Gynaecological Cancer and Cervical Screening

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What will be covered

• Understand the epidemiology, aetiology, diagnosis, management and prognosis of gynaecological cancers.
• Screening and management of premalignant conditions of the cervix.
Gynaecological Cancers = malignancies arising in the female reproductive tract

- Ovarian
- Cervical
- Endometrial/uterine
- Vulva
- Vagina
- Trophoblastic
“What do you know about ________”

Dressed In A Surgeon's Gown A Physician May Make Some Important Progress

- Definition
- Incidence (also Prevalence)
- Age
- (Sex)
- Geographical Distribution
- Aetiology (Causes and Risk factors)
- Pathology
- Macroscopic Pathology: Anatomical
- Microscopic Pathology: Histological, biochemical
- Symptoms and Signs
- Investigations
- Prognosis...

- ... and of course treatment options, which don't fit but you shouldn't forget.
General principles of cancer management

- History
- Examination
- Investigation (imaging, bloods, tissue sampling)
- Discussion at MDT (IOG guidelines)
- Management (curative or palliative)
- Follow-up & surveillance
Why do you need to care?

• 14% of all solid tumors in women and 11% of deaths from them.

• Cervical, endometrial and ovarian cancer represent 95% of all gynaecological cancers

• Worldwide, these tumours account for even larger share of cancer mortality
Uterine cancer: Endometrial Carcinoma

- 4th most common cancer in UK women
- Age profile: Most common between 60 and 69 years
Risk factors

- **Increased exposure to unopposed oestrogen**
- Obesity
- Menstrual history (Early menarche, late menopause, infertility due to failure of the ovaries, Failing to ovulate, oligo/amenorrhoea)
- Lower parity
- Endometrial hyperplasia
- PCOS
- Family history and other cancers
  - cancer of the colon, rectum or breast in the past
  - Maternal history
  - If you have several close relatives on the same side of the family who have had bowel cancer
  - Hereditary nonpolyposis colon cancer (HNPCC). Other than bowel cancer, womb cancer is the most common cancer linked with this syndrome.
Risk factors continued

• **Tamoxifen and raloxifene**
  Has a similar effect on the womb to oestrogen

• **Hormone replacement therapy (HRT)**
  Oestrogen only HRT increases the risk of womb cancer and is normally only prescribed to women who have had their womb removed (a hysterectomy).

• **Oestrogen only Contraceptive pills**
  Most types of birth control pills used today normally decrease the risk of womb cancer. These contain either a combination of oestrogen and progesterone (combination pills), or progesterone only (mini-pills).

• **Diabetes and high blood pressure**
  Link to obesity??

• **Ethnicity**
  Caucasian > african/afrocaribbean
  Common in Jewish women
Clinical presentation

• 90% of women will be diagnosed because of postmenopausal bleeding (PMB) or irregular vaginal bleeding

• Less common:
  – Pelvic/lower abdominal pain
  – Dyspareunia
  – Palpable uterus

• Symptoms of carcinomatosis
Red flag signs & symptoms

- PMB in women who are not on hormone replacement therapy (HRT)
- PMB in women that goes on for more than 6 weeks after stopping HRT
- PMB in women taking tamoxifen
- Pelvic mass
- Persistent intermenstrual bleeding (IMB) in women who have had a pelvic examination that was normal
Type

95% are adenocarcinomas

- Endometrioid adenocarcinomas (75%)
- Papillary serous carcinomas
- Clear cell carcinoma
Investigations

- Pelvic examination
- Bloods (FBC, CA125)
- Endometrial biopsy
  - Pipelle (aspiration)
  - Hysteroscopy
  - D&C
- Transvaginal ultrasound
- Further staging investigations
Prognosis - good

• Overall in England and Wales, between 7 and 8 out of every 10 women diagnosed will live for at least 10 years.

• Most are low grade. They tend to respond very well to treatment and many women are cured.
Treatment

• **Surgery**: TAH BSO
• Lymph node removal: grade 2 or 3 endometrial cancer.
• **Radiotherapy**
  – After surgery if:
    • The cancer had grown more than half way through the muscle wall of the womb
    • The cancer had grown down to the neck of the womb (cervix)
    • The cancer cells were judged to be grade 3 or 4 (high grade)
Modalities

• Surgery (total abdominal hysterectomy, bilateral salpingo-oophorectomy)
• Surgery plus adjuvant chemotherapy
• Surgery plus adjuvant irradiation
Complications of Radiation Therapy

Acute:
• Perforation
• Fever
• Diarrhoea
• Bladder spasm

Chronic:
• Proctitis
• Cystitis (a/w UTI)
• Fistula
• Enteritis
Case

• Kate, a previously fit 65 year old woman, presented to her GP with:
  • A 2 month history of dyspepsia
  • A 6 month history of fatigue
  • She commented that her trousers had become tighter over the previous 4 weeks
  • On examination her GP noted abdominal ascites and arranged for Kate to have some blood tests – which ones?

• CA-125 is a tumour marker which is elevated in approximately 85% of patients with stage III/IV ovarian cancer
• Blood test results:
  – CA-125: 2130
  – CEA: 18
  – FBC: Hb 10.1, WCC 5.6, PLT 230

• Which gynaecological cancer are you thinking of?

• What of the following risk factors are associated with ovarian cancer?
  – Prolonged use of the oral contraceptive pill
  – Pregnancy
  – Presence of BRAC2 mutation
Gynaecology review

- PV examination revealed a fixed left sided pelvic mass
- Ultrasound confirmed presence of left sided pelvic mass
- Diagnosis given and options discussed
- Which of the following surgical options is adequate and should be discussed with Kate?
  - TAH
  - TAH BSO
  - TAH BSO, LN sampling, peritoneal biopsies
• **Surgery:**
  Kate decided to have a TAH, BSO, omentectomy, lymph node sampling & multiple peritoneal biopsies.
  Surgical findings were:
  • a 12cm left sided ovarian tumour
  • omental cake
  • deposits noted over large and small bowel and surface of the liver
  • Optimal debulking was achieved.

**Pathology:**
  • Serous papillary adenocarcinoma of left ovary
  • Ascitic fluid positive for cancer cells
  • Multiple implants from bowel surface containing tumour of greater than 2cm
  • Lymph nodes not involved

• What stage is Kate’s ovarian cancer?

• **FIGO stage IIIC**
• Kate is referred to oncology: She has had an uncomplicated post operative recovery
• Post operative CA-125: 235U/ml
• What would you tell Kate her median 5 year survival is?
  – Stage III ovarian tumours have a 5 year survival of 20%
• Does Kate need any other treatment?
  – Kate should be advised to have chemotherapy using carboplatin & paclitaxel (taxol)
- **Chemotherapy:**

  After discussion about the rationale and potential toxicities of chemotherapy with carboplatin and paclitaxel Kate decides to proceed with treatment. CA-125 normalised by cycle 3

- Her treatment was complicated by the development of a moderate peripheral neuropathy from cycle 4
  - Her paclitaxel dose was reduced

- **Follow-up:**

  Kate attended outpatients 3 monthly initially

- 26 months following completion of chemotherapy CA-125 noted to be elevated at 189U/ml

- On questioning Kate tells you that she has been constipated and has had abdominal pain

- What is the likeliest explanation for this?
Ongoing management

- CT confirms progressive disease and Kate elects to have palliative carboplatin chemotherapy.

At assessment after 3 cycles of carboplatin CA 125 is still rising and CT scan confirms progressive disease with development of splenic metastases.

Kate describes symptoms of nausea, vomiting and abdominal pain
- On examination there is tenderness in the umbilical area
- An abdominal x-ray is arranged
- Abdominal x-ray showing small bowel obstruction with features of central gas shadows, no gas in large bowel and dilated small bowel
  She is admitted, her small bowel obstruction is managed with bowel rest, IV fluids, analgesics and anti-emetics via syringe driver, and her symptoms resolved.
• On discussion with her oncologist they decide that further chemotherapy is not appropriate and she is referred to the community palliative care team
• Over the next 4 months she requires regular visits to hospital for paracentesis
• Her bowel symptoms return and are managed with a subcutaneous infusion via a syringe driver.
Ovarian cancer

• Fifth most common cancer in females in the UK and the second most common gynaecological cancer after uterus.
• 6,600 new cases of ovarian cancer diagnosed each year in the UK, that is around 125 women every week.
• Ovarian cancer is more common in women who have been through the menopause: more than 8 in 10 new cases are diagnosed in women aged over 50 years.
• Since the mid 1970s, the incidence of ovarian cancer in women over 65 has increased by more than 40%.
• The incidence of ovarian cancer is highest in USA and Northern Europe and lowest in Africa and Asia.
How many women die from ovarian cancer?

- Fourth most common cause of cancer death in women in the UK and the most common cause of gynaecological cancer death.
- Around 4,300 women die of ovarian cancer each year in the UK.
Risk factors

- Age; more than 4 out of 5 cases are diagnosed in women over 50 years. Most common in postmenopausal women
- BRCA1 or BRCA2 gene mutation
- Nulliparous women
- HRT for more than five years
- Endometriosis
- Obesity

- Oral contraceptive use reduces the risk of ovarian cancer and the protective effect persists for many years after stopping the Pill.
- Breastfeeding lowers risk of ovarian cancer
Symptoms of ovarian cancer

• Frequently vague
• The more common symptoms of ovarian cancer include abdominal pain and bloating, fatigue, weight loss, urinary symptoms and occasionally abnormal vaginal bleeding
• One audit in the UK reported that nearly 80% of patients had had symptoms for less than four weeks when they presented at general practice
Diagnosis and staging of ovarian cancer

- Refer to nearest Cancer Unit
- Careful history
- Physical examination
- Pelvic examination and Pap smear
- Proctosigmoidoscopy, where indicated
- FBC and urinalysis
- Bloods, including CA-125
- Chest film, IVP, Barium enema, or CT scan
- Transvaginal ultrasound

- SURGERY
Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Percent</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>24</td>
<td>&gt;90%</td>
</tr>
<tr>
<td>II</td>
<td>6</td>
<td>70-80%</td>
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<tr>
<td>III</td>
<td>55</td>
<td>20-30%</td>
</tr>
<tr>
<td>IV</td>
<td>15</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>50%</td>
</tr>
</tbody>
</table>
Surgery and chemotherapy

- In women who have completed their families, or are post-menopausal, it is recommended that the uterus, fallopian tubes and ovaries are removed and relevant biopsies performed.
- In younger patients, consider fertility sparing treatment.
- In a situation where there is very advanced disease, all of which cannot be excised by surgery, many surgeons perform ‘debulking’ surgery.
- Prophylactic oophorectomy has been shown to decrease the risk of BRCA-mutation-related gynaecological cancers and breast cancer in BRCA1 and BRCA2 mutation carrier.
Non-malignant conditions that may elevate CA-125 concentrations

- Gynaecological
  - Acute PID
  - Adenomyosis
  - Benign ovarian neoplasm
  - Endometriosis
  - Functional ovarian cyst
  - Meig’s syndrome
  - Menstruation
  - OHSS
  - Unexplained infertility
  - Uterine myoma

- Nongynecological
  - Active hepatitis
  - Acute pancreatitis
  - Cirrhosis
  - Congestive heart failure
  - DM(poor control)
  - Diverticulitis
  - Mesothelioma
  - Nonmalignant ascites
  - pericarditis
  - Pneumonia
  - Post-op period
  - SLE
Omental disease
Case

• 45 year old P 2 + 3
• Intermenstrual and Post Coital Bleeding for 6 months
• What should the GP do now?
  – Cervical Cytology (Practice Nurse)
    • Poor views blood++
• “Severe Dyskaryosis”
• Urgent referral for Colposcopy
• Abnormal appearances
• Biopsy
Histology Cervical Squamous Cell Cancer

• Clinic
  – Diagnosis with CNS
  – MRI

• MDT
  – Clinical Nurse Specialist
  – Surgeon
  – Radiotherapist (Clinical Oncologist)
  – Medical Oncologist
  – Radiologist
Recommendation for Surgery

• Radical Hysterectomy, Bilateral Salpingo-ophorectomy, Pelvic Lymph Node Dissection
• Suprapubic Catheter
• Hospital for 7 days
• Catheter out when residual volume less than 50mls
• Clinic 2/52 for results
  – Stage 1b Cervical cancer
  – No Lymph Nodes involved
  – No radiotherapy
  – CNS support
  –Reviewed every 3/12 for first year
Cervical Cancer

- Worldwide cervical cancer is the 2nd most common cancer affecting women
- 80% cases occur in developing countries
- Deaths from cervical cancer have fallen markedly in the UK from 8.3 per 100,000 women in 1971 to 3.3 per 100,000 in 2000
- 11th most common cause of cancer deaths in women in the UK
Symptoms

- Abnormal vaginal bleeding (PCB, IMB, PMB), discharge
- Pain, urinary symptoms in advanced disease
NORMAL CERVIX
Risk factors

• Sexual behaviour (age of first intercourse, number of partners)
• Smoking
• Immunosupression (HIV, drugs)
• Viral infections: HPV 16, 18, (31, 33)
Cervix Uteri

Transformation Zone

Colposcopy
Pathology

• Pap smear - mild, moderate, severe dykaryosis
• CIN 1, 2, 3
• CIN 1 - 30% would clear with no treatment
• CIN3 - 60% may become invasive (10-20 years)

• 85-95% squamous
• 5% Adenocarcinoma
• Others e.g adenosquamous, small cell
Investigations

• T markers: CA125, CA19-9, CEA, SCC Ag.
• MRI (hydronephrosis), endo vaginal coils, sinerem, PET CT
• Pelvic and para-aortic LN
• Staging is clinical except for Stage 1a (histological), with radiology for hydronephrosis/distant mets
Treatment - CIN and superficial carcinoma

- CIN - excision LLETZ, cold knife cone, laser, hysterectomy, (ablation)
- Ia1 - cone biopsy (0.5% LNM)
- Ia2 - cone biopsy (7% LNM) ? hysterectomy
Invasive Cancer

• Ib1 - surgery if low risk of LNM (<4cm, well/mod diff., no LVSI, no LN on MRI)
• Radical Hysterectomy, pelvic lymphadenectomy +/- BSO
Radical Hysterectomy

- Removes corpus, cervix, parametria, upper third of vagina
- Uterine arteries divided at origin
- Ureters dissected through tunnel
- Uterosacral ligaments divided near rectum
- Typically combined with LND
- Oophorectomy not mandated
Chemoradiotherapy

- **Ib2 and greater**
- External beam to whole pelvis, followed by intracavity brachytherapy L4/L5 to bottom of obturator foramen, 1cm outside bony margin of pelvis
- Intracavity brachytherapy for 3cm tumours
- Para-aortic nodes in early stage disease if suspicious
- Cisplatin/5FU
Palliation

• Stents
• Urinary diversion
• RT
Total Exenteration
Fertility Preservation

- LLETZ
- Trachelectomy - vaginal, abdominal with laparoscopic LN
Trachelectomy
Survival

<table>
<thead>
<tr>
<th>Stage</th>
<th>Survival</th>
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</thead>
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<tr>
<td>Stage 0</td>
<td>100%</td>
</tr>
<tr>
<td>Stage I</td>
<td>85%</td>
</tr>
<tr>
<td>Stage II</td>
<td>66%</td>
</tr>
<tr>
<td>Stage III</td>
<td>39%</td>
</tr>
<tr>
<td>Stage IV</td>
<td>11%</td>
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Vulval Cancer

- Rare
- 80% diagnosed in women over 60
- Non-invasive pre-cancerous condition VIN ('vulval intraepithelial neoplasia') tends to be diagnosed earlier – 30s to 50s
Risk factors

• Human papilloma virus (HPV) infection
• Weakened immune system (from HIV or immunosuppressant drugs)
• Genital herpes infection
• Smoking
• Some chronic skin conditions
Vulval cancer

- Most common symptom is a persistent and lasting itch that does not improve
- Others include:
  - Pain or soreness
  - Thickened, raised, red, white or dark patches on the skin of the vulva
  - An open sore or growth visible on the skin
  - Burning pain when you pass urine
  - Vaginal discharge or bleeding
  - A mole on the vulva that changes shape or colour
  - A lump or swelling in the vulva
Vulval cancer

• **Squamous cell carcinoma**
  90% are this type. This type of cancer usually forms slowly over many years. Before it develops, there may be precancerous changes in the cells of the vulva. These can be there for several years.

• **Vulval melanoma**
  This is the second most common type of vulval cancer.

• **Adenocarcinoma**

• **Basal cell carcinoma**

• **Verrucous carcinoma**

• **Sarcomas**
Treatment

• When diagnosed and treated early, vulval cancer can be cured in over 90 percent of cases.

• Typically involves surgery, radiation therapy and in some cases, chemotherapy.

• **Surgery**: wide local excision, in which the cancer and some of the normal tissue around the cancer is removed.

• **Radiation Therapy**: Radiation may be used alone, before or after surgery.

• **Chemotherapy**
Gestational trophoblastic tumours (GTT)

- Rare tumors that involving abnormal growth of cells inside a woman's uterus.
- GTD tumors start in the cells that would normally develop into the placenta during pregnancy.
- GTD begins in the layer of cells called the *trophoblast* that normally surrounds an embryo.
- Most GTDs are benign (non cancerous) and they don't invade deeply. Some are cancerous.
- All can be treated.
- The main types of gestational trophoblastic diseases are:
  - hydatidiform mole (complete or partial)
  - invasive mole
  - *choriocarcinoma*
  - placental site trophoblastic tumor
  - Hydatidiform mole
Screening

• Is to seek early signs of a high-burden disease in a high risk group in which you can intervene effectively
Criteria for Screening Test

1. Simple & quick
2. Capable of being performed easily
3. Inexpensive
4. Acceptable to population
5. Accurate
6. Repeatable
7. Sensitive
8. Specific
Screening for cervical cancer

- Success story in the UK
- Despite an increase in HPV infection rates, mortality has remained relatively static
Cervical cancer is preventable

- Cervical smear (papanicolau smear/liquid based cytology)
- The screening interval is the time between smears
- 3 yearly if 25 to 49 years old
- 5 yearly if between 50 and 64
- 65+ Only those who have not been screened since age 50 or have had recent abnormal tests
Screening results

• ‘Inadequate smear’
• This could be because:
  – Not enough cells in the sample
  – an infection so cells not seen clearly
  – menstrual bleeding so too much blood to see the cells clearly
  – cervix was inflamed and so the cells could not be seen clearly enough
• 'borderline'
  – cell changes = near normal and likely will go back to normal on their own

• Abnormal smear results
• Abnormal smears can be reported in two different ways. In the UK:
• Mild or slight cell changes (mild dyskaryosis)
• Moderate cell changes (moderate dyskaryosis)
• Severe cell changes (severe dyskaryosis)
Management

- Inadequate/borderline
- Repeat smear
- **CIN 1 (mild dyskaryosis)**
  - Colposcopy or a repeat smear in 6 months
  - Three consecutive normal 6 monthly smears are necessary before returning to regular screening
- **CIN 2 (moderate dyskaryosis) or 3 (severe dyskaryosis/CIS)**
  - Require treatment e.g. LLETZ
Limitations of Cervical Smear

• Complex laboratory test
• Requires trained cytotechnician for reading and pathologist for review
• Continuous monitoring needed to maintain high-quality results
• Reports often take minimum 1-2 weeks to obtain
• Follow-up of women can be difficult
What’s new?

• **HPV vaccination**
  - September 2008 with all 12- to 13-year-old and 17- to 18-year-old girls being offered the vaccine.
  - A catch-up programme was also announced at this time with 13- to 18-year-old girls being offered the vaccine over the following two academic years.

• **HPV test**
  - More sensitive than smear tests at picking up pre-cancerous changes.
  - May require repeating less often e.g. five-yearly, rather than three-yearly for smears.
(11) Which of the following statements with regards to endometrial, ovarian and cervical cancer are TRUE: T F

True
False
False
False
True

(a) Ovarian cancer has the worst prognosis
(b) Cervical cancer is best treated with chemotherapy
(c) The number of cases of endometrial cancer has been reduced by good screening techniques
(d) Ovarian dermoid cysts are often malignant
(e) Cervical cancer is most commonly squamous

The overall prognosis from cases of ovarian cancer over 5 years is 30%. This compares to 55% for cervical cancer and 65% for endometrial cancer. Endometrial cancer has the best prognosis because patients often present with “post-menopausal bleeding” and seek advice from their GP at an early stage. Similarly the cervical screening regime in the UK picks up cases of cervical cancer at a pre-malignant stage and recognises those patients who will be at risk of cervical cancer. Unfortunately no accurate screening test exists for ovarian cancer and patients often present at a late stage (i.e. stage III-IV) which is difficult to treat. Cervical cancer and endometrial cancer are treated with surgery and or radiotherapy, dependent on the stage of the disease etc, and ovarian cancer is treated with surgery and or chemotherapy (e.g. taxol, cisplatin).

• Dermoid cysts of the ovary account for approximately 25% of ovarian neoplasms and are made from the primary germ layers: endoderm, ectoderm and mesoderm. As a result they can consist of hair, teeth, cartilage etc and only about 1% have a malignant potential.
• In Cervical cancer:  T  F

True
False
False
False
False

(a) Human papilloma virus types 16, 18, 31, 33 and 35 are associated with cervical cancer
(b) Cervical cancer affects about 1000 women in the UK each year
(c) Stage for stage, cervical cancer has a worse prognosis than endometrial cancer
(d) all patients with Borderline nuclear abnormalities on their cervical smears should be referred directly for colposcopy
(e) at colposcopy, citric acid allows clear demarcation of abnormal areas

Cervical cancer is most commonly squamous although glandular lesions are found in the older age group (40 yrs) and about 2800 cases happen in the UK each year (2002). The prognosis has improved over recent years because of the cervical screening picking up cases at a pre-malignant stage and the overall death rate is 1100 deaths in 2002 (cf. 1500 in 1993). Although the prognosis for cervical cancer is the same, stage for stage compared with endometrial cancer, because there are more cases of endometrial cancer which present at an earlier stage the overall prognosis for endometrial cancer is better (65% cf. 55% for cervical). Orange juice (citric acid) will be of no benefit in the colposcopy clinic! 5% acetic acid (dilute vinegar) is used and this shows up the abnormal cells with acetowhite changes. The abnormal cells have a high nuclear to cytoplasmic ratio, and thus contain a lot of protein. It is this protein which gives the acetowhite changes.
• (13) In Endometrial cancer:
  T  F

- True
- True
- False
- False
- True

- (a) It often presents with postmenopausal bleeding
- (b) Women taking oestrogen only HRT are at increased risk
- (c) May be screened for using CA125 and TV scanning
- (d) Commonly develops from leiomyomas
- (e) Polycystic ovarian disease is a recognised risk factor

Endometrial cancer often presents at an early stage, as soon as the cancer has invaded the endometrium (stage Ia). The peak incidence is at 61 yrs and over 75% occur in the postmenopausal age group. If women require HRT and they have a uterus in place then they must be given progesterone therapy as well as oestrogen. If they are on short term therapy, they can have a cyclical HRT (bleed every 21 days), but if they want to use it long term i.e. more than 1-2 yrs, and they are aware of the risks, e.g. breast cancer, DVT's etc, then they should be prescribed continuous combined preparations (e.g. kilovance) as long as no other contraindications exist. Those patients on continuous combined preparations have a lower risk of endometrial cancer compared with those on cyclical HRT. There is no screening test for endometrial cancer and although CA125 and ultrasound scans can help to detect ovarian cancer, they are of no use as screening tools for this condition at present.

- Leiomoyomas (fibroids) are often benign and less than 0.2% will become malignant leiomyosarcomas. Most leiomyosarcomas arise de novo, are rapid growing and have a bad prognosis.
- Patients with polycystic ovaries are at higher risk of endometrial cancer and diabetes later on in life.
(14) In Ovarian cancer:  T   F

False
False
**True**
False
False

(a) The commonest types of tumour arise from the "germ cell lines"
(b) Often present in the premenopausal age group
(c) The risk of developing ovarian cancer can be increased to 40% if > 2 first degree relatives have been affected
(d) It is commonly treated with radiotherapy
(e) It often presents at an early stage due to abdominal ascites

Over 70% of ovarian neoplasms develop from epithelial cell tumours (e.g. mucinous cystadenomas (commonest benign) or serous papilliferous (commonest malignant)). The remainder are germ cell tumours (e.g. dermoid cysts) or sex cord/gonadal stromal tumours (e.g. granulosa cell tumours). Most present in the post menopausal age group although the germ cell tumours may be seen in younger patients. The overall risk of ovarian cancer in women between 50-70 is 1:70. This increases to 5% in women who have 1 first degree relative with the disease, and 40% in women with 2 relatives. Although ascites can be recorded at any stage during the disease (e.g. Ic, IIc etc) this is often a late feature and patients commonly present with stage III or IV disease. If at all possible, debulking surgery is carried out and this may be followed by chemotherapy.