 50% sensitised, and if blood reacts with 100% of donors they are highly sensitised. Unfortunately, some highly sensitised candidates wait many years for a compatible transplant, although the antibodies responsible for sensitisation can decrease with time.

United Kingdom matching system

Within the United Kingdom, each transplant centre has a local list of recipients awaiting transplant. There is a national database held at NHSBT in Bristol. Each deceased donor is tissue-typed at the local transplant centre and the details sent to NHSBT, where the closest tissue match is found from the central computer. The kidneys are then sent to the recipient centre for transplant.

A new scheme for the national allocation of kidneys was adopted in the United Kingdom in 2006. The scheme is based on HLA matching, gives priority to paediatric and highly sensitised patients (i.e. patients with high levels of HLA antibodies), and uses a point score to differentiate between equally matched patients. The aim of this scheme was to reduce the variability in deceased donor waiting times across the United Kingdom.

The scheme has five tiers. Tier A kidneys are offered to paediatric patients with no mismatched HLA antigens at HLA-A, -B, and -DR (termed a 000 mismatched transplant) who are known to be highly sensitised. If there are no such patients in tier A, then kidneys are offered in tier B to 000 mismatched, nonsensitised paediatric patients. If there are no patients in either tier A or B then kidneys are offered in tier C to 000 mismatched adult patients who are highly sensitised. If no match is found in tier C then the offer moves to tier D which includes all other 000 mismatched adult patients and favourably matched (i.e. no mismatch at HLA-DR and a maximum of one mismatched antigen at both the HLA-A and HLA-B locus; 100, 010, 110 mismatch grades) paediatric patients. Tier E includes all other patients. Paediatric patients in tiers A and B are prioritised according to waiting time. In the remaining tiers, patients are prioritised according to a points score, including: waiting time, age, donor recipient age difference, and geographical location of patient relative to donor (NHSBT 2017a).

Review of the scheme has shown that matching is still relevant; however, advances in immunosuppression over the last 10 years have meant that only the most poorly matched grafts (two antigen mismatch at HLA-DR locus) are associated with worse outcomes when compared to 000 mismatched grafts (Johnson et al. 2010).

Deceased Donation

The majority of renal transplants currently performed in the United Kingdom are from deceased donors. Deceased donors fall into two categories: Donation after Brainstem Death (DBD) or Donation after Circulatory Death (DCD). DBD donors are patients whose death is confirmed using neurological criteria (also known as brain stem death or brain death), this is only possible in patients who are maintained on mechanical ventilation.

Causes of brain stem death

The most common causes of brain stem death are listed in Box 10.5.

Cerebral swelling resultant from trauma or anoxia and intracerebral bleeding can cause raised intracranial pressure, which forces the cerebral hemispheres through the tentorial hiatus, thus compressing the brain stem and interrupting its blood supply. Such herniation of the cerebral tissue is usually described as ‘coning’ and results in irreversible damage to the brain stem.

BOX 10.5

Common causes of brain stem death

- intracerebral bleed or infarction.
- head trauma.
- cerebral hypoxia due to:
 - respiratory arrest;
 - cardiac arrest.
- smoke inhalation/carbon monoxide poisoning.
- cerebral tumour.
- drug overdose.
- intracranial infection.

Certain conditions must be met before brain stem death testing can take place:

- the patient is deeply comatosed, unresponsive, and apnoeic with lungs artificially ventilated.
- there is a positive diagnosis or known condition that has led to the diagnosis of irreversible brain damage.
- potentially reversible causes of coma have been excluded.

Possible causes of coma that must be excluded are primary hypothermia (the patient's temperature must be greater than 34 °C for testing to take place), effect of depressant drugs, potentially reversible circulatory, metabolic and endocrine disturbances, and potential causes of apnoea. Testing will then take place to ascertain the absence of brain stem reflexes:

- the pupils are fixed and do not respond to sharp changes in light intensity;
- there is no corneal reflex;
- the oculovestibular reflexes are absent;
- no motor responses within the cranial nerve distribution in response to stimulation of any somatic area;
- there is no cough reflex response to bronchial stimulation by a suction catheter placed down the trachea to the carina, or gag response to stimulation of the posterior pharynx with a spatula;
- there is no evidence of spontaneous respiration or respiratory effort during the apnoea test (loss of capacity for spontaneous breathing).

Brain stem functions

The brain stem is responsible for the capacity to breathe spontaneously and the capacity for consciousness. If the brain stem is irreversibly damaged then there is loss of function and it is argued that 'death entails the irreversible loss of those essential characteristics which are necessary to the existence of a living human person'.

Brain stem death diagnosed by signs of irreversible damage to the brain stem is an accepted concept in most countries of the world.

Brain stem death diagnosis

Tests to diagnose brain stem death originated from the Harvard Medical School criteria (Harvard Medical School 1968) and were published in the United States in 1968. A UK Code of Practice for the diagnosis of brain stem death was agreed by the Conference of Medical Royal Colleges in 1976 and most recently updated in 2008. Available at http://aomrc.org.uk/wp-content/uploads/2016/04/Code_Practice_Confirmation_Diagnosis_Death_1008-4.pdf (accessed 20 June 2018).

Declaration of brain stem death

The UK Code of Practice recommends that brain stem death testing should be carried out by two medical practitioners who have been registered for a minimum of five years and 'who have expertise in this field'. At least one should be a consultant. Testing should be performed by two doctors together and should be performed completely and successfully on two occasions. Neither of the doctors should be a member of the transplant team or associated with potential transplant recipients.

Time of death

The time of completion of the first set of tests is legally the time of death, and this should be recorded as such on the death certificate.

Absolute contraindications to organ donation

- age > 85 years (on or after their 85th birthday)
- primary intracerebral lymphoma
- all secondary intracerebral tumours
- any active cancer with evidence of spread outside affected organ within three years of donation
- melanoma (except completely excised Stage 1 cancers)
- active (not in remission) haematological malignancy (myeloma, lymphoma, leukaemia)
- definite, probable, or possible case of human transmissible spongiform encephalopathy (TSE), including Creutzfeldt-Jakob disease (CJD) and vCJD (variant Creutzfeldt-Jakob disease), individuals whose blood relatives have had familial CJD, and other neurodegenerative diseases associated with infectious agents.
- TB: active and untreated
- West Nile Virus (WNV) infection
- HIV disease (but not HIV infection)
- history of infection with Ebola virus

Organ-specific contraindications for potential kidney donors

- chronic kidney disease (CKD stage 3B or worse, eGFR < 45)
- long term dialysis (that is, not acute relating to acute illness)

- renal malignancy: Prior kidney tumours of low grade and previously excised would not necessarily exclude donation
- previous kidney transplant (>6 months previously)

(NHSBT 2015)

The following conditions may preclude donation, but individual donors should be discussed with the Specialist Nurse for Organ Donation (SNOD) as they may still be suitable:

- bacterial meningitis
- viral meningo-encephalitis
- influenza
- tuberculosis
- bacteraemia
- abscesses
- MRSA
- malaria
- fungal infection
- unusual bacterial/fungal/protozoal infection
- chagas disease (*Trypanosoma cruzi*), apparent in some Latin American migrants

(SaBTO 2011)

It is recommended that critical care staff consider organ donation in all those with brain stem death and refer to the SNOD for a decision regarding medical suitability. General Medical Council (GMC) and NICE guidance both recommend that consideration for organ donation should be a routine part of end of life care and the wishes of the individual patient with regard to donation should be fulfilled wherever possible (GMC 2010, NICE 2011).

In order to keep transplants safe Department of Health guidelines state that 'certain medical and social information' must be given. Therefore, donor families are given an information sheet (Box 10.6) and asked to read these questions and answer 'to the best of their knowledge' (SaBTO 2011).

Requesting donation

In the United Kingdom, the legal requirements for organ donation are laid down in the Human Tissue Act (2004) (available at <http://www.legislation.gov.uk/ukpga/2004/30/contents>). This Act established the Human Tissue Authority (HTA) as the regulatory body for all matters concerning the removal, storage, use, and disposal of human tissues (except gametes and embryos) for scheduled purposes, and includes responsibility for living donor transplantation. The HTA's code of practice on consent sets out guidance on how the law should be applied, encompassing issues of consent.

In practice, it is the next of kin or the patient's executor who is usually approached to give permission for donation. If the patient has signed a donor card there is no statutory requirement to approach the family, but in practice the views of the family are always sought and if objections are raised donation does not occur.

If the next of kin cannot be notified, the body remains in the possession of the hospital. In such cases the hospital manager can give permission for donation as long as reasonable enquiries have been made and that there is no reason to believe that the deceased had expressed objections.

Religious beliefs

As far as it is known, no major religious groups in the United Kingdom object to the principles of organ donation and transplantation. Some groups feel that it is

BOX 10.6**Keeping transplants safe: donor data collected by the SNOD on the donor assessment form**

General Health: Visit to GP within 24 months (details)
 Diabetes, Cancer: investigations or treatment (details)
 Recent infections or contact with infection (details)
 Ever had hepatitis, jaundice, or liver disease (details)
 Neurosurgical surgery or implantation of dura mater before August 1992
 Blood transfusion before 1980
 Any type of brain disease (details)
 Ever received pituitary extract (details)
 History of autoimmune/chronic disease (details)
 Ever had serious infection, such as, TB, WNV, typhoid, toxoplasmosis, brucellosis, rabies, Lyme disease (details)
 Acupuncture, body piercing, tattoo, botox, or collagen injection (details)
 Ever had a sexually transmitted disease, such as syphilis, gonorrhoea, genital herpes, or warts (details)
 Travel risk assessment (details)
 Behavioural risk assessment: Alcohol, Smoking
 May be infected with HTLV (Human T cell lymphotropic virus), HIV, HBV, HCV
 Ever injected with nonprescription drugs
 Ever been given payment for sex with drugs or money
 Ever had oral/anal sex with another man (male donors only)
 Had sex within 12 months with a man who has had sex with another man
 Has been in prison for >3 days within last 12 months
 Had sex in the last 12 months with anyone who is HIV or HTLV positive, HBV or HCV positive, had sexually transmitted disease, given payment for sex, ever injected drugs, or ever had sex in any part of the world where HIV/AIDS is very common

only permissible if donors themselves had requested donation. These groups include, in particular, Orthodox Jews, Christian Scientists, and some Hindu groups. Jehovah's Witnesses have religious objections to blood transfusions, but feel that donating or receiving organs is a matter for all Jehovah's Witnesses to decide for themselves.

It is often thought that the Muslim faith does not support donation and anecdotal evidence suggests that British Muslims are, in general, reluctant to donate organs. However, recent legislation has approved donation and transplantation in Muslim countries such as Saudi Arabia. Also, a fatwa issued by the Muslim Law Council has stated that Muslims may donate organs. They may carry donor cards and their next of kin may give permission for donating. Previous reluctance to donate may have been cultural rather than religious and therefore information and liaison with Muslims will be vital in order to encourage donation.

Byrne et al. (2017) states that there is an increased prevalence of ESKD in those from ethnic minorities in the UK. Major causes are the higher incidence of hypertension and diabetes combined with other reasons that are, as yet, unknown. Although none of the major religions forbids organ donation, there are fewer deceased organ donations from this community. The reasons for this are complex but include mistrust of the NHS, lack of available culturally sensitive information, and lack of engagement with the community in general (Department of Health 2010). Language and cultural barriers seem to have inhibited the uptake of public health messages pertinent to organ donation and transplantation.

Strategies to increase the number of donors in the UK recognise the need to engage with black and minority ethnic groups in order to address the shortage of donor organs from this group (NHSBT 2014).

Other issues may also be adversely affecting the deceased donation rate from within *all* groups, particularly aspects relating to gaining consent from the bereaved.

Fear of increasing the distress of the family

Critical care staff have expressed fears that offering donation may increase the distress of the bereaved; however, experience suggests that offering the choice to donate, if performed with empathy, does not increase distress (Marck et al. 2016). Indeed, donor families report that the act of donation brings comfort and something positive in an otherwise negative situation. Family members were consoled by the fact that by consenting to donation they had allowed their relative to help others. In the presence of a diagnosis of brain stem death there can be no hope for the patient but donation can be an option offering hope of life for others.

Acceptance that death has occurred

It is crucial that the bereaved family have accepted the fact that death has occurred before donation is requested. In the case of brain stem death the acceptance of death is more difficult for the family as they are asked to accept a 'new concept of death'. The accepted concept and image of death involves a cold, lifeless body without a heartbeat; however, in the case of brain stem death the family are presented with an image of a warm patient with a heartbeat who appears (due to the ventilator) to be breathing. Therefore, the visual message is one of life but the verbal message is one of death. In such cases denial is often enhanced and relatives must struggle to understand and accept the situation. Denial may be particularly acute in the case of an intracerebral bleed where there is no outward sign of injury or trauma.

Clear communications must ensue, the core message being that there is no hope of recovery. Irreparable damage has occurred and, in the case of brain stem death, the brain has died – death of the brain stem is death of the person.

When to offer donation

It is damaging to approach the family too early, as trust may be lost. Several studies examined the reasons for relatives' refusal (for example, Simpkin et al. 2009) and noted that refusal could be attributed to several reasons, including concern about protecting the dead body, perceived quality of care during the current episode, timing of the request, and a limited understanding of brain death. It was recognised as being important for the family to have accepted that death has occurred before donation is offered, so to inform the family of the death and to request donation at separate meetings. The timing of the request and the skill of the person making the request were seen to have the greatest positive impact on gaining consent for donation.

Who should offer donation?

There is evidence that the SNOD is the best person to make the initial approach to the family to discuss donation (Hulme et al. 2016). The skill of the person making the approach to the family and the timing of the approach are important considerations that can positively influence consent rates.

How to offer donation

There are no 'right' words; each situation is unique and families will have their own individual responses. The family should be asked if they have any objection to donation rather than for permission to proceed. Some families will require time to consider their decision. Many relatives will have additional questions concerning the process of donation and its implications at this time. The family may require reassurance on the following issues:

- the donor will feel no pain.
- there will be dignity and respect throughout the donor surgery.
- the body will not be grossly mutilated or disfigured.
- the surgical wound will be sutured.
- they can view the body after surgery and the funeral will not be delayed.

The SNOD works closely with other healthcare professionals to answer further questions and to facilitate the wishes of the family. It can be reassuring to the family that he or she will be present throughout the surgery and at the end to oversee and continue care. They will also ensure that the bereaved can see the deceased after surgery in the chapel of rest if this is their wish.

Unconditional gift

It is important to stress that organ donation is a voluntary 'unconditional gift'. One case, much publicised, reported that the bereaved had stated that the organs 'must only be given to white recipients'. Such a condition is totally unacceptable and there is now legislation that prohibits the placing of any conditions when agreeing to organ donations.

Continuing care after donation

Letters of thanks containing brief anonymous information concerning the transplant recipients are given or sent to the donor family after the donation. Further help and support are also offered. Many families state that the news of the successful transplants is a source of comfort. More recently, transplant coordinators have arranged meetings between donor families and recipients. Such meetings have been requested by both parties and have followed careful counselling and preparation to ensure the willingness of all individuals involved.

Refusal to donate

As part of measures to improve organ donation rates in the United Kingdom, an audit of potential donors in all UK intensive care units and emergency departments commenced in 2003 and has continued until the present. The aim of the audit is to determine the number of potential organ donors. Results from the report for 2016/2017 indicate that 97.4% of patients who met the criteria for DBD were referred as potential donors and 85.6% of patients meeting the criteria for DCD were referred. Of the families approached regarding potential organ donation the report cites the following as the main reasons for refusal of consent:

- patient stated in the past they did not wish to be a donor (DCD 20.1%, DBD 21.3%).
- family were not sure the patient would have agreed to donation (DBD 15.3%, DCD 15%).
- family did not want surgery to the body (DBD 12.9%, DCD 8.6%).
- family felt it was against their religious/cultural beliefs (DBD 10.9%, DCD 2.8%).

Further analysis of the results of the audit show that the age and gender of the potential donor has little impact on the refusal rate, but relatives of ethnic minority groups are more likely to deny consent than those of white potential donors (NHSBT 2017c).

Refusal rates at this level represent a desperate lost potential. Therefore, it is vital that information programmes to allay fears and to present the successes of transplantation continue. It is also helpful to implement education for healthcare staff to examine the issue of requesting donation so that personnel will feel comfortable when offering this option of hope to the family.

Transplant coordinator groups have introduced workshops on breaking bad news and the approach for donation for nursing and medical colleagues working in intensive care and emergency departments. Such workshops use informed actors and provide a forum and a safe environment for staff to examine sudden traumatic death, the reactions of relatives, and responses that will facilitate the approach for donation.

If the family agree to donation, the ventilation continues and the preparations for the donor surgery are made, but if the family refuse donation then ventilation will cease.

It is always helpful for the family if the deceased carried a donor card, was registered as a donor on the National Register, or had discussed the issue with them. Most families want to fulfil the wishes of their loved one and if they know the thoughts of the deceased with regard to donation, then the question and decision can be made easier.

Clinical care of a potential organ donor

Brain stem death results in changes to normal homeostatic mechanisms; such changes will ultimately result in cardiac arrest. Once permission has been given for donation it is important to stabilise the condition of the donor to ensure optimal condition of the organs for transplantation. NHSBT provide guidance for critical care staff regarding the care required to optimise the donor prior to donation (NHSBT 2017d).

The role of the specialist nurse for organ donation

All renal transplant centres depend on local SNODs. They are senior practitioners who offer a 24-hour service to intensive care units with regard to organ donation. The specialist nurse's responsibilities are to:

- determine suitability of the potential donor;
- determine which organs/tissues can be donated;
- identify any risk factors for transmission of disease from potential donor to potential recipient.

Organisation of the organ donation procedure and surgery

The specialist nurse will be available to advise and support the donor family and critical care staff throughout the donation process. Organisation of the organ donation is complex and it is the specialist nurse's role to ensure the arrangements for donation are made with a minimum of distress to the donor family and the critical care staff. The majority of organ donations today are multiple donations and it is the specialist nurse who organises the necessary clinical tests, liaises with the various recipient teams, and arranges the donor surgery (Box 10.7).

BOX 10.7**Organ donation: role of the SNOD**

- complete and clearly document a comprehensive assessment of the donor including medical, behavioural, and travel history; communicate this information to the recipient transplant centres.
- key components of donor assessment:
 - gather information from health care team involved in current and past medical care including the patient's GP and allied health professionals.
 - review results of clinical investigations, including review of medical and nursing notes.
 - structured discussion with patient's next-of-kin/family.
 - full and detailed physical examination.
 - seek further specialist advice where necessary.
- organise any further clinical tests and blood tests
- liaise with NHSBT duty office.
- liaise with recipient teams.
- liaise with theatre staff and obtain theatre time:
 - accompany donor to theatre.
 - assist surgical teams.
 - support theatre personnel.
- final care of donor.
- contact with donor family offering information and/or support.
- information and thanks to donor hospital personnel.

Permission from the coroner

If the case comes under the jurisdiction of the Coroner (or Procurator Fiscal in Scotland), then permission must be obtained to proceed to organ donation. Cases that require Coroner or Procurator Fiscal permission include:

- road traffic accident;
- suspicious deaths/suicide;
- deaths less than 12 hours after surgery;
- traumatic deaths.

Permission will be granted if the donation will not interfere with the Coroner/Procurator Fiscal's legal responsibility to establish the cause of death. In some cases a Home Office pathologist will be present at the retrieval to document the procedure as part of the investigation into cause of death.

Removal of kidneys from a multiorgan donor

It is most common now for kidneys to be taken out as part of an operation from a multiorgan donor. This requires careful coordination between the liver, renal, and thoracic teams involved to make sure that there is no compromise to viability in any of the transplanted organs.

The exact details of the operation vary from centre to centre, but the principles include a generous incision giving good exposure to the organs of interest with the heart still beating, and placement of cannulae for in situ perfusion and cooling:

- a bilateral subcostal incision with a midline sternotomy is a common approach to the chest. The heart and lungs are inspected and mobilised first to allow rapid removal at a later stage.

- a careful laparotomy is carried out before dissection of the major blood supply to the liver. The common bile duct is transected and the gall bladder incised and flushed to prevent biliary autolysis.
- cannulae are placed into the aorta and portal vein via the mesenteric vein for perfusion. The distal inferior vena cava is cannulated and used for vascular drainage.
 - ventilation ceases when the aorta is cross-clamped. Perfusion starts simultaneously to minimise warm ischaemia.
 - the organs are removed; first, heart and lungs, followed by the liver, and then the kidneys. Careful cooperation between teams is required to minimise damage to the various organs. The pancreas is used for transplantation with increasing success; concurrent retrieval with the above organs has not been associated with adverse outcome.
 - before closure of the abdominal incisions, specimens of donor lymph nodes and spleen are removed for histocompatibility and tissue typing.

Surgical technique for deceased donor nephrectomy

If the kidneys are to be removed alone, bilateral nephrectomy is accomplished through a long midline incision or a bilateral subcostal incision. The kidneys are either taken out *en bloc* or individually on patches of inferior vena cava and aorta. The technique preferred in this centre entails the removal of an individual kidney on a patch of aorta and inferior vena cava. The technique is as follows:

- abdominal incision and laparotomy are performed as for multiorgan retrieval.
- the aorta is dissected up to the superior mesenteric artery and the inferior vena cava dissected above the renal veins.
- slings are placed around the aorta and the inferior vena cava above the bifurcation ready for tying at a later stage.
- a catheter is passed into the aorta through an incision just above the bifurcation. The balloon of the catheter is distended with fluid and ties placed around the aorta distal to the balloon to hold it in place. Care must be taken not to overdistend catheter balloons as this can obstruct the lumen of the catheter.
- a similar procedure is carried out with the inferior vena cava just above the confluence of the right and left common iliac veins, and the aorta and inferior vena cava below the catheters are tied off.
- the aorta is tied off in the upper abdomen and perfusion is started through the Foley catheter (Figure 10.3). As perfusion starts, ventilation is discontinued.
- the kidneys begin to get cold at this stage and, whilst the perfusion fluid is running through into the kidneys and out through the renal veins, the kidneys should be surrounded by ice to assist cooling and prevent rewarming from the adjacent tissues.
- the inferior vena cava above the renal veins is ligated and the blood from the kidneys drains out through the catheter in the inferior vena cava.
- after 2 l of perfusion fluid has flushed through the kidneys and the kidneys are cold, they can be mobilised and the cannulae removed.
- the inferior vena cava is split up the middle and along the back, taking care not to divide the right renal artery. The aorta is also divided anteriorly and posteriorly, taking care to avoid damaging the left renal vein which crosses in front of the aorta. Having done this, each kidney is taken out with a section of aorta, inferior vena cava, and long length of ureter and placed in iced saline, where it is reflushed with preservation fluid.
- normally, no further dissection is done at this stage, but the kidney is placed in sterile bags and sent at 4 °C to the receiving centre. Further dissection of the kidney is performed immediately before subsequent transplantation into the recipient.

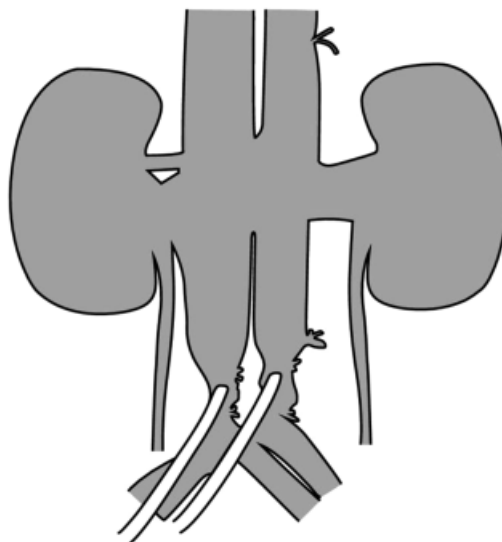


Figure 10.3 Perfusion catheters in situ for deceased donor nephrectomy.

Following removal, each kidney is examined for any surgical injury and unusual anatomy and is placed in a sterile bag with a small amount of perfusion fluid. This bag is then placed inside two further polythene bags to ensure sterility. The kidney is finally packed into a transport container with ice.

Organ preservation

The aim of preservation is to maintain the organ in an optimal condition until transplantation can occur. All living cells require oxygen to survive. Once the blood supply to the organ ceases, the lack of oxygen will result in cellular ischaemia. Cooling the organ will reduce the cellular metabolism and thus help to minimise subsequent damage. Ischaemia that occurs before the organ is cooled is termed warm ischaemia.

Warm ischaemia

If the blood supply to the kidneys is interrupted without cooling, the tubular cells suffer warm ischaemia resulting in acute tubular necrosis (ATN). ATN may be reversible if the warm ischaemia time is limited (approximately 45 minutes). However, should the warm ischaemia extend longer than one hour the glomeruli are likely to suffer irreversible damage and the kidney may not regain function. During DBD donation the ventilation and blood supply continue until the perfusion system is in place. As perfusion with cooled fluid commences, the ventilation ceases. Thus, the kidney is immediately cooled and the warm ischaemia is limited to approximately one to two minutes only.

Cold ischaemia

The ice should maintain the kidney at approximately 4°C, thus minimising ischaemic damage and enabling transport to the transplant centre. The time from the beginning of cooling to reperfusion and rewarming at the time of transplantation is termed the cold ischaemia time. Most kidneys can be stored for 24–48 hours if

necessary. However, evidence suggests that prolonged cold ischaemia has an impact on post-transplant outcomes, with a 4% increased risk of graft failure for every hour after 21 hours of cold ischaemia (Johnson et al. 2010).

Donation after circulatory death

Donation after circulatory death was previously known as non-heartbeating donation or donation after cardiac death (also abbreviated to DCD). This refers to organs retrieved for transplantation from a donor whose death is confirmed using cardiorespiratory criteria as opposed to neurological criteria. Prior to the introduction of brain stem death criteria in 1976 all organ donations came from donors who had suffered circulatory death; the introduction of this criteria and the ability to maintain potential donors on artificial ventilation led to the reduction in this practice. However, the lack of suitable organ donors in the intervening years has led to the increasing use of DCD donors. There are two categories of DCD donation: 'controlled' where there is planned withdrawal of life-sustaining treatment, or 'uncontrolled' where the donor suffers an unexpected cardiac arrest and resuscitation is not attempted.

Relative and absolute contraindications for DCD donation are the same as for DBD donation. To establish death the patient must be observed by the clinician for at least five minutes to ensure that irreversible cardiorespiratory arrest has occurred. Following this a double balloon triple lumen catheter is inserted into the femoral artery, the catheter is guided into the aorta, and the top balloon inflated to occlude the aorta. The lower balloon is then inflated and cold perfusion fluid is flushed through the catheter and into the kidneys. A further catheter is inserted into the femoral vein to allow the perfusion fluid to drain. This procedure allows the organs to be perfused with cold solution prior to removal, allowing time for the patient to be moved to the operating theatre whilst minimising warm ischaemic time.

DCD donation programmes vary worldwide. In the UK DCD donors make a significant overall contribution to deceased donation, representing 41% of all deceased organ donors in 2016–2017 (NHSBT 2017b). All DCD programmes in the UK at the present time are controlled, with no uncontrolled donation programmes currently active.

The time interval between treatment withdrawal and cold perfusion in the donor, known as warm ischaemia, can make DCD donors unsuitable to donate some solid organs such as liver and pancreas. Although this extended warm ischaemic time can affect short-term outcomes in kidney transplantation and lead to an increased incidence of delayed graft function, longer-term outcomes are improving.

There are ethical and legal questions to consider with the practice of DCD donation, for example to what extent should clinical interventions be undertaken in the dying patient in order to facilitate organ donation, such as admission to intensive care, arterial and venous catheterization, and inotropic support? In order to clarify the legal and ethical issues surrounding DCD donation The UK Donation Ethics Committee and the Academy of Medical Royal Colleges set out recommendations for practice related to DCD donation for those caring for dying patients. The guidance is based on two principles: firstly, that where donation is a possibility full consideration should be given to this when caring for a dying patient and, secondly, that donation is an integral part of a patient's end of life care if it is established that donation would be consistent with their wishes, values, and beliefs (UKDEC 2011).

The time between referral for donation and actual donation can be distressing for the family and friends of the patient and there is evidence that the time taken from decision to donate and actual donation can lead to some families refusing consent for donation (NHSBT 2017c). The SNOD will assume the same role as in

DBD donation and will provide support and assistance to both the donor's family and to the team providing care to the patient.

Living Relation Donation

In the early days of transplantation, live related transplants were the only possible option but, with the advent of deceased donation and improved immunosuppression regimes, most centres concentrated, in the main, on deceased donation with fewer live donor transplants. This was due, in part, to the fact that some clinicians struggled with the ethical issue of subjecting a healthy and fit person to the risks of major surgery that had no personal benefit for them, albeit there would be benefit to their family member.

Ethical issues

The core factors of the living donation debate involve the critical issue of a balance between 'doing good without doing harm' and the concept of altruism.

Physical wellbeing – doing good without doing harm

The donation will most certainly 'do good' in benefiting the recipient but may also 'do harm' to the donor, as the surgical procedure exposes the living donor to major clinical risks. Mortality from living donor surgery is low; however, donor deaths have been reported. Early postoperative complications may occur including chest infection, deep vein thrombosis, wound infection, and postsurgical depression amongst others. The lifetime risk of ESRD after kidney donation is low, occurring in less than 1:200 donors (0.5%) (BTS 2018). BTS guidelines (2018) recommend that counselling and consent of potential living kidney donors must include acknowledgement that the baseline risk of ESRD is increased by donation. Discussion with potential donors must be informed by those factors known to increase ESRD risk post-donation, including donor age, sex, race, BMI, and a family history of renal disease (BTS 2018).

Psychological wellbeing – doing good without doing harm

Undoubtedly, many living donors gain psychologically from the act of giving. Early studies suggest that donors describe the act 'as one of the most meaningful experiences in their lives' (Fellner and Marshall 1968). The satisfaction of helping a 'loved one' return to a normal lifestyle is very rewarding for many. Long-term follow-up of donors has demonstrated no adverse effects on psychological health or social status (Fournier et al. 2012).

Altruism

Altruism – the act of unselfishness – means giving freely without thought of reward. Much debate has surrounded this concept, with writers in the 1960s and 1970s questioning the fundamental reasons for giving. Kempf (1966) reported that although donors were 'consciously altruistic' there was 'considerable unconscious resentment' towards the recipient and towards hospital personnel who requested or encouraged the donation. Other studies suggested the presence of a degree of coercion or subtle familial pressure. There were also reports of financial incentives or other 'material rewards' offered by recipients to donors to encourage donation.

Although many of these early studies involved small numbers of donors and recipients, the negative findings led many centres to pursue deceased donor options.

Later studies in the 1970s and the 1980s reported more positive psychological findings (Smith et al. 1986) and this led to the development of more extensive live donor transplant programmes in many UK centres.

Recent studies have been supportive of live donation but have also noted psychological issues that may need to be addressed. A study of 262 live kidney donors found that 40% felt pressure to donate, with this most likely where there was a family relationship to the patient (Valapour et al. 2011).

Further studies have also reported positive findings. Fournier et al. (2012) investigated follow-up of 398 living donors who had donated between 1952 and 2008. The study concluded that there were no negative psychological effects on the donors in the long term.

Benefits for the transplant recipient

Although the ethical issues have been recognised and much debated, the decision to continue with living donation has usually been based upon the very real benefits that ensue for the recipient. Living donation has always demonstrated higher graft survival rates than deceased donation, regardless of genetic relationship or tissue matching. Although recent advances in immunosuppression have narrowed the gap between the two groups, in most cases the living donor grafts still have a better survival rate at one year and a significantly higher probability of function in the long term. The recipient benefits from a reduction in the time on dialysis, which is recognised as contributing to an improved outcome following transplantation.

The living donation can be planned to take place at the most suitable time (medically and socially) for the recipient and donor. As renal function deteriorates, transplantation can be planned for the predialysis phase (pre-emptive transplantation), thus avoiding the physical and psychological stress of dialysis adjustments. Studies have shown an improved outcome for recipients transplanted pre-emptively. Such benefits have encouraged the expansion of living donor programmes.

Transplant rates

Living donor programmes vary throughout the world but most European countries have a substantial live donor programme. In the countries covered by Eurotransplant, in 2016, almost 30% of kidney transplants were from living donors (Eurotransplant 2017; <http://statistics.eurotransplant.org>). Sweden, the United States, Denmark, and Greece also have relatively high rates. The United Kingdom had a low rate with only 5% of the total transplant programme resulting from living donation in 1981, but it was 35% in 2017 (Figure 10.4).

Living unrelated donation (genetically unrelated – emotionally related)

In Norway in the early 1990s, parents, siblings, adult children, uncles, aunts, grandparents, and spouses were accepted as donors. Spouses are, of course, genetically unrelated but were recognised as ‘emotionally related’. The Norwegian experience showed that transplantation between spouses (partners) could achieve graft survival rates equal to the best achieved with deceased donor organs. Similar results for transplantation between partners were reported in the United States (Terasaki et al. 1997). Centres across the world are now utilising spousal/partner donors and also other donors, who have a demonstrable relationship with the recipient, such as close friends. However, all centres stress that the donor must be well motivated and well informed before proceeding.

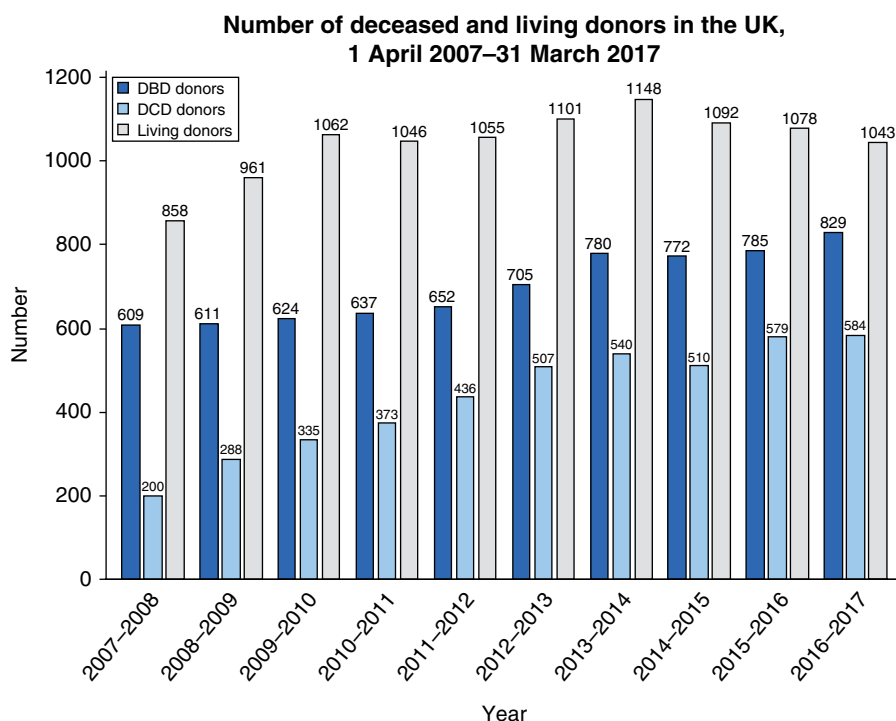


Figure 10.4 Number of deceased and living donors in UK, 1 April 2007–31 March 2017.
Source: from *Organ Donation and Transplantation Activity Report 2016/17*. NHS Blood and Transplant.

Buying and selling of organs

Living donor transplantation in the United Kingdom is controlled by strict laws to prevent the possibility of illegal practices such as financial payments and coercion. In the United Kingdom the Human Tissue Act 2004 came into place in 2006. This Act placed the principle of consent at the centre of living donation, and indeed to all issues relating to donation and the taking of, storage, and use of human tissues and organs. It covers England, Wales, and Northern Ireland, with the Human Tissue (Scotland) Act 2006 covering Scotland. The HTA, established in 2005, implemented the provisions of the Act and the EU Tissue and Cells Directive which also came into force in 2006. Under the Act, the approval process is the same for directed genetically or emotionally related organ donation. Local independent assessors (IAs), trained and accredited by the HTA, assess all donor/recipient pairs, and where the requirements are met, give approval to proceed. Prior to 2006, legislation precluded the use of altruistic donors who wish to give anonymously to the donor pool, however it is now possible for nondirected altruistic donation to take place, with the donor kidney being utilised in the same way as a deceased donor kidney. The new Act has also allowed the development of the National Living Donor Kidney Sharing Scheme (NLDKSS).

The buying and selling of organs does occur in some of the developing countries and is an accepted practice. Indeed, some clinicians have suggested that a similar system, strictly controlled by legislation, could be introduced in the UK to increase transplant rates. The ethical and moral ramifications would be immense and at present such a concept is illegal and totally unacceptable to most.

National Living Donor Kidney Sharing Scheme

The NLDKSS in the UK was introduced to allow donor and recipient pairs who were incompatible for transplantation to be matched with other donors and recipients in the same situation and the donors to be effectively ‘swapped’. This procedure can be carried out between more than two pairs, known as pooled donation. This scheme is administered by NHSBT and individual units are responsible for donor and recipient work-up prior to registering for the scheme. Matching runs are carried out on a three monthly basis and the units involved informed of any matches thereafter. Once units are informed of a match a cross-match blood test is arranged between relevant donors and recipients. Once results of the cross-match confirm that the transplant can proceed, the donor and recipient are interviewed by their local IA and a report submitted to the HTA. Once HTA approval is given the transplant must take place within six months, otherwise re-assessment by an IA will be required. The transplant operations take place simultaneously at each centre, with kidneys travelling from the donating unit to the receiving unit. Anonymity between donor and recipient is maintained in the same way as for deceased donation.

The future for living kidney donation

A review of the living donor kidney transplant programme in the UK in 2010 led to the development of the UK Strategy for Living Donor Kidney Transplantation (NHSBT 2011). This strategy was successful in its aim to increase overall UK live donation rates to 18 pmp. A further strategy was developed in 2014 (NHSBT 2014) to build on this success with three key objectives:

- to increase live donor transplant activity in the UK.
- ensure all suitable recipients have equitable access to live donor transplantation.
- to maximise opportunities for suitable donor and recipients to contribute to and to benefit from the NLDKSS.

Donor and recipient matching

Individual tissue type is inherited as half from each parent. Therefore, matching within a nuclear family unit will usually result in a potential donor who is HLA-identical, a one-haplotype match, or a mismatch.

Immunological aspects

Matching for the major histocompatibility complex (MHC) will take place, however. Figure 10.5 demonstrates tissue-type inheritance using the Donor-Related (DR) locus. Therefore, potential donors may be:

- HLA-identical, as with DR1:3 (siblings);
- a one-haplotype match, as with DR1:3 and DR1:8 (siblings);
- DR1:4 and DR1:3 (parent–child);
- unmatched, as with DR1:3 and DR4:8 (siblings).

The long-term graft survival rates are better with better matching, but a mismatched living donor kidney transplant gives better results overall than well-matched deceased donor transplants.

Psychological issues

The question of the possibility of living related donation may bring unity to a family group but it may also bring conflict. Parents will often offer to donate early in

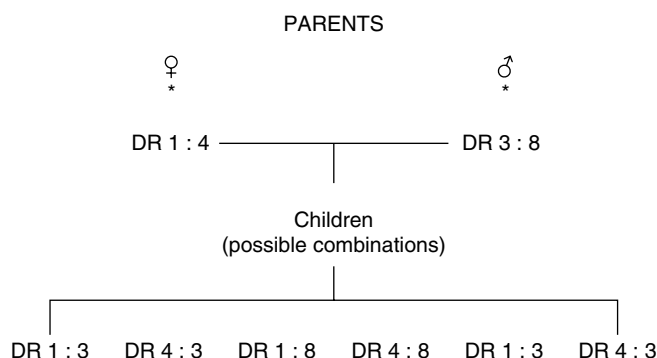


Figure 10.5 An example of tissue-type inheritance.

the disease process and are extremely well motivated, but problems can arise if one parent is 'more suitable' due to tissue matching or physical constraints. The 'less suitable' parent may feel rejected and excluded from the donation and transplant process.

Siblings may be willing or ambivalent and it may be difficult to express ambivalent feelings because of societal concepts of family loyalty and love. A sibling of a patient has expressed the wish that 'the request had never been made, as once verbalised it was impossible to refuse without feeling enormous guilt'. Married siblings may wish to donate but may encounter hostility from their partner who feels that the risks are too great and that responsibilities to the family of marriage are more important than loyalty to the family of birth.

Ongoing psychological support is a necessary part of a living donor programme. Donor and recipient must be well informed concerning the risks and benefits and also the psychological difficulties that may develop. Separate meetings, both for the donor and the recipient, with medical staff and nurse/counsellor should be planned so that feelings, fears, and anxieties can be discussed with honesty. The motivation to donate should be explored and, if appropriate, the donor offered the opportunity to withdraw without guilt or family conflict.

Similarly, the decision to receive should be explored and the recipient offered the opportunity to refuse. Some patients have refused living donation, preferring to wait for cadaveric grafts so as not to 'inflict my disease on my family'. The dynamics of the donor and recipient relationship must be well understood so that help and advice may be offered if difficulties arise.

Assessment and preparation of donors

The living donor must be:

- well-motivated;
- in excellent health with two normal kidneys and normal renal function;
- ideally compatible for blood group and cross-match with the recipient, although ABOi and HLAi transplantation is now possible.

The assessment and preparation for living donation are extensive and normally carried out in stages over several weeks or months. Different centres will conduct tests at different stages but most units complete the same catalogue of tests in order to ensure that the criteria are fulfilled. The British Transplant Society and Renal Association have produced guidelines on this. It is recommended that the potential recipient should be evaluated for suitability for transplantation as early as possible,

to avoid any unnecessary delay. Donor assessment should be organised in a way that is acceptable to the potential donor, avoiding the need for repeated visits and inconvenience to home and work life as far as possible. Grouping tests and investigations together can minimise extra visits to hospital and an organised and focused approach to the process is good practice (see Boxes 10.8 and 10.9). This is best organised and monitored by the living donor coordinator who becomes the point of contact for potential donors and liaises between the various members of the multidisciplinary team (MDT). A donor health questionnaire has been developed by the BTS (2018) (pp. 56–57) and this should be used for initial discussion and assessment with the donor.

BOX 10.8

Initial donor assessment

- donor previous medical history.
- blood group.
- tissue typing.
- urinalysis (urine microscopy, culture, and sensitivity, albumin/protein:creatinine ratio).
- blood pressure, pulse, weight, and height.

The aim is to identify unsuitable donors early in the process. If there are no contraindications at this point the donor will move on to the next stage of assessment.

BOX 10.9

Medical assessment and further investigations: see British Transplantation Society guidelines (2018) for detailed information on donor assessment

- full medical history and physical examination.
- history in relation to transmissible infection.
- repeat urea, electrolytes, creatinine.
- liver function tests, fasting glucose, bone profile.
- haemoglobin, blood count, and coagulation screen.
- viral screen.
- repeat urinalysis (urine microscopy, culture, and sensitivity, albumin/protein:creatinine ratio).
- measurement of glomerular filtration rate (GFR).

Clinical tests

- chest X-ray.
- ECG.
- imaging of kidneys to determine renal anatomy, initially by ultrasound (less invasive) and progress to preferred method of assessment of vessels, which may be by catheter angiography, digital subtraction angiography (DSA), computed tomography (CT), or magnetic resonance angiography (MRA).

Other tests as indicated, depending on family history and/or results of physical examination, for example glucose tolerance test, thyroid function, echocardiogram. The donor assessment procedure aims to ensure the suitability of the donor, to minimise the risks of donation, and to ensure suitability of the donor kidney for the recipient. Donor confidentiality should be maintained at all times. Donor assessment is generally carried out by medical and surgical teams that are not also caring for the recipient; this ensures separation of interest. The donor assessment process should be designed in such a way that straightforward noninvasive tests are carried out first, therefore, if donors are later found to be unsuitable they avoid the need to undergo invasive testing.

Throughout the assessment programme the donor is assured that it is possible to retract the offer to donate at any time. Such a decision will be strictly confidential and support and advice will be available. If the donor wishes, a medical reason not to donate can be provided. This medical reason is seen within the context of a 'benevolent decision' to enable the donor to retract without family conflict or distress, thus promoting full altruism.

Preoperative care for the donor

Two separate surgical teams are usually involved with a living related donation. The donor team assumes responsibility for donor care and the transplant team takes responsibility for recipient care. The donor and recipient are usually both nursed within the transplant centre in separate rooms. However, they may be nursed together if they so wish, if there are language or other difficulties.

The donor and recipient are usually admitted on the day before transplant and at this stage a further medical history and physical examination will be performed, along with an anaesthetic and physiotherapist assessment (see Box 10.10).

The immediate preoperative care for the living donor will be similar to that given to patients undergoing conventional nephrectomy. However, particular attention is paid to informed consent, preoperative hygienic care, and premedication.

Surgical technique of nephrectomy

Living donor nephrectomy is always emotionally taxing surgery and can be technically difficult. Thus, whilst very rare, the risks are certainly not negligible and major morbidity or death is very traumatic not only for the relatives but for the members of the surgical team themselves. The risk of death associated with living donor nephrectomy and the risks of short- and long-term complications must be fully explained. Following recent developments in case law (Montgomery), the clinician responsible for the living donor is required to give the HTA explicit assurance that the person intending to donate understands both the generic and specific material risks of donation. This includes information about generic risks to which any reasonable person or all donors would attach significance, as well as information about individual risks to which the person consenting to donation is likely to attach significance (BTS 2018, p.38).

BOX 10.10

Donor preoperative assessment investigations

- ECG.
- chest X-ray.
- DVT prevention and prophylaxis (see NICE <http://guidance.nice.org.uk/CG92>)

Blood tests

- final cross match.
- MRSA screening swabs (throat, nose, axilla, groin).
- urinalysis, urine for microscopy, culture, and sensitivity.
- biochemistry.
- liver function tests.
- haematology and clotting screen.
- baseline measurement of blood pressure, pulse, respiration rate, temperature, and weight and nursing admission procedure.

The traditional approaches for removing a kidney from a live donor are either transabdominal, intraperitoneal, or via the loin over the 11th or 12th rib, either spreading or removing the 11th or 12th rib. The intra-abdominal approach is usually through a transverse incision in the right or left upper quadrant. Laparoscopic nephrectomy, either hand assisted or totally laparoscopic, is the most common surgical technique used in the United Kingdom and may be transperitoneal or retroperitoneal in approach. The technique requires a high degree of training of surgeons. The donor is placed in the flank position and the abdomen insufflated with carbon dioxide gas. Entry ports are made into the abdomen for the camera and instruments. After isolating the kidney it is enclosed by a bag to aid removal through another incision. The hand-assisted laparoscopic technique entails an incision large enough to allow insertion of the surgeon's hand to assist with the laparoscopic procedure.

Generally the left kidney is preferred due to the longer left renal vein, however the right kidney may be used successfully if preferred or if there are extra arteries on the left. The presence of more than one artery can make the surgery more complicated and it is important that this is established pretransplant and the donor counselled of the relevant risks.

The kidney is carefully exposed and meticulous dissection is carried out with careful handling of the kidney and careful exposure of the renal vein and artery. The gonadal and adrenal tributaries of the renal vein are ligated and divided and often a posterior lumbar vein needs ligating and dividing as well. The renal artery is cleaned and exposed at its junction with the aorta and the ureter is identified and dissected down to the pelvic brim or just below, where it is ligated and divided. It is very important to avoid too much dissection in the hilum of the kidney and it is also essential to avoid stripping the ureter of its adventitia. The blood supply to the ureter normally comes from the renal artery, branches from the gonadal vessels and the external iliac artery, and branches of the superior vesicle artery. In a transplant kidney the blood supply to the ureter is entirely dependent on the renal artery and it is essential to keep a good amount of adventitia around the ureter to allow the blood to reach the distal ureter. One of the major complications after transplantation is ischaemia of the lower end of the ureter and this is normally due to stripping of the ureter or loss of a lower pole artery at the time of the donor surgery.

When the kidney is free and attached just by the artery and the vein, the artery is ligated and divided first, followed by the vein. The kidney is removed and placed in iced saline where perfusion is started immediately and, after careful inspection, any further dissection is carried out and a renal biopsy is taken.

Postoperative management: living donor

The postoperative care for the living donor is similar to the care given for a conventional nephrectomy. Laparoscopic nephrectomy is associated with a shorter hospital stay, reduced pain, and quicker recovery time than standard nephrectomy. In most centres, patient-controlled analgesia using an opiate is utilised. See BTS (2018) guidelines for more detailed information.

Hydration: fluid and electrolyte balance

Paralytic ileus may occur as a result of the retroperitoneal dissection and the handling of the bowel. Therefore, the intake of oral fluids must commence slowly and only increase as ileus resolves and bowel sounds are evident. In practice, hydration is maintained by intravenous infusion until oral intake is sufficient. Close monitoring of fluid and electrolyte balance is necessary until dietary intake is adequate.

The passing of urine may prove difficult due to the pain of movement and anxiety, so often a urinary catheter is inserted under anaesthetic so that urinary output can be closely monitored and pain minimised. The catheter is usually removed on the second postoperative day. Regular midstream urine specimens should be obtained for microscopy, culture, and sensitivity during hospitalisation. Monitoring of urine output is important to determine the function of the remaining kidney.

Wound management

Wound management should include regular inspection to exclude complications of bleeding and infection.

Emotional support

During the early postoperative period, emotional support should be offered, as should frequent information regarding the progress of the recipient. Donor and recipient should be reunited at the earliest opportunity and encouraged to spend time together. The donor may experience a feeling of anticlimax after the surgery due to a release of the preoperative tension and anticipation. Such anticlimax may combine with postanaesthetic 'blues' to form a mild depression with emotional lability. Staff should recognise the altruism of the act and offer understanding and reassurance.

Discharge

The majority of living donors will be discharged between the third and fourth postoperative day. It is recommended that they continue their postoperative recovery at home for approximately six weeks to two months. Return to work will be variable depending on type of employment and its physical and psychological demands. Physical monitoring may include one or two further assessments by the surgical team.

The minimum standard includes a follow-up appointment within four to six weeks after donation at the transplant centre and an annual review thereafter, either at the transplant centre, the referring nephrology unit, or in primary care. Additional reviews are arranged if clinically indicated. Within a maximum of 12 weeks, it is anticipated that the donor will have made a full recovery and returned to normal activities (BTS 2018). Emotional support should continue as appropriate, with help available if difficulties arise.

Reimbursement for the financial cost of donation such as loss of earnings and travel expenses is available via NHS England (NHS England 2017). The intention is to ensure the process of becoming a living donor has no financial incentive or disincentive.

There are some challenges in achieving life-long follow-up for all donors, particularly for non-UK residents. This is especially the case in countries where living donor transplantation is not an established practice or where individuals pay for healthcare. These donors must be provided with written advice about appropriate annual monitoring.

Increasing Donor Organ Supply

Deceased organ donor rates and kidney transplant rates in the UK have remained fairly constant since the early 2000s. Such rates are insufficient to meet demand and the renal transplant waiting list continues to rise. If the renal transplant rate

continues at the same level, many hopeful patients on dialysis will be denied their 'treatment of choice'. Extending living donor programmes has increased the supply of kidneys, livers, and in some cases lungs for transplantation but it is crucial that the United Kingdom continues to explore and introduce initiatives to increase deceased donor organ supply.

The Organ Donation Taskforce was formed by the Department of Health in 2008 to look at ways to increase organ donation. The UK at that time had the eighth lowest rate of organ donation in Europe (16.4 donors per million population in 2010) compared with 32.0 in Spain, the highest rate in Europe.

Figures released annually by NHSBT have indicated the number of organ donors has been increasing since 2008. Several factors contributed to achieving this goal:

- improved infrastructure to support organ donation and transplantation by the implementation of the SNOD and the Clinical Lead in Organ Donation (CLOD) roles.
- implementation of the National Organ Retrieval Service (NORS).
- development and implementation of the living kidney donor strategy.
- expanded DCD donor programmes.

Latest figures from NHSBT (2018) (available at <https://www.odt.nhs.uk>) showed an increase in deceased donors from 1940 in 2013/2014 to 2378 in 2017/2018. However, living donors have fallen slightly with 1116 in 2013/2014 to 972 in 2017/2018. There are still challenges to overcome with UK donor rates remaining lower than that of several other European countries such as Spain, Portugal, and France (see Table 10.2). The UK has one of the lowest consent rates in the Western

Table 10.2 Actual deceased organ donors across Europe in 2016.

Country	Deceased donors pmp in 2016
Greece	4.7
Switzerland	13.2
Sweden	19.7
Republic of Ireland	16.4
Poland	14.0
Holland	14.7
Germany	10.6
United Kingdom	21.5
Slovakia	13.3
Finland	24.7
Czech Republic	25.3
Belgium	30.8
Norway	20.9
Italy	24.7
Austria	25.2
France	28.7
Portugal	32.7
Spain	43.8

Source: Council of Europe (2017).

world with only 4 in 10 families consenting to donation. This rate is much lower amongst black, Asian, and minority ethnic (BAME) communities with this group accounting for only 5% of organ donors. End of life care with respect to donation has improved over the years in the UK but it is known that opportunities to donate are still being missed. There is also a wide variation in practice between UK units in terms of acceptance and usage of donor organs.

In response a new strategy has been developed by NHSBT in conjunction with all four of the UK Health Departments that aims to build on the work of the organ donation taskforce and to address these specific issues. The 'Taking Organ Transplantation to 2020' strategy has four key objectives:

- increase consent for donation to 80% (currently 57%).
 - increase the deceased donation rate to 26 pmp (currently 19.1 pmp).
 - transplant 5% more of the organs offered.
 - increase the deceased donor transplant rate to 74 pmp (currently 49 pmp).
- (Available at https://nhsbt.dbe.blob.core.windows.net/umbraco-assets-corp/4240/nhsbt_organ_donor_strategy_long.pdf (accessed 19 June 2018)).

It is recognised that to achieve these objectives will require a commitment from several areas: from society and individuals, from NHS staff working in areas related to donation and transplantation, and from NHS commissioners and NHSBT (NHSBT 2017e).

Opting in/opting out

Within the UK the general public are encouraged to 'opt in' by making the voluntary decision to donate organs. This decision is supported by carrying a donor card or joining the organ donor register and informing relatives of this wish. Thus, donation is a voluntary gift.

About 36% of people in the UK had joined the NHS Organ Donor register by 2017, which equates to over 23 million people. More people who have not registered will carry an organ donor card, however problems with this system are that in practice, the donor card may not be available at the time of death, or relatives may either be unaware of the donor's wishes or may choose to ignore them. Several patient groups, and the British Medical Association, have pressed for the introduction of an 'opt-out' system, whereby everyone is deemed to wish to donate unless they have registered an objection.

A soft opt-out system was introduced in Wales in December 2015. The system applies to those over 18 years of age who live and die in Wales. Those who have not opted out by registering their decision will be assumed to have consented to donate their organs. Early evaluation of the system shows promising results with an increase in the number of families giving consent for their relative to donate their organs, however this has not translated into an increase in the number of actual donors, thought to be due to an increase percentage of donors being unsuitable (Welsh Government 2017). There is however a high awareness and support for the system amongst the general public in Wales, much higher than for other parts of the UK (71% in Wales vs 49% in remainder of UK); this could be due to the increase in publicity surrounding the change in law, possibly leading to an increased awareness within the general public. However, with a true opting-out system the wishes of the family are not considered; the system in Wales will not override the wishes of the family but will hopefully make the decision to consent to donation an easier one for the family to contemplate.

The opt-out system will come into force in England from spring 2020, and will mean adults are presumed to be organ donors unless they have recorded their decision not to be. Families will still be involved before organ donation goes ahead.

It is hoped that the strategies described will continue to increase donation rates in the UK and achieve the targets set out. It is possible, however, that with growing waiting lists the demand may always outstrip supply.

Preoperative Management for a Recipient of a Renal Transplant

The transplant call

Transplant recipients report mixed reactions of relief, excitement, anxiety, and sadness when they receive the transplant phone call – relief that the waiting time may be over; excitement for the new life ahead; anxiety that the surgery may be difficult or that the transplant may fail; and sadness that a family elsewhere has experienced tragedy in order for the kidney to become available.

During the telephone conversation the recipient is informed that a transplant may be possible and to travel to the transplant centre and have nothing further to eat or drink. Brief questions are also asked to clarify current health status and to exclude any infections or other problems that may prevent transplantation.

Some centres contact two recipients for each transplant so that should a positive cross-match occur for one, a second recipient is already prepared, thus minimising the cold ischaemia time. It has been found that contacting two recipients can lead to repeated disappointments, anger, and depression, therefore it is preferable to only call one recipient to the transplant centre in the first instance.

Nursing admission

Upon arrival, the recipient and family are welcomed by the nursing team and helped to familiarise themselves with the unit. Brief information is given regarding the forthcoming blood and clinical tests; questions are answered and anxieties explored during the nursing admission procedure (Box 10.11).

BOX 10.11

Nursing admission procedure

- blood pressure, pulse, temperature, respirations.
- current weight: dry weight.
- past medical history – renal disease.
- dialysis history – current practice and date and time of last dialysis.
- current health status – recent relevant health events (i.e. blood transfusion/infections).
- normal urine output, if any.
- social information.
- allergies.
- name band applied.

Medical assessment

Immediate medical assessment and blood tests are required to assess fluid and electrolyte status (as dialysis may be needed prior to surgery); also to complete the final tissue typing cross-match test, if required, and therefore the medical assessment immediately follows the nursing admission procedure (Box 10.12).

Preoperative dialysis

The results of the medical assessment and blood tests will determine the need for dialysis. Fluid overload and electrolyte imbalance (particularly hyperkalaemia) must be corrected, as they represent an anaesthetic risk and may enhance post-transplantation difficulties.

Haemodialysis with minimal or no heparinisation is often necessary to ensure optimal weight and to reduce fluid overload and serum potassium levels.

Peritoneal dialysis patients may require rapid exchanges to achieve optimal fluid and electrolyte status. The peritoneal catheter exit site should be examined for any signs of infection and a swab taken for culture and sensitivity. Also, following the necessary exchanges, the catheter should be drained and a fluid specimen sent for microscopy, culture, and sensitivity and then the catheter capped, leaving the patient empty of fluid.

Information and emotional support

During the dialysis time, it is often possible to explore individual fears and anxieties and offer emotional support and information regarding postoperative medications and procedures. Recipients are often emotionally labile at this time ('tears and laughter') and require much emotional understanding and support.

Immediate preoperative care

It is usual for the physiotherapist to visit to commence chest physiotherapy and advice regarding postoperative mobility and for the anaesthetist to perform an assessment. Once the tissue typing cross-match has proved negative, the final preoperative preparation begins (Box 10.13).

BOX 10.12

Medical assessment procedure

- medical history.
- renal disease history.
- dialysis history.
- current health status – recent relevant events.
- allergies.
- medical examination.
- blood tests:
 - urea and electrolytes;
 - liver function tests;
 - tissue typing cross-match;
 - viral screen (as in pretransplant assessment);
 - cross-match for 2–4 units of blood available for transplant surgery.
- clinical tests:
 - chest X-ray;
 - ECG;
 - midstream specimen of urine, urinalysis.

BOX 10.13**Preoperative preparation**

- skin swabs/nose, throat, axilla, and groin swabs – for MRSA screening;
- swabs and dressings to other dialysis lines (i.e. permanent central venous catheters);
- suppositories (if required);
- bath/shower/hair wash;
- operation gown;
- marking and dressing (to protect) arteriovenous fistula from inadvertent use of invasive monitoring (e.g. intravenous lines, blood pressure cuffs) and to maintain warmth, thus avoiding clotting;
- antithrombosis stockings;

Preoperative medications such as immunosuppression, aspirin

Note: Transplant centres may use differing combinations of immunosuppressive medications. Medications given immediately preoperatively.

- premedication;
- diabetes mellitus: sliding-scale insulin as appropriate.

Surgical Technique for Renal Transplantation

Before transplantation begins, a catheter is placed into the bladder. This allows drainage of the bladder during the transplant operation and also allows the bladder to be filled with solution containing antibiotics to facilitate later identification of the bladder for reimplantation of the ureter. The right or left iliac fossa is the normal site for the transplant (Figure 10.6).

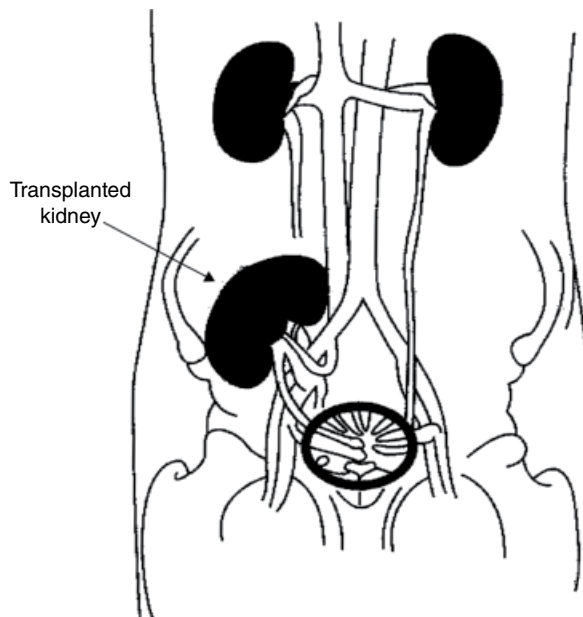


Figure 10.6 Position of the transplanted kidney.

- an incision is made curving from just above the pubic symphysis to just above the iliac crest.
- the inferior epigastric vessels are ligated and divided and an extraperitoneal approach is made down on to the iliac vessels.
- the external iliac artery and vein are freed and small branches or overlying lymphatics are ligated and divided.
- clamps are applied to the external iliac vein and the renal vein is anastomosed to the external iliac vein with continuous 5.0 Prolene sutures.
- clamps are then applied to the external iliac artery and the renal artery on its patch (known as the Carrell patch) is anastomosed with continuous 5.0 Prolene to the external iliac artery (Figure 10.7). Sometimes the internal iliac artery is used and an end-to-end anastomosis is performed.
- once the anastomoses are complete, the clamps are released, taking the venous clamps off first. The kidney normally perfuses quickly and one is often able to see immediate urine production.
- the bladder is then filled through the catheter and the ureter put into the bladder and then tunnelled submucosally to prevent urinary ureteric reflux (the Leadbetter–Politano technique). Most centres may use an extra vesicle technique which involves splitting the muscle, laying the ureter just above the bladder mucosa and so into the bladder, and closing the muscle over the top. If the bladder has been opened it is closed with two layers of Vicryl. A ureteric stent is placed in the ureter and left in situ for four to six weeks. This reduces the risk of ureteric stenosis.
- the wound is closed in the usual fashion and the bladder washed out at the end of the procedure.

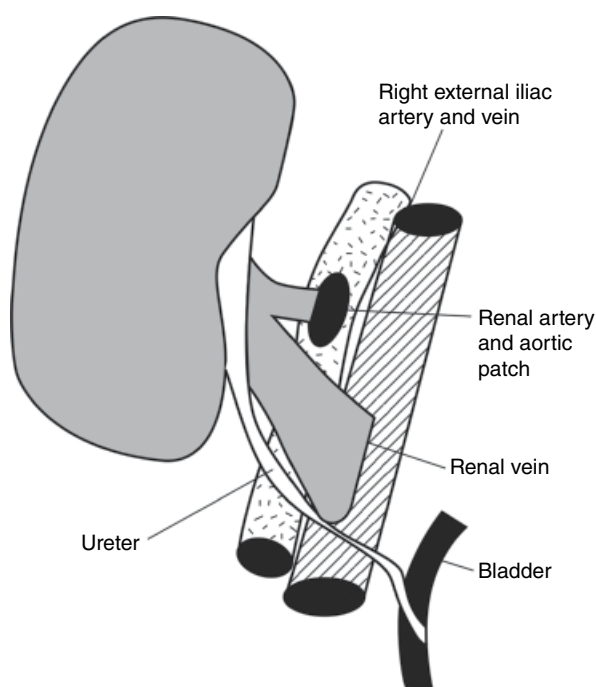


Figure 10.7 The surgical technique for renal transplantation.

10.13 Immunosuppression

Immunosuppression regimes

Until 1997, the most commonly used immunosuppression was a ‘triple-therapy’ regime involving ciclosporin (Sandimmun/Neoral), azathioprine (Imuran), and prednisolone. The advent of newer drugs has allowed centres to use differing combinations to ‘tailor’ immunosuppressive medications to individual recipients based on their risk of potential problems post-transplant, such as rejection, diabetes, non-adherence, and cancer. Immunosuppressive regimes are generally divided into induction (given at the time of transplant) and maintenance, with maintenance immunosuppression divided further to the early (less than three to six months) and late (more than six months) postoperative period. The aim of all immunosuppression protocols is to reduce rejection, maximise patient and graft survival, and to minimise adverse side effects. The early postoperative period is when the risk of rejection is highest, therefore this is the time of maximum immunosuppression. Combinations of immunosuppressive medications are given in order to minimise side effects of one particular drug whilst gaining adequate immunosuppressive effect. Dudley and Harden (2011) give an example of immunosuppressive regimens dependent on immunological risk (risk of rejection). Broad guidelines are as follows:

- induction therapy should be given to all recipients, IL2-RA for those in the low risk group, T-cell depleting antibody (TDA) to be considered for those in the high-risk group.
- maintenance immunosuppression with a CNI, an antiproliferative agent (mycophenolate/azathioprine), plus or minus steroids for low and medium risk.
- mycophenolic acid (MPA) based drugs given in preference to azathioprine as an antiproliferative agent.
- steroid avoidance/withdrawal can be used in the first postoperative week in low risk recipients.

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (NICE) updated guidance to the NHS in England and Wales on the use of immunosuppressive therapy for renal transplantation in adults in October 2017 (NICE 2017). The guidance recommends: interleukin-2 receptor antagonist (IL2-RA, basiliximab) for induction treatment. This should be used with a combination of a CNI and an antiproliferative agent. NICE (2017) recommends Tacrolimus and Mycophenolate Mofetil as the most clinically and cost-effective options.

This guidance represents the views of NICE, and health professionals are expected to take it into account when exercising clinical judgement. However, it does not override the individual responsibility of health professionals to make appropriate decisions for patients. Nevertheless the recommendations by NICE will be used as a guide by NHS commissioners and will therefore have implications for funding if individual clinicians deviate from using the recommended combination of immunosuppression agents.

Induction immunosuppression

Interleukin-2 Receptor Antagonist (IL2-RA): Basiliximab (Simulect)

Action Basiliximab works by binding specifically to part of the interleukin-2 receptor, which is only expressed on activated T lymphocytes. Basiliximab helps to prevent

proliferation of antigen-stimulated T cells and is used in combination with other immunosuppressives to form a baseline therapy.

Side effects None have been reported.

T-Cell depleting antibodies (TDA)

Action Inhibit and destroy circulatory lymphocytes through antibody action. TDAs are used as induction immunosuppression in high immunological risk recipients and as a treatment for rejection.

Muromab-CD3 (Orthoclone (OKT3)) monoclonal antibody

Side effects

- chest pain;
- pulmonary oedema;
- gastrointestinal disturbances;
- fever;
- chills;
- dyspnoea;
- infections.

This drug can cause rapid pulmonary oedema and therefore it is essential that the patient is evaluated for volume overload and given treatment if necessary prior to administration of the drug.

Antilymphocyte globulin (ALG), antithymocyte globulin (ATG) – polyclonal antibodies

Side effects

- rash;
- fever/chills;
- anaphylaxis;
- thrombocytopenia/leukopenia;
- myalgia.

Maintenance immunosuppression

Calcineurin inhibitors

Ciclosporin (Neoral/Sandimmune)

Ciclosporin is a natural peptide found in two strains of fungi. It was first introduced into clinical immunosuppression in 1983 and is a CNI. Neoral ciclosporin is in a microemulsion and is more reliably absorbed.

Action Ciclosporin inhibits interleukin-2 and interferes with the growth and activation of T lymphocytes.

Side effects Usually side effects are dose dependent and responsive to dose reduction. The commonest side effects include:

- nephrotoxicity – decreased GFR;
- hypertension;
- hepatic dysfunction;
- hirsutism;
- hyperlipidaemia;
- hyperkalaemia;
- hyperuricaemia;
- gum hypertrophy;

- hypomagnesaemia;
- hypertrichosis.

Other less common side effects include:

- muscle weakness;
- thrombocytopenia.

Absorption Ciclosporin is absorbed with variable efficiency by different individuals; therefore, regular monitoring of whole blood levels is necessary. The usual therapeutic range may be higher during the early post-transplant period, with maintenance doses aimed at lower levels. Therapeutic monitoring is usually by 12-hour postdose trough levels. It may take up to one month to stabilise levels post-transplant and continual monitoring is necessary at every clinic visit thereafter.

Some units perform C2 monitoring, i.e. measuring blood concentrations two hours postdose. C2 is thought to predict more accurately individual patient absorptions than traditional trough monitoring and potentially results in a reduced incidence of acute rejection episodes and acute renal dysfunction. However this method can be difficult to organise, relying on accurate timing of dose administration and sample collection to ensure accuracy.

Tacrolimus (FK506)

Tacrolimus is another CNI that, like ciclosporin, works early in T-cell activations. Its action inhibits interleukin-2 and other cytokines that cause early T-cell activation. It is available in an immediate release and prolonged release formulation.

Absorption As with ciclosporin, regular monitoring of whole blood levels is necessary.

Side effects Common side effects include:

- visual and neurological disturbances;
- hypertension;
- tremor, headache, insomnia;
- raised blood sugar level;
- leukopenia.

Antiproliferative agents

Azathioprine

Azathioprine is a derivative of the anticancer drug 6-mercaptopurine and was introduced into clinical practice in 1962.

Action Azathioprine inhibits both DNA and RNA synthesis and prevents growth of lymphocytes.

Side effects The main side effect is neutropenia. If the white blood cell count (WBC) drops to below $3.5 \times 10^9 \text{ l}^{-1}$ the dose should be reduced. If the WBC continues to fall the drug should be stopped temporarily.

Other side effects include:

- alopecia;
- general malaise;
- muscular pains;
- malignancy;
- pancreatitis (rare);
- altered liver function;
- cholestatic jaundice (rare).

Because of the risk of neutropenia, blood counts must be checked at intervals of no longer than three months.

Mycophenolate mofetil

Mycophenolate mofetil was licenced in 1995; it is metabolised to MPA. MPA is similar in effect to azathioprine but has a more selective action.

Action Mycophenolate mofetil acts by preventing activated lymphocytes from differentiating and proliferating and thereby limiting clonal expansion. In the United Kingdom, this drug was previously used in preference to azathioprine in selected patients who were considered to be at a higher risk of rejection than average, however it is now routinely used as part of maintenance immunosuppression.

Side effects

- gastrointestinal effects including: diarrhoea, constipation, nausea, vomiting,
- blood disorders: leukopenia, anaemia, pancytopenia

A formulation of MPA (Myfortic) is available with an enteric coating that some patients may find reduces gastrointestinal side effects.

Corticosteroids

Prednisolone

Action The action of corticosteroid preparations is complex and involves anti-inflammatory responses with blocking of T cells and interleukin-1.

Side effects

- cushingoid appearance;
- fluid retention;
- glaucoma;
- increased appetite;
- hypertension;
- psychosis;
- peptic ulceration;
- increase in blood sugar levels.

Side effects with long-term treatment:

- subcapsular cataract;
- pancreatitis;
- skin thinning;
- osteoporosis.

Many centres start steroid reduction at one month after transplant and aim to remove steroid therapy at one year after transplant because of the long-term side effects.

Mammalian target of rapamycin inhibitor (M-TORi) sirolimus (rapamycin)

Sirolimus acts later in the T-cell activation than CNIs. It inhibits interleukin-2-mediated signal transduction pathways. Sirolimus is not nephrotoxic, which gives it an advantage over CNIs. It was licenced for use in the UK in 2001. Due to its potential to delay healing, sirolimus is rarely used in the early post-transplant period. It also interacts with CNI to enhance toxicity so is rarely used in combination with these drugs.

Side effects

- delayed healing (lymphocoele);
- hypercholesterolaemia;
- hypertriglyceridaemia;

- thrombocytopaenia;
- increased blood levels of MPA;
- nose bleeds.

Everolimus Everolimus is similar to Sirolimus but has a shorter half-life and therefore a shorter time to achieve steady state concentration. Toxicity and side effects are similar to Sirolimus, particularly the interaction with CNI.

Belatacept (Nulojix)

Action Belatacept is a fusion protein that works by selectively blocking the process of T-cell activation. Licenced in the United Kingdom in 2011 for use in combination with corticosteroids and mycophenolate in maintenance immunosuppression, Belatacept is given by intravenous infusion according to a dosing schedule commencing on the day of transplant, then on day 5, week 2, 4, 8, and 12. Subsequent maintenance regime comprises monthly infusions. Evidence suggests improved patient and graft survival and improved renal function with Belatacept when compared to ciclosporin (Vincenti et al. 2016). Data are not yet available for long-term side effects but there is a potential increased risk for post-transplant lymphoproliferative disorder (PTLD). Depending on the long-term effects of this medication it may offer potential benefits for patients particularly with regard to the convenience of dosing and freedom from side effects of CNIs.

Side effects

- anaemia;
- diarrhoea, constipation, nausea, vomiting;
- urinary tract infection;
- peripheral oedema;
- hypertension;
- headache;
- electrolyte disturbance;
- leukopenia.

Renal Transplant Rejection

There are three types of renal transplant rejection:

- hyperacute rejection;
- acute rejection;
- chronic rejection or chronic allograft nephropathy (CAN).

Hyperacute rejection

Hyperacute rejection (Figure 10.8) occurs rapidly, within minutes or hours of revascularisation of the transplant. It is caused by:

- the presence of preformed cytotoxic antibodies in the recipient's blood (resulting from previous failed transplants, blood transfusions, or pregnancies) reacting against the donor's histocompatibility antigens;
- ABO incompatibility between the donor and the recipient.

The final lymphocytotoxic cross-match prior to transplant should demonstrate that cytotoxic antibodies are present and transplantation should not take place, thus a hyperacute rejection is a very rare phenomenon today.

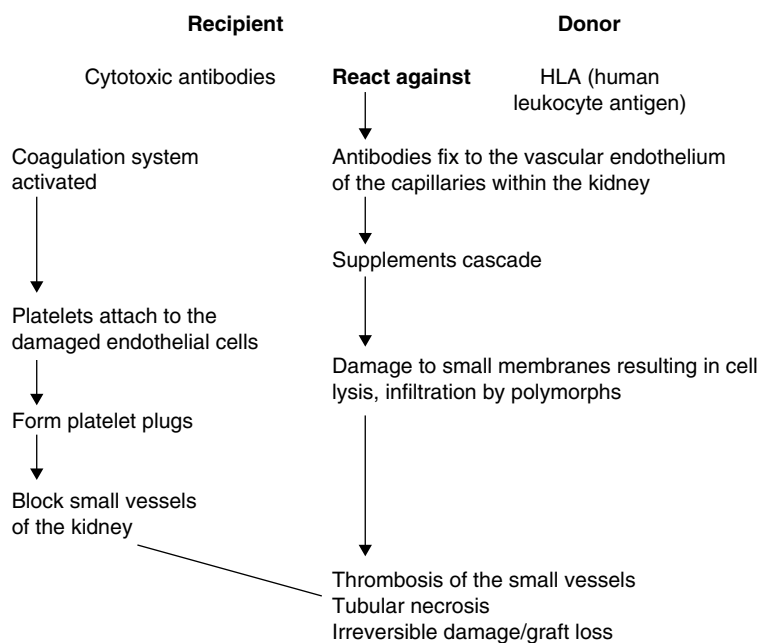


Figure 10.8 Histopathology of hyperacute rejection.

Hyperacute rejection may be observed during the transplant surgery. Instead of the kidney becoming distended and pink as the arterial and venous clamps are released, as is usual, with hyperacute rejection the kidney will remain flaccid and become blue. Damage is almost always irreversible and the graft is lost.

Acute rejection

Acute rejection (Figure 10.9) can be cellular and/or antibody-mediated rejection (ABMR) which commonly occurs between four days and two months after transplantation. Rejection is ideally diagnosed by biopsy of the graft in order to differentiate from other causes of graft dysfunction such as CNV toxicity or BK virus nephropathy. Acute cellular rejection is usually treated initially with corticosteroids; usual practice is to administer daily bolus doses of 500 mg intravenous methylprednisolone over a three-day period (one bolus each day). Cellular rejection that does not respond to treatment with high-dose steroids and rejection that is antibody mediated is treated with a course of TDA. Rejection often responds to treatment; however, a severe rejection episode may result in some loss of overall graft function. It is usual to increase the level of maintenance immunosuppression following an episode of rejection unless nonadherence or another reason for reduced levels of immunosuppression can be confirmed.

Transplant biopsy

A percutaneous biopsy of the transplant kidney is often the only reliable way to diagnose accurately the cause of graft dysfunction. Many patients are anxious about the biopsy procedure and the effect on the transplanted kidney and will require reassurance and explanation of the rationale for the procedure and the procedure itself. Many centres now perform biopsies as day case procedures, minimising hospital stay and disruption for the patient.

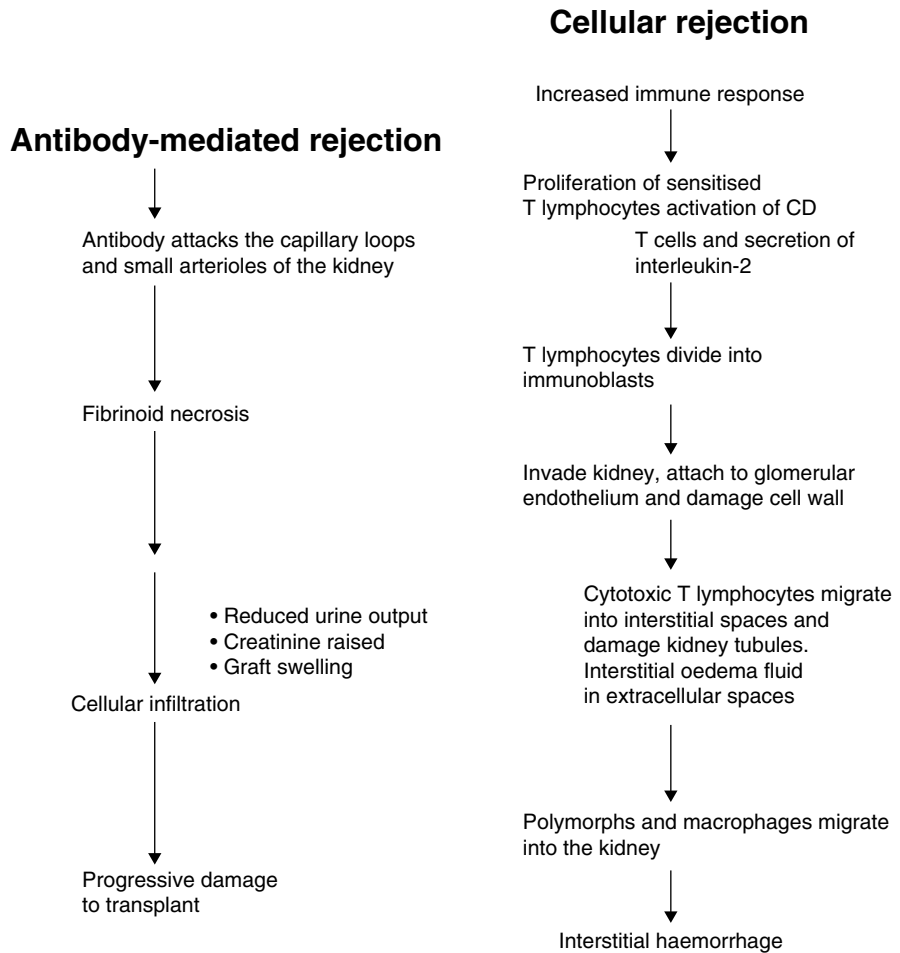


Figure 10.9 Histopathology of acute rejection.

It is recommended practice to send serum samples at the time of biopsy to check for the presence of HLA specific antibodies. This can aid the diagnosis of ABMR and ensure the correct treatment is given. Biopsy samples should be routinely stained for C4d deposition (to indicate ABMR) and SV40 antigen (BK virus), as appearances can be similar on histological examination.

Some centres perform 'protocol biopsies' that is, routine biopsies at set time periods post-transplant (e.g. at 3, 6, or 12 months) with the aim of optimising immunosuppressive regimes based on the results.

Chronic allograft injury

Chronic allograft injury (CAI) usually occurs over months or years but may occur much earlier. It is difficult to separate out the contribution of rejection from other factors detrimental to the kidney. The term chronic allograft injury encompasses all of these, meaning that permanent damage is seen on biopsy. There is a gradual occlusion of the lumen of the arteries of the kidney with interstitial fibrosis which destroys the graft. The exact mechanisms involved in CAI are still unclear and may be immunological or nonimmunological. Other factors include donor history and delayed graft

function, acute rejection episodes, hypertension, CNI toxicity, and infection. The first signs of CAI are usually a gradual worsening of renal function with proteinuria.

Postoperative Care and Complications for the Recipient of a Renal Transplant

Aims of care

The aim of postoperative management is to provide the appropriate care to support primary transplant function and to aid optimal recovery. Initial care involves close monitoring of physical and psychological health, with frequent assessments and adjustments in response to changes in health status.

Immediate postoperative care

In most cases the anaesthetist will insert a triple-lumen central venous line via the internal jugular vein immediately prior to surgery. This line facilitates monitoring of fluid status and central venous pressure (CVP) and allows infusion of fluids and medications during surgery and the early postoperative phase.

Cardiorespiratory status

Immediate baseline observations should be recorded, including blood pressure, pulse, respirations, and temperature. Such observations should continue every 30 minutes until stable and thereafter hourly or as appropriate. Twenty-four-hour ECG monitoring may be routine; however, in some centres such monitoring may only be used for patients in high-risk categories. Close monitoring of respiratory status is essential, as anaesthetic drugs and analgesia may be poorly excreted due to the reduced transplant function, thus depressing respiratory effort and increasing the risk of pulmonary complication. Early chest physiotherapy is essential.

Pain management

The experience of pain is unique to each individual and therefore the use of patient-controlled analgesia is a suitable therapy as it will provide satisfactory pain management, reduce recipient anxiety, and facilitate deep breathing and movement. An opiate derivative is commonly used. Pethidine is avoided because of the possible accumulation of metabolites in the presence of reduced renal function. Recipients often report that the presence of the urinary catheter causes the greatest discomfort. Severe pain in the graft in the early postoperative period may be indicative of swelling of the kidney as a result of venous thrombosis.

Hydration: fluid and electrolyte balance

Inadequate hydration may adversely affect transplant function; therefore, the maintenance of an acceptable venous pressure without the complication of fluid overload is an integral element of care. Fluid intake is usually administered through the central venous line. CVP measurements, recorded hourly, and urinary output measurements, recorded hourly, are used as a guide to appropriate fluid intake.

Fluid intake protocol usually involves fluids being administered through an infusion pump with hourly intake equal to the previous hour's output plus 50 ml, with the aim of achieving a CVP level of approximately 10–15 cm H₂O.

Peripheral line perfusion must also be included in the intake total. Infusion of dopamine may be introduced to help maintain pressure and improve transplant perfusion by reducing vasoconstriction of the smaller renal vessels. Monitoring of serum biochemistry and haemoglobin levels is ongoing and the results will determine the type of intravenous fluid given. Often 5% dextrose is alternated with normal saline. Blood transfusion is occasionally required.

Oral fluids are usually introduced within the early postoperative phase (as paralytic ileus is rare) and are gradually increased as appropriate. In uncomplicated cases the CVP line is removed after 24 hours and nutrition introduced.

Urine output: catheter care

A urinary catheter will be in situ following the transplant surgery, and the urine may be bloodstained due to the surgical procedures to the bladder and ureter. Clot formation may occur, resulting in pain and anuria. Gentle sterile bladder washouts can be performed to alleviate the problem and re-establish urine flow.

Twenty-four-hour urine output should be recorded and it is, of course, important to note the volume of urine passed from the native kidneys pretransplantation when assessing urinary totals. Daily urine analysis and biochemistry should be noted and daily catheter specimens obtained for microscopy, culture, and sensitivity. The catheter is usually removed on the fifth postoperative day. Some recipients may experience difficulty with voiding and also may have very limited bladder capacity due to pretransplant bladder atrophy. Reassurance and bladder retraining strategies usually help to solve these problems.

Wound management

A wound drain may be present and drainage should be monitored. Observation and aseptic dressing of the wound will be given as appropriate and the sutures removed when healing has occurred. The immunosuppression regime and other contributory factors such as diabetes or malnutrition may impede the healing process.

Infection control

Recipients are immunocompromised and therefore infection control procedures should be strictly followed. Handwashing should take place before and after each nursing and medical procedure and visitors should be monitored for infections. Medications should include prophylaxis against infection and additional treatments should be commenced if infection is suspected.

The recipient should be helped to achieve personal and oral hygiene of a high standard and aseptic techniques utilised with regard to wound, peritoneal catheter site, urinary catheter and CVC care. Catheter tips should be cultured for microscopy and sensitivity when removed.

Postoperative medications

In addition to immunosuppressive medications other medications are required post-transplant:

- antibiotic prophylaxis – particularly to prevent infection with *Pneumocystis carinii*;
- PPIs;
- nystatin to prevent oral candidiasis;
- aspirin, to minimise long-term cardiovascular risk;
- statin, to minimise cardiovascular risk;

- calcium supplements, to limit side effects of corticosteroids on bone mineral density;
- isoniazid, for prophylaxis against TB if required;
- valganciclovir, for prophylaxis against CMV infection if required.

Continuing care

Recipients usually recover quickly from the anaesthetic and begin early mobilisation to prevent complications. A light diet is introduced on day one. Constipation may be a problem due to anaesthetic, immobility and analgesia, and gentle laxatives or suppositories may be needed. Self-care is usually achieved by the fifth postoperative day.

Sadness may be linked to thoughts of the donor family and grief and guilt may be expressed that the transplant has resulted from 'another's tragedy'. It is often helpful to give recipients anonymous details such as age and gender of the donor, and to offer them the opportunity to write a letter of thanks to the donor family. The expression of thanks usually enables recipients to accept the gift of the organ and to move forward to their new lifestyle.

Anxiety is usually linked to the fear of complications such as rejection, infection, and graft loss. Recipients and their families require considerable support, understanding, and in-depth information during the early postoperative phase, particularly if difficulties occur.

Complications of renal transplantation

Renal dysfunction – acute tubular necrosis

The most common cause of delayed graft function after renal transplantation is ATN, which may be due to prolonged hypotension in the donor or prolonged ischaemia during the donor or recipient surgery. Dialysis support may be required until adequate transplant function is achieved. Haemodialysis, with reduced heparinisation, can be undertaken as necessary (a frequent clotting screen will be required), and peritoneal dialysis recommenced as long as the peritoneum has not been breached by surgery.

CNIs (ciclosporin, tacrolimus) are known to be nephrotoxic and may therefore prolong ATN.

Acute rejection

Many transplant recipients will experience at least one episode of acute rejection. Acute rejection may not present with overt symptoms; a mild increase in creatinine, indicating graft dysfunction, may be the only symptom, often picked up following a routine visit to the transplant clinic.

The clinical signs of acute rejection may include:

- renal dysfunction;
- pyrexia;
- reduced urine output;
- swelling and tenderness of the transplant;
- ankle oedema, weight gain;
- flulike symptoms.

Vascular complications

Transplant renal artery and renal vein thrombosis Thrombosis of the renal artery or renal vein is a rare complication. Clinical signs of graft thrombosis usually include pain in the graft, renal dysfunction, anuria, and hypotension. Diagnosis

may be confirmed by ultrasound scanning (see Chapter 7). Immediate surgical exploration should be undertaken. In the majority of cases the transplant will be lost.

Transplant renal artery stenosis Renal artery stenosis usually occurs between 6 and 12 months after transplantation. Signs include graft dysfunction and severe hypertension with a bruit on auscultation over the transplant. Diagnosis is confirmed by doppler ultrasound or angiography. In severe cases intervention may be required either by percutaneous transluminal angioplasty or surgery.

Urological complications

A major urological complication which may occur is avascular necrosis of the distal end of the transplant ureter, resulting in leakage of urine. Surgical reimplantation of the ureter will be required in most cases. This complication has become less common recently due to the use of a ureteric stent.

Infections

Bacterial infection

The clinical signs of infection are similar to those of rejection (pyrexia, tachycardia, flulike illness), therefore it is important that both possibilities are considered and investigations undertaken to exclude either cause. Transplant recipients are at increased risk of rejection due to immunosuppression, however, due to their impaired immune response, they may not display overt signs of infection until the infection has become more serious. It is therefore vital to monitor transplant recipients closely for signs and symptoms of infection and to investigate even seemingly innocuous symptoms. Infections in this group of patients can be life threatening if not treated appropriately and adequately.

Chest infections may result from *Pneumococcus*, *Haemophilus influenzae*, *Klebsiella*, and *Pneumocystis*. Infection may develop rapidly, resulting in the need for ventilation. Early treatment with appropriate antibiotic therapies is essential.

Fungal infections

Oral *Candida* is common and many centres give antifungal prophylaxis for a short time following transplantation. Oral hygiene of a high standard should be encouraged. Genital *Candida* may also occur and recipients may be reluctant to report this problem. Recipients should be informed that *Candida* is a potential problem and that treatment will be required.

Transplant recipients are at increased risk of serious fungal infections such as *Aspergillus*, *Cryptococcus*, and *Pneumocystis carinii*.

Viral infections

Cytomegalovirus

CMV infection is usually acquired during childhood and early adulthood and is a minor flulike illness. However, this minor illness can cause major complications in the immunosuppressed transplant recipient. CMV disease, after transplantation, may occur because of:

- reactivation of latent disease in a CMV-positive recipient. Such reactivation is generally classed as 'secondary CMV'.

- transmission of CMV from a CMV-positive donor to a CMV-negative recipient through the transplanted organ, or community acquired infection after the transplant. This is classed as 'primary CMV'.

CMV may also be transmitted through whole blood transfusions, hence many centres require that all patients receive CMV-negative blood.

CMV vaccinations for all transplant recipients in the pretransplant phase would be an ideal solution to this problem but, as yet, no clinically acceptable vaccines have been formulated. Also matching so that CMV-negative recipients receive CMV-negative grafts would help to minimise the difficulties experienced, but such matching is not always possible in practice. Therefore, primary CMV disease does occur and can cause significant morbidity and mortality.

The usual time for manifestation of CMV disease is four to eight weeks post-transplantation. Clinical signs include swinging pyrexia, rigours, malaise, and, in extreme cases, pneumonitis, retinitis, gastroenteritis, and encephalitis.

Valganciclovir is widely used as prophylaxis in high-risk recipients (such as CMV-negative recipients receiving CMV-positive grafts, or CMV-positive recipients receiving ATG).

Recipients are monitored for serological evidence of CMV activity and treated according to local guidelines. Oral valganciclovir has been used for treatment, although it is licenced only for prophylaxis, however, if the patient is unwell, admission to hospital and treatment with IV ganciclovir may be necessary.

Herpes simplex and varicella zoster virus

Herpes simplex (types I and II) can cause problems following transplantation. Oral and anogenital lesions may occur. Recipients may be reluctant to report such problems due to anxiety and embarrassment. Therefore, recipients should be aware that these lesions may arise and that they occur because of reduced immunity, not because of other social issues. Sympathetic and understanding care should be offered and antiviral treatment commenced.

Reactivation of latent VZV may also occur and present as classical 'shingle' lesions. Antiviral treatment is necessary to prevent systemic complications. Disseminated VZV (chickenpox) is dangerous in immunosuppressed patients, resulting in some cases of life-threatening illness with encephalitis, pneumonitis, and meningitis. Recipients must be aware of the problems associated with such viral infections and should be encouraged to report signs and symptoms or contact with infected others.

BK (polyoma) virus

Most BK virus infections are asymptomatic but it is implicated in ureteric stenoses, late haemorrhagic cystitis, and deteriorating graft function. Two factors may account for the increase in BK nephropathy: improvements in biopsy interpretation and the newer immunosuppressants now widely used. Presence of BK virus in biopsy samples can be confirmed by testing with SV40 staining. Infection is associated with deteriorating renal function but can often be controlled by reducing immunosuppression. BK virus is often detected during routine urinalysis; haematuria can be a sign of BK infection and urine should be sent to the laboratory for cytological examination. This will detect the presence of viral cells. This does not always indicate the presence of active virus in the graft and a serum sample tested for BK virus load can indicate the presence and the activity of the virus. Serological testing of viral counts is a useful tool to monitor the effect of reduction in immunosuppression following a diagnosis of BK virus nephropathy at biopsy.

Discharge of the Recipient from Hospital and Continuing Care

If recovery has been uncomplicated the transplant recipient may be discharged home on about the seventh to tenth postoperative day.

The educative and developmental intervention is very important for recipients of transplants. They must have sufficient knowledge to monitor their health status, be understanding of medication regimes, and report problems if they arise. Assessment of learning difficulties should be completed soon after transplant so that relevant interventions may be implemented to aid learning, knowledge, and eventual independence. Physical barriers such as impaired sight and hearing can be aided by electronic blood pressure monitoring equipment. Language and literacy difficulties can be resolved with diagrammatic information, translations, and medication presented in daily dosette boxes, all promoting personal independence, although family members may be included in teaching sessions as appropriate.

The nurse may assess learning abilities (with an informal, nonthreatening discussion) post-transplant and plan a teaching information programme, implement this programme, and evaluate progress. Information is given as appropriate both verbally and in the form of a written information booklet. At the time of discharge the recipient should have the following knowledge (Box 10.14).

Drug charts and monitoring booklets should be utilised as part of a self-medication programme introduced as recovery allows or on the second postoperative day.

Immediately after discharge, recipients will be seen very frequently in the outpatient clinic and it is important that nursing intervention identifies developmental needs so that the recipient's knowledge base continues to expand and psychosocial care is offered. Reports suggest that some recipients feel that only the renal function and transplant progress is monitored, not the rehabilitation of the 'whole person'. Therefore, holistic care is essential, addressing psychosocial needs with physical needs; such care may be most appropriately offered by a transplant nurse practitioner who can offer continuity of care as well as understanding and support.

The aim of ongoing care is to empower the recipient to achieve optimal individual rehabilitation. It is essential to help the recipient achieve a balance between monitoring health and gaining normality. One of the most important post-transplant psychosocial tasks that the recipient needs to accomplish is the gradual relinquishing of the sick role and the eventual return to nonpatient status. Medical and nursing staff can give a confusing message by referring to recipients as patients and demanding strict adherence to rigid health protocols, whilst at the same time insisting that transplantation offers a return to 'normality'.

Flexibility of care, understanding, and encouragement are required to enable recipients to take control of their lives and achieve the highest quality of life possible. Ongoing health monitoring will continue and problems may occur, but advice and support should be available throughout the complete transplant experience.

BOX 10.14

Recipient pre-discharge knowledge

- understand the action, dosage, and side effects of medication and the need for adherence.
- awareness of how and where to obtain repeat prescription for all medications.
- recognise the signs of potential complications such as rejection and infection and ensure awareness of how and when to alert transplant personnel in the light of any of these changes.
- have telephone numbers of the transplant centre and know how to contact staff.
- ensure aware of arrangements for follow-up and the importance of regular attendance.

Ongoing care: information and support for transplant recipients

- peritoneal dialysis catheter: if transplant function is satisfactory, the peritoneal dialysis catheter is removed at six weeks to three months after transplant, although there is evidence that removal at time of transplant is advantageous (Warren et al. 2012). The ureteric stent is usually removed endoscopically four to six weeks after transplant, although many transplant surgeons attach the stent to the urinary catheter at the time of surgery allowing the stent to be removed with the catheter. This practice may reduce the incidence of post-transplant urinary tract infection due to early removal of the stent and avoidance of the need for an invasive procedure.
- diet: follow a normal diet, but taking care with weight gain due to increased appetite and freedom from the renal diet. If cholesterol or lipid levels are raised, dietary restrictions may be necessary. (See Chapter 13.)
- vaccinations and travel: transplant recipients should not receive live vaccines. Therefore, it is important to consult the transplant centre before travel immunisations are given. Foreign travel is encouraged but recognition of possible infection sources is necessary so that suitable precautions may be taken.
- skin care: immunosuppression predisposes recipients to skin damage from trauma and sun and increases the risk of skin malignancies. Therefore, dermatological monitoring and advice should be given and recipients should use high factor sun block during sun exposure and report any skin lesions. Many centres refer their patients for a baseline dermatological assessment after transplantation.
- fertility: female patients should be aware of fertility issues and be given advice with regard to birth control measures. Condoms or the mini-pill are the most appropriate therapies but intrauterine devices can be useful. Recipients of both sexes should, ideally, wait at least one year before considering pregnancy. Advice should be available with regard to pregnancy risks in individual cases. Patients of both sexes must be told that they should inform the clinic if they have any plans for pregnancy, so that any medical issues or drug changes can be discussed. Recipients cannot breastfeed after delivery as the immunosuppression may transfer to the baby.
- employment: recipients may return to work as soon as they feel able as long as graft function and health are satisfactory and employment does not put either at risk. Help should be available for those recipients seeking employment.
- health education: smoking is discouraged due to the risk of enhanced cardiorespiratory and vascular complications. Exercise and activity are encouraged, although contact sports such as rugby or martial arts may put the graft at risk. Female patients should have regular cervical smears and breast examinations due to the increased risk of malignancy. Male patients should be monitored for potential malignancies and encouraged to perform testicular self-examination.
- psychological health: psychological support should be available to help with sexual problems, body image problems and marital problems.
- social needs: help and advice should be available for social needs such as benefits, housing, and return to work.

Pancreas-Kidney Transplantation

Pancreatic transplantation is of proven clinical benefit for patients with type-1 diabetes who are undergoing renal transplantation, and is usually carried out at the same time, as simultaneous pancreas-kidney transplant (SPK). The procedure has

an increased mortality and morbidity risk due to the complexity of the surgery but for those patients suitable to undergo the procedure the long-term benefits often outweigh these risks.

Barlow et al. (2017) reported that recipients of both pancreas and kidney transplants SPK from 2001–2014 ($n = 1739$) which resulted in a functioning pancreas graft, had significantly better kidney graft and patient survival than those with just a kidney graft ($n = 385$) or those with a failed pancreas graft. However, the authors found that kidney-pancreas grafts for recipients with Type-1 diabetes do not confer an overall survival advantage compared with kidney-only transplants.

SPK transplantation can not only restore renal function and allow freedom from dialysis but enables discontinuation of insulin and retardation of the complications of diabetes. Immunosuppression for kidney-pancreas transplantation is similar to that for kidney alone.

Survival rates post SPK transplant in the UK are:

- patient survival at 1 year – 97% and at 5 years – 89%
- graft survival at 1 year – 88% and at 5 years – 78%

Figure 10.10 shows pancreatic transplant activity in the UK, with the number of patients registered on the SPK waiting list at 224 on the 1st March 2017.

The pancreas is a fragile gland and is easily damaged by trauma, poor perfusion, or duct obstruction. Surgical placement of the pancreas is determined by the need to allow drainage of the pancreatic enzymes. Drainage may be either into the bladder, with vascular connections to the external iliac artery and vein, or into the duodenum. Enteric drainage can avoid the problems associated with bladder drainage such as dysuria, haematuria, metabolic acidosis. Patients with a neurogenic

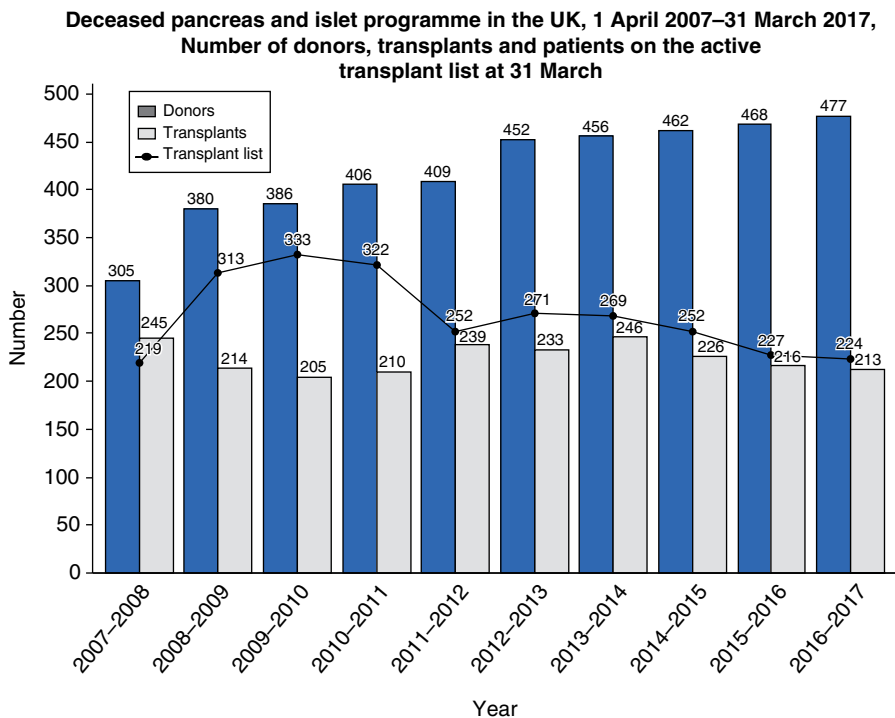


Figure 10.10 Deceased pancreas and islet programme in the United Kingdom, 1 April 2007–31 March 2017. Source: from: *Transplant Activity in the UK 2016–2017*. NHS Blood and Transplant.

bladder can develop ‘reflux pancreatitis’ from inadequate bladder emptying. In the post-transplant period, urinary tract infections are common and pancreatic enzyme activation can lead to ‘chemical’ cystitis or urethritis in those with bladder drainage. Patients may subsequently develop urethral stricture or disruption, haematuria, or perforation of the bladder or duodenum. Urinary drainage, however, allows monitoring of amylase excretion in the urine, which may offer the ability to detect pancreas rejection early. Transplantation of a pancreas and a kidney from the same donor allows manifestations of kidney allograft rejection to guide treatment as kidney graft rejection is believed to precede or parallel pancreas rejection. Surgical problems related to exocrine pancreatic drainage and allograft pancreatitis are usually due to leakage or fistula formation leading to fluid collections, pseudocysts, or abscesses surrounding the pancreatic graft. Due to the loss of pancreatic secretions rich in sodium and bicarbonate into the urinary tract, pancreas transplant recipients are susceptible to metabolic acidosis and dehydration. All recipients must increase fluid and salt intake, but may require additional oral bicarbonate supplementation (Hakim 2013).

Causes of pancreas graft loss include vascular thrombosis, pancreatitis, infection, and rejection. Vascular thrombosis may occur, in part, because of the low circulatory flow through the pancreas but can also accompany pancreatitis or rejection. Hyperamylasaemia is common after transplantation and may be either asymptomatic or indicative of symptomatic pancreatitis.

Patients with type-2 diabetes have relative contraindications for pancreatic transplant – they are usually older by the time end-organ damage develops, and may have significant vasculopathy. Despite this there is some evidence that outcomes of SPK transplantation are superior to kidney transplantation alone in this group of patients (Margreiter et al. 2013). The authors of this study however did report increased levels of vascular disease in this recipient group and found the most common cause of graft loss was death of the recipient. This evidence suggests that SPK transplantation may be beneficial in a carefully selected group of patients with type-2 diabetes.

Conclusion

A successful renal transplant can provide the best quality of life for those with ESKD. This chapter has discussed the ever-evolving clinical care and management for people who have donated and also received kidney transplants. Renal nurses are advised to keep abreast of newly published evidence-based guidelines in order to provide the best and safest care they can.

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CHAPTER 11

Nondialytic Options and the Role of Palliative Care

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Learning Outcomes

- to describe the palliative care needs of patients with end-stage kidney disease (ESKD) who follow the nondialytic (conservative management) pathway or who withdraw from dialysis.
- to understand the range of symptoms patients with advanced kidney disease experience, and how to assess and address them.
- to understand which patients require consideration of their end-of-life care needs.
- to review the role of the renal nurse when providing palliative and end-of-life care.

Introduction

This chapter considers the needs of patients with ESKD, their partners, carers, and families. This is a sensitive time, when their health may be declining, and (for some) when the end of their life may be approaching. Both kidney and palliative care specialists (Grubbs et al. 2017) continue to identify the significant and growing need for palliative care within nephrology. The focus of the chapter is on those who choose not to dialyse and follow a conservative pathway, but the care of the smaller number of those who withdraw from dialysis is also discussed. Both groups of patients present specific challenges to the nurses caring for them. Renal nurses may also be asked to help patients and families as they consider the decision for or against dialysis. This is a challenging decision, particularly for those who have multiple comorbid conditions where the benefits of dialysis are less clear.

Numbers of Patients

Chronic kidney disease (CKD) is a disease that is found across the age spectrum but is more commonly seen in older people. The prevalence of Stage 1–5 CKD in the UK population is estimated to be 13% (Evans and Taal 2015). While not all of these patients will progress to end-stage disease, the numbers requiring renal replacement therapy (RRT) have been increasing steadily in recent years, as the population ages. Over the last 40 years there have also been many changes which have increased our understanding and improved life expectancy for people with ESKD. Medical and technological advances have led to increased availability of treatment for renal problems and an ability to treat older people who have other illnesses. The Renal Registry report for 2015 suggests that the number of people on RRT is continuing to rise, with an annual growth rate of 4.3%, and that older patients treated by haemodialysis make up a disproportionate amount of the numbers accepted for RRT (Byrne et al. 2017). In 2015 approximately 120 people per million population (pmp) were accepted for renal replacement, and in 2015 there were over 61 256 people receiving RRT in the United Kingdom.

The need for RRT is also influenced by ageing of ethnic minority populations. These groups have a higher prevalence of renal problems due to higher rates of diabetes mellitus and hypertension. Between 2011 and 2036 the prevalence of CKD stages 3–5 is expected to increase by 8.3% and will be particularly noticeable within the black and minority ethnic groups and older people (Public Health England 2014).

The Importance of Nondialytic (Conservative) Care

The median age of patients starting RRT is 66.4 years, and 16% are over 75 years (Byrne et al. 2017). Worldwide, the use of RRT is expected to double by 2030 (Thaminda et al. 2015). With increased age there is usually increased comorbidity; 67% of those over 65 have one or more comorbidities when commencing dialysis. For those over 85 years, about 30% die within one year of commencing dialysis (Byrne et al. 2017). There are many factors that can influence the treatment choices for these older patients, especially for those over 75 years. Dialysis has been shown to have very limited survival advantage in those with high levels of comorbidity (Chandna et al. 2011; Murtagh et al. 2007a) and this, combined with the high burden of treatment with dialysis (Jones et al. 2018), has led to the development of conservative management pathways (where dialysis is not commenced).

Unfortunately, the UK Renal Registry does not yet collect data on those managed without dialysis, so it is hard to know how many patients with ESKD opt to follow a nondialytic (conservative) pathway. Local data indicate it may be about 15–20% of those in managed nephrology care at Stage 5 CKD. Morton et al. (2016) showed that approximately 14% of patients assessed were likely to follow a palliative (conservative) pathway. These patients were, on average, older than the patients commencing RRT (median age of 80 versus 64 years old) and more likely to have lost a partner. In this study those who opted for RRT were less likely to receive specialist palliative care. They were also more likely to die in hospital rather than at home or in a hospice.

The Palliative Approach

Palliative care is a relatively new discipline, emerging in the 1960s, through the inspiration of Dame Cicely Saunders and others. The World Health Organisation definition of palliative care (World Health Organisation 2012) is widely accepted (see Box 11.1).

BOX 11.1**Definition of palliative care (World Health Organisation 2012)**

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, psychosocial and spiritual.

Palliative care:

- provides relief from pain and other distressing symptoms;
- affirms life and regards dying as a normal process;
- intends neither to hasten or 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 or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications.

Source: WHO (2012).

It is important to recognise that this definition is not disease orientated but patient focused, and also reflects changes made to move away from a disease-specific definition, such as cancer, to an understanding that palliative care should be available to all with a life-threatening illness. It also encompasses early introduction of a palliative approach, while enabling a person to continue with life-prolonging therapies, such as dialysis.

Palliative care aims for a holistic approach to care of patients and families, in situations where the disease is advanced, progressive, and incurable. It encompasses physical, psychological, practical, and spiritual aspects of care, and includes consideration of the needs of families and informal carers. For those with ESKD, it is not yet clear what model of palliative care provision should be adopted; whether palliative care should be provided predominantly by renal professionals, by specialist palliative care professionals, or by primary care professionals, or (most likely) by some combination of these three groups. Much will depend on the configuration and availability of local services. Palliative care has been, and still is, at different stages of development throughout the world. It is a dynamic concept that all practitioners should integrate into their daily practice; a patient-centred approach to care in advanced disease with a focus on quality of life and management of symptoms (Etkind et al. 2017). It may be inappropriate to move a person to a different group of healthcare professionals just because of their stage of life. One of the big influences on and challenges to practice therefore is the integration of the extensive knowledge and experience in palliative care from the specialist palliative care field into nephrology practice, for the benefit of patients and families.

Recent Government and Other Initiatives

Recent political and national developments in the United Kingdom have given considerable impetus to development of clinical services for those approaching the end of life. In the United Kingdom, nephrology was one of the first specialities to adapt

the national End-of-life Care Strategy (Department of Health 2011) and make specific recommendations for the ESKD population. A framework for implementing end-of-life care in advanced kidney disease was produced (NHS Kidney Care 2015). This has had an important impact within renal units, to ensure that improvements in palliative and end-of-life care for those with advanced kidney disease are achieved.

Internationally 'The KDIGO Controversies Conference on Supportive Care in CKD' has defined a useful guide to clinical and research activities aimed at improving outcomes in people living with advanced kidney disease. The work includes development of globally relevant guidelines (Davison et al. 2015). In addition, Davison et al (2019) have written a recent paper detailing recommendations for the care of patients receiving conservative kidney management.

It is important to distinguish between palliative and end-of-life care. Meghani (2004) cautions against using the terms synonymously; end-of-life care incorporates palliative care, but not all palliative care will be related to end-of-life care. Palliative care interventions, which focus on a holistic approach, may be both appropriate and very helpful throughout the renal illness from diagnosis and can often markedly improve quality of life in a sustained way. If symptom burden is high and quality of life is poor, despite disease-based interventions, then this is the time to consider palliative care, whatever the expected prognosis.

Communication, Decision-Making, and Planning

Patient communication

As disease progresses and the end of life approaches, skilled communication becomes increasingly important in the delivery of effective patient care. Communication between patient and nurse is important; patients want to know what to expect as their illness advances, and they value professionals who can talk openly about death and dying (Davison and Simpson, 2006; Mandel et al. 2017). Contrary to the beliefs of many professionals, openness does not remove hope but helps to focus it in a more realistic way.

Information needs to be delivered at a pace that each individual patient can manage. It is important to ensure there is the time and conditions for difficult questions to be asked and answered, since many factors will prevent such questions being explored. Communication between the patient and their family also becomes increasingly important to patients as death approaches, and nurses have a key role in facilitating this. Sometimes, understandably, family members adopt a protective attitude towards each other, shielding each other from bad news, but this is not always helpful, particularly if the patient is seeking openness and honesty (Noble et al. 2014).

Information also needs to be carefully matched to each patient's preference for information and for involvement in decisions. In general, doctors and nurses tend not to raise their concerns about a patient's declining health and worsening prognosis unless a patient asks about this, and patients often wait for professionals to raise such matters. This can lead to a collusion of silence, where both continue to focus on other (often disease-related) issues, and do not address underlying concerns about declining health.

At the same time, the patient's choices about end-of-life care need to be explored. If open communication does not occur, choices are likely to be more limited. An example of this is the preference to die at home if possible; this cannot be facilitated if initial communication and discussions about the implications of the illness have not taken place. Box 11.2 provides some suggestions of useful 'opening questions' that nurses can use to help enable a patient or their family to raise their concerns readily.

BOX 11.2**Suggested questions to explore patient concerns**

How do you think things are going with your health overall?
 Have you any worries about your health?
 What concerns you most at present?
 Have you any worries about the future?
 Do you want to know more about your illness and what to expect?
 What is most important for you to achieve?
 What are your most important hopes?
 What are your biggest fears?
 What would most improve your quality of life at present?
 What is most important to you: quality or length of life?
 How is your family handling your illness?
 Have you given any thoughts to what treatments you might or might not want in the future?

For patients with ESKD, some specific considerations are important. Firstly, some patients will be living with their renal condition over a long period of time. It can be more difficult, then, for both patient and professional to perceive the change from living with a long-term condition to a decline in health towards death. If health professionals do not see this change, they may well deny the patient and their family the opportunities they need to understand their illness and address and plan for their remaining time. Secondly, the pattern of decline may be more uncertain than for other terminal conditions such as cancer. The limited available evidence suggests that prognosis in conservatively managed patients varies considerably, depending partly on the underlying cause of the renal failure and on which other comorbid conditions coexist (Chandna et al. 2011; Etkind et al. 2017). Dealing with this uncertainty is hard for both patient and professional and it needs to be honestly acknowledged in any communication. Thirdly, renal professionals rightly focus on active disease management. End-of-life care requires a change of focus from a primarily disease-centred approach to a more patient-centred approach. Disease management takes a much lower priority, particularly as the end of life approaches. Controlling symptoms, attending to psychosocial and spiritual needs, and anticipating future care needs all become as important, or more important, than renal expertise. Nurses may feel uncertain about their skills in this area, particularly if they work with patients at the end of life infrequently.

Family communication

Effective end-of-life care cannot be delivered without good family communication. However, the ethical and legal responsibilities of the nurse are predominantly to the patient, so it is important to seek patient agreement before any communication with the family, particularly if that communication takes place away from the patient. In the final days of life, increasing uraemia may mean that patients are often confused, and increasingly lack the ability to make decisions for themselves. It is important, therefore, to ensure from the beginning that relevant family members are involved in any management decisions (if the patient wishes) and that they are aware of the patient's end-of-life preferences, before the patient becomes less well. O'Hare et al. (2017a) highlights that failing to incorporate family and friends into patient care may not only cause distress, but can result in missed opportunities to improve advance care planning.

Communication within the team

A number of key decisions will be made with patients as they approach the end of their life. These include decisions around withholding or withdrawing dialysis, decisions around preferred place of care and death, and cardiopulmonary resuscitation (CPR) decisions, amongst others. Each of these should be communicated to the whole renal team. Patients will often see different professionals at each clinic visit or hospital admission, and it is important that patient and family are given clear and consistent messages.

A wide variety of nonrenal healthcare professionals may also be involved in end-of-life care, ranging from the general practitioner and district nurses to specialist palliative-care professionals (who may be community, hospital, or hospice based). Time and energy therefore needs to be devoted to communicating any decisions made to all members of the team, including those providing care out of hours, and those who may be called in a crisis, both at home or in hospital.

Dialysis decision-making

As disease advances, decisions may be made either to withdraw dialysis, or to follow a conservative pathway. This raises complex and challenging issues (Noble et al. 2017). These issues have been reviewed and guidelines have been developed in the United States to inform dialysis decision-making (Renal Physicians Association 2010). The guidelines are built on shared decision-making, recognising that patients are individuals and have their own history, perspectives, and preferences.

People with kidney disease are known to have widely differing preferences for involvement in decisions, but generally receive less information than they want and have less involvement in decisions than they prefer (Hussain et al. 2015). Some nephrologists feel that most, if not all, patients requiring RRT should receive dialysis, but there is growing recognition that, for some patients, dialysis may not greatly increase survival while adding a considerable treatment burden. For these patients, conservative management (care without dialysis, but with management to minimise disease progression, and full supportive and palliative care) may be a better option, although any final decision will depend on patient preferences as well as professional advice. Work by Chandna et al. (2011) and others has shown that patients with poor functional status and high levels of comorbidity do not do well on dialysis. Foote et al. (2016) also describe poor survival in older patients on dialysis, but recognise that survival alone is an insufficient measure of outcome – they also recommended future research should explore hospitalisations, quality of life and symptom burden.

Following a conservative management pathway sometimes demands especially difficult decision-making, since it requires weighing up patient preferences, estimated survival on or off dialysis, anticipated quality of life on or off dialysis, and the treatment burden with dialysis. Estimating survival and quality of life is difficult for the individual patient. These factors including symptom burden, survival, and quality of life continue to be studied in patients who are managed conservatively (O'Hare et al. 2017b).

Advance planning

Effective and appropriate care can only be delivered by planning ahead and anticipating future care needs. It is therefore important to explore sensitively with patients (and their family, if desired) what their wishes are for future care, or in the event of a sudden deterioration or crisis. Relatively few patients choose to write a

BOX 11.3**The principles underlying the UK Mental Capacity Act 2005**

- a person must be assumed to have capacity unless it is established that he/she lacks capacity.
- a person is not to be treated as unable to make a decision unless all practicable steps to help him/her to do so have been taken without success.
- a person is not to be treated as unable to make a decision merely because he/she makes an unwise decision.
- an act done, or decision made, under this Act for or on behalf of a person who lacks capacity must be done, or made, in his/her best interests.
- before the act is done, or the decision is made, regard must be had to whether the purpose for which it is needed can be as effectively achieved in a way that is less restrictive of the person's rights and freedom of action.

formal advance directive, but all should be offered the chance to discuss preferences for future care and management. These discussions should be carefully documented and revisited regularly (since preferences may change).

Advance directives are written documents which specify a patient's preferences, in anticipation of loss of the capacity to make his or her own decisions, when they are less well. In the United Kingdom, the Mental Capacity Act (which became law in 2005) clarifies the legal status of such documents, and also makes provision for a person to be named to represent the patient's preferences in their place (known as Lasting Power of Attorney). The Mental Capacity Act is based on five principles designed to protect people who lack capacity to make particular decisions, but also to maximise their ability to make decisions, or to participate in decision-making, as far as they are able to do so. The principles are outlined in Box 11.3.

There are other ways to facilitate planning, including use of tools such as the Preferred Place of Care document (Pemberton et al. 2003). This was developed to promote discussion around patients' preferred place of care and death. It provides an accessible patient-held record which records their preferred wishes. Anticipating and planning for acute admissions is also particularly important for some patients, especially those with cardiac disease, who may be more liable to develop fluid overload or acute pulmonary oedema.

Whether specific documents or advance directives are used or not, every patient should, as their disease progresses, have the chance to discuss their future care, concerns, hopes, and preferences. The responsibility lies with the professional to ensure that these opportunities arise. These issues should be addressed early and systematically, remembering that both patients and professionals find it hard to introduce and address such matters (Luckett et al. 2017).

Careful consideration should be given to resuscitation status, since this may be an issue during hospital admission. CPR in this group of patients may be inappropriate, depending on prognosis and comorbidity. It is important to recognise that there is no ethical obligation to discuss CPR with patients who are terminally ill, if this treatment is judged to be futile and therefore would not be provided (NHS Kidney Care 2015).

Care of Patients Managed Without Dialysis

People who are being managed conservatively need much more than just symptom management (see Box 11.4). Achieving these goals requires a shift from a predominantly disease-focused approach towards more patient-centred management

BOX 11.4**The needs of patients managed conservatively**

- skilled communication to facilitate the 'not for dialysis' decision, to explain disease progression and prognosis, and to facilitate future management decisions, in accordance with the patient's information preferences.
- regular review(s) of the 'not-for-dialysis' decision.
- continuing disease management to maximise and maintain residual renal function.
- continuing disease management to minimise symptoms.
- regular and detailed assessment of symptoms.
- proactive intervention to control symptoms.
- advance planning as the illness progresses, to:
 - avoid inappropriate acute admissions;
 - avoid inappropriate reversal of 'not-for-dialysis' decision;
 - enable place of care preferences to be met if possible.
- ongoing psychological and social care.
- involvement and support of family as appropriate.
- spiritual care, especially as the end of life approaches.
- detailed and expert end-of-life care in the final days or weeks.

Source: Murtagh et al. (2016).

(the disease itself, while it must not be neglected, is less important than overall quality of life, and patients should be encouraged to decide what treatment they can or cannot tolerate as the illness progresses). Careful judgements need to be made as to when to discontinue onerous treatments; these will often depend on perceived burden and patient preference.

Symptoms Towards the End of Life

Common physical symptoms that patients with CKD report are lack of energy or fatigue, itching (pruritus), pain, sleep disturbance, and restless legs (see Box 11.5).

A number of studies report fatigue as extremely common (42–89%), (Artom et al. 2014). Pruritus has been studied extensively; some of the larger studies suggest that 40–70% of patients may be troubled by this symptom. Pain has been infrequently studied but the few studies of it suggest more than 50% of patients have pain (Davison et al. 2014). Sleep disturbance and the related symptom of restless legs have been studied more often, and appear to affect 30–52% of patients. Anxiety and depression may also be experienced by some patients. Reports of how common these problems are depend on how they are defined and sought. Screening questionnaires are positive in approximately 40% of patients, but fewer patients (23%) have depression diagnosed at formal psychiatric interview (Palmer et al. 2013). A variety of other less common symptoms have been described, including anorexia, constipation, cough, dyspnoea, nausea, and vomiting. Most evidence comes from patients receiving dialysis; some symptoms (such as muscle cramps, pruritus, and restless legs) may be dialysis related, and will occur less often in conservatively managed patients, while other symptoms are disease related and will worsen with declining renal function.

As the illness progresses, symptoms may worsen. Symptoms in the last days of life, in both people who are being conservatively managed and people withdrawing from dialysis, may follow different patterns but there have been very few studies of

BOX 11.5**Symptoms commonly experienced in stage 5 CKD**

- fatigue or lack of energy.
- itching (pruritus).
- pain.
- sleep disturbance.
- restless legs.
- anxiety and/or depression.
- anorexia.
- constipation.
- cough and dyspnoea.
- nausea and vomiting.

symptoms in either group at the end of life. Cohen et al. (2000) have carried out one of the few studies on dialysis withdrawal, and they describe pain, agitation, myoclonus (involuntary jerking of muscles), fatigue, and dyspnoea each occurring in at least one in four patients in the last days of life.

Symptom assessment

The most important step is to identify symptoms when they are present. This is best done by asking the patient about potential or extant symptoms, in a systematic way; with an organised and sequential enquiry focusing on distinct areas such as cardiovascular, respiratory, and musculoskeletal systems. Symptom questionnaires such as the Patient Outcome Scale symptom module (renal version) may be helpful and are freely available at pos-pal.org (accessed 1 March 2019). Symptoms may go unrecognised in ESKD partly because the focus may have been on the disease itself and not the symptoms per se. Symptoms may also be related to other coexistent illnesses (comorbidity), not to the renal disease, which may render systematic enquiry challenging. Many, if not most, of such patients will have several comorbid conditions and management of symptoms may fall to a variety of health professionals. However, these patients will have an eGFR result of $<15 \text{ ml min}^{-1}$, and health professionals inexperienced in renal care may have insufficient experience to confidently and effectively undertake relevant clinical management. The key to effective, high-quality symptom control is proactive, detailed, and thorough symptom assessment at regular intervals, to pre-empt patients reporting symptoms, or for new symptoms to emerge.

Careful attention should be given to the underlying cause of each symptom. As an example, pain may be more related to comorbid conditions than the renal disease itself; with ischaemic pain from peripheral vascular disease, neuropathic pain from polyneuropathy (often related to diabetes mellitus), bony pain from osteoporosis, or musculoskeletal pain from a variety of causes, all typical common examples. Less often, there may be specific discomfort related to the primary renal disease, such as: bone pain from renal osteodystrophy (the dystrophic growth of bone caused by disturbances in the metabolism of calcium and phosphorus), cyst pain in polycystic kidney disease, or the infrequent but acute pain of calciphylaxis, (the accumulation of calcium in small blood vessels within the skin, resulting in painful ulceration).

Symptom management

Management of symptoms in CKD is further complicated by the altered pharmacology of drug metabolism and excretion in advanced renal impairment, with a

potentially high risk of toxicity and side effects. The symptomatic presentation of such toxicity or adverse reactions may also be unclear because of comorbid conditions. A brief outline of the most frequent or challenging symptoms is given here, but more detail can be found elsewhere, such as in Chambers et al. (2010).

Constipation

This is common, and usually multifactorial. Fluid reductions, poor mobility, and drug side effects are common contributors. A stool softener such as lactulose may be useful, as may faecal bulking agents such as isphagula husk. These agents may need to be combined with a stimulant laxative such as senna or bisacodyl (Bouchoucha et al. 2004).

Fatigue or lack of energy

This is one of the commonest problems and can prove challenging to manage clinically.

Interventions such as erythropoietin replacement and iron supplementation may be prescribed to maintain haemoglobin between 110 and 120 mg dl⁻¹ and may need to be continued even when prognosis is short, because of the symptomatic improvement they may provide. Nutritional advice and support under the guidance and input of a dietician should be carefully considered. Nonpharmaceutical measures can also be considered such as exercise and cognitive behavioural therapy (Artom et al. 2014).

Nausea and vomiting

It is important to try to identify the cause of such upset if effective management is to be achieved; the clinical history may be invaluable in this regard. Gastroparesis (reduced gastric motility, usually presenting with early fullness, vomiting after eating, and relief of nausea with vomiting) may respond to metoclopramide, which increases gastrointestinal transit time, at the risk of inducing uncomfortable spasm. Nausea as a direct result of high levels of toxic metabolites in the blood ('uraemic nausea') is typically more constant and less closely related to eating; haloperidol (powerful centrally acting sedative antipsychotic agent) may prove effective. This is very effective but doses may be limited by sedation. Other centrally acting antiemetic agents such as ondansetron may also be used, especially if nausea is drug-related. Persistent nausea or vomiting near the very end of life can be treated with levomepromazine.

Pain

Pain management needs to be tailored, both to the individual patient and to the specific cause of the pain. If the cause cannot be removed or reduced, then pain medication should be given according to the World Health Organisation 'analgesic ladder' (www.who.int/cancer/palliative/painladder/en; accessed 1 March 2019). This consists of three steps:

- Step 1: a non-opioid, usually paracetamol; either orally or parenterally.
- Step 2: opioids for mild to moderate pain.
- Step 3: opioids for moderate to severe pain.

Initial analgesia should start with the lowest appropriate step. It is important to understand that if the full dose is insufficient for relief, then using another medication from the same 'step' does not usually provide any better relief and it may be more effective to move up to the next step. Tramadol is an effective Step 2 opioid, although this drug should be used at a reduced dose and at an increased dose interval in Stage

5 CKD (Broadbent et al. 2003). Use of Step 3 opioids in Stage 5 CKD is highly problematic: morphine and diamorphine in particular tend to accumulate and readily cause toxicity. Fentanyl is a safer choice, although available formulations may prove restrictive (Murtagh et al. 2007b).

According to the cause of the pain, additional (adjuvant) medication may need to be used alongside opioids. This is particularly true of neuropathic pain, which may respond well to centrally acting agents such as gabapentin; being mindful of toxicity in patients with impaired renal excretory capacity.

Pruritus

Dry skin is very commonly associated with pruritus, and should be actively managed with liberal regular emollients (such as aqueous cream). High serum levels of calcium, phosphate, magnesium, and parathyroid hormone have all been associated with pruritus to a greater or lesser extent (Lugon 2005), and should be sought and actively managed, if present. Oral antihistamines are often used, although there is little evidence for benefit, whilst topical antihistamines such as crotamiton may be equally, or additionally, effective, especially when sparingly combined with a topical steroid such as 1% hydrocortisone. If pruritus disturbs sleep, a sedative antihistamine (such as chlorpheniramine) given at night may be useful. Other treatment options include naltrexone (not with opioids), capsaicin cream (especially if pruritus is localised) or thalidomide (caution with handling).

Restless legs and sleep disturbance

These two symptoms frequently coexist. Simple measures, such as avoiding caffeine, avoiding alcohol in the evenings, and reducing daytime sleep, are important in facilitating sleep. Hypnotics, such as zolpidem, zopiclone, or temazepam can be used, although doses should be reduced in Stage 5 CKD without dialysis, and risk of dependence should be considered carefully if prognosis is months or more.

Restless legs should be managed specifically with reduction in caffeine (coffee), theophylline (tea), and any aggravating medications (such as tricyclic antidepressant drugs). Active treatment of anaemia and low ferritin (which are both associated with restless legs) should be considered. Major tranquilisers such as clonazepam or dopaminergic agents may be prescribed, although these may be associated with re-emergent symptoms as tolerance develops, or with rebound symptoms after a dose reduction or withdrawal. For these reasons, the lowest possible doses should be used, and intermittent rather than continuous use may be helpful.

Psychological and Social Issues

There are numerous psychological and social implications of living and dying with CKD, many of which are similar to other life-threatening or chronic diseases. The patient, together with their carer or family, faces various potential changes and these can be related to factors such as role change, appearance, sexuality, financial challenges, and becoming more physically dependent on others. It is important that timely discussions occur, to ensure that the patient and their family are prepared for and supported through potential changes as they are made aware of services and benefits that may be of benefit.

Psychological aspects of care are addressed more fully elsewhere (Chambers et al. 2010), but failure to address psychosocial issues can lead to 'technical' treatment without healing. It is also important to provide support to the family caregivers; by doing this, the patient is additionally supported. The involvement of the multidisciplinary

team is key to effective management in this important arena. The timely intervention of an occupational therapist can help promote independence and safety, which provides timely support for both patients and carers. Mindfulness techniques can help patients and carers reconnect with their bodies and experience life more fully. They encourage living in the present as opposed to dwelling on the past or worrying about the future and are endorsed by Kidney Care UK, the UK's support charity for people affected by kidney disease.

Spiritual Care

Palliative care considers the whole person, their family, and carers. It is important to consider all aspects and dimensions of each patient's existence, since psychological, social, and spiritual issues are important. For example, as Davison (2005) identifies, unless the psychological, social, and spiritual components of pain are addressed, pain may not be relieved adequately.

The term 'spiritual' is ill defined and can mean very different things to different people and cultures. To add to the confusion, the terms 'spiritual' and 'religious' are frequently used interchangeably, which is semantically incorrect and may introduce confusion to an important area of care. Spirituality is to do with meaning, not necessarily through formal religious beliefs, while religion is an expression of spiritual beliefs through a more formal framework (Speck et al. 2004). Spiritual care should be integrated into practice to ensure that the whole person is represented and considered within the contexts of both their existence and their care. Illness, and the end of life in particular, involves mind and spirit, not just what happens to the body, and it is therefore important that care of all such domains are included in overall care.

Spirituality is often neglected until the end of life is perceived as being very near, leaving little time for spiritual care or resolution of important issues. The closeness of death, and the prospect of facing mortality, can have significant effects on both patient and family, as well as on healthcare professionals. Sometimes people look for meaning in what is happening, or ask the question 'why me?' There may be issues of guilt, or some families may be facing multiple losses or another recent bereavement. Knowledge and discussion of spiritual needs should help address these issues as death approaches, although attentive, active listening is frequently the most important skill in spiritual care.

The provision of access to a bereavement service is also important. Some renal units offer an annual memorial service as part of their bereavement care. Families of patients who have died in the previous year are invited to the service, as well as renal professionals. It is an opportunity for all to acknowledge the loss, to continue to provide support, and often helps families progress in their bereavement journey.

Conclusion

The needs of patients with kidney disease (and their families) as they become less well and as they approach the end of life are complex. They need skilled and open communication from an early stage, advance planning, high-quality symptom control, and good psychological and spiritual care. Their families may also need bereavement care. Effective delivery of such care also requires communication with, and coordination of, the network of professionals who may be involved, including primary care, renal, and specialist palliative care professionals, as well as families and informal carers.

It is imperative that nephrology nurses develop generic palliative care skills to ensure that appropriate care, including good symptom relief, is given to patients and their families at all stages of their disease trajectory. In addition, partnerships with specialist palliative care providers need to be nurtured to ensure that their timely intervention can be of full benefit, and that there is maximum sharing of expertise and experience. The overall aim is to enable the last months and days of each patient's life to be lived as fully as possible, and for them to achieve a good death. It is a challenging area for nephrology nursing practice, but one that cannot and must not be ignored.

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CHAPTER 12

Renal Care in Infancy, Childhood, and Early Adulthood

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Learning Outcomes

- to gain an understanding of the physiological differences between children and adults.
- to develop an appreciation of the psychosocial impact of chronic kidney disease (CKD) and renal replacement therapies on children and their families.
- to identify the key differences in the management of CKD, dialysis, transplantation, and acute renal failure in children.
- to be able to identify important issues around transition, and the transfer of young people to adult services.

Introduction

The aim of this chapter is to address the unique needs of infants, children, and young adults who have kidney damage. The challenge is to meet the needs of the patients and their parents within each of these age groups.

Infants and young children are dependent upon their parent/carer for their global needs, and as they mature, they are increasingly able to become self-caring. The NHS England service specification for paediatric nephrology services (NHS Commissioning Board [now known as NHS England] 2013) recognises that children and young people with renal disease require care from full multidisciplinary teams to ensure support for their physical, psychosocial, and emotional needs. The approach taken with this client group needs to be flexible, and the multiprofessional team needs to be diverse to support this. Specialist units will commonly comprise not only medical staff and specialist nurses but also specialist dietitians, social workers, hospital play specialists, hospital school teachers, psychologists, pharmacists, and youth workers.

Kidney disease in childhood is rare and in the United Kingdom care is delivered in only 13 tertiary centres. Wherever possible, efforts are made to treat children as close to home as possible and a network model of care is encouraged (BAPN 2008).

Key concerns are the psychosocial impact of a condition, which will often be long-term, on both the child and their family (Department of Health 2006a). A recent study has reported poorer overall quality of life, and poorer physical, school, emotional, and social functioning in children with mild-to-moderate CKD compared with healthy children (Gerson et al. 2010). The prevention of complications that may have an impact on the health of the child throughout their future, on transfer to adult services, is also important.

The following sections will highlight both the physiological and psychosocial differences between children and adults, and how renal replacement therapies need to be adapted accordingly.

Physiology in Childhood – Impact on Renal Care

There are several key areas where physiology in childhood differs from adulthood.

Growth

Children should be continually growing, with accelerated growth spurts during infancy and adolescence.

Normal birth weight is 3.3–3.5 kg and during infancy growth varies between 6–240 g a week, with an expected 25 cm length increase in the first year. This gradually declines to 2 kg per year with 5 cm height increase until the pubertal growth spurt (Shaw and McCarthy 2015).

Several factors have an influence in growth including diet, genetic inheritance, and growth hormone production, which are discussed further below.

Fluid balance

Seventy-five percent of the body is comprised of water in newborn infants, decreasing to 45% in young adults. There is also a greater proportion of extracellular water in infants; therefore water is more easily lost, particularly during pyrexia (Mondozzi et al. 2015).

Renal anatomy

Neonates' kidneys are affected by the removal of blood flow from the placenta, leading to a reduction in glomerular filtration rate (GFR) and renal blood flow.

At birth the kidneys have the correct number of nephrons, but they are immature. Newborns have small underdeveloped glomeruli, short loops of Henle, and an underdeveloped renal cortex.

There is a reduced ability to concentrate urine, and also to secrete hydrogen ions. This becomes particularly important if the infant enters into a state of metabolic acidosis.

GFR does not reach close to adult values until a child reaches one to two years of age (Ring and Camille 2015).

Careful consideration is needed when monitoring children and that age-appropriate parameters are used. Age-appropriate reference ranges should be consulted for biochemistry results throughout childhood (see Table 12.1).

Blood pressure increases with size/age. Height centile charts should be used to monitor blood pressure in children with short stature for accuracy. This will include

Table 12.1 Biochemistry reference ranges for children.

Sodium (mmol l ⁻¹)		132–142
Potassium (mmol l ⁻¹)	<1 month	3.0–6.6
	>1 month	3.0–5.6
Bicarbonate (mmol l ⁻¹)		22–32
Urea (mmol l ⁻¹)		2.5–6.5
Albumin (g l ⁻¹)		34–45
Calcium (mmol l ⁻¹)	<1 year	2.4–2.8
	1–2 years	2.3–2.7
	3–16 years	2.2–2.6
Phosphate (mmol l ⁻¹)	<4 weeks	1.2–3.1
	5 weeks–6 months	1.5–2.4
	6 months–1 year	1.5–2.1
	1–3 years	1.2–2.0
	3–6 years	1.0–1.8
	6–15 years	1.0–1.7
	Adult	0.8–1.4
Creatinine (μmol l ⁻¹)	<5 years	<44
	5–6 years	<53
	6–7 years	<62
	7–8 years	<71
	8–9 years	<80

many children with renal disease (National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents 2005).

Chronic Kidney Disease

The common causes of CKD in children are different from those experienced in later life, as indicated in Table 12.2. In comparison with the numbers seen in the adult population, it is difficult to gain accurate figures. In 2014, data suggested that the incidence of established renal disease (ERD) was 60.4 pmarp (per million age-related population) and 9.4 pmp (per million population) as a whole (Byrne et al. 2017).

The presenting symptoms of CKD commonly seen in children are shown in Box 12.1.

Table 12.2 Common causes of ERD in children.

Tubulointerstitial disease 53.4%
Glomerular disease 16.9%
Familial/hereditary diseases 14.9%
Systemic diseases affecting the kidney 4.3%
Other 9.8%

Source: Byrne et al. (2017).

BOX 12.1**Presenting symptoms of CKD in children**

- failure to thrive or anorexia.
- nausea, vomiting and loss of appetite.
- lethargy.
- headaches and high blood pressure.
- reduced urine output or polyuria/polydipsia, possibly wetting.

Children can present at any age and at different stages of renal disease. It is important that investigations are undertaken to determine cause and therefore the interventions required. Dialysis may be necessary in some cases, however many children can be treated conservatively.

Some conditions are familial and therefore siblings may also need to be assessed, even if they are asymptomatic. In rare cases a parent and one or more children may be dialysis dependent, and a thorough plan of psychosocial support is a necessity in this situation.

Conservative management

Providing the biochemistry is stable, children can be maintained without dialysis for some time. This applies for children with both CKD and Acute Kidney Injury (AKI). Several interventions can be incorporated into conservative management. These interventions continue into the established phase of CKD, and may be temporarily used to support children in an acute phase of renal disease.

Diet (also see Chapter 13)

Poor appetite, gastrointestinal reflux, and vomiting are common problems seen in children and infants with CKD.

It is important that a paediatric renal dietitian is involved in the management of children with renal disorders (NICE 2013b). Dietary control can assist in delaying the need for dialysis and all of the medical and psychosocial problems associated with it. Adequate nutrition is also important for growth and neurological development.

Energy requirements should be based upon EAR (estimated average requirement) for chronological age, or height age if the child falls below the second percentile (Royle 2015).

Individualised dietary guidance is needed for each family, based on the child's biochemistry, stage of CKD, and renal replacement therapy used. Negotiation with food allowances is often needed with older children, to improve adherence to the nutritional plan. Clear education is needed for the child and their parents, to ensure understanding of the necessity of restricting many of the favourite childhood foods, such as chips and pizza. Sodium, potassium, and phosphate intakes often need to be altered. Patients with renal tubular disorders, such as Bartter's Syndrome, are at risk of electrolyte and fluid imbalances (Ring and Camille 2015). Supplements are often required. Protein intake may also need to be modified to balance growth requirements against potential uraemia.

High-energy food and drinks are encouraged, as it can be difficult to achieve EAR when on an altered diet.

It is common for younger children and infants in particular, to refuse to eat, and enteral feeding via the nasogastric or gastrostomy route is often required.

Gastrostomy feeding in particular has been shown to be a valuable tool in nutritional support. It has also been associated, with other factors, in improved growth of young children (Rees et al. 2011).

Socialisation with food is still important, with the end goal of transplantation in mind. Feeding problems can remain in a small number of children following a successful transplant and speech and language therapy can be required. Conversely, in older children advice is often needed to prevent excessive weight gain, particularly when taking corticosteroids as immunosuppression.

Fluid management

The approach to fluid management will be dependent upon whether the child concerned has a reduced urine output or is polyuric.

Patients who have a reduced urine output will usually be given a fluid allowance, and also be prescribed a diuretic regimen. The common guideline used is to add 400 ml m⁻² surface area/day to the average daily urine output, to allow for insensible losses (Royle 2015).

Some children are polyuric and great care needs to be taken to ensure that fluid intake is sufficient to prevent dehydration.

Along with dietary changes, it is the reduction in fluid allowance that older children often find the most difficult to adhere to. It is important to give advice on ways of managing fluid. Fluid overload is a contributor to hypertension in many patients, and therefore can impact in cardiovascular health.

Blood pressure

As with adults, hypertension is a complication that children with renal disease may experience. It is essential that accurate measurements are taken, to enable effective treatment of hypertension. Cardiovascular complications are a major cause of mortality and morbidity in adult patients. Slowing the progression of CKD, avoiding long-term dialysis, and, if possible, conducting pre-emptive transplantation may represent the best strategies to decrease the risk of premature cardiac disease (Mitsnefes 2012).

Prevention of early complications is therefore essential, with hypertension being one of the most modifiable. Hypertension has also been associated with acceleration of renal disease and there is evidence that intensified blood-pressure control, with target 24-hour blood-pressure levels in the low range of normal, confers a substantial benefit in terms of slowing kidney disease progression (ESCAPE trial group et al. 2009).

Blood pressure increases with age, and there are reference guidelines to assist in patient management. As children with renal insufficiency are often short in stature their height should be used as a reference, rather than chronological age. It is recommended that systolic blood pressure should be maintained below the 90th percentile for height and sex (Byrne et al. 2017). There are charts based upon gender, age, and height which should be used (Lurbe et al. 2016).

The British Hypertension Society has guidelines on blood pressure measurement, which include some guidance on children <http://www.bhsoc.org>. Blood pressure measurement in children can be difficult to obtain. There are a limited number of oscillometric devices that are validated for use in children. Abnormal readings should be confirmed manually, when used (Lurbe et al. 2016). Many paediatric renal units measure blood pressure manually. See Box 12.2 for a summary of blood pressure measurement guidelines.

Very small children can be uncooperative, and it is usually difficult to hear Korotkoff sounds in small children using a stethoscope. As a result, Doppler devices

BOX 12.2**Key principles in blood pressure measurement**

The bladder in the cuff should cover 80–100% of arm circumference.

Doppler devices are the recommended method in children under two years.

Inflate to 30 mmHg above the estimated systolic pressure.

Deflate the cuff at 2–3 mmHg s⁻¹.

Record the reading to the nearest 2 mmHg.

Blood pressure should be compared to centile charts for height, age and gender.

are recommended in children under two years of age. Single readings should not be used to direct management, because white coat hypertension can be particularly problematic in children. Ambulatory blood pressure monitoring is often used to assist in correct treatment of hypertension enabling monitoring away from the hospital environment (Flynn 2011).

Anaemia

Anaemia is also associated with an increased risk of cardiac morbidity and mortality, and also affects growth and development. Haemoglobin should be maintained between 95 and 115 g l⁻¹ in the under twos and 100–120 g l⁻¹ in older children (NICE 2015a). Initially oral iron supplementation with nutritional management is sufficient in managing anaemia. However as renal function deteriorates (usually GFR <60 ml⁻¹ min⁻¹ 1.73 m⁻²) erythropoietin stimulating agents may need to be introduced. Most children with established kidney disease require treatment.

Intravenous iron is usually given on an as-required basis, however weekly doses for children on haemodialysis can be effective in counteracting the blood loss experienced. Whenever possible, blood transfusions are to be avoided.

Growth and bone health

Growth problems are common in children with renal disease, and monitoring is essential. This becomes a particular issue when GFR decreases below 25% (Hodson et al. 2012). Height/length, weight, and head circumference in the under twos should be measured and recorded on a growth chart (Royle 2015).

Renal bone disease is a major contributor to growth problems. Close monitoring of phosphate levels and parathyroid hormone is essential. Dietary modification should begin when abnormal results are seen (NICE 2013b).

Diet has a major impact on growth, including control of calcium and phosphate levels. Phosphate-binding medication is often required, with calcium-based binders recommended as a first line (NICE 2013b; Royle 2015). In infants and young children this is added as a suspension into feeds, whereas older children follow similar regimes to adults. Adherence can be a problem, and education and negotiation is essential to identify a regime that is realistic.

The 19th UK Renal Registry (Byrne et al. 2017) report suggests that 33.3% of children and young people under 18 years of age on dialysis have hyperphosphataemia, so Vitamin D analogues may be required. Combining these treatments can control serum calcium levels and prevent the development of hyperparathyroidism (Bacchetta et al. 2012). Progression to tertiary hyperparathyroidism can make long-term treatment very difficult, and may ultimately lead to the need for a parathyroidectomy. Vascular calcification is also a major concern, and can be a contributing factor in cardiovascular complications (Bacchetta et al. 2012).

Growth problems in children with renal disorders have been associated with deranged secretion of growth hormone and resistance. Recombinant growth hormone can be effective (Hodson et al. 2012) and this treatment should be considered. This should be carefully managed in conjunction with an endocrinologist to minimise complications.

Nephrotic Syndrome

Nephrotic syndrome is the most common glomerular disease in childhood. The disease is predominantly seen in preschool children with an incidence of 2–4 cases per 100 000 in the United Kingdom (Krishnan 2012). It is four to six times more common in the UK Asian population (Lennon et al. 2009).

Nephrotic syndrome is characterised by a triad of symptoms: proteinuria (early morning protein to creatinine ratio greater than 200 mg mmol^{-1}), hypoalbuminaemia (plasma albumin less than 25 g l^{-1}), and generalised oedema (Lennon et al. 2009). Oedema develops when a loss of plasma protein leads to a fall in oncotic pressure and water leaks into the interstitial space. Elevated plasma cholesterol frequently occurs.

Acquired nephrotic syndrome can be secondary to infection, allergic disorders, or systemic disease such as Henoch–Schönlein purpura, although it is most commonly idiopathic. Seventy per cent of paediatric patients respond well to corticosteroid therapy and can be classed as having steroid sensitive nephrotic syndrome (SSNS) (Bierzynska and Saleem 2017).

The treatment of SSNS is with prednisolone, $60 \text{ mg m}^{-2} \text{ day}^{-1}$ until urinary remission, followed by $40 \text{ mg m}^{-2} \text{ day}^{-1}$ on alternate days for a further 28 days. The child is considered to be in remission when the urine has been negative of protein for three consecutive days. Relapse occurs when there is proteinuria of 3+ or more on dipstick for three consecutive days after remission (Krishnan 2012). Relapse occurs in approximately 70% of children, requiring high-dose steroid treatment, which is weaned after four weeks. The use of high-dose steroids for prolonged durations can have serious side effects including weight gain, mood swings, hypertension, and increased blood sugar. Alternative therapies are now routinely considered and Rituximab is commissioned for the treatment of relapsing SSNS (NHS England 2015).

Renal biopsy is only indicated if remission is not achieved within 28 days of commencing treatment.

Nursing care of children with nephrotic syndrome

Accurate monitoring of fluid balance is essential along with daily weight and regular blood pressure measurement. Frequent assessment of oedema is necessary and mobilisation should be encouraged to disperse oedema. In children with significant oedema, a fluid allowance of 750 ml daily for children under five years and 1000 ml daily for those over five years should be considered. Although oedema may be present, hypovolaemia may occur due to the shift of fluid into the interstitial space. Diuretics should therefore be used with extreme caution and daily monitoring of serum electrolytes is necessary. In severe cases of oedema or hypovolaemia, 20% albumin infusions may be prescribed. Albumin should be administered with caution and frequent observations made during and after the infusion.

Urine should be checked for protein daily and a teaching programme should be arranged for children and carers, so that they can continue with urinalysis following discharge. Advice about steroid dosage and potential side effects should be given. Referral to a paediatric renal dietician is recommended. A healthy eating

plan should be observed with a no-added salt diet. Monosaturated or polyunsaturated fats should be used to prevent hyperlipidaemia.

In cases of frequent relapse or steroid resistance, second-line nonsteroidal treatment is necessary. These children should be referred to a paediatric nephrologist. Minimal change nephrotic syndrome has a favourable prognosis. Children who present with this syndrome between one to eight years of age are likely to respond to steroid treatment. The disease usually burns out before childhood leaving no residual renal damage (Hodson et al. 2012).

Congenital nephrotic syndrome

This is a rare, inherited disorder, which usually presents in the antenatal stage or within the first three months of life (Jalanko 2009). It is characterised by heavy proteinuria, oedema, and hypoalbuminaemia. Unlike childhood nephrotic syndrome, the disease cannot be controlled with the use of corticosteroids.

Daily albumin infusions are necessary and central venous line insertion is recommended to facilitate this. Ultimately, nephrectomy and renal replacement therapy is required. Early referral to a paediatric nephrology centre is crucial.

Renal Replacement Therapy

Transplantation

Transplantation is the treatment of choice for children with ERD. In 2016 75.3% of children with ERD were transplanted (Byrne et al. 2017). Normal renal function provides children with better opportunities for growth and development. In addition, successful transplantation maximises the amount of education and normal childhood activities, which may be compromised during dialysis.

Allocation of deceased donor transplants currently gives priority to paediatric recipients (under 18 years of age) or young adults of 19 years of age who have been on the list since age 18 years. This was agreed as children are likely to require more than one kidney transplant in their life time and a good match at first transplant will mean less difficulty in finding a suitable donor in the future.

It is possible to transplant kidneys from adult donors depending on the size of the child's abdominal cavity. If the donor kidney is disproportionately large, it may be placed intraperitoneally. However, the extraperitoneal position is preferable as this preserves the peritoneum for dialysis and avoids long-term complications.

Transplantation into very small children is rarely successful. Most transplant surgeons require children to weigh approximately 10 kg or have reached at least 22 months of age before transplantation is considered. This is due to the risk of infarction in small vessels postoperatively. Children receiving renal replacement therapy from birth therefore require the maintenance of dialysis access up until this time. This places a significant burden on the carers and a challenge for professionals.

Living donor transplantation

With the decrease in the number of deceased donors, living donor transplantation is on the increase and is now routinely considered as an early option. In children, the donor is most frequently a parent, although donation from grandparents has been reported. UK law prohibits minors from donating a kidney and therefore siblings under 18 years are not considered. For children placed on the deceased donor waiting list, the avoidance of parental antigens will allow living related transplantation to be considered in the future.

Living related donation (LRD) is advantageous in that families are able to plan the timing of the transplant, which allows them to consider employment, education, and family arrangements. It is recommended that children receiving kidney transplants must be cared for within a paediatric unit (NHS Commissioning Board 2013) therefore there is the potential for the recipient and the donor to have surgery at different hospitals simultaneously. Professionals need to pay attention to the psychosocial needs of the family during this time, as often the nondonating parent must divide his or her time between the two sites. Supportive care could be provided in terms of video links and assistance with transport.

Pre-emptive transplantation

Transplantation prior to the need for dialysis is considered to be the gold standard for treatment of ERF and was achieved in up to 33.2% of transplanted children in the United Kingdom from 2011 to 2015 (Renal Registry 2017). The benefits of transplant before dialysis include: less interruption of schooling and family life, preservation of the peritoneum and vessels for future dialysis treatments, improved growth and development, and reduction in the symptoms of established renal failure.

A child is generally considered for transplantation once the GFR has fallen below $10\text{--}15\text{ ml min}^{-1}1.73\text{ m}^{-2}$ and dialysis is anticipated within 12–24 months and/or a significant complication of growth failure is present. In addition, pre-emptive transplantation should be considered if the child exhibits symptoms of ERD, i.e. renal bone disease, poor growth, fatigue, and inability to take part in normal childhood activities.

Care of the child after kidney transplantation

Nursing care of the child following renal transplant must be in a designated high dependency nursing area in order to ensure close monitoring. Postoperative complications include bleeding, vascular thrombosis, and delayed graft function (Williams 2012). After the first 48 hours recovery is generally fast and, if there are no complications, children can be discharged 7–10 days following transplant.

Careful attention to kidney function and immunosuppression levels is necessary, and children are usually seen as an outpatient several times a week in the first four weeks. Due to the long travelling distances to the specialist centre for paediatric patients, close collaboration with local health centres and district hospitals is encouraged so that blood tests can be taken locally and results sent to the tertiary centre.

Immunosuppression

There is currently no standard immunosuppression regimen for children and young people undergoing renal transplantation. However NICE guidance (2017) recommends Basiliximab, Tacrolimus, Mycophenolate Mofetil, and rabbit anti-human thymocyte immunoglobulin as initial options to prevent organ rejection in children and young people. There are newer immunosuppressant agents targeting different sites in immune activation pathways, such as sirolimus and everolimus. Experience with these drugs in the paediatric population is evolving although potential nonadherence to the immunosuppressive regimen can be prevalent resulting in serious clinical consequences (Dobbels et al. 2010).

Complications

There are several potential complications following paediatric renal transplant. Hypertension is recognised as an important risk factor for cardiovascular morbidity and graft survival in transplanted children, with post-transplant hypertension occurring in 60–90% of transplanted children (Seeman 2007). Causes include: immunosuppression therapy, graft dysfunction, stenosis, and weight gain. Ideally,

hypertension should be confirmed using 24-hour automated blood pressure monitoring. The systolic blood pressure should be maintained at <90th percentile for age, gender, and height. (+1.28SD = 90th percentile) or 130/- mmHg, whichever is lower.

Other complications include urinary-tract infection, rejection, and recurrence of primary disease. Regular follow up and 24-hour access to the nephrology centre is essential.

Preparation for dialysis and transplant

Prior to commencing renal replacement therapy children, young people, and their carers need to be given information regarding treatment options. In order for them to make an informed choice, information that is appropriate to age and understanding must be available. Hospital play specialists, trained to prepare children for procedures, are invaluable members of the paediatric multiprofessional team. Evidence shows that appropriate preparation for family members prior to treatment may prevent trauma later (Waby et al. 2005). Consideration must also be given to siblings who may feel distressed by the treatment and are concerned about family separation (Batte et al. 2006).

There are a number of investigations that are required within the preparation period. These are summarised in Box 12.3.

Immunisation

Live vaccines should not be given in children who are immunosuppressed. In order to receive optimal protection against infectious diseases children should be given a full course of primary immunisations prior to transplant listing. In addition to routine childhood immunisation, hepatitis B, BCG, and varicella zoster vaccine should be given to nonimmune children. The quadrivalent human papillomavirus (HPV4) vaccination is recommended (Public Health England, Department of Health 2017)

Dialysis

Although every attempt is made to transplant pre-emptively and hold off dialysis this is not always possible. Peritoneal dialysis (PD) is often the dialysis of choice if a transplant is not available, however some families may choose haemodialysis. It is important that children and their families are aware of all of the options available, and that they are actively involved in the decision-making process.

BOX 12.3

Investigations required prior to renal replacement therapy

- Blood group
- Tissue type
- Cytotoxic antibodies
- Parental cross-match (if requested)
- Immunisations
- 24-hour urine collection
- ECG
- Urological opinion
- Urodynamics, if indicated

Other professionals also require information when children progress onto dialysis. General practitioners and community health staff should be informed of changes in the child's treatment.

School and nursery visits are also often required to provide training and support to teachers and other carers who may be responsible for the child (NHS England 2013).

Peritoneal dialysis

In 2015 PD was used as the initial renal replacement therapy in 44% of children with ERD, however use of PD as a first treatment has fallen since 2001. This may be due to an increasing number of live donor transplants; also, increasing life stress on families may lead to parents choosing in-centre haemodialysis to reduce the burden of care on the family. One benefit of PD in paediatric patients is the reduced disruption to normal life. It is the recommended therapy in children under the age of two (National Institute for Health and Care Excellence 2011). In many paediatric units automated PD is the most frequent mode of delivery. This is usually carried out overnight reducing the impact on schooling in particular. Machines can deliver fill volumes as low of 60ml with reduced recirculation of fluid using specialised sets, therefore enabling most infants to be dialysed this way. Infants requiring lower volumes are usually hospitalised following transfer from Neonatal Services.

Another advantage of this method is the reduction in times the catheter is accessed, reducing the potential for contamination and therefore infection. Fill volumes are usually calculated based on surface area ($1.2\text{--}1.4\text{lm}^{-2}$) (BAPN 2008), or weight $30\text{--}50\text{mlkg}^{-1}$.

Ambulatory PD is less frequently used for younger patients. Young adults may choose this method, as it gives them more freedom during the evenings and it is estimated that less than 30% of paediatric patients use this mode of PD.

There is no optimum PD fluid prescription for children and the type of fluid and dwell time is determined on an individual basis depending on size and tolerance rather than an optimal dialytic exchange volume (Fraser et al. 2015).

- parental/carer burnout is always an issue. Whenever possible young adults are taught to undertake their own dialysis, with the support of another family member. However, with young patients there is a reliance on their relatives to provide this treatment. Where possible, respite care provision should be made available.
- infection is a major concern in the paediatric population. Peritonitis can quickly lead to systemic illness in very young children. There is also the long-term treatment of the child/young person to consider and they may sometimes face a return to dialysis at a later date. Therefore, it is very important to prevent sclerosis of the peritoneum due to either repeated or single severe peritonitis episodes, increasing the longevity of this type of dialysis. Changes in treatment modality may be required if a child has repeated peritonitis episodes. Research into prevention and treatment is ongoing as a result.

Periodic updating of families on technique is recommended as this may reduce the risk of infections from practices at home. A great difficulty can be in maintaining hygiene in infants wearing nappies and who do not understand that their catheter/line should be kept clean. Therefore fasten-through vests and tubigrip can be useful tools in preventing them from tampering with any type of access.

Haemodialysis

Haemodialysis is often the second choice of dialysis in children. This is due to the frequency it can be offered, and the impact on the child and family. It is recommended

that children should be cared for in a specialist paediatric renal unit. However, because of the very small numbers of children requiring this treatment there are only 13 paediatric renal units in the UK. This inevitably leads to children travelling to receive this treatment. As a result, the psychosocial impact of haemodialysis can be considerable for children and their families (Kaur and Davenport 2014). 13% of children in the UK with ERD were treated with haemodialysis in 2015 (Byrne et al. 2017) reflecting this.

School provision is important for older children and young adults who dialyse three to four times a week are unable to attend school with their peers on dialysis days. Preschool children need distraction as well as play programmes to promote their global development.

Families need support, particularly those with children under 16, who must be transported with an escort each time they attend the hospital.

There can also be technical difficulties when children require haemodialysis.

Vascular access

Central lines are frequently used as a form of chronic access, particularly in children awaiting transplantation for which dialysis will hopefully be a relatively short-term treatment. A range of sizes is required for the patient group cared for in paediatric renal units.

There is a risk of occlusion and infection, as with any central venous access device. Complications are carefully monitored.

Arteriovenous fistulae are used, more for older patients with a longer-term need for dialysis. Use in younger patients is limited by vessel size and nursing expertise. Play preparation and the use of anaesthetic creams are very important in these patients, as this is a painful procedure (Kaur and Davenport 2014).

The challenge in children is maintaining access sites for the future, which can become very problematic in children receiving renal replacement therapies from a very early age.

Prescribing dialysis and adequacy

Standardised treatment regimens cannot be used in patients on paediatric programmes. Guidelines on prescribing haemodialysis safely must be adhered to, to ensure adequate dialysis whilst preventing complications of over-efficient dialysis such as disequilibrium. Common guidelines are a pump speed of $6\text{--}8\text{ ml}^{-1}\text{ min}^{-1}\text{ kg}^{-1}$ (BAPN 2008). It is also important to use a circuit less than a maximum of 10% (ideally 8%) of the child's total circulating volume (see Box 12.4). A variety of line volumes and dialysers need to be available to meet these requirements.

Where this is not possible it can be necessary to prime the dialysis circuit with albumin or blood. If blood is used repeatedly, the same donor should be requested. This will reduce the sensitisation effects for future transplantation (Kaur and Davenport 2014).

BOX 12.4

Blood volume calculation

Neonates	90 ml kg^{-1}
Infants and children	80 ml kg^{-1}
Adults	65 ml kg^{-1}

Source: from Willock and Jewkes (2000).

Guidelines recommend initial treatment should use a dialyser with a surface area no more than 75% of the child's own surface area (BAPN 2008). This is usually increased in size up to the child's surface area to achieve a Urea Reduction Rate (URR) of at least 65%. An equilibrated Kt/V of >1.2 can also be used.

Careful consideration is also needed in guiding fluid removal on dialysis; $0.2 \text{ ml}^{-1} \text{ min}^{-1} \text{ kg}^{-1}$ of fluid is the upper limit commonly used for guiding fluid removal whilst dialysing. Additional fluid removal is undertaken via isolated ultrafiltration, sequentially followed by the prescribed dialysis. However, greater than a 5% reduction in fluid in one session is not advised (BAPN 2008). Blood volume monitoring can be used to guide fluid removal and can be a useful tool in assessing dry weight (Michael et al. 2004). Due to the continual growth of children, it can be difficult to establish dry weight. Regular reviews are required to prevent frequent hypotensive episodes during dialysis.

High flux dialysis remains the more common treatment in many units for these patients, and is recommended for any child on dialysis for extended periods due to the risk of amyloidosis (Fischbach et al. 2012). Haemodiafiltration is variable in its use.

Home haemodialysis

Historically home haemodialysis was not widely used in paediatric units, as transplant waiting times have been low and set up of home therapy lengthy. However, the advent of portable home haemodialysis machines which do not require water treatment is changing this. Research into the effect of this treatment is limited, but the suggested benefits of treatment flexibility and frequency are leading to an increase in interest nationally (Hothi et al. 2016).

Acute Kidney Injury

AKI is characterised by a reversible increase in plasma creatinine and urea and by the inability of the kidney to regulate fluid and electrolyte balance.

The management of AKI in children has improved with advances in treatment for infants and children (Goldstein 2011). Critically ill neonates and children with congenital cardiac disease and those receiving solid organ transplants are susceptible to AKI. There is also evidence of increased incidence of AKI in children with malignancy, sepsis, and those receiving nephrotoxic medications (Goldstein 2011). There is increasing emphasis on calculating the risk of AKI and early treatment (KDIGO 2011). The paediatric RIFLE criteria stratify AKI in children into five groups (R = risk, I = injury, F = failure, L = loss of kidney function, E = end-stage renal disease) enabling earlier recognition and intervention (Hayes and Christian 2012). It is suggested that up to 10% of all children treated in intensive care units suffer a degree of kidney injury, with sepsis and fluid overload now frequently treated with renal replacement therapy (Basu et al. 2011).

Cause

The causes of AKI in childhood are commonly divided into three groups: prerenal, intrinsic, and postrenal. Prerenal injury occurs when blood flow to the kidney is reduced as in cardiac insufficiency, renal vein or renal artery thrombosis, and hypovolaemia. In infants and small children hypovolaemia is commonly due to dehydration following gastrointestinal losses. Studies have shown that AKI in childhood due to dehydration is largely preventable with early management.

Intrinsic renal disorders are those that occur following damage to renal parenchymal cells. These include malignancy, congenital malformation, glomerulonephritis and haemolytic uraemic syndrome (HUS).

Postrenal disorders include urethral obstruction (valves, phimosis), ureteral obstruction, and neurogenic bladder. These conditions require intervention by a paediatric urologist with nephrology liaison.

Treatment

NICE guidance (2013a) for AKI covers care and management for children and young people, as well as adults. It is not necessary to refer children or young people to a paediatric nephrologist when there is a clear cause for AKI and the condition is responding promptly to medical management. The guidance also states that management of AKI needs to be discussed with a paediatric nephrologist as soon as possible and within 24 hours of detection when one or more of the following is present:

- a possible diagnosis that may need specialist treatment (for example, vasculitis, glomerulonephritis, tubulointerstitial nephritis, or myeloma);
- AKI with no clear cause;
- inadequate response to treatment;
- complications associated with AKI;
- stage 3 AKI (according to [p]RIFLE, AKIN, or KDIGO criteria);
- a renal transplant;
- CKD stage 4 or 5.

It is also important to consider referral to a paediatric nephrologist for children and young people who have recovered from an episode of AKI but have hypertension, impaired renal function, or 1+ or greater proteinuria on dipstick testing of an early morning urine sample.

If renal replacement therapy is needed, the type of RRT depends on the circumstances, the skill of the nursing staff, and the therapies available. Traditionally, PD has been the treatment of choice for children with AKI in renal centres. The advantage of PD is that it can be provided as a continuous therapy, which does not require vascular access. In addition, PD does not rely on specialist nursing expertise although prior experience with this therapy is advisable if using an automated machine. For units without this expertise, manual PD sets for infants and children are available. Bicarbonate dialysis solutions should be considered for use in infants or children who have lactate intolerance.

PD in AKI must be commenced as soon as possible and there is therefore a risk of leakage. Small volumes of $10\text{--}20\text{ ml kg}^{-1}$ ($300\text{--}600\text{ ml m}^{-2}$) of continuous cycling therapy are recommended to prevent complications.

Haemodialysis is commonly used to treat children with AKI cared for within paediatric renal centres, when PD has failed or is contraindicated. Haemodialysis is suitable for rapid fluid and toxin removal. The disadvantages of this therapy are the need for vascular access, a water supply that is often only available within paediatric nephrology units, and the need for specialist nurses.

Continuous renal replacement therapy (CRRT) in the form of continuous haemofiltration or continuous haemodiafiltration is increasingly seen as the preferred modality for the treatment of AKI in paediatric intensive care units (Goldstein 2011). CRRT is often used in critically ill patients on PICU as it minimises haemodynamic perturbations associated with intermittent haemodialysis (Hayes and Christian 2012). Children require vascular access of a sufficient size to deliver appropriate blood flow through the filter. A dual lumen central venous line of a

minimum 6.5 fg is recommended. Equipment must be calibrated to deliver blood pump speeds as low as 20 ml min⁻¹. Recommended fluid removal should not exceed 0.02 ml kg⁻¹/min⁻¹. As in haemodialysis the extracorporeal circuit size should not exceed 10% of the child's circulating blood volume. In infants, regular blood priming is necessary if the line volume exceeds the child's extracorporeal volume.

Haemolytic Uraemic Syndrome

This is a common cause of AKI in childhood. HUS is characterised by haemolytic anaemia, thrombocytopenia, and AKI in the absence of disseminated intravascular coagulation (Inward 2008). The *E. coli* 0157 bacteria cause approximately 90% of HUS cases. Children usually present with bloody diarrhoea, nausea, and vomiting. Consequently, children with HUS are often misdiagnosed with surgical problems. Early investigation of renal function and blood film is essential, and transfer to a tertiary referral centre is recommended (Inward 2008).

Approximately 60% of children with HUS require dialysis during the acute stage of the illness (Sheiring et al. 2010). Supportive treatment such as blood transfusion and treatment of hypertension is also required. Seventy percent of children with HUS recover renal function. However, approximately 25% need treatment for high blood pressure and CKD management.

Atypical HUS (aHUS) may occur during childhood. This is associated with factor H deficiency (Fremeaux-Bacchi et al. 2005). AHUS is a chronic, rare, progressive condition that causes severe inflammation of blood vessels and the formation of blood clots in small blood vessels throughout the body, a process known as systemic thrombotic microangiopathy. Children may present with the symptoms of renal failure but there is often no preceding diarrhoeal illness. Until recently treatment involved regular plasma exchange or plasma infusion to prevent established kidney disease. However, since 2015, Eculizumab, a human monoclonal antibody that binds to complement C5 and blocks prothrombotic and proinflammatory processes, has been commissioned for the treatment of aHUS (NICE 2015b).

Transition to Adult Services

Adolescence is recognised as a time of physiological, emotional, and psychological change. Transfer from paediatric to adult renal services during this critical time can be stressful for young people, their carers, and health professionals. Poorly planned transition has been associated with an increased risk of nonadherence to treatment and serious consequences in terms of morbidity, mortality, and social and educational outcomes (Department of Health 2006b). A reported 35% of young people lose their transplant within 36 months of transfer to adult services (Harden et al. 2012).

A seamless transition plan is essential. This should consider clinical, educational, and social outcomes for young people. The transition process should start as early as 11 years of age with involvement from the young person, his or her carers, and health professionals from paediatric and adult teams. Starting to plan their transition as early as possible can lead to a better experience for young people moving from children's to adult services. Early planning allows a more gradual process (NICE 2016). Flexibility of the time of transfer is important, and should depend on the individual young person's needs rather than a fixed age. An age range of 14–24 years should be considered (Webb et al. 2010).

A UK consensus statement (Webb et al. 2010) recommends that young people should be able to achieve specific competencies prior to transfer to an adult unit. Examples of such competencies are the ability to understand and organise medications, and to manage hospital appointments.

It is acknowledged that paediatric services differ in terms of staffing resources and patient numbers. The key to successful transition is to manage the expectations of young people and their carers. Preparation for change is essential and joint clinics with multiprofessional adult and paediatric teams are recommended. Young people should be given a choice as to whether parents and carers are present at clinic appointments. Specific young adult clinics where young people can receive support from peers are valuable. The participation of youth workers, trained to provide social and informal educational support, is recommended and where possible the appointment of a hospital youth worker should be considered (Hilton and Jepson 2012).

Conclusion

As this chapter has highlighted, providing treatment for children with renal disorders has different challenges from the adult population. In addition to treating the renal-associated complications, there are the additional issues around growth, development, and the psychosocial impact on the whole family (Marciano et al. 2011).

The British Association of Paediatric Nephrology (<https://renal.org/bapn> accessed 1 June 2018) identifies standards for care, and markers for good practice in the service provision for children and young people. The challenge for all paediatric nephrology services is to ensure that these standards are achieved, and the highest quality care is provided for these children and young people.

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CHAPTER 13

Renal Nutrition

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Learning Outcomes

- to describe the historical background to renal nutrition and dietetics.
- to evaluate nutritional management in the predialysis phase.
- to identify the dietary principles of haemodialysis (HD) peritoneal dialysis (PD) and transplantation.
- to discuss the role of the nurse in giving dietary advice.

Introduction

Dietary treatment has always been regarded as an important part of managing patients with advanced kidney disease (AKD), before and during renal replacement therapy (RRT). During the 1960s many patients were treated with diet alone. The renal diet was adapted to dialysis and transplantation once these modes of RRT became available during the 1970s and early 1980s. Nowadays, chronic fluid overload, hyperphosphataemia, and protein energy malnutrition are amongst the most common problems. These can lead to long-term complications if not resolved and adversely affect outcome of treatment and the quality of life of patients with renal disease, who may require treatment for many decades. This chapter will address the important issues of dietary management and the role it plays in the overall treatment of AKD.

Historical Review of Dietary Management

Predialysis treatment (1960–2000)

HD was only accepted as a regular form of RRT for selected patients at the end of the 1960s. Prior to this period, patients approaching ERF (established renal failure) with gastrointestinal symptoms were advised to follow a very low-protein diet

(VLPD). The best-known diet at the time was the Giovanetti diet, containing 20 g protein of high biological value (HBV) to cover essential amino acid requirements. An intake of 50 kcal kg^{-1} body weight (BW) was recommended to prevent loss of muscle and maintain nitrogen balance. This diet was prescribed to selected patients with a creatinine clearance of 3 ml min^{-1} or a plasma urea level of 33 mmol l^{-1} (200 mg dl^{-1}) and was the only treatment available to improve the well-being of patients, until regular HD treatment became available.

It became apparent in later years that a badly managed protein-reduced diet contributed to malnutrition before patients started HD. This prolonged the rehabilitation period and also contributed to the outcome of treatment, with an increased morbidity and mortality (Ikizler and Hakim 1996).

During the 1980s there was a renewed interest in protein allowance as protein restriction in partially nephrectomised rats delayed the progression of renal disease. This was the hyperfiltration/hyperperfusion hypothesis (Brenner 1983). It was more difficult to prove the same effect in humans. High-energy diets containing no more than $0.6 \text{ g protein kg}^{-1} \text{ BW day}^{-1}$ were prescribed during the early stages of chronic renal disease to asymptomatic patients, who not surprisingly found this difficult to follow for extended periods of time.

In the United States, the National Institutes of Health (NIH) stated in 1993 that the nutritional health of a patient prior to dialysis was an important indicator of outcome and that all patients were entitled to receive a nutritional assessment by a trained renal dietitian. In the absence of obvious malnutrition, a moderate low-protein diet of up to $0.7\text{--}0.8 \text{ g protein kg}^{-1} \text{ BW day}^{-1}$ should be prescribed. When malnutrition was present, the amount of energy was increased and the amount of protein raised to $1.0\text{--}1.2 \text{ g kg}^{-1}$ to allow for nutritional repletion or to counter the catabolic effects of stress. Dietary prescriptions should also include guidelines for energy, fat, carbohydrate, fluid, sodium, phosphate, and potassium as well as other nutrients and micronutrients (NIH 1993). The NIH had also commissioned a large multicentre study to ascertain once and for all the efficacy of low protein diets. The Modification of Diet in Renal Disease (MDRD) study compared diets with different levels of protein reduction at different levels of renal impairment. The diets ranged from usual intake to VLPD supplemented with ketoacids and combined with phosphorus restriction. The results of this two-year study, which had been launched in 1985, were finally published in 1994 (Klahr et al. 1994).

The MDRD study showed that, in the absence of severe proteinuria and hypertension, a reduction of protein intake by $0.2 \text{ g kg}^{-1} \text{ BW}$ resulted in a modest reduction in the rate of progression. There appeared to be no further advantage in using a VLPD supplemented with essential amino acids. However, it did reveal that subjects accustomed to a 'Western' diet containing typically $>1.2 \text{ g protein kg}^{-1} \text{ day}^{-1}$ found it very difficult to achieve the designated protein restrictions of $<0.6 \text{ g protein kg}^{-1} \text{ day}^{-1}$. The report cautioned that, whilst lowering blood pressure and protein intake appeared to be safe, both must be carefully monitored.

Several meta-analyses were subsequently conducted, which included studies such as the MDRD study. Fouque et al. (2000), Pedrini et al. (1996), and Ginn et al. (1999) concluded that dietary protein reduction effectively slows the progression of diabetes mellitus (DM) and nondiabetic renal disease.

On the basis of these analyses as well as expert opinion, National Kidney Foundation (NKF)/Dialysis outcomes quality initiative (DOQI) published the 'Clinical practice guidelines for nutrition in chronic renal failure' (Kopple et al. 2000) and the European Dialysis and Transplant Nurses Association/European Renal Care Association also published guidelines shortly afterwards. The suggested protein and energy requirements for patients with advanced chronic kidney disease

Table 13.1 Suggested protein and energy requirements versus degree of renal function.

GFR ^a (ml min ⁻¹)	Protein (g kg ⁻¹ IBW)	Energy (kcal kg ⁻¹ IBW)
>50	normalise	30–35
25–50	0.6–1.0 ^b	30–35
<25	0.6–0.75 ^b	30–35
<10 start dialysis		

^a GFR – glomerular filtration rate.
^b Protein should contain at least 50% sources of high biological value (HBV). 35 kcal kg⁻¹ IBW for active patients and 30 kcal kg⁻¹ IBW for sedentary or older patients, i.e. >65 years of age.

(CKD), not on dialysis, are summarised in Table 13.1 and take the patient's ideal body weight (IBW)¹ as well as the residual renal function into consideration.

The debate about whether to reduce protein (and how low to go) continues to this day. In support of protein reduction, a low-protein diet will reduce the burden of waste products that have to be removed: nitrogen compounds, acids, phosphate, and also potassium. This potentially has beneficial effects on reducing symptoms of uraemia and controlling the development of problems such as acidosis and renal bone disease.

The main deleterious effect of the low-protein diet is the risk of malnutrition; energy requirements are difficult to meet (although not impossible) without resorting to sources of carbohydrate and fat, which may have an impact on cardiovascular disease (CVD). Vitamin and mineral intakes also have to be monitored closely. Those clinicians not in favour of low-protein diets argue that the risk of malnutrition outweighs any benefits that may be gained from the (very moderate) reduction in the rate of decline in kidney function (Johnson 2009). Even the most recent Cochrane review which analysed the results from 10 studies and 2000 patients concluded that the optimal level of protein prescription could still not be confirmed (Fouque and Laville 2009).

As there are many different elements to patient care prior to starting dialysis, a more realistic approach to protein recommendations is usually taken.

Current Concepts of Predialysis Dietary Intervention

The nutritional content of the diet should be specifically adapted to each patient's individual needs and personal circumstances. This should result in the reduction of metabolic waste products, which can otherwise accumulate as chronic disease progresses. Most patients will receive some nutrition information in the predialysis phase, although it is very variable and dependent on dietetic staffing levels. The Renal Nutrition Group of the British Dietetic Association (BDA) has designed a flow diagram which outlines the nutritional care of a person with CKD (Figure 13.1). It is recognised that 'diabetes and hypertension are the leading causes of CKD in middle and higher income countries accounting for approximately 35 and 25% of kidney disease' (Palmer et al. 2017). Therefore, in CKD stages 1–3 the focus is on weight management, diabetes control, hypertension, and lipid management as described in the National Institute for Health and Care Excellence (2014) clinical

¹ See Appendix 13.A for calculation of IBW.

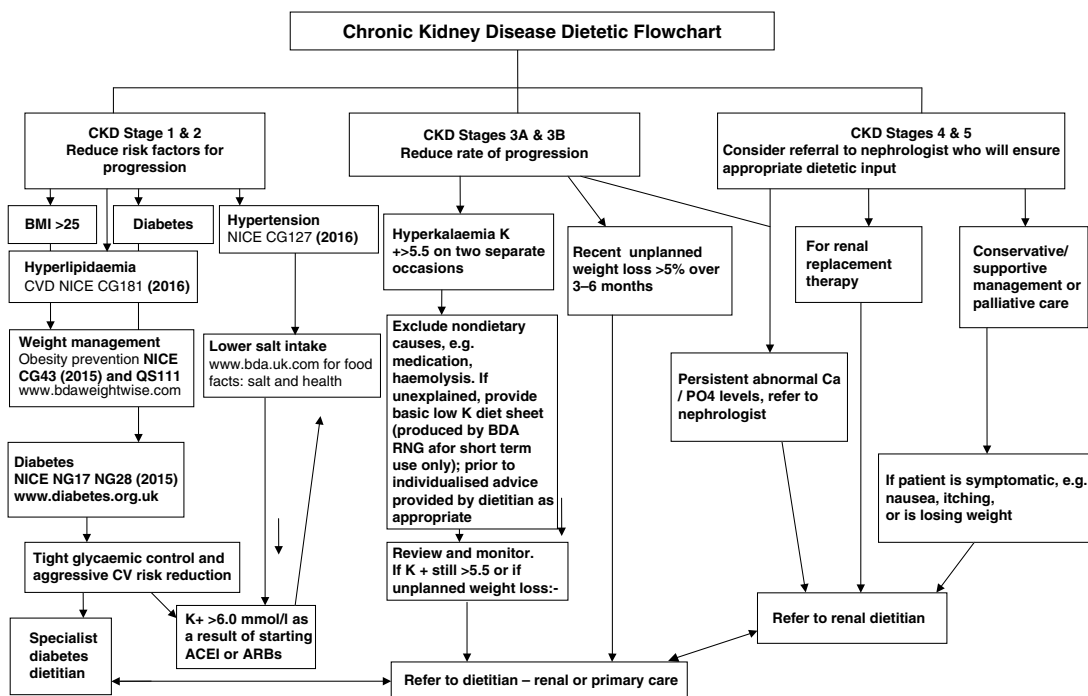


Figure 13.1 Flow chart for dietary treatment of chronic kidney disease (CKD); stages 1–5.

guideline CG182. This guideline also describes three points regarding lifestyle advice relevant to the management of CKD:

- encourage exercise, achieve healthy weight and stop smoking;
- ensure malnutrition is prevented;
- offer dietary advice to people with progressive CKD regarding potassium, phosphate, protein, calories, and salt when indicated. However, low-protein diets less than $0.6\text{--}0.8\text{ g kg}^{-1}\text{ day}^{-1}$ are not recommended. ‘Kidney Disease Improving Global Outcomes’ KDIGO (2012) guidelines suggest lowering protein intake to $0.8\text{ g kg}^{-1}\text{ day}^{-1}$ in adults with glomerular filtration rate (GFR) less than $30\text{ ml min}^{-1}\text{ 1.73 m}^{-2}$ in selected individuals and also recommend not exceeding $1.3\text{ g protein kg}^{-1}\text{ day}^{-1}$ in adults at risk of progression.

Self-management of blood pressure, smoking cessation, exercise, diet, and medication is encouraged.

From stage 3 (usually 3b) to stage 5, the problems of preventing and controlling renal bone disease, hyperkalaemia, anaemia, acidosis, and malnutrition come to the fore.

The Renal Association (RA) of the UK concur with all of these points and they have produced specific clinical guidelines which cover the key elements of care, many of which also have nutritional implications:

- detection, monitoring, and care of patients with CKD: includes management of hypertension, diabetes, and cardiovascular risk factors. It also discusses management of hyperphosphataemia and hyperkalaemia (MacGregor and Taal 2011) now archived.
- CVD in CKD (Holt and Goldsmith 2010) now archived.
- CKD mineral and Bone Disorders (Steddon and Sharples 2015).
- anaemia of CKD (Mikhail et al. 2017).
- nutrition in CKD; focus is on malnutrition (Wright and Jones 2011; now archived and in process of being rewritten).
- clinical Practice Guideline Post-Operative Care in the Kidney Transplant Recipient (Baker et al. 2017).
- clinical Practice Guideline on PD in adults and children (Woodrow et al. 2017).

Hypertension

Sodium (Na) and fluid retention occur in most types of renal disease and contribute to high blood pressure. The National Institute for Health and Care Excellence (2014) guideline and the KDIGO (2012) guidelines recommend that, to improve blood pressure control, patients should be advised to reduce dietary salt and alcohol intake, stop smoking, achieve a healthy weight, and take regular exercise aiming for levels of below 140/90 mmHg (130/80 mmHg if the person has diabetes or high levels of proteinuria). A recent systematic review found that salt reduction not only reduced blood pressure but also reduced proteinuria; however, longer-term studies are needed to see if this improved progression of kidney disease and reduction of cardiovascular events in people with CKD (McMahon et al. 2015).

A moderate salt-reduced diet (about $80\text{--}120\text{ mmol Na}$) will facilitate the action of antihypertensive medication such as diuretics and the commonly used angiotensin converting enzyme (ACE) inhibitors. RA guidelines and also the current government Food Standards Agency (FSA) guidelines for the general population recommend a maximum salt intake of 6 g day^{-1} or 100 mmol sodium . However, KDIGO (2012) guidelines recommend a sodium intake of 90 mmol , which is equivalent to a salt intake of 5 g day^{-1} . In practice this is not simple as many people rely

on the purchase of processed foods (see Appendix 13.B). About 80% of our salt intake is hidden in processed foods, including staple food items such as bread and breakfast cereals. Patients should be advised as follows:

- prepare meals using fresh ingredients.
- use spices and herbs to add flavour to food.
- only use a little salt in meal preparation.
- avoid adding salt to food after preparation.
- avoid excessive amounts of salty foods such as cured and processed foods; this includes takeaway meals.
- avoid using salt substitutes containing potassium salts such as potassium chloride (KCl).
- avoid meals prepared with monosodium glutamate. This is added to enhance the taste of food in restaurants, takeaway outlets, and ready-to-eat meals sold in supermarkets.
- read food labels and check for additives like monosodium glutamate and salt substitutes. Note that $1 \text{ mmol Na} = 23 \text{ mg Na}$; $2 \text{ g (2000 mg) Na} = 5 \text{ g NaCl} = 90 \text{ mmol Na}$.

A small proportion of patients are 'salt losers' (due to a specific renal pathology) and need to add salt to their meals and/or use salt supplements.

The KDIGO guidelines for the management of blood pressure in renal disease also recommend the following:

- maintaining a healthy BW (Body mass index (BMI) $20\text{--}25 \text{ kg m}^{-2}$).
- undertaking exercise compatible with cardiovascular health and tolerance. Aiming for 30 minutes, five times a week.
- alcohol intake should be no more than two standard drinks per day for men and one standard drink per day for women (acknowledging that the definition can vary between countries).

Cardiovascular Risk and Hyperlipidaemia

The traditional risk factors of age, gender, lipid levels, and blood pressure contribute to risk of CVD in patients with renal disease; additionally other risk factors include calcium and phosphorus imbalance, hyperhomocysteinaemia, inflammation, and possibly anaemia (Holt and Goldsmith 2010). The National Institute for Health and Care Excellence (2014) CG182 guidelines do not recommend the use of a risk assessment tool (such as QRISK2) to assess CVD risk in people with an estimated glomerular filtration rate (eGFR) less than $60 \text{ ml min}^{-1} 1.73 \text{ m}^{-2}$ and/or albuminuria, simply stating that these people are at increased risk of CVD.

Recommendations from the K/DOQI (2003a) guidelines were that CKD was a high-risk factor for CVD and that 'major findings from randomised trials in the general population are applicable to patients with CKD, until proven otherwise'. More recent intervention trials in the renal population have now supported this statement and blood pressure and lipid levels should be well controlled using a combination of lifestyle changes and medication, including ACE inhibitors for blood pressure and statins for cholesterol. Lifestyle changes include: weight loss where necessary to achieve a healthier BMI, having a cardioprotective diet, stopping smoking, avoiding excess alcohol, and taking regular exercise (NICE CG182 section 1.2, NICE CG181 section 1.3.27).

Archived recommendations from RA state lipid and HbA1c (haemoglobin A1c) levels should be: low-density lipoprotein (LDL) $<2 \text{ mmol l}^{-1}$ or a 30% from baseline, total cholesterol $<4 \text{ mmol l}^{-1}$ or a 25% reduction from baseline, triglycerides

$<1.7\text{ mmol l}^{-1}$, HbA1c between 6.5 and 7.5% ($48\text{--}58\text{ mmol mol}^{-1}$) which are lower than standard NHS (National Health Service)/ British Heart Foundation Guidelines; non-high-density lipoprotein non-HDL cholesterol should be lower than 4 mmol l^{-1} and total cholesterol should be 5 mmol l^{-1} or less. Due to the association with hyperhomocysteinaemia, folate and B_{12} levels should be monitored every six months in CKD stages 4/5 and 'nutritionally at risk' patients should be recommended to take nutritional supplements.

As well as BMI, the National Renal Data Set recommends that waist and hip circumference should be measured. An excess of body fat, particularly round the waist, is linked with metabolic disturbances including raised inflammatory cytokines and insulin resistance. In patients with CKD a raised waist: hip ratio has been associated with increased myocardial infarction and fatal coronary artery disease (Elsayed et al. 2008). Significant correlations have been shown between the presence of inflammation (measured by CRP [C-reactive protein], TNF α [tumour necrosis factor], and fibrinogen) and carotid plaques in patients preparing for dialysis, who have simultaneously demonstrated signs of muscle/protein wasting (low serum creatinine, LBM [lean body mass], and urea nitrogen appearance); the so-called malnutrition–inflammation–atherosclerosis (MIA) syndrome. It is unclear whether CRP is raised in response to endothelial cell damage or whether CRP and other acute phase reactants such as IL-6 are actually involved in the initiation and progression of atherosclerosis (Stenvinkel 2003).

The systematic review by Palmer et al. (2017) found some evidence for beneficial effects of dietary interventions in CKD including use of the Mediterranean diet. More studies are still needed to elucidate the role of diet, exercise, and weight reduction in reducing the risk of CVD and MIA in patients with CKD.

Interventions in Patients with Diabetes

The results of the Diabetes Control and Complications Trial (DCCT) (Type 1 diabetes) and the UK Prospective Diabetes Study (UKPDS) (1998) (Type 2 diabetes) showed that the careful control of blood glucose and hypertension significantly decreases the renal complications of diabetes which often begin with the appearance of microalbuminuria (UKPDS 1998; Yale 2005). Observational studies indicate improved cardiovascular risk with good glycaemic control. RA guidelines recommend a target HbA1c of 6.5–7.5% ($48\text{--}58\text{ mmol mol}^{-1}$) stating the benefits mentioned above. Other guidelines, for example KDIGO guidelines (2012) and Caring for Australians with Renal Impairment (CARI), also give a caveat that 'less stringent goals ($>7\%$) may be more appropriate for patients with a history of hypoglycaemia, limited life expectancy, advanced microvascular or macrovascular complications, or extensive comorbid conditions' (Chadban et al. 2010). Medication to control hyperglycaemia will need to be adjusted regularly as requirements diminish and renal function declines.

A Cochrane systematic review by Robertson et al. (2007) concluded that reducing protein intake does seem to slow progression of diabetic nephropathy, although in a nonsignificant way; that is, increasing time to dialysis by only two months. They noted that compliance with such a protein-reduced diet was difficult to achieve and also added that factors worth considering included changing the type of protein: vegetable versus animal, fish/white meat versus red meat. This may be a more practical and achievable approach than restricting the amount of protein, however the trials evaluating the effectiveness only involved small numbers of patients. The CARI guidelines also agree that there was insufficient evidence to support the use of lower protein intakes to slow down progression of nephropathy in type 2 diabetes (Chadban et al. 2010). The Diabetes

UK guidelines base their recommendations regarding protein reduction on the systematic review by Robertson et al. (2007) and suggest that a six-month trial of reduced protein may be initiated and continued if there is a response.

With the rising levels of diabetes in the population there needs to be a concerted effort in primary care to maximise blood glucose and blood pressure control, in order to prevent nephrology services from being overwhelmed with patients who have diabetes.

Calcium, Phosphate, and Vitamin D Metabolism

The first signs of impaired calcium (Ca) and phosphate (P) homeostasis arise early in renal impairment (CKD 2) as parathyroid hormone (PTH) levels start to rise. This is due to phosphate retention and impaired hydroxylation (activation) of vitamin D, which results in reduced absorption of Ca from food in the small intestine. The ensuing hypocalcaemia stimulates an increased release of PTH, which, in an attempt to normalise plasma calcium levels, releases calcium and phosphate from the bone (eventually causing weakened bones). As renal disease progresses the release of calcium and phosphate from the bone and reduced excretion of phosphate in the urine leads to hyperphosphataemia.

Monitoring of calcium, phosphorus, PTH, calcidiol (25OH vitamin D), and alkaline phosphatase (ALP) is recommended from CKD stage 3b (progressive) (Steddon and Sharples 2015). Treatment can include the use of: calcium supplements, vitamin D (including activated forms, alfacalcidol, and calcitriol), calcimimetics, dietary phosphate restriction, and phosphate binders or transport blockers (Sexton and Vincent 2004). The NICE guidelines CG157 (2013) recommend that a specialist renal dietitian should carry out a dietary assessment and give individualised information and advice on dietary phosphate management.

Calcium supplements

The recommended daily calcium intake for predialysis patients is 1000–1500 mg. If this is not being reached (particularly if protein intake is low), calcium supplements may be needed but should be taken in between meals, preferably at bedtime, to maximise calcium absorption.

‘Active’ vitamin D

Vitamin D is a fat-soluble vitamin and is obtained from a small number of foods but mostly from exposure to sunlight (this may be reduced in the elderly and certain ethnic groups). It needs to be converted to an active form by hydroxylation in the liver and kidney. The use of active forms of vitamin D, alfacalcidol, and calcitriol can be troublesome. On the one hand, they reduce PTH levels (which will reduce the negative effects on bone) but, simultaneously, calcium and phosphate absorption from the gut increases, which can lead to hypercalcaemia and hyperphosphataemia if not monitored closely. The precipitation of this excess calcium and phosphate in the soft tissues (blood vessels, coronary arteries, and aortic valves), is considered to be one of the major causes of morbidity and mortality in adults, particularly young adults, with renal failure.

Steddon and Sharples (2015) recommend measuring calcidiol levels from stage 3b and supplementing if levels show insufficiency ($<75 \text{ nmol l}^{-1}$). As vitamin D has many metabolic roles, there is a strong rationale for ensuring adequate levels of this hormone, not simply to normalise bone metabolism (Armas and Heaney 2011).

Dietary phosphate reduction

The RA has advised that 'patients need dietary advice to reduce dietary phosphate'. Although the optimal time to start a reduction in phosphate intake/commence phosphate binders has not been established, the KDIGO (2017) guidelines recommend:

In patients with CKD G3a–G5D, we suggest limiting dietary phosphate intake in the treatment of hyperphosphatemia alone or in combination with other treatments. It is reasonable to consider phosphate source (e.g. animal, vegetable, additives) in making dietary recommendations.

The older K/DOQI guidelines (2003b) recommend specific intakes of phosphorus such that:

Dietary phosphorus should be restricted to 800 to 1,000 mg/day (adjusted for dietary protein needs) when the serum phosphorus levels are elevated (1.49 mmol/l (>4.6 mg/dL)) at Stages 3 and 4 of CKD, and >1.78 mmol/l (5.5 mg/dL) in those with kidney failure (Stage 5).

UK guidelines suggest maintaining serum phosphate between 0.9 and 1.5 mmol l⁻¹ and calcium should be within the normal reference range in Stages 3b to 5 CKD.

Calcium and phosphate are obtained from most foods with high protein content. Examples are milk and its products: cheese and yoghurt. Phosphorus also appears in high-fibre cereal products, fish with edible bones, offal, pulses, and nuts. Absorption from the gastrointestinal tract varies between 30 and 80%, and phosphorus from vegetable sources is less bioavailable.

Appendix 13.D shows high-phosphorus foods, not all of which have alternatives with comparable nutrient content, and therefore total elimination from the diet is not feasible. Recently, more attention has been paid to phosphate-containing food additives (Benini et al. 2011) and current dietary information needs to be modified in order to take into account not just phosphate content but also bioavailability. Hyperphosphataemia is difficult to control by dietary manipulation alone and needs to be combined with phosphate binders. A moderate protein reduction will also tend to reduce phosphate intake which is one of the arguments in favour of a protein reduction in the predialysis population. However, the impact on other nutrients must always be considered. For example, wholemeal products contain more phosphorus as well as more fibre, yet fibre also improves bowel habits and the general well-being of patients. Serum phosphate levels may rise (by 0.25 mmol l⁻¹) with a high-fibre diet, however, the benefits of a high fibre intake outweigh the risk of hyperphosphataemia and if necessary, phosphate binding agents can be increased.

Phosphate binders

Phosphate binding occurs in the stomach and small intestine and reduces the absorption of phosphate into the body. If calcium and aluminium salts are used as oral binders, these initially dissolve in the acid environment of the stomach and then form an insoluble precipitate with phosphate. This product is eliminated via the gastrointestinal route (not the kidneys). However, a high gastric pH (i.e. less acidic), found generally in the elderly and particularly in people taking H₂-receptor antagonists such as ranitidine, can reduce the effectiveness of the binders and hyperphosphataemia can result.

Phosphate binders should be taken with food, particularly main meals and snacks containing phosphate, and with milk-based nutritional supplements. Ideally, the dose of the binder should be altered to reflect the phosphate content in a particular meal.

Both the calcium and aluminium in the binder are absorbed to some extent and this has given rise to worries about aluminium toxicity and calcium overload, with many recent guidelines suggesting that use of calcium-based binders should be restricted (KDIGO 2017). More recently developed phosphate binders such as sevelamer hydrochloride (Renagel), lanthanum carbonate, and iron-based binders do not contain calcium or aluminium and sevelamer has an added benefit in that it also binds cholesterol. Calcimimetic agents are recommended for use in patients with hyperparathyroidism and control of calcium and phosphate in Stage 5 CKD (Steddon and Sharples 2015).

Hyperkalaemia

Plasma potassium levels are tightly controlled in the body and, in order to maintain normal levels, 90% of potassium is usually excreted by the kidney with the remainder excreted via the gastrointestinal route. Progressive renal failure is often complicated by hyperkalaemia (plasma potassium $>5.5 \text{ mmol l}^{-1}$) and may occur when renal function has declined to a GFR of 5 ml min^{-1} despite normal urine output. Hyperkalaemia can also occur at an earlier stage when patients receive ACE inhibitors or angiotensin II receptor binders (ARBs) for blood pressure control. This can be exacerbated if combined with a high intake of potassium-rich foods and is potentially life threatening, particularly as it is not associated with physical warning signs and requires immediate treatment. Dietary and nondietary causes of hyperkalaemia should be investigated at the same time.

Examples of nondietary causes are:

- metabolic acidosis;
- increased catabolism (and conditions which cause cell destruction: rhabdomyolysis, gastrointestinal bleed);
- endocrine abnormalities;
- drugs such as potassium supplements (i.e. slow K), some laxatives, potassium-sparing diuretics, ACE inhibitors, ARBs, and nonsteroidal anti-inflammatory drugs (NSAIDs);
- constipation (and drugs that exacerbate constipation, for example iron tablets).

Dietary management

Dietary sources of potassium are listed in Appendix 13.E. A dietary intake of no more than $60\text{--}70 \text{ mmol d}^{-1}$ ($1 \text{ mmol kg}^{-1} \text{ IBW}$) is sufficient to prevent or treat hyperkalaemia in the presence of an adequate urine output or dialysis treatment. However, serum K levels, in patients who are not on dialysis and not passing much urine, taking a 50 mmol potassium diet, can rise by 1 mmol d^{-1} despite gastrointestinal adaptation to increase potassium excretion.

Most foods contain potassium, but vegetables and fruits are major sources; some varieties contain more than others. Staple foods such as potatoes, yam, sweet potatoes, green bananas, and plantain are high in potassium, but should be included in a potassium-reduced diet. Potassium-containing salts such as dipotassium phosphate, are used as food additives but in small quantities. Of greater concern is the use of KCl as a substitute for sodium chloride as part of the food manufacturers' attempt to reduce the sodium content of food.

Patients should receive dietary advice regarding the potassium content of specific foods, avoiding or at least limiting the quantities eaten of those that are high. Cooking techniques such as boiling (and throwing away the water) will remove some of the potassium in vegetables. Cooking methods which *retain* potassium include cooking in a pressure cooker or microwave, stir-frying, roasting, and casseroles of vegetables.

Potassium and high-fibre foods

Constipation is a common problem for patients receiving PD, older, and sedentary patients. High-fibre cereal products are recommended to prevent constipation and can have a beneficial effect on hyperlipidaemia. Some high-fibre foods are high in potassium, although studies have shown that the overall effect of a high fibre diet on serum potassium was not significant – increasing serum potassium levels by about 0.3 mmol l^{-1} (Sutton et al. 2014).

Potassium exchange resins

Potassium binders such as calcium or sodium ion-exchange resin (i.e. calcium or sodium resonium) may be used to control hyperkalaemia. Calcium resonium is a gritty textured powder and is best taken with a sweet drink to mask its taste. Calcium ions (or sodium) are exchanged for potassium ions in the gut and the potassium is then eliminated. The long-term use of calcium resonium can lead to severe constipation (unless appropriate laxatives are prescribed) and is therefore not used for routine control of plasma potassium levels.

Anaemia

Anaemia due to renal impairment can be diagnosed when $\text{GFR} < 45 \text{ ml min}^{-1}$, i.e. CKD stage 3b, although it is more prevalent in stage 4 CKD (Mikhail et al. 2010). It can impact on general nutritional status by causing general lethargy, taste changes, and a poor appetite, hence it is always worth checking the patient's haemoglobin and ferritin levels if they present with these symptoms. Anaemia is also involved in the pathogenesis of left ventricular hypertrophy (LVH) and therefore increases the risk of CVD. A serum ferritin of $< 100 \text{ ng ml}^{-1}$ or a transferrin saturation of $< 20\%$ indicates relative iron deficiency. It is important to ensure an adequate intake of iron, B_{12} , and folate. Vitamins B_6 and C also have important roles in erythropoiesis. The consumption of foods which are high in iron, such as red meat, offal, and pulses may be reduced in a renal diet, particularly if protein- or phosphate-restricted diets have been prescribed. A potassium-lowering diet may result in decreased iron, folate, and vitamin C intakes.

If oral iron (Fe) supplements are used, $200\text{--}300 \text{ mg Fe day}^{-1}$ is required to restore iron status. These can cause side effects such as constipation and black stools. They can also interact with other medication such as the calcium-containing phosphate binders. In order to obtain a rapid improvement in iron status, intravenous preparations are more often used (NICE Guideline NG 8 2013).

Acidosis

Metabolic acidosis is a feature of CKD and has a detrimental effect on muscle and bone metabolism. Recent guidelines suggest that bicarbonate levels are normalised using oral sodium bicarbonate (KDIGO 2012; NICE 2014), CARI guidelines note that in early CKD, a balanced diet rich in fruit and vegetables (alkaline producing) can be beneficial.

Malnutrition

Irrespective of whether a therapeutic diet is recommended to treat any of the other problems listed above, all patients at CKD stages 4 and 5 should receive a dietary assessment and be screened for malnutrition (Campbell 2013). A patient with poor nutritional status at the start of dialysis will have a poor outcome in terms of survival and therefore it is important to prevent malnutrition from occurring at the outset.

Regular dietary follow-up in clinic or by telephone should help to maintain optimal nutritional status by ensuring that a balanced diet is being achieved, i.e. one that contains adequate macronutrients (protein, fat, carbohydrate) and micronutrients (vitamins and minerals). If specific dietary reductions are advocated, it is important that the impact of these reductions on the intake of other nutrients, as well as the social effects, are fully evaluated. The diet should provide sufficient dietary freedom and enable the patient to lead a near-normal life. This means that dietary flexibility must be incorporated and appropriate carers, relatives, or friends should be involved whilst educating the patient to promote maximum dietary adherence.

Nutritional assessment

A full nutritional assessment includes collection of information from these six main categories:

- anthropometry: circumferences; mid-arm circumference (MAC), Mid-arm muscle circumference (MAMC), waist and hip; BIA (bioelectrical impedance analysis), Dual-energy X-ray absorptiometry (DEXA);
- biochemistry: Urea, creatinine, electrolytes, haemoglobin (Hb), and micronutrient screen;
- clinical; comorbidities, medication;
- dietary intake, and an estimation of requirements;
- environment: social circumstances, health, and religious beliefs;
- function: physical function, activity levels; sit to stand, grip strength.

RA guidelines recommend that patients with a GFR $<20 \text{ ml min}^{-1}$ who are not on dialysis, should have a nutritional assessment every two to three months.

Body composition changes

The K/DOQI (2003a) guidelines have indicated the need for more information regarding 'the appropriate parameters to be used for assessment of body composition'. Nonetheless, simple 'bedside' measurements can indicate a decline in nutritional status as long as oedema and signs of fluid overload are identified. These include actual BW (in comparison with IBW), weight loss of 5% in three months, and BMI $<20 \text{ kg m}^{-2}$ (Wright and Jones 2011). These authors of the RA guideline 'Nutrition in CKD' also recommend use of the Subjective Global Assessment (SGA), where a grading of B/C on a three-point scale or a score of 1–5 on the 7-point scale indicate declining status.

Insufficient energy intake will lead to protein catabolism, which may present as muscle wasting. This can be detected using hand grip strength and other measures of physical function (sit to stand, shuttle test). MAMC can be estimated from measurements of MAC and triceps skinfold. Conditions that exacerbate protein/muscle loss include sarcopenia (muscle loss due to ageing), inflammation, acidosis, and lack of activity/exercise. Blood biochemistry may indicate whether there is inflammation

(raised CRP, low albumin, raised white cell count) or acidosis (low bicarbonate levels) and if present, appropriate treatment should commence. There is growing evidence that low vitamin D levels and raised PTH are determinants of sarcopenia. Visser et al. (2003) and Wright and Jones (2011) suggested that supplementation of ergocalciferol or cholecalciferol may be beneficial in undernourished CKD patients.

Where there is an energy deficit, fat stores will also be used to provide energy. This initially may not be a problem, particularly if the patient is obese and can therefore mobilise these excess stores. The advantages of not having excess body fat include a decreased risk of CVD, hypertension, and diabetes. Formation of a fistula or insertion of a Tenckhoff catheter is also more difficult in patients who are overweight or obese. However, fat is used to insulate the body, to provide cushioning for bones, and to provide an energy source when food intake is poor. Recent evidence has shown that whereas being underweight increases mortality in patients on dialysis, being overweight may actually confer some advantage, at least in the first few years of dialysis (Friedman 2006). This is reflected in the K/DOQI guidelines (2003a) that have stated that a BMI of up to 28 kg m^{-2} is acceptable. The UK RA guidelines (now archived) recommend that patients with a $\text{BMI} > 30 \text{ kg m}^{-2}$ should receive advice to assist weight loss (MacGregor and Taal 2011).

Nutritional requirements

Protein

Protein is an important nutrient for the repair and maintenance of tissue and for growth.

Quantity The level of dietary protein intake should maintain nitrogen balance (in a well-nourished adult) or be sufficient for growth (in children) and repair (in patients recovering from malnutrition or illness). For instance, if a patient consumes a high protein diet ($> 1.2 \text{ g kg}^{-1} \text{ IBW}$), a reduction to $1.0 \text{ g kg}^{-1} \text{ IBW}$ may initially be sufficient, which can be reduced to $0.8 \text{ g kg}^{-1} \text{ IBW}$ if renal function deteriorates at a later stage. This is an acceptable protein allowance for long-term use and it meets the maintenance requirement of 0.66 g kg^{-1} advised by WHO/FAO. The archived RA guideline 'Nutrition in CKD' (Wright and Jones 2011) recommended that a protein intake of no less than 0.75 g kg^{-1} is realistic and required an energy intake of $35 \text{ kcal kg}^{-1} \text{ day}^{-1}$ to prevent malnutrition and the more recent NICE guidelines CG187 (2014) do not support an intake below $0.8 \text{ g kg}^{-1} \text{ day}^{-1}$.

Quality The quality of protein is affected by its digestibility and amino-acid content. Meat, fish, eggs, milk, and soy protein are usually referred to as containing HBV protein because of the levels of essential amino acids when compared with a reference protein. Proteins from plant sources (cereals, vegetables, pulses, and nuts) may be limited in lysine, threonine, methionine, and cysteine and have poorer digestibility. Despite this, the amino acid content of a UK vegetarian diet is comparable with UK omnivores. Rice-based vegetarian diets have poorer amino acid content (compared with wheat-based diets) as well as lower digestibility. In order to ensure that a reduced-protein diet contains adequate levels of all the amino acids, it is particularly important for vegetarians to have proteins from a variety of sources including cereals, pulses, and legumes.

Energy

Protein, fat, carbohydrate, and alcohol all contribute to a person's energy intake.

Quantity Example: to calculate energy requirements for a 70 kg person (IBW):

$$70 \times 30 - 35 \text{ kcal} (126 - 150 \text{ kJ}) = 2100 - 2450 \text{ kcal} (8.8 - 10.3 \text{ MJ})$$

The range of energy requirements, 30–35 kcal kg⁻¹, is similar to the result obtained using the Schofield equations for basal metabolic rate and assumes a physical activity level of 1.3–1.4, which is low (Todorovic and Micklewright 2007). Patients with increased metabolism due to infection, injury, or increased activity levels should have their requirements calculated using equations such as Schofield or Oxford with appropriate factors added for metabolic stress and activity levels.

Quality The quality of foods providing energy is as important as the quantity. CVD and some cancers are associated with a high proportion of saturated fat in the diet. Hypertriglyceridaemia (common in patients with renal disease) is associated with high intakes of rapidly absorbable carbohydrates and alcohol. If a protein reduction has been advised, there has to be an increase in calories to make up the deficit. This could take the form of monounsaturated fat (olive oil) and carbohydrates with a medium to low glycaemic index (pasta, basmati rice, new boiled potatoes, some fruits).

Micronutrients: vitamins and minerals

Vitamins and minerals regulate metabolic pathways and some of the most observable clinical features of uraemia (anaemia and renal bone disease) are caused, or at least exacerbated, by vitamin and mineral deficiencies. Metabolism of protein, carbohydrate, and fat will be affected by deficiencies of vitamins and minerals. These can arise because uraemia alters their serum levels and body stores and also interferes with their function. Drug interactions can affect the absorption and utilisation of minerals (such as calcium, iron, zinc, and magnesium) and vitamins (such as B₆, folate, and B₁₂) (Jankowska et al. 2017).

Requirements for these three vitamins may be higher in renal disease in order to treat hyperhomocysteinaemia, which is a risk factor for CVD. Dietary reductions that limit protein, phosphate, and potassium intake will inevitably limit the intake of various micronutrients. A low-protein diet can contain low levels of B vitamins (B₁, B₂, B₆, B₁₂), iron, calcium, and zinc (Hadfield 1992). A low-potassium diet will limit intake of folic acid, vitamins C and E, as well as phytochemicals such as fructo-oligosaccharides, phytosterols, and polyphenols. A review by Steiber and Kopple (2011) found that vitamin deficiencies (particularly B₁ and B₆) in CKD stages 3–5 were common, with intake of other B vitamins decreasing with lower protein intake.

However, there may be reduced renal losses of some nutrients. Vitamin supplements containing the fat-soluble vitamins A and E are contraindicated in patients with renal disease. Vitamin A metabolites are less well excreted and accumulate over time; toxicity has been reported in patients receiving total parenteral nutrition containing a high dose of vitamin A. High-dose vitamin E supplementation may potentially disrupt the clotting mechanisms. A more recent literature review cited articles that found evidence of vitamin deficiency in 60–97% of patients with CKD 3–5 and recommended ensuring that people at least meet the recommended nutrient intake which, in the United Kingdom, is 1 µg kg⁻¹ day⁻¹ (Steiber and Kopple 2011). It is recommended that vitamin and mineral status should be included in the nutritional assessment.

Prevention and treatment of malnutrition should be started during the predialysis phase. Many renal departments hold multidisciplinary education sessions for patients to provide information on treatment options, diet, and support from social services. Ideally an expert patient, a specialist renal nurse, dietitian, social worker, and consultant should be involved in the sessions, with access to a counsellor if available. All patients should also receive individual dietary advice, and frequent monitoring is essential to accommodate any changes in renal function.

Nephrotic Syndrome

Nephrotic syndrome (NS) is characterised by proteinuria $>3 \text{ g day}^{-1}$, which results in hypoalbuminaemia and generalised oedema. Hyperlipidaemia, clotting problems, and hypertension are also present. Loss of immunoglobulins and proteins that bind iron, copper, zinc, and vitamins A and D can result in an increased risk of infections and general malnutrition. The syndrome can arise in diseases that primarily cause glomerular damage such as focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), and minimal change nephropathy (MCN) or secondary to other diseases, including diabetic nephropathy and autoimmune disease such as systemic lupus erythematosus (SLE). Treatment aims to control oedema, reduce proteinuria, and treat complications which arise including infections, hyperlipidaemia, and clotting problems. Diet therapy has a role to play in several of these areas (Table 13.2).

Protein reduction

Historically, in NS, a high-protein diet was advised with the aim of replacing protein losses. This is now thought to cause further damage to the glomerular basement membrane and exacerbate the proteinuria. An intake of $0.8\text{--}1 \text{ g protein kg}^{-1} \text{ IBW day}^{-1}$ is now recommended. This can result in reduced proteinuria, and improvements in other biochemical parameters such as, phosphate, lipid, renin, and fibrinogen levels (thromboembolism is increased in NS: 10–30% of adult patients with NS may develop clotting problems). Not all studies have shown a corresponding increase in plasma albumin levels.

Hyperlipidaemia

The incidence of myocardial infarction has been reported as five to six times greater in NS compared with normal. Increased liver synthesis of lipoproteins and impaired metabolism of triglycerides results in raised triglycerides and cholesterol. Standard lipid lowering advice can be given as well as the use of lipid lowering agents such as 5-hydroxy-methyl-glutaryl-coenzyme A (HMG-CoA) reductase inhibitors (statins) and bile acid sequestrers.

Table 13.2 Management of nephrotic syndrome (NS).

Symptom	Dietary management
Hypertension and oedema	Dietary sodium reduction: $80\text{--}100 \text{ mmol day}^{-1}$. Fluid reductions may also be necessary, depending on the response to medication. Target weight loss $0.5\text{--}1 \text{ kg day}^{-1}$. ACE inhibitors commonly used (monitor potassium levels).
Proteinuria/hypoalbuminaemia	Moderate protein reduction: $0.8\text{--}1 \text{ g kg}^{-1} \text{ IBW day}^{-1}$. Good control of blood glucose in diabetes. Medication can include steroids to treat the primary disease. ACE inhibitors also help to reduce proteinuria (monitor potassium levels).
Hyperlipidaemia	Standard lipid lowering advice; 30% calories from fat. Statins and bile acid sequestrants.
Lower immunity	A balanced, nutritious diet will help prevent protein–energy malnutrition (PEM) and maintain micronutrient levels: monitor for signs of vitamin D deficiency and anaemia.

Dietary Management: Dialysis

Historical review

Since the early 1990s, considerable progress has been made regarding modes and quality of treatment. Regular HD became available from the mid-1960s onwards when patients were initially selected for treatment, so were usually young and free from concomitant disease. Dietary management was aimed at controlling the patient's fluid balance and biochemistry. During these early days of dialysis, a strict diet (by present standards) was followed by many patients, which consisted of a daily intake of: 50 g protein, 50 mmol sodium, 50 mmol potassium, 3500 kcal, and 300 ml fluid.

As the quality of dialysis treatment improved during the 1970 and 1980s, dietary reductions were relaxed to a daily intake of 60 g protein, 60 mmol sodium, 60 mmol potassium, 2500–3000 kcal, and 300–500 ml fluid. Even this slightly more generous HD diet was nutritionally incomplete without the use of high-energy, low-electrolyte supplements and several books were published during the following years to promote dietary education (Vennegoor 1992).

During the early 1980s CAPD (continuous ambulatory peritoneal dialysis) became established as a new chronic dialysis technique, although it had been used since the 1960s for patients who were haemodynamically too unstable for HD. By the mid-1980s, the diet for both HD and PD was similar to that prescribed today: 1–1.2 g protein kg IBW⁻¹ day⁻¹ for HD and 1.2–1.5 g protein kg IBW⁻¹ day⁻¹ for PD (Vennegoor 1992).

Current concepts of dialysis dietary management

Specific dietary requirements will need adjusting when the mode of therapy (HD, PD, or transplantation) commences or changes. Current recommendations for dietary requirements are shown in Table 13.3.

Protein

During HD approximately 6–12 g of amino acids are lost per session. For PD, 8–12 g protein, in addition to 3 g amino acids, are lost per day. On the basis of these figures alone the additional dietary protein required to replace these losses can be calculated as 0.1 g kg⁻¹ day⁻¹ for patients on HD and 0.2 g kg⁻¹ day⁻¹ for patients on PD. Some authors have argued that, as the minimum safe protein intake for healthy individuals (and in the predialysis phase) is approximately 0.75 g kg⁻¹ day⁻¹, the recommended minimum intake on dialysis should be as follows: 0.9 g kg⁻¹ day⁻¹ for HD and 1 g kg⁻¹ day⁻¹ for PD. These are slightly lower levels than that recorded in Table 13.2 and, for *some* patients who are metabolically stable (i.e. not catabolic) nitrogen balance studies have shown that intakes at this level can be sufficient. As with any patient, in order to ensure that they are not becoming malnourished, it is important to measure nutritional status using a number of different methods such as those used in SGA (McCann 1996). See Appendix 13.B.

Energy requirements

An intake of 35 kcal kg⁻¹ IBW is recommended to maintain nitrogen (protein) balance in patients on HD and PD. For sedentary and older patients, 30–35 kcal kg⁻¹ IBW is sufficient. Underweight patients may need additional calories (and supporting micronutrients) to encourage weight gain, whilst overweight patients may need

Table 13.3 Dietary recommendations for patients on renal replacement therapy (RRT).

	HD	PD	TXP
Protein (g kg ⁻¹ IBW)	1.0–1.2(1.1–1.4) ^a	1.0–1.2	EAR
Energy (kcal kg ⁻¹ IBW)	30–35	30–35	EAR
Na (mmol day ⁻¹) ^b	80–100	80–100	80–110
K (mmol kg ⁻¹ IBW)	1.0	1.0–1.3	Free
P (mmol day ⁻¹) ^c	31–45(26–32)	31–45 (26–32)	Free
Vitamins	Yes	Yes	Not required
Phosphate binders	Yes	Yes	Not required

Notes: HD, haemodialysis; PD, peritoneal dialysis; TXP, transplantation; IBW, ideal body weight; EAR, estimated average recommendations (national agreement).
^aProtein and energy intake for HD and PD based on Renal Association guidelines (Wright and Jones 2011) and (Naylor et al. 2013).
^b80–110 mmol equals 1800–2500 mg sodium.
^cadjusting for protein requirement, i.e. 0.32–0.6 mmol phosphate g⁻¹ protein.
Source: Sodium, potassium and phosphorus intake for HD and PD based on EDTNA/ERCA and EBPG nutritional guidelines.

a calorie adjustment to encourage weight loss if appropriate (Todorovic and Micklewright 2007; Wright and Jones 2011).

Dextrose (glucose) is used as an osmotic agent in PD for the removal of fluid. Up to 70% of this glucose is absorbed through the peritoneum and this can exacerbate hyperglycaemia, hyperlipidaemia, and obesity. The amount of glucose absorbed increases as the osmotic strength of the dialysate increases. When calculating energy requirements for patients on PD, the glucose (and hence calories) absorbed from the dialysate needs to be included in the calculation. Glucose absorption may provide approximately 70 kcal for a 2l 1.36% exchange, 130 kcal for a 2l 2.5% exchange and 200 kcal for a 2l 3.86% exchange. Daily intake from this source could be between 100 and 300 g glucose (400–1200 kcal), depending on the strength and size of the exchanges used and may be one of the factors that leads to an increase in central obesity and associated metabolic changes in PD patients. Recent PD guidelines discourage the use of the higher glucose solutions and suggest the use of glucose polymers or amino acid-containing solutions (Woodrow et al. 2017). Icodextrin is a PD solution which contains glucose polymers with a larger molecular weight than glucose and is an effective osmotic agent. The calorie uptake is only half that of a comparable 3.86% exchange whilst achieving the same level of ultrafiltration. Some improvements in glycaemic control have been measured in patients who have diabetes, using one icodextrin exchange per day. See Chapter 9 for more information.

Sodium and fluid

Once a patient becomes oliguric and eventually anuric, the intake of salt and fluid will need to be reduced to control interdialytic weight gain (IDWG) with HD and fluid balance with PD. Excessive IDWG in patients on HD contributes to hypertension prior to HD treatments, necessitating antihypertensive medication.

A reduced fluid allowance is probably the most difficult part of the dialysis diet to cope with. Up to 86% of patients may exceed an IDWG guideline of 1.5 kg day⁻¹ and there appears to be no difference between those who have diabetes and those who do not. Some groups of patients with different ethnic backgrounds appear to have additional problems with IDWG. Indo-Asian patients in particular may often

be unable to adhere to their fluid allowances and this is attributed to a higher fluid and salt content of traditional foods and meals (de Brito-Ashurst et al. 2011).

Most renal centres in the United Kingdom regard an IDWG ranging from 1.5 to 2.0 kg as acceptable. Considering the differences in size of patients, it may be more appropriate to base IDWG on dry weight using 4–4.5% as an acceptable IDWG (European Best Practice Guidelines, EBPG 2007). However, an upper limit is recommended for patients with BMI > 25 kg m⁻².

Sodium intake: the mechanism of thirst

It is important to remember what causes thirst. The sodium level in the body is finely tuned in healthy individuals as well as those with kidney disease. Too much dietary salt will cause the plasma sodium level to rise (transiently) and the thirst mechanism in the brain to act. It is then necessary to drink sufficient fluid to normalise the sodium level.

A sodium intake of 80–110 mmol day⁻¹ can help control thirst. This can be achieved by following the advice listed in the earlier section on hypertension.

Excessive IDWG may not always be due to poor understanding of dietary advice. Even 'solid' food contains some fluid and patients with a good appetite will have higher IDWG; this can be established with a detailed dietary assessment, indicating a high protein and energy intake.

Fluid includes anything liquid at room temperature (apart from vegetable oils) and also includes jelly, ice cream, ice cubes, gravy, soups, sauces, and custard. A daily fluid allowance of 500–750 ml in addition to the average daily urine output is usually sufficient to prevent excess IDWG in patients on HD. Patients undergoing PD can usually increase their intake to at least 750 ml plus average daily urine output. This amount may be modified depending on the level of ultrafiltration which is achieved with the lower strength exchanges of PD fluid. The following additional tips can help the patient keep to their fluid allowance:

- measure the daily fluid allowance in a water jug: take out the equivalent amount after having a drink or if food with a significant amount of fluid is eaten.
- divide the fluid allowance throughout the day.
- use a small cup or glass instead of a mug or large glass.
- drink only half a cup each time if possible.
- ice cubes may be more thirst quenching, but each cube contains 30 ml fluid (two tablespoons): lemon juice or other flavourings can be added.
- rinse the mouth with water; gargle but do not swallow.
- stimulate saliva production by sucking a piece of lemon or grapefruit, sherbets, or chewing gum.
- try artificial saliva sprays.
- take medicines with meals unless contraindicated.
- when going out, save the allowance of fluid to allow for an extra drink when socialising.
- a daily weight check in the morning before breakfast will reveal the rate of fluid accumulation in between HD treatments and the fluid status on PD.

Potassium

Some patients starting dialysis continue to produce fairly good quantities of urine. This helps to some extent with the excretion of sodium, potassium, and, of course, fluid. However, the urine is often described as 'poor quality' in that the level of these solutes are lower than usual and plasma potassium levels should be monitored closely. The risk of hyperkalaemia is greater in patients who do not pass urine. The

dietary intake of potassium should be reduced to approximately $1 \text{ mmol kg}^{-1} \text{ IBW}^{-1} \text{ day}^{-1}$ for patients on HD. Hyperkalaemia can be a frequent problem, especially on HD, and dietary indiscretion is sometimes partly to blame, although the amount of potassium removed during dialysis can vary by as much as 70%. Patients on PD may have a more relaxed dietary potassium reduction, as potassium is constantly removed with PD and hypokalaemia has even been observed.

A detailed diet history should be taken for all patients so that the main sources of potassium in the patient's diet are known and the level of reduction and dietary advice given is based on a risk assessment of their usual dietary intake, urine output, and plasma potassium levels. Other reasons for hyperkalaemia should be investigated simultaneously as previously described. Some patients on HD consume foods with high potassium content during the first couple of hours on dialysis. However, the transit of food and fluid through the gastrointestinal tract may be slower whilst the patient is dialysing and so it is advisable to put a limit on this consumption as the potassium may not be completely removed.

Phosphorus

The recommended intake varies from 1000 to 1400 mg ($31\text{--}45 \text{ mmol day}^{-1}$), or approximately $0.5\text{--}0.6 \text{ mmol}$ phosphorus per gram of protein up to 45 mmol day^{-1} . However, some guidelines (EBPG 2007) are stricter than the previous nutritional guidelines as they suggest a maximum of 0.4 mmol phosphorus per gram of protein per day. It is recognised that with higher protein recommendations the phosphorus intake also increases, and there has to be a balance between reductions which prevent hyperphosphataemia and preserving an adequate and acceptable diet for the patient to follow (Lynch et al. 2011). Close collaboration of the multidisciplinary team is required to prevent hyperphosphataemia. A combination of achieving an adequate dialysis prescription, phosphate binders which are acceptable to the patient and taken at the right dose at the right time, and clear dietary messages have been shown to improve phosphate biochemistry (Yokum et al. 2008; Caldeira et al. 2011; Gonzalez-Parra et al. 2012) although long-term improvements on mineral and bone disorders require larger, well-designed RCTs (randomised controlled trials) (Liu et al. 2015). For patients receiving dialysis phosphate levels should be maintained between 1.1 and 1.7 mmol l^{-1} .

Vitamins and minerals

During dialysis the small molecules, such as water-soluble vitamins, are removed; losses are even higher with high flux HD. The fat-soluble vitamin A is a larger molecule and vitamin A metabolites are therefore more difficult to remove and could lead to toxicity. However, with a functioning kidney there are also vitamin losses and so the question is whether dialysis removes greater amounts of vitamins than would normally occur. Evidence of vitamins at risk includes thiamin (B_1) in PD patients, pyridoxine (B_6) and ascorbic acid (vitamin C) in PD and HD, and folate in HD (Jankowska et al. 2017). To reduce cardiovascular risk, UK RA guidelines recommend monitoring folate and B_{12} every three months if patients remain anaemic. Ascorbic acid is easily dialysed in both HD and PD. A high-dose vitamin C supplement should be avoided to prevent hyperoxalosis; 60 mg may be sufficient with a normal dietary vitamin C intake, while a supplement of 500 mg vitamin C may increase serum oxalate levels. Oxalate deposits as crystals in soft tissues such as muscle tissue and vital organs, and may increase the risk of myocardial infarction, muscle weakness, and bone disease.

Table 13.4 Suggested daily dosage of vitamins for patients with ERF (EBPG and UK guidelines).

Vitamins	EBPG	RNI (UK)
Vitamin A	0	600–700 µg
Vitamin E	400–800 (0) iu	no DRV given
Vitamin B ₁	1.1–1.2 (1.5) mg	0.8–1 mg
Vitamin B ₂	1.1–1.3 (1.7) mg	1.1–1.3 mg
Vitamin B ₆	10 (10) mg	1.2–1.4 mg
Vitamin B ₁₂	2.4 (6) µg	1.5 µg
Folic acid	1000 (800–1000) µg	200 µg
Pantothenic acid	5 (10) mg	no DRV given
Niacin	14–16 (20) mg	13–17 mg
Biotin	30 (300) µg	>10 µg
Vitamin C	75–90 (60) mg	40 mg

Notes: RNI, recommended daily intake. Dietary reference values (DRV) for food energy and nutrients for the United Kingdom.

The results of the Dialysis Outcomes and Practice Patterns Study (DOPPS) showed that water-soluble vitamin supplementation is associated with a 15% decrease in mortality (Fissell et al. 2004). At the time of the study only 3.4% of patients from the UK renal units were receiving water-soluble vitamins compared with 72% in the US. This has had an impact on the UK guidelines, which now recommend water-soluble vitamins for those undergoing HD (Wright and Jones 2011), and there seems to be a greater awareness and use of water-soluble vitamins on UK renal units (Hunt 2011). Table 13.4 lists the suggested daily recommendations in the United Kingdom and Europe (EBPG 2007).

Early reviews identified that deficiencies of iron, zinc, copper, manganese, and chromium are most likely to occur as a result of dietary restrictions, drug nutrient interactions, and protein losses (Wolk 1993; Rocco and Makoff 1997). Iron may need to be supplemented to maintain ferritin levels above 100 ngml⁻¹. The EBPG guidelines (EBPG 2007) do not recommend routine zinc or selenium supplements but note that if symptoms of these deficiencies are detected (including thyroid dysfunction due to low selenium) then a three- to six-month trial is warranted. A more recent review of trace element deficiency in patients on HD identified 128 studies and concluded that levels of zinc, selenium, and manganese were lower than control groups. They highlighted an association between zinc deficiency and increased risk of infection which requires further investigation in the renal population (Tonelli et al. 2009).

Malnutrition

Malnutrition is a complication of HD and PD and its consequences have been well documented since these techniques became available (Carrero et al. 2013; Ikizler et al. 2013). Effects of malnutrition are:

- failure to thrive;
- increased morbidity;

- delayed wound healing;
- decreased resistance to infection;
- electrolyte imbalance;
- prolonged hospitalisation;
- muscle wasting (skeletal muscle as well as heart/lung, etc.);
- loss of protective subcutaneous fat;
- lethargy/apathy;
- increased mortality.

Causes of malnutrition

There are several overarching reasons for malnutrition in patients on dialysis and these are multifactorial in origin:

- reduced dietary intake:
 - reduced appetite;
 - existing malnutrition at the start of dialysis due to uraemia or unsupervised predialysis dietary restriction;
 - conflicting dietary recommendations, e.g. increasing protein whilst decreasing the intake of phosphorus;
 - dietary recommendations which decrease palatability of food: decreased salt intake, decreased fat or sugar intake;
 - coexisting gastrointestinal disease (i.e. gastroparesis) or other comorbidities such as cardiac failure, cancer, stroke;
 - multipharmacy prescriptions;
 - inadequate provision of nutrients in food provided by hospitals or nursing homes;
 - financial constraints;
 - decreased physical ability (shopping, cooking);
- reduced appetite;
 - raised cytokines; TNF α ;
 - inadequate dialysis leading to uraemia;
 - suppression of appetite due to PD; this may be due to glucose absorption, abdominal pressure from the dialysate fluid, or constipation;
 - anaemia or other micronutrient deficiencies; zinc, B vitamins;
 - old age; taste, sight changes;
 - depression;
- increased nutritional losses;
 - losses during dialysis: vitamins, minerals, proteins, and amino acids;
 - persistent proteinuria;
 - protein loss during peritonitis;
 - altered metabolism;
 - inflammatory response as a result of the dialysis process; the presence of inflammatory cytokines results in appetite loss, muscle breakdown, and low albumin;
 - untreated acidosis: muscle and bone metabolism is impaired;
 - inadequate dialysis: buildup of waste products and cytokines;
 - low physical activity: low anabolic stimulation of muscle and bone;
 - intercurrent illness/infections, causing raised requirements, increased cytokines;
 - hyperparathyroidism: muscle and bone metabolism is impaired;
 - resistance to insulin, growth hormone, and insulin-like growth factor;
 - low 'active' vitamin D: muscle and bone metabolism is impaired.

Comorbidities and drug nutrient interactions also have an impact on all of these four main points.

Detection of malnutrition

As discussed, the detection of malnutrition should involve monitoring a number of components: anthropometry, biochemistry, clinical, diet, and exercise/activity. Many screening tools only include two of these components. For example the Malnutrition Universal Screening Tool (MUST) incorporates anthropometry (weight, weight change) and diet. SGA includes anthropometry, clinical, diet, and exercise/activity although adapted versions have also included measurement of biochemistry (Kalantar-Zadeh et al. 2001). The Canada-USA (CANUSA) Peritoneal Dialysis Study Group showed the relative risk of death on PD increased with age, insulin-independent diabetes mellitus, CVD, low serum albumin, and worsening nutritional status. Malnutrition (identified by SGA) correlated strongly with an increase in number of days hospitalised (CANUSA Peritoneal Dialysis Study Group 1996).

Albumin has often been used as a marker for poor nutritional intake, and although it is certainly correlated with poor outcome (increased morbidity and mortality) it is probably the case that the conditions which cause a low albumin have an impact on nutrition as well as albumin, i.e. they co-correlate.

The use of different methods to determine the extent of malnutrition has led to some differences in the stated prevalence. British Association for Parenteral and Enteral Nutrition (BAPEN) (a charitable association that raises awareness of malnutrition and works to advance the nutritional care of patients) has been coordinating the use of MUST in UK hospitals. The annual audit has indicated that the prevalence of malnutrition in renal inpatients is 30%. However, using other scoring systems the prevalence has been much higher at 64–90%. The issue lies with the sensitivity and specificity of MUST. When MUST was compared with SGA in 64 patients on HD, the sensitivity was 31% and the specificity was 95%; that is, it had poor ability to detect ‘true cases’ of malnutrition (Fisher et al. 2010). In addition, MUST is a poor detector of malnutrition in liver disease which is similar to kidney disease in that it can be a long-term condition which features many metabolic changes including fluid overload (Arora et al. 2012).

Protein energy wasting

An expert working party convened by the International Society of Renal Nutrition and Metabolism (ISNMRD) has attempted to simplify the nomenclature used to describe malnutrition in renal disease (Fouque et al. 2008). The term they feel encompasses the changes indicating decreased nutritional status is ‘protein energy wasting’ (PEW). They define this as a ‘state of decreased body stores of protein and energy fuels’ which is ‘often associated with diminished functional capacity’. It includes syndromes such as MIA, but they emphasise that PEW, as can be seen from the list above, is not just due to an inflammatory component (although it is estimated that up to 50% of patients with renal disease show evidence of an ongoing inflammatory response).

Management of malnutrition

Assessing nutritional status

Whichever methods of assessment are used to assess nutritional status, they should be done regularly and systematically for all patients as physical deterioration can occur rapidly and is difficult to reverse. It is important to

identify malnutrition so early rehabilitation and improved clinical outcomes are possible. The National Institute for Health and Clinical Excellence (NICE) guidelines (National Institute for Health and Clinical Excellence 2006a), recommended that 'All hospital in-patients on admission and out-patients at first appointment should be screened for presence or risk of malnutrition'. Screening should take place weekly for inpatients, and within one month of starting dialysis for outpatients (Wright and Jones 2011). A new inpatient screening tool has recently been validated and has been shown to be reliable when used by nurses admitting patients to specialist renal wards (Jackson et al. 2018).

The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines (ESPEN 2002) have described the prerequisites of a useful assessment tool. This tool should have the following features:

- good predictive validity – the individual identified 'at risk' will benefit from intervention;
- good content validity – includes 'all' relevant components of the problem it is meant to solve;
- high reliability – small inter-observer variation;
- practical;
- linked to 'specific protocols for action';
- rapid and simple, so that it can be performed by admitting staff or community healthcare teams.

The authors of the K/DOQI guidelines recommended that further work needed to be carried in order to 'identify and validate' the optimal panel of measures for screening and assessment of nutritional status in patients with renal diseases (K/DOQI 2000). In the meantime, nutritional assessment should incorporate a number of complementary measures that at least include dietary assessment and body composition measures (Engel et al. 1995; EBPG 2007). The MUST tool (Stratton et al. 2003) and SGA contain both these elements, although the shortcomings with MUST have already been discussed. SGA has been validated for use with patients with renal diseases and is recommended by the RA guidelines (Wright and Jones 2011) and by the ISNMRD who also recommend regular nutritional screening (a minimum of every three months) of albumin, weight, BMI, malnutrition-inflammation score, and protein and energy intake (Ikizler et al. 2013).

Methods of dietary assessment

Methods of dietary assessment include:

- twenty-four-hour recall: this is quick and assesses recent intake.
- three-day food diary: can include a weekend day and one HD day and gives a better illustration of the variety of foods eaten. It may also reveal the disruption to meal times caused by a dialysis day – for HD patients significant decreases in all nutrients can occur three days out of seven.
- urea content of 24-hour urine samples in predialysis patients and urine plus dialysate collection in patients undergoing PD can be used to calculate urea nitrogen appearance. This is equivalent to dietary protein intake in nutritionally stable patients (PD dialysate collection can also be used to estimate protein losses).
- in patients on HD, changes in plasma urea measurements (collected for dialysis adequacy tests) can be used to calculate the protein catabolic rate (PCR). This is only equivalent to protein intake in patients who are nutritionally stable. Urinary urea also needs to be included in the calculation.

Techniques to Assess Body Composition

The best-known techniques are:

- height and weight (BMI), percentage weight loss over time. The minimum data set and diagnostic criteria for malnutrition recommended by the RA include: BMI < 20 kg m⁻², actual BW < 85% ideal weight, unintentional oedema-free weight loss of 5% in three months or 10% in six months.² A minimum BMI of 23 kg m⁻² is recommended (EBPG 2007).
- mid-upper arm anthropometry: MAC, tricep skinfold, MAMC. MAC is easy to perform, noninvasive, and training can reduce observer error repeatable to an acceptable degree. Skinfolds are more prone to observer error; a measure of muscle function may be a better way of assessing muscle mass (e.g. grip strength, sit-to-stand test or walking test). MAMC can be calculated from a measurement of MAC and the triceps skinfold.
- bioelectrical impedance: quick and noninvasive, but it is an indirect measure and it is influenced by hydration and electrode placement (Lindley et al. 2005). BIA measurement of phase angle may be helpful in determining hydration state. RA guidelines recommend that BIA and handgrip strength may be useful in those diagnosed at risk of or with malnutrition. A review of BIA technology by NICE also found some evidence that this technique can result in better fluid management compared to clinical judgement (NICE 2015).
- DEXA: measures bone mineral content and density. It relies on assumptions about hydration status which may not be valid in patients with renal diseases, particularly for the measurement of lean body mass. However, DEXA is expensive.

Hypoalbuminaemia

It had always been assumed that serum albumin was a reliable marker of nutritional status, however this relationship has been questioned as other causes of low albumin are also common in renal disease including fluid overload and inflammation (Friedman and Fadem 2010). As stated, a low albumin is certainly predictive of a poorer outcome and an important predictor of morbidity and mortality. Later studies revealed that albumin was also a marker for morbidity and mortality in PD.

The correct diagnosis is crucial for appropriate medical management as there are several potential causes of hypoalbuminaemia:

- decreased synthesis due to poor nutritional intake – albumin has a half-life of two to three weeks, therefore complete starvation can take at least this length of time to make an impact on plasma levels. In ‘partial’ starvation, where patients are not quite meeting their requirements and are slowly losing weight, albumin levels can be maintained for months even when substantial amounts of weight are lost, due to adaptive mechanisms.
- decreased synthesis due to the acute phase response – this is part of the body’s immune response to cell damage which can arise through trauma, infection, or cancer. The cytokine IL6 is thought to be the mediator which instructs the liver to reduce production of certain proteins (albumin, transferrin) and increase production of others (CRP, ferritin). This interrelation between CRP and albumin may explain why a low albumin has been associated in so many studies with increased morbidity and mortality.

²SGA is included in the minimum data set for all patients with CKD stages 4 and 5.

- the presence of inflammation can also cause the endothelium to become 'leaky', with the redistribution of albumin pools, for example from vascular spaces to the intervascular space, which may have an impact on the efficacy of dialysis.
- albumin losses due to proteinuria, dialysis losses, or peritonitis.
- dilution – if the patient is fluid overloaded, for example before a HD session, or if dry weight needs to be adjusted. For example, 3 l overload can dilute plasma albumin from 42 to 37 g l⁻¹.
- albumin assay methods vary – it is important to use the same method of measurement each time (bromocresol green or bromocresol purple) or if comparing patients based at different renal units.

Subjective global assessment

SGA is an assessment of nutritional status and was first performed with surgical patients (Detsky et al. 1987). It is based on patient history and physical examination. A simple questionnaire is usually completed by a trained nurse or dietitian.

History

The history includes weight changes, dietary intake, gastrointestinal symptoms, and functional status and can include comorbid disease.

Physical examination

Physical examination takes into account loss of subcutaneous fat, muscle wasting, oedema, and ascites. Each section is rated on a three- or seven-point scale by the interviewer. An overall score is then assigned depending on the severity of symptoms. For the three-point scoring system subjects are given a score of A, B, or C: A for well nourished, B for mild–moderate malnutrition, and C for severe malnutrition. The seven-point score subdivides these categories into: A, A–, B+, B, B–, C+, C, or sometimes a numerical score is used: SGA scores of 6–7 (well nourished), 3–5 (mild–moderate undernutrition), and 1–2 (severe undernutrition) (Appendix 13.B).

The seven-point SGA was developed for the CANUSA study (Churchill et al. 1996) and was found to positively correlate with BMI, percentage body fat, and MAMC (Visser et al. 1999). A 1-unit lower SGA score was associated with a 25% increase in the relative risk of death and a 1-unit increase in score was associated with reduction in days hospitalised. Reproducibility was good: 81–91% when two observers were compared. A prospective longitudinal study of 1600 patients concluded that SGA could distinguish different degrees of PEW and confirmed that a greater degree of PEW was associated with increased mortality (de Mutsert et al. 2009).

K/DOQI Guidelines (K/DOQI 2000) stated that 'SGA is a valid and clinically useful measure of protein- energy nutrition status in maintenance dialysis patients'. The UK RA and EBPG (2007) also supports the use of the three- or seven-point SGA.

Protein energy wasting

Measures which the ISNMRD panel recommend to diagnose PEW include:

- serum chemistry: albumin, prealbumin, cholesterol.
- body mass: unintentional weight loss, total body fat percentage.
- muscle mass: muscle wasting, MAMC, creatinine appearance.
- dietary intake: protein intake, energy intake.

They acknowledged that, whilst nutritional scoring systems such as SGA will to some extent identify PEW, they will not provide a definitive diagnosis (Ikizler et al. 2013).

Treatment of malnutrition

A thorough assessment should identify the nutritional state of the patient and any modifiable causes of deterioration. This is the diagnosis stage in the Dietetic (Nutrition) Care Process outlined by the British (American) Dietetic Association and illustrated with respect to patients with renal disease (Memmer 2013). Although there are usually several possible causes and potential treatments (Carrero et al. 2013; Ikizler 2013; Ikizler et al. 2013), a protocol should be in place so that an initial intervention can be started immediately (a good example of this in patients who do not have renal disease is illustrated by the MUST tool, which describes the actions to be taken for each level of malnutrition). This may require nursing staff to start monitoring the patient using food charts or to start appropriate supplements (suitable for patients with renal disease) in the first instance and alert the renal dietitian. The dietitian will carry out a full nutritional assessment, however identifying and targeting the multiple barriers to achieving good nutritional status requires a team approach and the correct interventions and care plan can result in improvements in several nutritional parameters.

The primary aim of nutrition support is for patients to meet their nutritional requirements (macro- and micronutrients) in the least invasive, most effective way. The patient's protein and energy intake can be calculated from food intake charts or a 24-hour recall and the nutrient deficit can be calculated using a very simple formula:

$$\text{requirements} - \text{current intake} = \text{nutrient deficit}$$

This deficit has to be met using the following methods of nutrition support:

- oral – for patients who are able to eat and drink normally: fortified foods or foods with a high nutrient content or sip feeds; support and encouragement with eating if necessary.
- nasogastric or gastrostomy feeding for patients who are unable or unwilling to eat or drink normally. Oral and tube feeding can be combined (for example, tube feeding overnight, whilst the patient sleeps, and encouraging normal eating/drinking during the day).
- intraperitoneal amino acids (IPAA) with PD.
- intradialytic parenteral nutrition (IDPN) during HD.
- total parenteral nutrition (TPN) for patients whose gastrointestinal tract is not functioning sufficiently.

Nutrition support is ineffective without close teamwork and each member of staff agreeing to carry out specific roles. All healthcare workers directly involved in inpatient care should receive training in the following (National Institute for Health and Clinical Excellence 2006a):

- the importance of nutrition;
- the correct use of appropriate screening tools and indications for nutrition support and delivery;
- when and where to seek advice on nutrition support.

Oral nutritional support

The key stages in providing oral nutritional support (ONS) are:

- identifying any barriers preventing the patients from meeting their requirements and referral to other specialists, if necessary;
- involving the patient in deciding which type of supplementation is appropriate.

Barriers to meeting requirements

Gastrointestinal problems should be identified by a nutrition screening tool. If chewing and/or swallowing are a problem, the consistency of food may need to be modified. The catering department will have to be notified and it may be appropriate to refer to the speech-and-language therapist. People who lose weight rapidly often find that their dentures no longer fit properly, however this problem cannot usually be remedied during the patient's stay. Thrush infections are common in undernourished patients or patients who are prescribed immunosuppressants. This can cause a sore mouth, taste changes, and swallowing problems and can be relatively easily treated with antifungal agents. Constipation and diarrhoea are equally deleterious to the patient's appetite, and need to be identified and treated.

Motivating and encouraging the patient at meal times is often necessary and needs to be supervised by a member of the nursing team. Actively involving older people in their nutritional care and allocating a nurse to oversee their nutritional needs can improve intake by 30% (Pederson 2005). If active depression is an underlying cause, it may be useful to involve the help of a counsellor.

Prior to admission, the patient may have had a long period of deterioration due to the lack of ability or facilities to cook and shop. These problems may be resolved by a social worker and involvement of other family members or friends. If physical weakness is a problem, a physiotherapist or occupational therapist can suggest exercises to strengthen the patient or tools to assist the patient.

In hospital, physical weakness may prevent the patient cutting up their food or removing packaging. Poor vision may also be a problem. Assistance must be provided when these problems are identified. Loss of muscle mass is one of the main consequences of malnutrition and, in elderly people in particular, this leads to decreased capacity for the activities of daily living, loss of independence, and decline in mental status.

Physical activity and physiotherapy can improve muscle mass and should be part of nutrition support in the elderly patient (Suetta et al. 2004). Studies in patients on dialysis have shown improvements in muscle fibre and general muscle structure, as well as exercise capacity, after a training programme has been initiated (Kopple et al. 2005; Heiwe and Jacobson 2011; Koufaki et al. 2015). However, other authors have found a disappointing response to resistance exercise training (Ikizler 2011) and it may be that acidosis, which is prevalent in patients with kidney disease, actually worsens during exercise, thus preventing a more positive outcome (Clapp and Bevington 2011). Nonetheless, both UK and European guidelines promote physical activity in patients undergoing dialysis and recommend that patients should be given the opportunity to participate in regular exercise programmes (EBPG 2007; Wright and Jones 2011; Koufaki et al. 2015).

Food supplementation

This may involve providing fortified foods, snacks, or drinks with high nutritional content. Some of these can be given between meals so that the patient can eat little and often. Examples of these foods include sweet biscuits, cakes, cheese and biscuits, yoghurt, and mousses.

Supplement drinks, mousses, and soups are available as well as protein and energy powders and liquids, although the latter are more likely to be added during food preparation. In order to metabolise protein and energy supplements efficiently, the full range of micronutrients are required and an appropriate multivitamin and mineral supplement may be also given. The supplement drinks and desserts should be prescribed as a medicine and their listing on the drug chart may help improve distribution and monitoring of intake. The drinks may be milkshakes,

juice drinks, or yoghurt drinks. The flavours can include various fruits, vanilla, chocolate, neutral, and savoury. Mousses and bars are available and may be useful for patients with reduced fluid allowances.

The renal dietitian will be aware of the nutritional content of any supplements as well as potassium and phosphate content. The ratio of protein to energy may vary, which may suit the needs of different patients. A malnourished patient's potassium and phosphate intakes are usually poor and they may even have low plasma levels, however it is always necessary to be aware of the potassium content; powdered drinks which require the addition of milk may be unsuitably high in potassium. The patient will usually need to continue phosphate binders unless they are extremely malnourished.

Nursing and/or catering staff need to ensure that the supplements/fortified foods are given to the patient at the right time, at the correct temperature, and that they are actually consumed by the patient.

Nasogastric and gastrostomy feeding

The insertion of a gastrostomy feeding tube enables long-term tube feeding to be carried out without the discomfort of a nasogastric (NG) feeding tube. NICE guidelines recommend gastrostomy placement if NG tube feeding is not appropriate or if feeding is likely to be required for more than four weeks. Renal formulae are available with reduced electrolyte content but high nutrient density to reduce the fluid intake. Surveys have shown that the majority of (nonrenal) patients (83%) accepted the gastrostomy feeding well. Gastrostomy tubes may be placed via a percutaneous endoscopic method (PEG) or radiological method (RIG). In comparison with NG feeding there were fewer complications, greater comfort, better quality of life, and better nutritional efficacy (Loser et al. 2005). In adult patients on HD, there have been fewer reports of gastrostomy use, although gastrostomy feeding in children seems more successful and perhaps some lessons need to be learnt from the techniques used in paediatrics (von Schnakenburg et al. 2006).

Renal-specific formulae

Low-electrolyte, low-fluid supplements and feeds, and multivitamin supplements have been developed for patients who have kidney disease. Even these adapted nutrition support regimens may not result in the best possible outcomes because they do not supply enough of the relevant nutrients, and they may even add to the burden of nutrients which cannot be efficiently utilised at the time. The metabolic changes in renal disease have already been mentioned and these include the inflammatory response, which may involve rapid turnover of immune cells, increased antibody production, and production of acute phase proteins (such as CRP and fibrinogen). This creates an increased demand for certain nutrients such as branch chain amino acids, omega-3 fatty acids, and glutamine. Future research will continue to investigate targeted nutrition, which aims to supply essential nutrients such as glutamine, arginine, and DNA precursors, or attempts to attenuate the inflammatory response using omega-3 essential fatty acids in order to reduce catabolism in patients with kidney disease.

A meta-analysis of the effects of oral supplements and enteral tube feeding in dialysis patients concluded that albumin levels and overall dietary intake improved. More research was required to investigate other clinical end points (anthropometry, quality of life, physical function) and also to determine whether renal-specific formulae had any advantage over standard feeds (Stratton et al. 2005).

Nutritional peritoneal dialysis

Dialysate containing 1.1% amino acid solution will provide a net gain of 18 g amino acids from one 2 l exchange. It is important to ensure that energy requirements are being met otherwise the aim of achieving a positive nitrogen balance will not be met. Studies have indicated an improvement in nitrogen balance with increases in albumin; the dialysate seems to be well tolerated (Taylor et al. 2002; Tjiong et al. 2005). Use of amino acid-containing dialysate will also reduce the overall amount of glucose absorbed during dialysis (Woodrow et al. 2017).

Intradialytic parenteral nutrition

Parenteral formulas containing 50–70 g amino acids, and 1000 kcal from fat and carbohydrate, can be safely delivered via the venous return during the HD treatment. Glucose monitoring during treatment is essential to prevent hyperglycaemia and fluid balance can be adjusted accordingly. An oral multivitamin and mineral supplement may be required to ensure efficient use of the protein and calories. The cost of IDPN is 10 times that of oral supplementation, therefore the latter method should be encouraged first. Case reports have shown the good safety profile of this technique (Dukkipati et al. 2010), although patients must be monitored for refeeding syndrome, hyperglycaemia, and hypertriglyceridaemia. A systematic review only identified three RCTs comparing IDPN with alternative means of nutrition support and stated that there was insufficient evidence to demonstrate net benefit or harm (Sigrist et al. 2010; Ikizler et al. 2013) however a recent RCT showed improved nutritional parameters in malnourished patients given IDPN compared with standard nutrition support (Marsen et al. 2017). In the United Kingdom, IDPN is often used after alternative feeding methods have been tried (and failed) or discounted, because of the burden it would place on the patient and their carer.

Monitoring nutritional support

This may require daily recording of food intake charts and weighing the patient regularly. Food records are best completed as the meal is being finished in order to observe the patient and note any problems, as well as record the amount and type of food eaten. Patients can often forget what they have eaten within a couple of hours. Monitoring of biochemistry and fluid balance is also crucial for patients with renal disease (very low as well as high levels of potassium and phosphate are possible) and most renal units have computer systems that can identify values outside of the normal range and create an alert for action to be taken. Repeat assessments of nutritional status should occur six to eight weeks after starting dialysis (the first measurement taken within one week of starting treatment), and then repeated every four to six months for stable patients. Those identified as malnourished will be assessed much more frequently, e.g. dietary intake and oedema-free weight may be assessed weekly but other body composition measures may take longer to change; arm anthropometry such as MAC can be repeated monthly.

Transplantation

Renal transplantation is thought to offer the patient with AKD the best chance of rehabilitation and a good quality of life.

Postoperative transplant care

Appetite may initially be poor postoperatively and steroids can increase protein catabolism; therefore, both kidney and gastrointestinal function should be

monitored. The rate at which biochemistry and urine output return to normal can vary (sometimes within a couple of days after surgery, or it can take several weeks) and needs to be monitored closely. There may be an ‘oliguric stage’ where fluid and electrolyte reductions are still required. This can progress to a polyuric stage, where intravenous support may be necessary to prevent fluid and electrolyte levels dropping below normal; dehydration at this stage can damage the new kidney. Nutritional requirements and the need for nutrition support can be assessed as previously described. Uncomplicated surgery increases metabolic rate by 5–20% and this should be included in the protein and energy requirements.

Long-term post-transplant care

The advice given to patients should include healthy eating (with some advice on food hygiene), exercise, and avoidance of smoking, excess alcohol intake, and exposure to too much sun (Baker et al. 2017). One of the positive aspects of transplantation is that the dietary changes are usually relaxed; however it is necessary to reinforce advice on healthy eating to help reduce the risk of obesity, CVD, diabetes, and also cancer.

Nutrient requirements are based on recommendations for the general population. The ‘Eat Well Plate’ is an appropriate model on which to base nutritional advice and meal suggestions.

Cardiovascular disease

CVD is the cause of 60% of deaths in transplanted patients and the incidence of CVD is five times greater than expected for age and gender. The main risk factors are obesity, hypertension, hyperlipidaemia, diabetes, sedentary lifestyle, and smoking. The EBPg (2002) for renal transplantation also list hyperhomocysteinaemia as a risk factor.

Obesity is common with a successful transplant and is multifactorial:

- the patient’s appetite increases due to increased feeling of well-being and release from dietary constraints. Relaxation of restrictions after transplant can lead to a more liberal intake of high-calorie foods such as dairy products, fried potato products, and chocolate.
- steroids stimulate the patient’s appetite.
- activity and exercise levels may be low. Patients are often reluctant to exercise because of lack of confidence and low exercise tolerance owing to previous inactivity.
- the combination of an increased calorie intake and low activity levels leads to a rapid gain in body fat.

Obesity contributes to hypertension, hyperlipidaemia, and insulin resistance and these in turn contribute to CVD. Transplant medication is also partly responsible for raising lipid levels. Graft survival is also lower in the obese and the patient should be made aware of the risk of obesity at an early stage, pretransplant if appropriate. Patients with a BMI > 30 kg m⁻² prior to transplantation are advised to lose weight and post transplant patients are advised to aim for a BMI < 25 kg m⁻² (Baker et al. 2017), although this is not recommended by NICE (2018).

Target lipid levels are the same as the general population (National Institute for Health and Clinical Excellence 2006b; Baker et al. 2017).

Other CVD risk factors are:

- elevated levels of serum triglyceride and cholesterol are found in 36 and 63% of transplant patients respectively;
- arterial hypertension is present in 60–85% of patients;

- post-transplant diabetes affects 4–18% of patients;
- raised waist circumference.

Control of calorie intake and increasing energy expenditure through activity and exercise are usually necessary. Additionally, poor eating habits may have formed whilst adhering to the dietary allowances on dialysis; intake of fruit and vegetables and other ‘cardio-protective’ foods, such as oily fish, are often low (very few patients have the recommended five portions of fruit and vegetable per day, or fish twice a week). Regular reinforcement of healthy eating advice can help reduce weight gain, improve lipid levels, and also help control hypertension.

Bone disease

There may be some improvement in bone parameters post-transplantation but bone turnover abnormalities can persist. An improved lean body mass (muscle) and bone strength may result from diet and exercise advice. Patients with or at high risk of developing osteoporosis may need to avoid steroids; DEXA scanning can be used to monitor the condition. The Royal College of Physicians guidelines for steroid-induced osteoporosis are recommended (Royal College of Physicians 2002). These guidelines discuss the importance of vitamin D and calcium intake, and weight-bearing exercise to improve bone health. They also discourage smoking, excess weight, and excess alcohol intake which are also discussed in the RA Guidelines (Baker et al. 2017).

Diabetes

The development of new-onset diabetes after transplantation (NODAT) is exacerbated by immunosuppressive agents: steroids, tacrolimus, and ciclosporin. Elderly, African-Caribbean, and Hispanic patients are most at risk. Graft loss is four times greater for patients who have diabetes. Fasting blood glucose should be checked every three months in all nondiabetic transplanted patients. Diet and exercise interventions help reduce the risk of metabolic syndrome and developing diabetes (Diabetes UK 2011).

Summary of dietary advice for renal transplant recipients

- monitor biochemistry and blood pressure control, in particular lipid levels (cholesterol and triglycerides), blood glucose, potassium, bone minerals, PTH, and haemoglobin.
- aim for acceptable BMI: the ‘Eat Well Plate’ is an appropriate food model to use.
- emphasise eating a variety of fruit and vegetables: aim for at least five portions per day.
- encourage high-fibre foods (soluble and insoluble).
- encourage fish, particularly oily fish, lean meats, and pulses.
- foods high in sugar, saturated fat, and salt should be used sparingly.
- dairy products should be low fat, with attention to meeting calcium requirements.
- alcohol consumption should be within usual recommendations.
- be aware of good food hygiene practices (Baker et al. 2017) and follow FSA food hygiene advice.
- encourage physical activity and regular exercise.
- avoid smoking and too much sun exposure.

Ideally a team of specialists should be available to help with the rehabilitation of transplanted patients, including the dietitian, nurse, physiotherapist, social worker, and counsellor.

Dietary Management in Paediatrics

CKD may present after birth or later in life and can proceed to established renal failure during childhood. Growth and neurodevelopment depend strongly on nutrition during early childhood and can be profoundly affected by CKD (Fischbach et al. 2011; Wesseling-Perry et al. 2012). This is especially the case during infancy and in very young children where spontaneous nutritional intake is poor (Foster et al. 2012). Abnormal changes in bone mineralisation of the growing skeleton have been shown to begin as early as CKD stage 2 (Wesseling-Perry et al. 2012). With evidence of suboptimal growth in up to 35% of children with CKD (Seikaly et al. 2007; Rodig et al. 2014), this may be affecting their future education and employment prospects (Broyer et al. 2004; Rocha et al. 2011). The factors contributing to growth and final adult height in those individuals requiring dialysis during childhood are multifactorial, predominantly driven by nutrition, metabolic and hormonal alterations, and comorbidities (Mekahli et al. 2010; Harambat et al. 2014). However, intensive feeding and early transplantation have been shown to achieve a mean adult height within the normal range in patients without comorbidities (Mekahli et al. 2010), with an overall improvement in post-transplantation final adult heights over the past two decades (Fine et al. 2010).

In order to optimise nutrition and growth, early nutritional intervention is essential and must be maintained on a long-term basis. Early nutritional assessment should include the regular monitoring of growth (weight, height, and head circumference) and dietary analysis by means of food diaries or dietary recall. Optimising the amount, type, source, and ratio of phosphate-to-protein during the early stages of CKD, despite normal serum phosphate levels, may affect the rate of disease progression (KDIGO 2017). A healthy balanced diet, rich in natural sources of meat and plant-based foods, should be encouraged. Home-cooked meals are preferable, as processed foods contain a significant amount of additives (in particular, inorganic phosphates and sodium) (Kalantar-Zadeh et al. 2010). The nutritional prescription should consider energy, macronutrients, fluids, sodium, potassium, micronutrients, and calcium/phosphorus/vitamin D.

As children progress to end-stage kidney disease (CKD stages 4 and 5), the dietitian must respond to the changing and evolving dietary needs of the child. The fluctuating clinical and biochemical disturbances demand the regular review of biochemistry and fluid balance. As serum phosphate and potassium levels start to rise, nutritional measures continue to play a significant role in the management and optimisation of cardiac and bone health. When serum phosphate levels are normal, in the context of serum PTH concentrations exceeding the target range, a moderate dietary phosphate restriction is encouraged to prevent and manage hyperparathyroidism, whilst optimising growth, nutrition, and bone mineralisation. Optimal dietary management requires the constant appraisal and readjustment of each child's bespoke nutritional prescription by an experienced dietitian (Royal College of Paediatrics and Child Health [RCPCH] 2011), and the review of prescribed medication such as phosphate binders and anti-reflux agents to augment their effects (Ibrahim et al. 2013). The KDOQI (2005) guidelines recommend starting to monitor bone biochemistry at CKD Stage 2.

Infants and children may present with particular problems such as anorexia, vomiting, and body image changes, causing significant anxiety for parents (Tong et al. 2010). An understanding of the psychosocial effects of CKD often proves to be as important as the dietary advice (Nicholas et al. 2011; Foster et al. 2012).

Ultimately, the dietary management of children with CKD is dependent upon age, stage of CKD (K/DOQI 2008), and an individual nutritional assessment, with

particular attention paid to growth parameters. Oral nutritional supplements may have an important role, and are frequently used (Rees and Jones 2013). However, experience has shown that attempting to achieve adequate nutrition orally can be stressful for families (Tong et al. 2010) due to issues relating to vomiting, palatability, and compliance.

A proactive approach to maintaining good nutrition and growth, without the use of growth hormone, has resulted in a programme of early instigation of dialysis or pre-emptive transplantation, in combination with nutritional support (Laakkonen et al. 2010). Early and intensive nutritional management is recommended in the KDOQI nutritional guidelines (2008). Although NG tubes are used successfully, supplementary feeding using a gastrostomy button device may be more suitable in the long term (Foster et al. 2012; Rees and Jones 2013). However, there is some concern that gastrostomy feeding may predispose to obesity (Sienna et al. 2010), especially when children are relatively inactive. This is of particular concern in children receiving PD, due to the absorption of glucose from the dialysate. The gastrostomy button also provides a convenient route for the administration of medication and fluids, which has undoubted benefits for the child and family.

Dialysis is seen only as a holding measure before transplantation. Most children do very well and resume normal eating and drinking post-transplant (Pugh and Watson 2006). However, even if the transplant is successful, with normal renal function attained, concerns remain that there may be a prolonged transition to exclusive oral nutrition in infants and children who commenced nutritional support via an enteral route early in life. Support should be provided to encourage oral stimulation from the time of commencement of tube feeding (Pugh and Watson 2006). Such children may continue to require a period of nutritional support post-transplant. Conversely, the lifting of dietary reductions and initiation of steroid treatment in other children may require energy intake to be reduced to prevent rapid weight gain and obesity – a growing problem in children with CKD (Foster et al. 2010; Rodig et al. 2014). The use of steroid-sparing regimens alongside a healthy, no-added-salt diet and exercise should be encouraged with ongoing dietetic advice.

Maintaining good nutrition in this group of children requires the collaborative efforts of a multidisciplinary team (Foster et al. 2012). An agreed philosophy of nutritional care and dietetic time to attend ward rounds regularly, outpatient clinics, and psychosocial meetings are essential. Home and school visits with frequent telephone contact are also invaluable support measures.

Conclusion

This chapter has provided the opportunity for the reader to improve current theoretical and practical knowledge of renal nutrition. However dietary advice is constantly changing as a result of new research findings and evidence-based guidelines. It is important that a positive effort is made to continuously review practice and to always involve patients in the decision-making process.

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13.A: Calculation of Body Mass Index and Ideal Body Weight

Body mass index (BMI) can be calculated by dividing the weight in kg by the height in metres squared. If the patient has oedema the BMI will be overestimated and is not valid. In estimating oedema-free body weight (BW_{ef}), weight should be measured after haemodialysis (HD) or after drainage of dialysis fluid in peritoneal dialysis (PD).

A person weighs 65 kg and is 1.70 m tall.

$$BMI = 65 / (1.7 \times 1.7) = 22.5 \text{ kg m}^{-2}$$

Normal range: 18.5–24.9.

Underweight <18.5.

Preobese (overweight): 25–29.9.

Obese class I: 30–34.9.

Obese class II: 35–39.9 (obese).

Obese class III: >40 (morbidly obese).

The K/DOQI guidelines recommend the use of adjusted oedema-free body weight (aBW_{ef}) to calculate protein or energy requirements or to assess intake. The following method can be used. Standard body weight: a BMI between 18.5 and 24.9 kg m^{-2} and its corresponding weight in kilogrammes, is considered within the normal range (WHO 1998). However, given the increased mortality of patients at the lower end of the 'normal' range, it may be prudent to calculate the standard weight for a BMI of 23 kg m^{-2} and this can be used in the equation below. The following equation has been suggested:

$$IBW = aBW_{ef} = BW_{ef} + ((\text{standard body weight} - BW_{ef}) \times 0.25)$$

These figures should be used to calculate protein and energy requirements for individual patients.

The important point for audit purposes and comparison across renal units is to note clearly how you have calculated ideal body weight (IBW). As there is no consensus regarding this issue a simpler method would be to use the weight corresponding to a BMI of 23 kg m^{-2} .

13.B: Seven-Point Subjective Global Assessment

Name Hospital No. D.o.B.....

Date					
Overall weight change over last 6 months					
❖ Gain (7)/<5% loss (6)					
❖ 5–10% sustained loss (4–5)					
❖ >10% sustained loss (1)					
❖ >10% loss but gaining (relative to dry weight) (2–3)					
❖ >5–10% loss but gaining (4)					
Weight change over past 2 weeks					
❖ No change/normal weight (6–7)					
❖ Increased/increasing (rate 1 score above previous) (3–4–5)					
❖ Stable but below normal (relative to dry weight) (2–3)					
❖ Decreased/decreasing (1)					
Change in dietary intake compared to normal					
❖ Good intake/no change/small change (7)					
❖ Borderline intake/decreasing (3)					
❖ Poor intake/no change (2)					
❖ Poor intake/increasing (3–4–5)					
❖ Poor intake/decreasing (1)					
Duration/type of change in diet					
❖ <2 weeks, normal diet (7)					
❖ >2 weeks, sub-optimal normal diet (3)					
❖ Full fluid diet/NG (3–4–5)					
❖ Hypocaloric liquids (2)					
❖ Starvation (1)					
GI symptoms					
Nausea, Vomiting, Diarrhoea, Anorexia					
❖ None/few intermittent symptoms (7)					
❖ Some symptoms >2 weeks (3–4–5)					
❖ Most/all symptoms >2 weeks (1)					
Subcutaneous fat (triceps/chest)					
❖ Little or no depletion (6–7)					
❖ Moderate depletion some/all areas (3–4–5)					
❖ Severe depletion most/all areas (1–2)					
Muscle wasting (quads/deltoids)					
❖ Little or no depletion (6–7)					
❖ Moderate depletion some/all areas (3–4–5)					
❖ Severe depletion most/all areas (1–2)					
Total score:					

13.C: Foods with a High and Low Sodium (Salt) Content

It may not be possible to eliminate all the listed foods or meals, unless a low-sodium alternative is available. A compromise may be reached by allowing some salty foods for sandwiches or main meals, but preparing the rest of the meals at home without salt. Adding herbs and spices during meal preparation or thereafter compensates for the loss of salt.

Foods with a high sodium content	Suitable alternative (always check with dietitian)
Dairy products	
Salted butter or margarine	Use unsalted or salt-reduced alternatives instead
Cheese, cheese spreads	
Meat and meat products	
Canned and cured meat products such as bacon, gammon, salt beef, corned beef, ham, tongue, all types of sausages, pâtés	Fresh-cooked meat Fresh-cooked poultry Fresh-cooked fish
Meat pies, quiches, and sausage rolls	Home-cooked meals
Processed meals	
Fast food-type meals	
Vegetables	
Canned vegetables, sauerkraut, instant potato powder, salted potato crisps	Fresh or frozen vegetables
Nuts	
Roasted and salted nuts	
Miscellaneous	
Salt, sea salt, salt substitutes such as Lo Salt, Solo, Selora	Herbs, spices
Mayonnaise, salad dressings	Homemade dressings, i.e. French dressing
Bottled sauces, pickles	Vinegar, lemon, lime juice
Canned or packet soups or ready-made soups	Homemade soup
Pasta sauce, curry paste, soya sauce	Homemade sauces
Meat or yeast extracts and bouillon cubes, packet gravy, gravy cubes or powders	Use herbs and spices for curries Use fresh ingredients for pasta dishes
Foods containing monosodium glutamate	
Salted savoury snacks	
Asian foods	
Poppadums, samosas, other savoury snacks, chutneys, pickles, chevra, chana	
Greek foods	
Taramasalata, canned vine leaves, houmus	Homemade houmus
Chinese foods	
Dried fish, salted fish	
Peking duck and similar products	

13.D: Foods with High and Low Phosphorus Content

All foods with a high protein content also contain a fair amount of phosphorus. However, some of these foods are an essential part of the diet and cannot be eliminated.

Foods with a high phosphorus content	Suitable alternative (always check with dietitian)
Cereals	
Natural Bran, All-Bran, Bran Flakes, Bran Buds, cereals containing nuts	All other breakfast cereals Porridge
Rye bread	Wholemeal or white bread, croissant
Crispbread containing rye	Puri, pitta bread, chapatti, naan
Oatcakes, scones	Yorkshire pudding
Soya flour	Flour, barley, sago Semolina, tapioca, cornflour, custard powder Pasta, noodles, rice, wild rice
Dairy products	
Milk, yoghurt (see allowance allocated by renal dietitian)	Cream, crème fraîche
Evaporated and condensed milk	Fromage frais, quark
Milk powder, Horlicks	Cottage cheese and curd cheese
Most types of hard cheese, e.g. cheddar	Full-fat or reduced-fat cream cheese, such as Boursin, Philadelphia, roulé, marscapone, riccota
Stilton, cheese spread	
Eggs (no more than one daily); however, these quantities may need to be adapted for vegetarian diets	Egg white, meringue
Meat and meat products	
Liver, kidney, liver pâté and liver sausage, black pudding	Beef, veal, lamb, pork, chicken, turkey, sausages, meat pies (see meal plan suggested by the renal dietitian)
Fish and fish products	
Fish with edible bones, such as anchovies, herring, kippers, pilchards, salmon, sardines, sprats, whitebait, fish roe, fish paste	Fresh or smoked fish, such as cod, haddock, halibut, plaice, mackerel, tuna, fish fingers, fish cakes Canned fish, such as tuna, salmon with all bones removed Cockles, mussels, squid Occasionally use: crab, lobster, prawns, scampi, trout
Vegetables	
Pulses, such as dried peas, dried beans, lentils, baked beans, chickpeas	All other vegetables
Savoury snacks	
All types of nuts such as peanuts, peanut butter	Popcorn, corn snacks
Bombay mix, chevra, chana, ganthia	
Poppadoms	
Sweets	
Chocolate, cocoa powder, Ovaltine, Mars bars, Snickers, Bounty, halva, burfi with nuts	Sweets, barley sugars, butterscotch, mint, fruit pastilles, starburst, sherbets, jelly babies, wine gums, marshmallows, Turkish delight, chewing gum, plain toffee and fudge, lollipops, ice lollies
Cakes and pastries	
Chocolate cake, Battenburg cake	All other types of cakes, biscuits, pastries
Any cakes and pastries containing chocolate or nuts	Doughnuts, cream cakes, gingerbread

Biscuits

Chocolate biscuits, Jaffa cakes
All biscuits containing nuts or chocolate

Plain biscuits, such as Digestives

Cream crackers, Rich Tea, shortbread, sponge fingers, cream-filled biscuits

Puddings

Milk pudding, custard, bread pudding, Christmas pudding, sponge

Pancakes, pastries, sweet or savoury, fruit jelly, sorbets, plain ice cream, cheesecake

Chocolate mousse, chocolate ice cream, desserts containing nuts and chocolate

Beverages

Milk and milk drinks, such as milkshakes, Build-up, Complan, Nutrament, drinking chocolate, cocoa, Bourneville, Ovaltine, Jamaican punch, some soft drinks contain added phosphate

Tea, coffee

Soft drinks, fruit squash, lemon barley, blackcurrant drink, lime juice cordial, Crushe syrup, rosehip syrup

Condiments and miscellaneous

Meat and yeast extracts, such as Marmite, Bovril, Vegemite

Sugar, jam, marmalade, honey, lemon curd, golden syrup

Marzipan, peanut butter, seeds such as sesame, tahini, chocolate and nut spread

Gelatine, yeast, pickles, chutney, tomato ketchup, tomato purée, lemon juice, vinegar, mustard, mayonnaise, salad cream, salad dressing, tartar sauce, chilli sauce, soya sauce, herbs, and spices, apple sauce, cranberry sauce, redcurrant jelly, horseradish, mint sauce, mint jelly

13.E: Foods with High, Medium, and Lower Potassium Content

Potassium is found in many foods including milk which may be restricted, but also protein-rich foods such as meat, fish, and pulses. The tables below should only be used as a guide in combination with up-to-date food composition tables and manufacturers' data.

Foods with a high potassium content**Savoury snacks**

- Bombay mix, curu snacks, all nuts including peanuts, all types of seeds, potato crisps, potato hoops, twiglets, vegetable samosas

Sweets and sweet snacks

- Chocolate; plain, milk, white, and all sweets containing chocolate
- Liquorice allsorts, toffees, fudge, and other sweets containing nuts, chocolate
- Dried fruit; dried apples, dried apricots, dried banana chips, currants, dates, dried figs, prunes, raisins, sultanas, other dried fruit
- Marzipan, treacle

Beverages

- Coffee in excess
- Milk powder and drinks containing milk powder, such as Ovaltine, Horlicks, Complan, Build-up, drinking chocolate, milk shakes, Nutrament, cocoa powder.

Foods with a lower potassium content

- Popcorn, corn snacks such as tortilla chips, rice cakes and rice-based snacks, wheat-based snacks

- Sugar, jam, marmalade, honey, lemon curd, golden syrup

- Boiled sweets, barley sugar, peppermint, Turkish delight, jelly babies, fruit pastilles, fruit gums, sherbets, marshmallows, lollipops, ice lollies, chewing gum

- Crystallised, glace fruit

- Tea (milk from allowance)

- Soft drinks; with low real fruit juice content, tonic, soda water, ginger beer, lemonade, fizzy water, bitter lemon
- Fruit squash

(Continued)

Foods with a high potassium content	Foods with a lower potassium content
● Milk shakes ● All fruit juices unless exchanged for fruit, cane sugar juice, vegetable juices; tomato juice, carrot juice Alcohol ● Ale, barley wine, beer, cider, lager, red wine, white wine, sherry, port, Cereals and cereal products ● All bran, bran flakes, oatbran flakes, cereals with dried fruit, nuts, or chocolate ● Oat cakes, rye crispbread ● All puddings, cakes, biscuits, and cereal bars containing dried fruit, nuts, or chocolate Condiments and flavourings ● Tomato ketchup, tomato chutney, tomato puree, coconut ● Meat and yeast extracts ● Salt substitutes containing potassium chloride (KCl) Dairy, fats, and oils Yoghurts, milk puddings, custard, evaporated, and condensed milk	● Rice, Oat milk ● Spirits ● Corn flakes, rice crispies ● Rice, barley, sago, semolina, tapioca ● Flour, noodles, pasta ● Bread, croissant, chapati, pitta bread, puri ● Plain cake, biscuits, pastry (icing sugar, butter icing) ● Spices; including, cinnamon, chilli powder, coriander, cumin, curry powder, ginger, mustard powder, nutmeg, pepper, turmeric ● Herbs; (fresh or dried) basil, bayleaf, coriander, dill, mint, oregano, parsley, sage, tarragon, thyme ● Garlic, lemon juice, Tabasco, vinegar ● Piccalilli, horseradish, chutney, and pickles Cream; double, single, whippingButter, lard, vegetable oils, and margarines

13.E.1: Potassium Portions

Potassium portions or exchanges can be used to encourage variety. Fruits and vegetables contain potassium in varying quantities. A patient may be advised to have (daily) one portion from the potato/tuber and pulse exchange list, two portions from the vegetable list, or two portions from the fruit list. This however depends on biochemistry, body size, and the diet as a whole and patients may be advised to avoid certain foods in the high-potassium list.

Cooking methods such as boiling and throwing the water away will remove some potassium. Steaming, baking, stir-frying, pressure cookers, and microwaving will not remove potassium.

Potatoes, tubers, and pulses: Note: one portion contains approximately 10mmol potassium. 150 g boiled potatoes may be replaced by: 75 g baked potato in skin or 75 g new potatoes or 75 g roast potato or 75 g boiled green banana or plantain; 50 g chips (two tablespoons) or six oven chips or two potato croquettes; 150 g boiled parsnips; 150 g ravioli or spaghetti in tomato sauce; 150 g yam, sweet potato, dasheen, eddoes, coco yam, boiled breadfruit; 150 g rice and peas (without coconut); 150 g soaked and boiled butter beans, haricot beans, black-eyed beans, baked beans in tomato sauce, dried peas, split peas, chick peas, lentils; 100 g red kidney beans, boiled. Vegetables: Each portion contains approximately 5 mmol (200 mg) potassium. Quantities are based on fresh or boiled and drained vegetables unless indicated.

High; As a guide, one portion is 75 g (1–2 tablespoons): beetroot (boiled)	Medium; As a guide, one portion is 100 g (2–3 heaped tablespoons): aubergine	Low; As a guide, one portion is 150 g (3–4 heaped tablespoons): asparagus (6 medium spears)
brussel sprouts (6) fennel okra (6 pods) spinach mushrooms (boiled in water first) tomatoes (fresh, canned). fried onion vegetable juices Raw vegetables: a small portion of a mixture of salad:beetroot, red cabbage, carrots celery, chicory, coleslaw corn kernels, cucumber, lettuce mustard and cress, peppers (red, green, yellow, or orange) radish, spring onions tomato (no more than half a tomato), watercress. Fruit: Each portion contains approximately 5 mmol (200mg) potassium. Quantities are based on fresh, stewed or canned fruit.	french beans broccoli celery courgettes curly kale leeks mangetout capsicum / peppers (red or green) sweetcorn kernels, on the cob or baby sweet-corn, fresh, or canned turnip	runner beans beansprouts bamboo shoots cauliflower carrots globe artichoke red, white or Savoy cabbage marrow pumpkin peas (processed, canned, frozen, mushy peas) onions boiled, pickled, or silverskin spring greens.
High; As a guide, one portion is 50–75 g (1–2 tablespoons):	Medium; As a guide, one portion is 100 g or 3 tablespoons:	Low; As a guide, one unit of fruit is 150 g or 5 tablespoons:
1 fresh apricot ½ small banana blackcurrants 5 dates (fresh or dried) 1 figs (fresh) 4 greengages (fresh) gooseberries (fresh or stewed) grapes 1 kiwi fruit 6 prunes (dried or canned) redcurrants rhubarb (stewed or canned) Fruit juices	apricots (canned in syrup or juice) blackberries (fresh or stewed) 12 cherries 6–8 kumquats 1 lemon or lime loganberries (fresh) 6 lychees (fresh) 3 slices mango melon 1 nectarine paw paw (papaya) 1 medium peach (fresh or in natural juice) pineapple (1 medium thick slice) 2 pomegranates plums: 1 large or 2 small raspberries (fresh) (about 20) 1 sharon fruit 8 small strawberries.	1 apple 1 clementine ½ grapefruit a thin slice of watermelon 1 small orange 2 passion fruits 1 medium-sized pear 1 satsuma 1 tangerine.

CHAPTER 14

Quality Improvement in Kidney Care

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Learning Outcomes

- to explain what is meant by quality improvement (QI).
- to identify what is meant by patient safety.
- to understand the process of implementing and evaluating clinical practice guidelines.
- to plan and evaluate the components of an audit of kidney care.
- to be familiar with the basic techniques in QI methodology.

Introduction

In 1998, the UK Secretary of State announced specific measures to ensure that ‘all patients should receive a first-class service’ (Department of Health 1998). The document in which this announcement was made highlighted that there were unacceptable variations in performance and practice, and in clinical outcomes. In England, Lord Darzi’s National Health Service (NHS) Next Stage Review report put ‘quality at the heart of everything we do’ (Department of Health 2008), whereas the more recent publication *Equity and Excellence: Liberating the NHS* commits to establishing improvement in quality and healthcare outcomes as the primary purpose of all NHS-funded care, placing patient safety ‘at the heart of the NHS’ (Department of Health 2011). In 2014, the ‘Five Year *Forward View*’ highlighted that unless there is a reduction in variation in quality and safety of care, then ‘patients’ changing needs will go unmet, people will be harmed who should have been cured, and unacceptable variations in outcomes will persist’ (Department of Health 2014).

This chapter will explore the ways in which renal nurses can promote a high-quality service, through understanding of QI methods, use and evaluation of best practice guidelines, and insight into clinical audit. Nurses have a vital role to play in the promotion of quality care in the renal specialty and are in a key position to understand the needs of individual patients and their carers.

Quality Improvement

QI has been defined as ‘the combined and unceasing efforts of everyone (healthcare professionals, patients and their families, researchers, payers, planners and educators) to make the changes that will lead to better patient outcomes (health), better system performance (care) and better professional development’ (Batalden and Davidoff 2007). Quality healthcare (Health Foundation 2013) needs to be:

- timely – reducing waits and delays.
- effective – providing services based on evidence and which produce a clear benefit.
- person-centred – establishing a partnership between practitioners and patients to ensure care respects patients’ needs and preferences.
- efficient – avoiding waste.
- equitable – providing care that does not vary in quality because of a person’s characteristics.
- safe – avoiding harm to patients from care that is intended to help them.

Patient Safety

Patient safety is the avoidance of unintended or unexpected harm to people during the provision of health care. There are two comprehensive resources available that can provide renal nurses with practical help in addressing patient safety issues. One is NHS Improvement (UK) (<https://improvement.nhs.uk>; accessed 1 August 2018) and the other is the Institute for Health Improvement (USA) (<http://www.ihl.org>; accessed 1 August 2018).

NHS Improvement supports providers of care to minimise patient safety incidents and drive improvements in safety and quality. This is achieved by issuing safety alerts, summaries of how NHS Improvement has reviewed and responded to patient safety issues, and running a national programme to support and encourage a culture of safety, continuous learning, and improvement across the health and care system. One example where NHS Improvement has supported the kidney community is the release of an alert in 2016 to support NHS providers in diagnosing, treating, and managing acute kidney injury https://improvement.nhs.uk/documents/251/Patient_Safety_Alert_Stage_2_-_AKI_resources.pdf (accessed 1 August 2018).

The Institute for Healthcare Improvement (IHI’s) work is focused in five key areas:

- Improvement Capability;
- Person- and Family-Centred Care;
- Patient Safety;
- Quality, Cost, and Value;
- Triple Aim for Populations (applying integrated approaches to simultaneously improve care, improve population health, and reduce costs).

One example from IHI (Luther and Resar 2013) describes a methodology that helps frontline staff to ‘see’ patient safety problems in their systems and enables them to solve the problems and share that learning with others. The methodology is constructed around an informal unit visit and designed to be a ‘conversation’ about safety issues, versus an inspection or evaluation. This approach seeks to identify problems as they occur and solve them as soon as they are seen. A renal nursing manager could implement this type of ‘conversation’ with staff on a monthly basis. A detailed example is shown in Table 14.1.

Table 14.1 The patient safety conversation.

The unit visit conversation		
Conversation steps	Specific duties	Desired outcomes
1. Organise the visit to the unit beforehand	● Select a mix of frontline staff (six to eight) ● Select a small leadership team ● Arrange for at least 60 minutes of conversation	● A cross-section of staff working on the unit are included in the conversation ● Schedule enough time for all staff to be able to discuss their work ● The location selected for the conversation will minimise interruptions
2. Arrange for all participants to describe the jobs they do	● Establish a nonthreatening atmosphere ● Limit this part of the conversation to the first 10 or 15 minutes ● Focus this portion of the conversation on understanding the work and the work environment	● Frontline staff trust that this conversation is not about assessing their personal work performance ● Staff are willing to talk about their work, how they do it, and how they add value to the patients and the organisation
3. Assess the work environment using 'anchoring questions'	● Use questions like: 'What causes a bad day for you?'; 'When was the last time a case was delayed?'; 'What makes some people with diabetes more difficult to manage?' ● Use these questions to learn about both clinical and nonclinical situations ● Steer discussion away from solutions	● A specific example of a defect around which to anchor subsequent questions to staff about frequency, type of patient involved, previous attempts to fix the defect, or what might happen if it were resolved ● A discussion that is completely nonthreatening and blame free, to allow for maximum sharing of information ● 10–15 defects that can be easily surfaced during a 60-minute conversation and compiled on a written list
4. Debrief	● First, debrief the team asking the above-mentioned questions ● Debrief the frontline team	● A list of defects that the front line has surfaced ● Buy-in from the frontline staff for possible action ● Buy-in from the questioning team as to the need for action
Source: 'The Unit Visit Conversation' in Tapping Front Line-Knowledge. Cambridge, Massachusetts: Institute for Healthcare Improvement; [Jan/Feb 2013]. (Available on www.ihl.org)		

Clinical practice guidelines

Over the past 20 years, the renal specialty has seen the emergence of a number of national and international standards for renal care. When the government's way of setting clear national standards was announced in 1998, the main strategy for this was through National Service Frameworks (NSF) and through a National Institute for Clinical Excellence (NICE). In early 2004 and early 2005 the NSF for Renal Services were published. This was the first NSF to be published in two parts and although the original publications were disseminated almost one decade ago, their publication has had a tremendous impact on how renal services have developed.

National Service Frameworks

Part One of the NSF for Renal Services (Department of Health 2004) set five standards and identified 30 markers of good practice that would help the NHS and its

partners manage demand, increase fairness of access, and improve choice and quality in dialysis and kidney transplant services. Part Two of the NSF for Renal Services (Department of Health 2005) sets four quality requirements and identified 23 markers of good practice to help the NHS limit the development and progression of chronic kidney disease (CKD), minimise the impact of acute kidney injury, and extend palliative care to people dying with kidney failure. Each of these documents is discussed in further detail in relevant chapters of this book.

In September 2005 a summary of progress to date towards achieving the standards and early actions set out in the Renal NSF, together with a review of the modernisation programme supporting delivery of the NSF, was published by the Department of Health (2005). In 2007 a second progress report was published and in 2009 another report (Department of Health 2009) highlighted the successes from the previous five years.

In June 2006 the *National Service Framework for Renal Services: Working for Children and Young People* was published. This document related specifically to the care of children and young people in greater detail. It also brought together the recommendations from the NSF for Children, Young People, and Maternity Services, to make an accessible, user-friendly document for all those with an interest in services for children and young people with kidney disease.

Many related projects and documents have been published following publication of the NSF for Renal Services. In 2013 the *Kidney Health: Delivering Excellence* (KHDE) report was published. The authors created a set of 16 ambitions for excellent kidney care, from early identification through to conservative care. The ambitions were:

1. Awareness and Identification – reduce cardiovascular risk.
2. Prevent or delay disease progression.
3. Inform self-management.
4. Deliver person-centred care.
5. Prevent and treat acute kidney injury.
6. Preparation and choice.
- 7, 8, and 9. Improve outcomes from transplantation, equity, increase numbers, and live well with a transplant.
10. and 11. Deliver better dialysis consistently and support patients to live well.
12. Improve the care of children and young people.
13. Access to and awareness of the multiprofessional team.
14. Treat and support people with rare diseases.
15. Research – produce a national strategy.
16. Conservative care – choice and multiprofessional support.

In 2017 the authors reviewed the 2013 KHDE report and were optimistic that the report's ambitions will continue to develop (<https://www.kidneycareuk.org/news-and-campaigns/news/kidney-health-delivering-excellence>; accessed 1 August 2018). However, some areas required further attention, including QI. As a result, a new QI ambition, Ambition 17, was added for 2017.

The kidney community promotes, encourages and supports continuous quality improvement and sharing of best practice by all healthcare workers to deliver better, safer, less variable and more efficient care. (KHDE 2017)

Kidney Quality Improvement Partnership

The Kidney Quality Improvement Partnership (KQIP) (a collaboration to support improvement across the renal community) now provides a focus for this ambition.

KQuIP is a dynamic network of kidney health professionals, patients, and carers who are committed to developing, supporting, and sharing QI in kidney services in order to enhance outcomes and quality of life for patients with kidney disease. KQuIP builds on rather than replaces existing QI structures by helping kidney services to embed QI into daily practice; understand and reduce unwarranted variation in care; and spread and share good practice. The KQuIP hub (<https://www.thinkkidneys.nhs.uk/kquip/hub>; accessed 1 August 2018) provides a variety of resources, including case studies, that will support you in developing QI projects for the benefit of patients.

In renal nursing practice we are fortunate to have a variety of clinical standards and guidelines to help us achieve clinically effective practice. In other words, many of the clinical guidelines that are available have been based on research evidence or expert opinion, so we do not have to examine all aspects of our care as it has already been done for us. There now follows a review of the most important clinical standards and guideline documents available for renal nurses.

National Institute for Health and Care Excellence (NICE)

The National Institute for Health and Care Excellence produces and disseminates clinical guidelines based on relevant evidence, associated clinical audit methods, and information on good practice. The Institute identifies new and existing health interventions, collects evidence, considers the implications for clinical practice, disseminates the findings, implements at a local level, and monitors the impact. The guidelines produced by NICE that are specifically relevant to renal practice are to be found in Table 14.2.

For further details, see the NICE website www.nice.org.uk/guidance (accessed 1 August 2018).

NICE quality standards are a concise set of statements designed to drive and measure priority QIs within a particular area of care. The standards are derived from the best available evidence and are developed independently by NICE, in collaboration with NHS and social care professionals, their partners, and service users.

The NICE quality standards are central in supporting the government's vision for an NHS and Social Care system focused on delivering the best possible outcomes for people who use services, as detailed in the Health and Social Care Act 2012. A quality standard for CKD was published in 2011 and covers the identification, assessment, and clinical management of CKD in adults. NICE quality statements for Renal Replacement Therapy (RRT) were published in 2014 and are shown in Box 14.1.

Table 14.2 Renal-specific NICE guidance (since 2010).

Year of publication	Topic
2011	Peritoneal dialysis
2013	Acute kidney injury (to be updated 2020)
2013	Management of hyperphosphataemia
2014	Chronic kidney disease (CKD) (to be updated 2020)
2015	Foot problems in diabetes
2015	Managing anaemia
2015	Diabetes management (Type 1 and Type 2 both published)
2018	Renal Replacement Therapy

BOX 14.1**NICE quality statements for RRT (2014)**

Statement 1. Adults preparing for or receiving renal replacement therapy, and their family members or carers, undertake individualised education programmes at specialist renal centres.

Statement 2. Adults who will need renal replacement therapy are offered a pre-emptive kidney transplant, if they are medically suitable.

Statement 3. Adults on dialysis are offered a kidney transplant, if they are medically suitable.

Statement 4. Adults with established kidney failure who are starting planned dialysis have a functioning arteriovenous fistula (AVF) or peritoneal dialysis catheter.

Statement 5. Adults who need long-term dialysis are offered home-based dialysis.

Statement 6. Adults using transport services to attend for dialysis are collected from home within 30 minutes of the allotted time and collected to return home within 30 minutes of finishing dialysis.

Statement 7. Adults who have a suspected acute rejection episode have a transplant kidney biopsy carried out and reported on within 24 hours.

Statement 8. Adults receiving haemodialysis have their vascular access monitored and maintained using systematic assessment.

Source: National Institute for Health and Care Excellence (2014).

The quality measures accompanying the quality statements aim to improve the structure, process, and outcomes of healthcare, although expected levels of achievement for quality measures are not specified.

Best Practice Guidelines from International and National Renal Associations

In 1990, the European Dialysis and Transplant Nurses' Association/European Renal Care Association (EDTNA/ERCA) commenced work on writing European clinical standards and in 1995 published European Standards for Nephrology Nursing Practice (Van Waelegheem and Edwards 1995). This document was published alongside the European core curriculum for a postbasic course in nephrology nursing (Kuentzle and Thomas 1995). These standards were one of the first publications that recommended specific guidelines for renal nursing practice. In recent years, renal nurses have had access to a variety of multi-professional best practice guidelines and a summary of these are outlined below.

Kidney Disease Outcome Quality Initiative/KDIGO

KDOQI (Kidney Disease Outcome Quality Initiative, originally called DOQI or Dialysis Outcome Quality Initiative) provides evidence-based clinical practice guidelines developed by volunteer physicians and healthcare providers for all stages of CKD and related complications, from diagnosis to monitoring and management.

KDOQI guidelines not only address dialysis but all stages of CKD. The first set of guidelines developed by KDOQI on the evaluation, classification, and stratification of CKD were published in February 2002.

In 2004 there were further developments as it was recognised that there was a need for a more uniform and global approach to the process of developing clinical guidance. The name under which the initiative is now incorporated is 'Kidney Disease: Improving Global Outcomes' (KDIGO). Its mission statement is 'Improve the care and outcomes of kidney disease patients worldwide through promoting coordination, collaboration and integration of initiatives to develop and implement clinical practice guidelines'. KDIGO is led by an international board comprised of approximately 50 members. The majority of the board members are practicing nephrologists, but also included are patient representatives, plus delegates from other medical specialties and disciplines – nephrology nurses, dietitians, and social workers.

Since the original development of the DOQI guidelines in haemodialysis and peritoneal dialysis, there have been developments in certain areas of care, such as blood pressure, diabetes, and living kidney donors. For further information, visit www.kdigo.org (accessed 1 August 2018).

Renal Association

Within the United Kingdom, the Renal Association published the third edition of *Treatment of Adult Patients with Renal Failure – Recommended Standards and Audit Measures* in 2002. From mid-2006 the Clinical Practice Guidelines of the UK Renal Association have been published in modular form. Table 14.3 shows the current and upcoming modules and expected review date.

Other Guidelines

A variety of clinical practice guidelines are available including the European Best Practice Guidelines (EBPG). The EBPG are published on behalf of the European Renal Association/European Dialysis and Transplant Association and can be found at

Table 14.3 Renal Association clinical practice guidelines.

Module	Date	Review due
Treatment of acute hyperkalaemia in adults	2014	2019
Planning, initiation, and withdrawal of RRT	2014	2019
Vascular access for haemodialysis	2015	2020
Water treatment facilities, dialysis water, and dialysis fluid quality for haemodialysis and related therapies	2016	2011
Peritoneal dialysis	2017	2022
Postoperative care of the kidney transplant recipient	2017	2022
Anaemia in chronic kidney disease (CKD)	2017	2022
CKD-mineral and bone disorders (CKD-MBD)	2018	2023
Blood-borne viruses	2018	TBC

Source: For further information on the Renal Association guidance, visit the website: <https://renal.org/guidelines> (accessed 1 August 2018).

<http://www.european-renal-best-practice.org/content/erbp-official-documents> (accessed 1 August 2018). The International Society of Peritoneal Dialysis guidelines can be found at <https://ispd.org/ispd-guidelines> (1 August 2018).

Evaluation of Guidelines

There are numerous local, national, and international guidelines that renal nurses can access for achieving clinically effective practice, although Mead (2000) questions how useful these guidelines can actually be in promoting good practice. She summarises her debate with the following recommendations – guidelines are guides, not rules; practitioners must critically appraise the included evidence; national guidelines must be adapted to local circumstances; and it is vital to ensure judicious and selective guideline development.

It is helpful to have a checklist to evaluate how useful guidelines are to a local renal nursing team. The following questions could be used for evaluation:

- are the guidelines based on evidence, expert opinion, or both?
- what is the quality of the evidence? (Does it consist of well-conducted clinical studies, reports, opinions, and clinical experience of respected professionals?)
- are the guidelines specific enough?
- are the guidelines local, national, or international?
- have patients been involved in the development?
- do the guidelines measure nursing?

The last point is difficult to evaluate as, of course, nurses do not work in isolation and therefore all members of the multiprofessional team contribute to patient outcome. But it is important that nurses recognise that it is nursing that they have to measure, and not necessarily the easier-to-measure variables such as blood pressure, potassium level, Kt/V , and haemoglobin levels. What matters to patients is the depth of the communication, the skill of the teaching, and the quality of their life, and although it is recognised that all of these are very difficult to measure, nurses must strive to evaluate these as part of the audit process.

Audit

The National Institute for Health and Care Excellence provides clinical audit tools for all clinical guidelines. The aim of the clinical audit is to make the process of developing clinical audit projects easier through the provision of ready-to-use criteria, including exceptions, definitions, and data source suggestions. One example is the suggestions for clinical audit that accompany the clinical guideline on anaemia management. Here you can review clinic audit tools and other resources to put the guidelines into practice and improve patient care www.nice.org.uk/guidance/ng8/resources (accessed 1 August 2018)

Quality and Service Improvement Methods

The Model for Improvement (Langley et al. 2009), is a simple, yet powerful tool for accelerating improvement. The Model for Improvement implements small tests of change using Plan-Do-Study-Act (PDSA) cycles. See Figure 14.1.

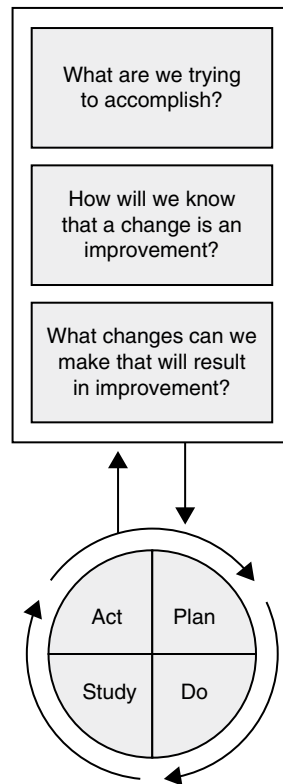


Figure 14.1 The model for improvement. Source: Institute for Healthcare Improvement (2012).

The Healthcare Quality Improvement Partnership (HQIP) was established in April 2008 to promote quality in healthcare, and in particular to increase the impact that clinical audit has on healthcare QI. HQIP does provide comprehensive information on QI tools, theories, and techniques that can be applied to a wide variety of situations (www.hqip.org.uk/resource/guide-to-quality-improvement-methods; accessed 1 August 2018) and also QI programmes (www.hqip.org.uk/national-programmes; accessed 1 August 2018).

One popular QI method used in renal care is the application of a care bundle. Care bundles are groups (bundles) of high-impact evidence-based healthcare interventions. Implementation of a care bundle can provide a structured way in which to improve the processes of care and patient outcomes. They are defined as a small, straightforward set of evidence-based practices (usually three to five) that, when performed collectively and reliably, have been proven to improve patient outcomes (Institute for Health Improvement 2018).

Success is defined as the application of *all elements* of the bundle at *every opportunity*. The idea of defining reliable practice in this ‘all-or-nothing’ approach is known as ‘composite reliability’. A care bundle approach aims to achieve a 95% level of reliability. Thus they can be used as tools to improve efficiency and also effectiveness – a smarter way of working that could be applied to renal nursing practice. Care bundles have been used with good effect to reduce the rate of infection in those with central venous catheters. A renal vascular access audit (NHS Information Centre 2011) showed that at first dialysis, 39% of patients had a tunneled central line, and 20% had a nontunneled central line. After adjusting for sample size, bloodstream infections were more common in patients with catheters

compared with other types of vascular access: 6 episodes/100 patients for an AVF, 13 episodes/100 patients for a nontunnelled venous catheter, and 8 episodes/100 patients for tunnelled catheters.

Units could implement and evaluate the use of a care bundle by using one of the examples of a care bundle for central venous catheters that are widely available.

Conclusion

Increasingly, renal nurses are being asked to identify and implement ways to improve the quality of care they provide. There are now a wide variety of resources available to help them, including those from NHS Improvement, the IHI, and KQuIP. However, it is important to remember that patients must be at the centre of any QI intervention and must also be included in the planning phase. Renal nurses are increasingly contributing to the culture of continuous QI in patient care and have a very important role to play in patient safety initiatives.

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