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Cases of gynecology. Part I

**Tutorial for practical lessons of obstetrics and gynecology
for students of the 5th course of medical
faculty**

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ABBREVIATIONS

APH	antepartum haemorrhage
BMI	body mass index
CIN	cervical intraepithelial neoplasia
COCP	combined oral contraceptive pill
CT	computerized tomography
CVS	chorionic villous sampling
DUB	dysfunctional uterine bleeding
ECG	electrocardiogram
FSH	follicle-stimulating hormone
GP	general practitioner
Hb	haemoglobin
hCG	human chorionic gonadotrophin
HIV	human immunodeficiency virus
HRT	hormone-replacement therapy
INR	international normalized ratio
IUCD	intrauterine contraceptive device
IUS	intrauterine system
IVF	in vitro fertilization
LH	luteinizing hormone
LLETZ	large-loop excision of the transformation zone
LMP	last menstrual period date
MoM	multiples of the median
MRI	magnetic resonance imaging
OAB	overactive bladder syndrome
PCA	patient-controlled analgesia
PCOS	polycystic ovarian syndrome
PMB	postmenopausal bleeding
PMS	premenstrual syndrome
POP	progesterone only pill
PPH	postpartum haemorrhage
SLE	systemic lupus erythematosus
SPD	symphysiopelvic dysfunction

STI sexually transmitted infection

TCRF transcervical resection of a fibroid

T3 tri-iodothyronine

T4 thyroxine

UTI urinary tract infection

WHO World Health Organization

CASE 1: INTERMENSTRUAL BLEEDING

History

A 49-year-old woman presents with intermenstrual bleeding for 2 months. Episodes of bleeding occur any time in the cycle. This is usually fresh red blood and much lighter than a normal period. It can last for 1–6 days. There is no associated pain. She has no hot flushes or night sweats. She is sexually active and has not noticed vaginal dryness. She has three children and has used the progesterone only pill for contraception for 5 years. Her last smear test was 2 years ago and all smears have been normal. She takes no medication and has no other relevant medical history.

Examination

The abdominal examination is unremarkable. Speculum examination shows a slightly atrophic-looking vagina and cervix but there are no apparent cervical lesions and there is no current bleeding.

On bimanual examination the uterus is non-tender and of normal size, axial and mobile. There are no palpable adnexal masses.

INVESTIGATIONS

		<i>Normal range</i>
Haemoglobin	12.7 g/dL	11.7–15.7 g/dL
White cell count	$4.5 \times 10^9/L$	$3.5–11 \times 10^9/L$
Platelets	$401 \times 10^9/L$	$150–440 \times 10^9/L$

Transvaginal ultrasound scan and hydrosalpinxography are shown in **Fig. 1.1**.



Figure 1.1 Transvaginal ultrasound image showing mid-sagittal view of the uterine cavity after installation of saline (hydrosalpinxography).

Questions

- What is the diagnosis and differential diagnosis?
- How would you further investigate and manage this woman?

ANSWER 1

The diagnosis is of an endometrial polyp, shown in the ultrasound image as a mass, surrounded by the instilled fluid, within the endometrial cavity (Fig. 1.1). These can occur in women of any age, although they are more common in older women and may be asymptomatic or cause irregular bleeding or discharge. The aetiology is uncertain and the vast majority are benign. In this specific case all the differential diagnoses are effectively excluded by the history and examination.

! Differential diagnosis for intermenstrual bleeding

- Cervical malignancy
- Cervical ectropion
- Endocervical polyp
- Atrophic vaginitis
- Pregnancy
- Irregular bleeding related to the contraceptive pill

Management

Any woman should be investigated if bleeding occurs between periods. In women over the age of 40 years, serious pathology, in particular endometrial carcinoma, should be excluded. The polyp needs to be removed for two reasons:

1. to eliminate the cause of the bleeding
2. to obtain a histological report to ensure that it is not malignant.

Management involves outpatient or day case hysteroscopy, and resection of the polyp under direct vision using a diathermy loop or other resection technique (Fig. 1.2). This allows certainty that the polyp had been completely excised and also allows full inspection of the rest of the cavity to check for any other lesions or suspicious areas. In some settings, where hysteroscopic facilities are not available, a dilatation and curettage may be carried out with blind avulsion of the polyp with polyp forceps. This was the standard management in the past but is not the gold standard now, for the reasons explained.

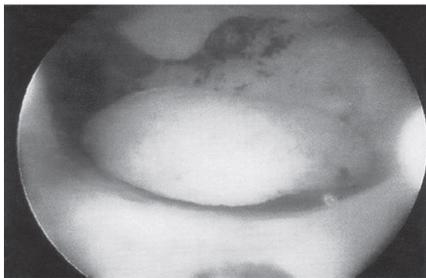


Figure 1.2 Hysteroscopic appearance of endometrial polyp prior to resection (see colour insert).

KEY POINTS

- Any woman over the age of 40 years should be investigated if bleeding occurs between the periods, to exclude serious pathology, in particular endometrial carcinoma.
- Hysteroscopy and dilatation and curettage is rarely indicated for women under the age of 40 years.

CASE 2: INFERTILITY

History

A 32-year-old woman has been trying to conceive for nearly 3 years without success. Her last period started 7 months ago and she has been having periods sporadically for about 5 years. She bleeds for 2–7 days and the periods occur with intervals of 2–9 months. There is no dysmenorrhoea but occasionally the bleeding is heavy.

She has been pregnant once in the past at the age of 19 years but that pregnancy was terminated for personal reasons. She had a laparoscopy several years ago for pelvic pain, which showed a normal pelvis.

Cervical smears have always been normal and there is no history of sexually transmitted infection. The woman was diagnosed with irritable bowel syndrome when she was 25, after thorough investigation for other bowel conditions. She currently uses metoclopramide to increase gut motility, and antispasmodics.

Her partner is fit and well, and has two children by a previous relationship. Neither partner drinks alcohol or smokes.

INVESTIGATIONS		
		<i>Normal range</i>
Follicle-stimulating hormone	3.1 IU/L	Day 2–5 1–11 IU/L
Luteinizing hormone	2.9 IU/L	Day 2–5 0.5–14.5 IU/L
Prolactin	1274 mu/L	90–520 mu/L
Testosterone	1.4 nmol/L	0.8–3.1 nmol/L
Thyroid-stimulating hormone	4.1 mu/L	0.5–7 mu/L
Free thyroxine	17 pmol/L	11–23 pmol/L
	Day 21 progesterone was requested but no period occurred for 3 months and therefore the test was not performed	

Questions

- What is the diagnosis and its aetiology?
- How would you further investigate and manage this couple?

ANSWER 2

The infertility is likely to be secondary to anovulation. Normal testosterone and gonadotrophins and high prolactin suggest the likely cause of anovulation is hyperprolactinaemia. Hyperprolactinaemia may be physiological in breast-feeding, pregnancy and stress. The commonest causes of pathological hyperprolactinaemia are tumours and idiopathic hypersecretion, but it may also be due to drugs, hypothyroidism, ectopic prolactin secretion or chronic renal failure. In this case the metoclopramide is the cause, as it is a dopamine antagonist (dopamine usually acts via the hypothalamus to cause inhibition of prolactin secretion, and if this is interrupted, prolactin is secreted to excess). Galactorrhoea is not a common symptom of hyperprolactinaemia, occurring in less than half of affected women.

!Drugs associated with hyperprolactinaemia (due to dopamine antagonist effects)
<ul style="list-style-type: none"> • Metoclopramide • Phenothiazines (e.g. chlorpromazine, prochlorperazine, thioridazine) • Reserpine • Methyl dopa • Omeprazole, ranitidine, bendrofluazide (rare associations)

The metoclopramide should be stopped and the woman reviewed after 4–6 weeks to ensure that the periods have restarted and that the prolactin level has returned to normal. If this does not occur, then further investigation is needed to exclude other causes of hyperprolactinaemia, such as a pituitary

micro- or macroadenoma. It would be advisable to carry out a day 21 progesterone level to confirm ovulatory cycles.

As with all women attempting to conceive, she should have her rubella immunity checked and should be advised to take periconceptual folic acid until 12 weeks of pregnancy to reduce the risk of neural tube defects.

If the woman fails to conceive after correction of hyperprolactinaemia, then a full fertility investigation should be planned with semen analysis and tubal patency testing (laparoscopy and dye test, hysterosalpingogram or hysterosalpingocontrastsonography (hyCoSy)).

KEY POINTS

- A full drug history should be elicited in women with amenorrhoea or infertility.
- Galactorrhoea occurs in less than half of women with hyperprolactinaemia.
- Day 21 progesterone over 30 nmol/L is suggestive of ovulation.

CASE 3: AMENORRHOEA

History

A 33-year-old woman complains that she has not had a period for 3 months. Four home pregnancy tests have all been negative. She started her periods at the age of 15 years and until 30 years she had a normal 27-day cycle. She had one daughter by normal delivery 2 years ago, following which she breast-fed for 6 months. After that she had normal cycles again for several months and then her periods stopped abruptly. She was using the progesterone only pill for contraception while she was breast-feeding and stopped 6 months ago as she is keen to have another child. She reports symptoms of dryness during intercourse and has experienced sweating episodes at night as well as episodes of feeling extremely hot at any time of day. There is no relevant gynaecological history. The only medical history of note is that she has been hypothyroid for 10 years and takes thyroxine 100 mg per day. She does not take any alcohol, smoke or use recreational drugs.

Examination

Examination findings are unremarkable.

INVESTIGATIONS		Normal range
Haemoglobin	12.2 g/dL	11.7–15.7 g/dL
White cell count	$5.1 \times 10^9/L$	$3.5\text{--}11 \times 10^9/L$
Platelets	$203 \times 10^9/L$	$150\text{--}440 \times 10^9/L$
Thyroid-stimulating hormone	3.6 mu/L	0.5–7 mu/L
Free thyroxine	21 pmol/L	11–23 pmol/L
Follicle-stimulating hormone	45 IU/L	Day 2–5 1–11 IU/L
Luteinizing hormone	30 IU/L	Day 2–5 0.5–14.5 IU/L
Prolactin	401 mu/L	90–520 mu/L
Oestradiol	87 pmol/L	Day 2–5 70–510 pmol/L
Testosterone	2.3 nmol/L	0.8–3.1 nmol/L

Questions

- What is the diagnosis?

- What further investigations should be performed?
- What are the key points in the management of this woman?

ANSWER 3

This woman has symptoms of amenorrhoea as well as hypo-oestrogenic vasomotor symptoms and vaginal dryness. The diagnosis is of premature menopause (premature ovarian failure), confirmed by the very high gonadotrophin levels. High levels occur because the ovary is resistant to the effects of gonadotrophins, and negative feedback to the hypothalamus and pituitary causes increasing secretion to try and stimulate the ovary. Sheehan's syndrome (pituitary necrosis after postpartum haemorrhage) would also cause amenorrhoea but would have inhibited breast-feeding and all menstruation since delivery.

Premature menopause (before the age of 40 years) occurs in 1 per cent of women and has significant physical and psychological consequences. It may be idiopathic but a familial tendency is common. In some cases it is an autoimmune condition (associated with hypothyroidism in this case). Disorders of the X chromosome can also be associated.

! Effects of premature menopause

- Hypo-oestrogenic effects:
 - vaginal dryness
 - vasomotor symptoms (hot flushes, night sweats)
 - osteoporosis
 - increased cardiovascular risk
- Psychological and social effects:
 - infertility
 - feeling of inadequacy as a woman
 - feelings of premature ageing and need to take HRT
 - impact on relationships

Further investigation

Osteoporosis may be prevented with continuous oestrogen replacement, but progesterone should also be given simultaneously (cyclically or continuously) to prevent the increased risk of endometrial carcinoma from unopposed oestrogen. Bone scan is necessary for baseline bone density and to help in monitoring the effects of hormone replacement. Chromosomal analysis identifies the rare cases of premature menopause due to fragile X syndrome or Turner's syndrome mosaicism.

Management

Osteoporosis may be prevented with oestrogen replacement, with progesterone protection of the uterus. Traditional HRT preparations or the combined oral contraceptive pill are effective, the latter making women feel more 'normal', with a monthly withdrawal bleed and a 'young person's' medication. In terms of future fertility, this woman's options are in vitro fertilization (IVF) with donor oocytes, adoption or the acceptance of only having one child. Occasionally premature menopause is a fluctuating condition (resistant ovary syndrome) whereby the ovaries may function intermittently. Contraception should therefore be used if it would be undesirable to become pregnant. Patient support organizations are a good source for women experiencing such an unexpected and stigmatizing diagnosis.

KEY POINTS

- Premature menopause (<40 years) occurs in 1 per cent of women.
- Oestrogen replacement is essential for bone and cardiovascular protection.
- It may be possible to conceive with IVF using donor oocytes.

CASE 4: PRIMARY INFERTILITY

History

A couple attends the gynaecology clinic because of failure to conceive. They stopped using condoms for contraception 19 months ago. There are no apparent sexual difficulties, and they have been having intercourse two to three times per week. In the last 6 months ovulation has been confirmed by the woman reporting a change in cervical mucus and a positive home urinary ovulation kit, and they have been having intercourse around this time.

The woman is 27 years old, with regular 29-day menstrual cycles and no previous gynaecological problems. Both the woman and her partner are generally healthy and have been together for 7 years. Neither reports any previous sexually transmitted infection.

Examination

The woman's investigations are normal, with normal gonadotrophins (LH and FSH), and confirmation of ovulation with a day 21 progesterone test. Chlamydia test is negative and she is immune to rubella. Hysterosalpingogram confirms patent fallopian tubes and normal morphology of the endometrial cavity.

INVESTIGATIONS		
The semen analysis for her partner is as follows:		
Parameter		Normal range (World Health Organization)
Semen volume	3.2 mL	>1.5 mL
Total sperm number	9.6 million	39 million per ejaculate
Sperm concentration	3 million/mL	>15 million/mL
Total motility (progressive and non progressive)	9%	>40%
Live spermatozoa	45%	>58%
Sperm morphology (normal forms)	3%	>4%



Figure 4.1 Transvaginal ultrasound scan.

Questions

1. What does the semen analysis show?
2. What further information should you ascertain from the man?
3. What does the ultrasound show and what is the significance of this in this case?
4. What further investigation and management would you plan for the management of this couple's infertility?

ANSWER 4

Semen analysis interpretation

Normal ranges for semen characteristics are published by the World Health Organization (WHO). The nomenclature applied to abnormal semen quality depends on the degree of abnormality and the specific type of abnormality. In this case the sample would suggest oligoastheno-terato-zoospermia (total number and concentration of spermatozoa, and percentages of both progressively motile and morphologically normal spermatozoa, all below the lower reference limits).

Further information to be ascertained

The history from the man is insufficient. Further enquiries should include:

- Occupation (infertility has been associated with occupational exposure to chemicals and with scrotal temperature)
- Smoking history
- Alcohol intake
- Previous medical history (cystic fibrosis, mumps or testicular torsion may affect fertility)
- Recent viral illness (may also affect spermatogenesis)

It should be confirmed that the semen sample was provided following the recommended procedures:

- Collected after at least 48 h but no more than 7 days of sexual abstinence
- Delivered to the laboratory within 1 h of production
- Collected by masturbation and ejaculated into a clean glass or plastic container, protected from extremes of temperature (below 20°C or above 40°C)

Ultrasound findings

The image shows an ovary which is polycystic in morphology. This is not a relevant factor for this couple as she has regular periods and the day 21 blood test confirms ovulation.

Further investigation and management

The abnormal sperm quality is the likely cause of infertility, but the semen analysis must be repeated to confirm that it is not a transient effect, e.g. of a recent viral illness. Causes of oligospermia may be pretesticular (such as pituitary tumours, smoking or medication), testicular (such as varicocele, trauma, mumps or Y chromosome deletions) or posttesticular (such as prostatitis or cystic fibrosis causing vas deferens obstruction). Referral to an andrologist can be useful in these cases as some causes of oligospermia are amenable to treatment.

He should also be examined for scrotal size and morphology. Testicular biopsy may be indicated to rule out pathology. Percutaneous sperm aspiration from the testis can be carried out in a man with complete azoospermia from an obstructive cause (not relevant for this couple where the man does have some sperm in the seminal fluid).

Assuming the semen quality remains poor on repeat analysis after 3 months, then the couple will need assisted conception with in vitro fertilization and intracytoplasmic sperm injection (direct injection of a single sperm into an egg) to achieve a pregnancy.

CASE 5: INFERTILITY

History

A 38-year-old woman is seen in the clinic because of infertility. She is gravida 2 para 1 having had a daughter 13 years ago, and a miscarriage 2 years later. She separated from her former husband and has now married again and is keen to conceive, especially as her new partner has no children.

Her last period started 45 days ago. She says that her periods are sometimes regular but at other times she has missed a period for up to 3 months. The bleeding is moderate and lasts for up to 4 days. There is no history of pelvic pain or dyspareunia, and no irregular bleeding or discharge. Alcohol intake is minimal and she does not smoke or take other drugs. There is no medical history of note and she takes no regular medication.

Her partner is 34 years old and is also fit and healthy with no significant history of ill-health or medications.

Examination

There are no abnormal features on examination of either partner.

INVESTIGATIONS (DURING THE NEXT MENSTRUAL CYCLE)		
Normal range		
Day 3 follicle-stimulating hormone (FSH)	11.1 IU/L	Day 2–5 1–11 IU/L
Day 3 luteinizing hormone	6.8 IU/L	Day 2–5 0.5–14.5 IU/L
Prolactin	305 mu/L	90–520 mu/L
Testosterone	1.3 nmol/L	0.8–3.1 nmol/L
Day 21 progesterone	23 nmol/L	
Semen analysis report: normal volume, count, normal forms and motility. Hysterosalpingogram report: the uterine cavity is of normal shape with a smooth regular outline. Contrast medium is seen to fill both uterine tubes symmetrically and free spill of dye is confirmed bilaterally.		
Transvaginal ultrasound scan report: the uterus is anteverted with no congenital abnormalities, uterine fibroids or polyps visualized. Both ovaries are of normal morphology, volume and mobility. No follicles are noted.		

Questions

- What is the cause of the infertility?
- What are the further investigation and management options?

ANSWER 5

Women with irregular periods often do not ovulate. Anovulation in this case is confirmed by the low day 21 progesterone level. The commonest cause of anovulation is polycystic ovaries, but in this case the ovaries show normal morphology and the androgen levels are normal. The noticeable abnormality is the high FSH level and the fact that no follicles are visualized at ultrasound scan.

This is suggestive of anovulation from premature failure of ovarian function. The woman is not menopausal because she still has periods, although irregular, and the FSH is only marginally raised. However it is known that FSH levels above 10 IU/L are associated with a poor prognosis for conception using the woman's own ova.

Further investigation

The FSH should be repeated, as it is possible that this could be a sporadic result or poorly timed sample, and therefore confirmation is needed before continuing on to treatment.

Anti-Mullerian hormone (AMH) is a further test of ovarian reserve and ovarian responsiveness in women with infertility. It decreases with number of ovarian antral follicles and it can be used to predict likelihood of ovarian response and pregnancy with assisted conception. Optimal fertility is associated with AMH levels of 28–48 pmol/L, whereas levels less than 5 pmol/L are suggestive of poor success rates with natural or assisted conception.

Management

As there is such a poor prognosis for conception either naturally or with in vitro fertilization using the woman's own ova, she should be counselled about assisted conception using donor eggs. Donated oocytes are fertilized with the partner's sperm and then implanted into the uterus. The woman needs appropriate luteal phase support, most commonly with progesterone pessaries.

! Counselling issues for this couple

- Psychological:
- the woman may feel that her ovaries are 'ageing' prematurely and this may have an effect on her self-esteem and sexuality.
- the stress associated with assisted conception is significant and many couples find that this in itself puts a large burden on their relationship.
- Funding: public funding may not be available as the woman already has one child.
- Consideration of alternative options: adoption, surrogacy and acceptance of not being able to have a child together should be explored with the couple.

KEY POINTS

- FSH above 10 IU/L is associated with poor prognosis for fertility.
- Infertile couples should be encouraged to explore all options, including accepting childlessness and adoption as well as assisted conception techniques.
- Low AMH is associated with poor fertility. Values less than 5 pmol/L are associated with a very poor chance of IVF success.

CASE 6: SHORTNESS OF BREATH AND ABDOMINAL PAIN

History

A 73-year-old woman has been admitted with shortness of breath. On further questioning she says she has been unwell for about 8 weeks. She has decreased appetite and nausea when she eats. She has lost weight but her abdomen feels swollen. She has generalized dull abdominal pain and constipation, which is unusual for her. There are no urinary symptoms. She has always been healthy with no previous hospital admissions. She is a widow and did not have any children. Her periods stopped at 52 years and she has had no postmenopausal bleeding. She has never taken hormone-replacement therapy.

Examination

She appears pale and breathless on talking. Chest expansion is reduced on the right side, with dullness to percussion and decreased air entry at the right base. The abdomen is generally distended with shifting dullness. There is a mass arising from the pelvis. Speculum examination is normal, but on bimanual palpation there is a fixed left iliac fossa mass of about 10 cm diameter.

INVESTIGATIONS

	Normal range	
Haemoglobin	9.2 g/dL	11.7–15.7 g/dL
Mean cell volume	82 fL	80–99 fL
White cell count	$4.1 \times 10^9/L$	$3.5\text{--}11 \times 10^9/L$
Platelets	$197 \times 10^9/L$	$150\text{--}440 \times 10^9/L$
Sodium	135 mmol/L	135–145 mmol/L

Potassium	4.0 mmol/L	3.5–5 mmol/L
Urea	5.1 mmol/L	2.5–6.7 mmol/L
Creatinine	89 mmol/L	70–120 mmol/L
Alanine transaminase	18 IU/L	5–35 IU/L
Aspartate transaminase	17 IU/L	5–35 IU/L
Alkaline phosphatase	78 IU/L	30–300 IU/L
Bilirubin	12 mmol/L	3–17 mmol/L
Albumin	30 g/L	35–50 g/L
CA-125	118 ku/L	<30 ku/L

Chest X-ray and abdominal computerized tomography (CT) scan are shown in Figs. 6.1 and 6.2 respectively.

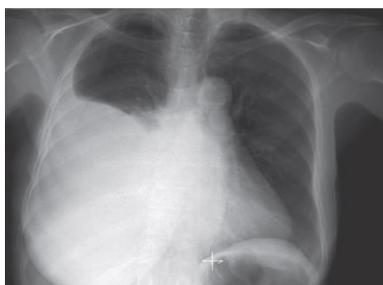


Figure 6.1 Chest X-ray



Figure 6.2 Abdominal CT scan.

Questions

- What is the likely diagnosis?
- How should this woman be further investigated?
- If the diagnosis is confirmed how should she be managed?

ANSWER 6

The history and examination are suggestive of a right pleural effusion and ascites. The presence of a pelvic mass would suggest that this is due to an ovarian or bowel problem. The chest X-ray confirms the effusion, and the CT shows a left-sided pelvic tumour and ascites. There are also solid areas in the anterior abdominal wall that represent omental infiltration by the tumour. CA-125 is a non-specific marker for ovarian carcinoma. The diagnosis is therefore likely to be that of ovarian cancer which commonly presents with systemic symptoms when metastatic disease is already evident.

! Confirmation of the diagnosis and management

The surgical aphorism ‘there is no diagnosis without a surgical diagnosis’ means that tissue needs to be obtained to confirm the diagnosis. Laparotomy should be performed with three objectives:

1. obtaining tissue for diagnosis
2. staging the disease according to the extent of tissue involvement
3. primary debulking – to perform a total abdominal hysterectomy and bilateral salpingo-oophorectomy and to reduce all abdominal tumour deposits to a volume of less than 2 cm. This allows optimal effect of chemotherapy following surgery. Lymph node dissection and omental resection are usually part of the procedure.

Prior to any treatment this woman also needs drainage of her pleural effusion for symptomatic relief and optimization for anaesthetic.

The prognosis for ovarian cancer is poor, as most women present at stage 3 or 4.

! Ovarian cancer staging and prognosis

Stage		Prognosis (5-year survival rate)
Stage 1 Confined to the ovaries	1A One ovary affected, ovarian capsule is intact 1B Both ovaries affected, ovarian capsules intact 1C Ovarian capsule is ruptured, tumour on ovarian surface or malignant cells detected in ascites or peritoneal washings	90%
Stage 2 Pelvic spread	2A Extension or implantation into the uterus and/or fallopian tubes (no malignant cells in ascites/peritoneal washings) 2B Extension to another organ in the pelvis (no malignant cells in ascites/peritoneal washings) 2C As for 2A/B plus malignant cells in ascites/peritoneal washings	65%
Stage 3 Peritoneal metastasis outside the pelvis and/or regional lymph node metastasis (includes liver capsule metastasis)	3A Microscopic peritoneal metastasis beyond the pelvis 3B Macroscopic peritoneal metastasis beyond the pelvis (max. diameter 2 cm) 3C Macroscopic peritoneal metastasis beyond the pelvis (max. diameter >2 cm) and/or distant lymph node metastases	35%
Stage 4 Distant metastasis beyond the peritoneal cavity (or liver parenchymal metastasis)		20%

KEY POINTS

- CA-125 is a non-specific marker for ovarian cancer.
- Ovarian cancer commonly presents late (stage 3/4) and prognosis is poor.
- Staging and primary treatment is by laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy and debulking.
- Neoadjuvant chemotherapy (preoperative chemotherapy to shrink the tumour mass down so that debulking surgery is more likely to be successful) may also be considered depending on the extent of disease on imaging.

- Chemotherapy is often effective adjuvant therapy.

CASE 7: ABDOMINAL SWELLING

History

A 35-year-old African-Caribbean woman has noticed abdominal swelling for 10 months. She has to wear larger clothes and people have asked her if she is pregnant, which she finds distressing having been trying to conceive. She has no abdominal pain and her bowel habit is normal. She feels nauseated when she eats large amounts. She has urinary frequency but no dysuria or haematuria.

Her periods are regular, every 27 days, and have always been heavy, with clots and flooding on the second and third days. She has never received any treatment for her heavy periods. She has been with her partner for 7 years and despite not using contraception she has never been pregnant.

Examination

The woman has a very distended abdomen. A smooth firm mass is palpable extending from the symphysis pubis to midway between the umbilicus and the xiphisternum (equivalent to a 32-week size pregnancy). It is non-tender and mobile. It is not fluctuant and it is not possible to palpate beneath the mass. On speculum examination it is not possible to visualize the cervix. Bimanual examination reveals a non-tender firm mass occupying the pelvis.

INVESTIGATIONS

Normal range

Haemoglobin	6.3 g/dL	11.7–15.7 g/dL
Mean cell volume	68 fL	80–99 fL
White cell count	$4.9 \times 10^9/L$	$3.5\text{--}11 \times 10^9/L$
Platelets	$267 \times 10^9/L$	$150\text{--}440 \times 10^9/L$

Magnetic resonance images (MRIs) of the abdomen and pelvis are shown in Figs. 7.1 and 7.2.

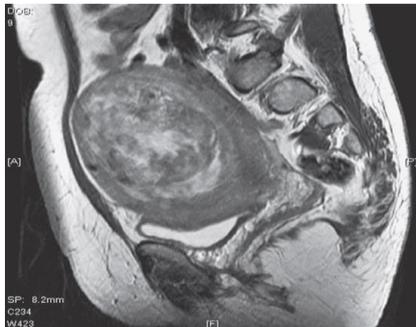


Figure 7.1 MRI of the abdomen and pelvis



Figure 7.2 MRI of the abdomen and pelvis.

Questions

- What is the diagnosis?
- How would you further investigate and manage this woman?

ANSWER 7

The woman has a large uterine fibroid (leiomyoma). This is causing menorrhagia and hence the microcytic anaemia from iron deficiency. Urinary frequency occurs due to the pressure of the large mass on the bladder. It is also likely that the fibroid is accounting for her infertility history, although this warrants investigation as a separate problem.

Fibroids are benign tumours of the myometrium which may be extrinsic (subserous) as in this case. Alternatively they may be intramural or submucosal (projecting into the endometrial cavity).

! Typical presentations of fibroids

- Menorrhagia
- Abdominal mass
- Pressure effect from pressure on the bladder, stomach or bowel
- Infertility

Fibroids are not typically painful unless they undergo degeneration, usually in pregnancy.

African-Caribbean women tend to develop fibroids more commonly than other ethnic groups.

Further investigation

Ferritin and folate levels should be checked to confirm the iron-deficiency status. It is also advisable to arrange renal function tests and a renal tract ultrasound, as very large fibroids can cause ureteric obstruction and hydronephrosis, which would need urgent treatment.

Management

The woman should be treated for her anaemia with ferrous sulphate. The menorrhagia can be reduced with tranexamic acid during menstruation. Gonadotrophin-releasing hormone analogues temporarily shrink fibroids and cause amenorrhoea to allow correction of iron deficiency. Gonadotropin-releasing hormone agonists (GnRHa) are useful in stopping bleeding temporarily to allow anaemia to recover prior to surgery, but are associated with hypoestrogenic side effects such as hot flushes and night sweats. Treatment with ulipristal acetate (a selective progesterone receptor modulator (SPRM) with progesterone agonist and antagonist properties) also effectively controls excessive bleeding and reduces the size of the fibroid with less side effects. Definitive treatment for fibroids is traditionally by hysterectomy or myomectomy. Myomectomy is favourable for this woman who is keen to have a family, so conservation of the uterus is essential. Uterine artery embolization also causes fibroid degeneration by interruption of the blood supply. However research into long-term safety and potential effects on uterine function during pregnancy are not clear.

KEY POINTS

- Fibroids may be small and incidental or occupy most of the abdomen.
- Anaemia should be suspected in any women with menorrhagia.
- Treatment of fibroids depends on the presence of symptoms and the necessity to preserve fertility.
- The optimal operative approach depends on the size and location of the fibroids.

CASE 8: ABNORMAL CERVICAL SMEAR

History

A 28-year-old woman attends the colposcopy clinic after an abnormal liquid-based cytology smear test. She is very anxious as she thinks that she might have cervical cancer. The smear is reported as 'severe dyskaryosis'. She had a previous normal result at age 25 years. She has not had any postcoital or intermenstrual bleeding.

Her first sexual relationship started at the age of 14 years and she has had several partners since then. She lives with her current partner who she has been with for 3 years. She was diagnosed with genital herpes several years ago but has not had any attacks for at least 3 years. She smokes 15–20 cigarettes per day and drinks only at the weekends.

She has an intrauterine contraceptive device *in situ*.

Examination

The cervix is macroscopically normal. At colposcopy, acetic acid is applied and an irregular white area is apparent to the left of the os. Lugol's iodine is applied and the same area stains pale while the rest of the cervix stains dark brown. A biopsy is taken.

INVESTIGATIONS

Cervical biopsy report: the sample received measures 4 × 2 mm and contains enlarged cells with irregular nuclei consistent with CIN3.

Questions

- How should this patient be managed?

ANSWER 8

The colposcopy findings show an abnormal area on the left of the cervix. The abnormal tissue stains white with acetic acid because abnormal cells have high-density nuclei which take up the acetic acid more than normal cells. In contrast, abnormal cells have lower glycogen content than normal cells and stain less well, remaining pale when iodine is applied.

The diagnosis is of CIN3 (cervical intraepithelial neoplasia). This is a tissue diagnosis as opposed to dyskaryosis which is an observation of cells from a smear. The degree of dyskaryosis and CIN often correlate, but a dyskaryosis report is not a diagnosis. After a smear showing severe dyskaryosis she has an 80–90 per cent chance of CIN 2 or 3 being found histologically on biopsy at colposcopy.

Management

CIN3 needs to be treated to prevent progression possibly over several years to cervical carcinoma. The commonest treatment is large-loop excision of the transformation zone (LLETZ) – removal of abnormal cervical tissue with a diathermy loop. Most women tolerate this under local anaesthetic. The LLETZ sample needs to be examined histologically both to confirm removal of all the abnormal tissue, and to ensure that there is not a focus of carcinoma within the sample.

Assuming that all of the abnormal cells are excised, with clear margins, at the time of LLETZ treatment, then six-month follow-up should be arranged where she should have a repeat smear and human papilloma virus (HPV) screening. If both are negative then she can go back to 3-yearly smear tests. If either is positive then annual smears remain necessary for 10 years.

She should be strongly advised to stop smoking as this is a significant modifiable risk factor for cervical carcinoma.

! Advice after LLETZ procedure

- The patient may have light bleeding for several days.
- If heavy bleeding occurs she should return as secondary infection may occur and need treatment.
- She should avoid sexual intercourse and tampon use for 4 weeks, to allow healing of the cervix.
- Fertility is generally unaffected by the procedure, though cervical stenosis leading to infertility has been reported, and midtrimester loss from cervical weakness is rare.

KEY POINTS

- Dyskaryosis refers to abnormality from a smear.
- Dysplasia and cervical intraepithelial neoplasia are histological terms from a biopsy sample.
- High-grade CIN should be treated to prevent long-term progression to cervical carcinoma.
- Human papilloma virus (HPV) testing is a triage tool to identify women at high risk of progression to more severe cervical pathology.

CASE 9: ANAEMIA

History

A 39-year-old woman is referred from the haematologist, with anaemia. She had been complaining of increasing tiredness and shortness of breath for 3 months, with frequent headaches.

Her periods occur every 24 days and the first day is generally moderate but the second to fourth days are very heavy. She uses tampons and sanitary towels together. She has no pain. Her last smear test was normal 2 years ago. She has had no previous gynaecological problems and takes no medication.

Examination

The woman is slim with pale conjunctivae. Abdominal, bimanual and speculum examination are unremarkable.

INVESTIGATIONS

		<i>Normal range</i>
Haemoglobin	6.3 g/dL	11.7–15.7 g/dL
Mean cell volume	66 fL	80–99 fL
White cell count	$9.1 \times 10^9/L$	$3.5\text{--}11 \times 10^9/L$
Platelets	$300 \times 10^9/L$	$150\text{--}440 \times 10^9/L$
Ferritin	9 mg/L	6–81 mg/L
Iron	7 mmol/L	10–28 mmol/L
Total iron-binding capacity (TIBC)	80 mmol/L	45–72 mmol/L

Blood film: hypochromic microcytic red cells

Transvaginal ultrasound scan report (day 4): the uterus is normal size and retroverted. The endometrium is smooth and thin measuring 3.1 mm. Both ovaries are normal.

Questions

- How do you interpret these findings?
- What is the likely underlying diagnosis?
- How would you manage this woman?

ANSWER 9

The blood count shows anaemia with reduced mean cell corpuscular volume and low mean cell haemoglobin suggestive of a microcytic anaemia. Iron deficiency is the commonest cause for this picture and is confirmed by the low ferritin and iron, with raised iron-binding capacity. The anaemia accounts for the breathlessness, tiredness and headaches.

Menorrhagia is the commonest cause of anaemia in women, and in this case is supported by the history of excessive bleeding. The woman herself may not recognize that her periods are

particularly heavy if she has always experienced heavy periods or if she thinks it is normal for her periods to become heavier as she gets older.

As no other cause of heavy bleeding is apparent from the history and the ultrasound is normal, then the underlying diagnosis is one of exclusion referred to as dysfunctional uterine bleeding (DUB).

Dysfunctional uterine bleeding

Excessive heavy, prolonged or frequent bleeding that is not due to pregnancy or any recognizable pelvic or systemic disease.

Management

The anaemia should be treated with ferrous sulphate 200 mg twice daily until haemoglobin and ferritin are normal. It may take 3–6 months for iron stores to be fully replenished. Tranexamic acid (an antifibrinolytic) should be given during menstruation to reduce the amount of bleeding. It is contraindicated with a history of thromboembolic disease.

The levonorgestrel-releasing intrauterine device is used for its action on the endometrium to reduce menorrhagia, often causing amenorrhoea, though it is commonly associated with irregular bleeding for the first 3 months. The combined oral contraceptive pill is effective for menorrhagia in young women (below 35 years).

If these first-line management options are ineffective then endometrial ablation should be considered, which destroys the endometrium down to the basal layer. It is successful in 80–85 per cent of women and they should have completed their family and use effective contraception. There are several approved minimally invasive endometrial ablation techniques with broadly similar efficacy: these include use of radiofrequency waves, electrocautery, microwaves, heated saline, or a heated balloon. Amenorrhoea occurs in 30–60 per cent of women with 70–90 per cent describing their satisfaction as good or excellent.

Hysterectomy is considered a ‘last resort’ for DUB, due to the associated morbidity.

KEY POINTS

- A woman’s perception of bleeding is not always proportionate to the actual volume lost, so haemoglobin should be checked in any woman suspected of menorrhagia.
- DUB is a diagnosis of exclusion.
- A hierarchy of first-, second- and third-line treatment should be used in management

CASE 10: ABSENT PERIODS

History

A 25-year-old woman presents with the absence of periods for 9 months. She started her periods at the age of 13 years and had a regular 28-day cycle until 18 months ago. The periods then became irregular, occurring every 2–3 months until they stopped completely. She has also had headaches for the last few months and is not sure if this is related. She has a regular sexual partner and uses condoms for contraception. She has never been pregnant. There is no previous medical history of note.

She works as a primary school teacher and drinks approximately 4 units of alcohol per week. She does not smoke or use recreational drugs. She jogs and swims in her spare time.

Examination

The woman is of average build. The blood pressure and general observations are normal. The abdomen is soft and non-tender and speculum and bimanual examination are unremarkable.

INVESTIGATIONS		
	<i>Normal</i>	
Follicle-stimulating hormone	7 IU/L	Day 2–5 1–11 IU/L
Luteinizing hormone	4 IU/L	Day 2–5 0.5–14.5 IU/L
Prolactin	1800 mu/L	90–520 mu/L
Testosterone	1.8 nmol/L	0.8–3.1 nmol/L
Magnetic resonance imaging (MRI) scan of the head is shown in Fig. 10.1.		

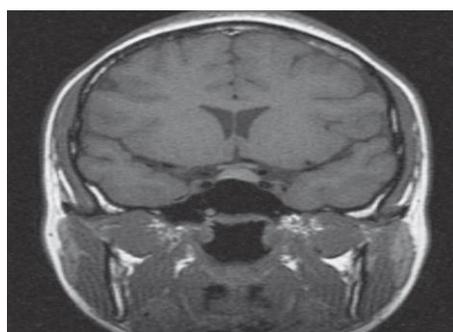


Figure 10.1 MRI scan of the head.

Questions

- What is the diagnosis?
- Are any further investigations indicated?
- How would you manage this patient?

ANSWER 10

The investigations show a high-prolactin and a space-occupying lesion in the pituitary fossa in the region of the anterior pituitary as detailed in Fig. 10.2. This is consistent with a pituitary adenoma (prolactinoma).

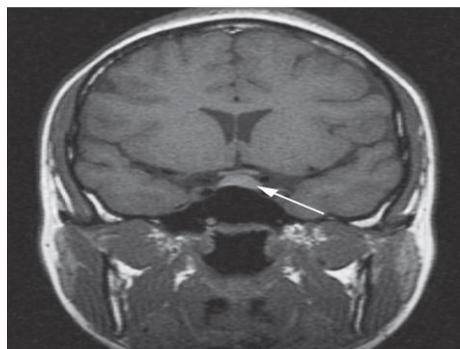


Figure 10.2 Arrow shows a small asymmetrical enlargement of pituitary gland, representative of a small pituitary adenoma (prolactinoma).

Prolactin should always be measured in a woman with amenorrhoea. Care should be taken in interpreting the results, as levels up to 1000 mu/L can be found as a result of stress (even due to venepuncture), breast examination or in association with polycystic ovarian syndrome. Above 1000 mu/L the usual cause is a pituitary adenoma (micro- or macroscopic).

! Differential diagnosis of secondary amenorrhoea

- *Hypothalamic:*
 - chronic illness
 - anorexia
 - excessive exercise
 - stress
- *Pituitary:*
 - hyperprolactinaemia (e.g. drugs, tumour)
 - hypothyroidism
 - breast-feeding
- *Ovarian:*
 - polycystic ovarian syndrome
 - premature ovarian failure
 - iatrogenic (chemotherapy, radiotherapy, oophorectomy)
 - long-acting progesterone contraception
- *Uterine:*
 - pregnancy
 - Asherman's syndrome
 - cervical stenosis

Further investigation

Visual fields should be checked, as visual field defects may be present with a large tumour. Thyroid function should be tested as hypothyroidism is also a cause of amenorrhoea. The other important investigation in any woman with amenorrhoea is a pregnancy test, although with this history this would be very unlikely. (Prolactin is also raised in pregnancy.)

Management

Most prolactinomas respond to medical treatment with bromocriptine or cabergoline. These are both dopamine agonists, which inhibit prolactin secretion from the anterior pituitary. Cabergoline is generally the first-line agent in the management of prolactinomas and idiopathic hyperprolactinaemia due to higher affinity for D2 receptor sites, more rapid resolution of prolactin levels, menstruation and return of ovulatory cycles and a better side effect profile.

Maintaining the prolactin level below 1000 mu/L causes menstruation (and ovulation) to return in most women. This can be continued indefinitely or until pregnancy is achieved if the presenting complaint is of infertility.

KEY POINTS

- Hyperprolactinaemia is a common cause of secondary amenorrhoea.
- Prolactin levels up to 1000 u/L may be due to non-pathological causes such as stress.
- Prolactinomas can usually be treated effectively with medical suppression, and surgery is only indicated rarely.

CASE 11: POSTMENOPAUSAL BLEEDING

History

A 58-year-old woman awoke with blood on her nightdress, which was bright red but not heavy. There were no clots of blood and there was no associated pain. The bleeding has recurred twice since in similar amounts.

Her last period was at the age of 49 years and she has had no other intervening bleeding episodes. She suffered hot flushes and night sweats around the time of her menopause, which have now stopped. She is sexually active but has noticed vaginal dryness on intercourse recently.

She has always had normal cervical smears, the last one being 7 months ago. She had two children by spontaneous vaginal delivery and had a laparoscopic sterilization aged 34 years. She has never used hormone-replacement therapy (HRT). She takes atenolol for hypertension and omeprazole for epigastric pain.

Examination

She is slightly overweight. Abdominal examination is normal. The vulva and vagina appear thin and atrophic and the cervix is normal. The uterus is small and anteverted and with no palpable adnexal masses. An outpatient endometrial biopsy is taken at the time of examination and sent for histological examination.

INVESTIGATIONS

Transvaginal ultrasound scan is shown in Fig. 11.1.

Endometrial biopsy report: the specimen shows atrophic endometrium with no evidence of inflammation, hyperplasia or malignancy.



Figure 11.1 Transvaginal ultrasound scan showing a midsagittal view of the uterus and endometrial 'stripe'. The endometrial thickness is measured to be 2.8 mm.

Questions

- What is the likely diagnosis?
- How would you manage this patient?

ANSWER 11

Postmenopausal bleeding is considered to be caused by endometrial cancer until proven otherwise. However only 10 per cent of women with postmenopausal bleeding are diagnosed with endometrial cancer.

! Causes of postmenopausal bleeding

- Endometrial cancer
- Endometrial/endocervical polyp
- Endometrial hyperplasia
- Atrophic vaginitis
- Iatrogenic (anticoagulants, intrauterine device, hormone-replacement therapy)
- Infective (vaginal candidiasis)

In this case the endometrium is <3 mm on ultrasound, which effectively excludes an endometrial malignancy or polyp. The normal endometrial biopsy report confirms the absence of endometrial

pathology. The smear history is normal, and the cervix appears normal, excluding cervical cancer. She is not taking any medication that may predispose to abnormal bleeding.

The diagnosis of atrophic vaginitis can therefore be made by exclusion of serious causes, and is backed up by the history of vaginal dryness at sexual intercourse and the atrophic vulva and vagina noted on examination.

Management

Treatment is hormonal with a course of topical oestrogen given daily for 3 weeks and then twice weekly for maintenance, for an initial period of 2–3 months. An alternative solution is to give a combined form of systemic HRT to protect the endometrium.

Some women are reluctant to use HRT because of the associated risks, and therefore advice should be given about vaginal lubricants which decrease discomfort but have no reparative value. If bleeding recurs after treatment or the diagnosis is in doubt, then further investigation with hysteroscopy and biopsy, ideally as an outpatient procedure is needed.

KEY POINTS

- Women with postmenopausal bleeding (PMB) should be considered to have endometrial cancer until proven otherwise.
- Endometrial thickness, endometrial biopsy and hysteroscopy are used to investigate PMB.
- Endometrial thickness less than 4 mm in a woman with postmenopausal bleeding reduces the probability of carcinoma to less than 3 per cent (although individual protocols may use different cutoff levels).
- Atrophic vaginitis can be treated with courses of topical oestrogens.

CASE 12: PAINFUL PERIODS

History

A 43-year-old woman is referred from her general practitioner (GP) with painful periods. She says that her periods have always been quite heavy and painful but that in the last 2–3 years they have become almost unbearable. She bleeds every 24 days and the period lasts for 7–9 days with very heavy flow from day 2 to day 6. The pain starts approximately 36 h before the onset of the bleeding and lasts until about day 5. The pain is constant, dull and severe, such that she cannot do any housework or any social activities during this time. Her GP has prescribed paracetamol and mefenamic acid in combination, which she says ‘takes the edge off’ but does not fully relieve the symptoms.

She has had four normal deliveries and her husband had a vasectomy several years ago.

There is no history of intermenstrual or postcoital discharge and she has no abnormal discharge. Her smear history is normal, the most recent being 18 months ago. She takes citalopram for depression but currently reports her mood as fine. She does not drink alcohol or smoke.

Examination

The abdomen is soft and there is vague tenderness in the suprapubic area. The cervix appears normal. On bimanual palpation the uterus is approximately 10 weeks size, soft and bulky. She is tender on palpation but there is no cervical excitation, adnexal tenderness or adnexal masses.

INVESTIGATIONS

Transvaginal ultrasound scan is shown in Fig. 12.1.

Transvaginal ultrasound report: there is asymmetrical uterine enlargement, with a thickened posterior uterine wall. There are ill-defined cystic spaces within the posterior myometrial wall. There is an indistinct myometrial-endometrial border. Both ovaries appear normal in size and morphology.



Figure 12.1 Transvaginal ultrasound scan showing a midsagittal view of the uterus.

Questions

- What is the likely diagnosis?
- How would you further investigate and manage this woman?

ANSWER 12

The symptoms of dysmenorrhoea and menorrhagia and the ultrasound report suggest a diagnosis of adenomyosis. This is a benign condition whereby functioning endometrial glands and stroma are found within the myometrium. With each period bleeding occurs from the endometrial tissue into the smooth muscle, with associated pain. It tends to occur in women over 35 years and risk factors include increased parity, termination and previous caesarean section. The condition may commonly be found in association with endometriosis. Classically the diagnosis may only be made histologically after hysterectomy for dysmenorrhoea. More recently however the diagnosis can be suspected by ultrasound or magnetic resonance imaging (MRI) scan.

! Causes of dysmenorrhoea

- Idiopathic
- Premenstrual syndrome
- Pelvic inflammatory disease
- Endometriosis
- Adenomyosis
- Submucosal pedunculated fibroids
- Iatrogenic (e.g. intrauterine contraceptive device (IUCD) or cervical stenosis after large-loop excision of the transformation zone (LLETZ))

Further investigation

If the diagnosis is in doubt then an MRI scan may be requested. Hysterectomy to obtain histological diagnosis would be inappropriate.

Management

The initial management involves analgesia such as mefenamic acid and codydramol. Tranexamic acid reduces the amount of bleeding, and this may secondarily reduce the amount of pain.

Suppression of menstruation with gonadotrophin-releasing hormone analogues is a short-term measure. The levonorgestrel-releasing intrauterine device is another option to locally suppress the endometrial tissue, and may resolve the pain.

As a last resort hysterectomy should be performed.

KEY POINTS

- The prevalence of adenomyosis is unknown, as diagnosis is only confirmed by hysterectomy.
- It is a cause of menorrhagia and dysmenorrhoea in older women.
- Hysterectomy may be avoided by use of analgesia or hormonal suppression.

CASE 13: POSTCOITAL BLEEDING

History

An 19-year-old woman is referred with postcoital bleeding. It has occurred on approximately seven occasions over the preceding 6 weeks. Generally it has been a small amount of bright red blood noticed a few hours after intercourse and lasting up to 2 days. There is no associated pain.

Her last menstrual period started 3 weeks ago and she bleeds for 4 days every 28 days. Her periods were previously quite heavy but are now lighter since she started the combined oral contraceptive pill (COCP) 6 months ago. There is no history of an abnormal discharge or offensive odour and she has no dyspareunia.

She has had three sexual partners and has been with her current partner for 10 months. She has never been diagnosed with any sexually transmitted infection and has never had a smear test. She had an appendectomy at the age of 7 years and was diagnosed with epilepsy in childhood but has been off all medication for 8 years.

Examination

The abdomen is soft and non-tender. Speculum examination reveals a florid reddened area symmetrically surrounding the external cervical os with contact bleeding. The uterus is normal sized, anteverted and non-tender. There is no cervical excitation and the adnexae are unremarkable.

Questions

- What is the differential diagnosis?
- What further investigations would you perform for this woman?
- If your investigations are negative what is the likely diagnosis and how would you manage the woman?

ANSWER 13

Postcoital bleeding in a young woman is common and normally benign. In this specific case the examination findings are consistent only with cervical ectropion, malignancy or infection.

! Differential diagnoses of postcoital bleeding in a young woman

- Cervical ectropion
- Chlamydia or other sexually transmitted infection (STI)
- Cervical malignancy
- Complication of the COCP
- Endocervical polyp

INVESTIGATIONS

An STI screen should be performed:

- endocervical swab for chlamydia
- endocervical swab for gonorrhoea
- high vaginal swab for trichomonas (and candida, not a STI, but possibly a cause of irregular bleeding from vaginitis).

A cervical smear should also be taken to exclude cervical intraepithelial neoplasia or malignancy prior to treatment.

Management

Assuming the swabs and smear are negative then the diagnosis is of cervical ectropion. This is particularly common around the time of puberty, in women using the COCP, and in pregnancy. It is not of clinical significance and is generally an incidental finding but warrants treatment if it causes embarrassing and troublesome bleeding (or discharge in some cases).

There are three options for treatment:

1. stop the COCP and use alternative contraception
2. cold coagulation of the cervix
3. diathermy ablation of the ectocervix.

KEY POINTS

- Cervical ectropion is very common and usually incidental and asymptomatic.
- It occurs particularly in pregnancy and with use of the COCP.
- Postcoital bleeding should always be investigated to exclude significant pathology.

CASE 14: RECURRENT MISCARRIAGE

History

A 34-year-old woman is referred from the emergency room with vaginal bleeding at 6 weeks and 5 days' gestation. Bleeding started 2 days ago and was initially spotting but has now increased so that she needs to change a sanitary towel regularly. There is a mild dull lower abdominal pain.

She normally has a regular 28-day cycle. In the past she has used the combined oral contraceptive pill but stopped 3 years ago when she and her partner decided to start a family.

She is gravida 3 para 0. Her first pregnancy ended in a complete miscarriage 2 years ago. Five months ago she had a missed miscarriage at 9 weeks and underwent surgical management.

There is no gynaecological history of note. Medically she is fit and healthy, except for mild asthma for which she takes inhalers.

The woman's mother died from a pulmonary embolism after her last child. Her brother also had a deep venous thrombosis at the age of 29 years. Her sister has two children, both born preterm because of severe pre-eclampsia.

Examination

The abdomen is non-distended but tender suprapubically. The cervical os is open and products of conception are removed from the os and sent for histological examination. The bleeding subsequently settles.

INVESTIGATIONS		
		<i>Normal range for pregnancy</i>
Haemoglobin	11.1 g/dL	11–14 g/dL
White cell count	$3.9 \times 10^9/L$	$6–16 \times 10^9/L$
Platelets	$201 \times 10^9/L$	$150–400 \times 10^9/L$
Anticardiolipin antibody: positive Lupus anticoagulant: positive Histology report: chorionic villi are seen, confirming products of conception.		

Questions

- What is the likely underlying diagnosis for the recurrent miscarriages?
- What further investigation should be performed?
- How should this patient be managed?

ANSWER 14

Raised anticardiolipin antibodies and lupus anticoagulant are suggestive of antiphospholipid syndrome.

! Diagnosis of antiphospholipid syndrome

- The presence of one of the clinical features:
 - three or more consecutive miscarriages
 - midtrimester fetal loss
 - severe early-onset pre-eclampsia, intrauterine growth restriction or abruption
 - arterial or venous thrombosis
- And haematological features:
 - anticardiolipin antibody or lupus anticoagulant detected on two occasions at least 6 weeks apart

Thus in this case the diagnosis must be confirmed by a second positive anticardiolipin test after at least 6 weeks. She should also be tested for antinuclear and anti-double-stranded DNA antibodies as antiphospholipid syndrome may be secondary to systemic lupus erythematosus (SLE).

Management

Oral low-dose aspirin and low-molecular-weight subcutaneous heparin from the time of a positive pregnancy test should be given in subsequent pregnancies to improve the likelihood of a successful live birth.

In the case of this woman, with such a strong family history of thrombosis and proven antiphospholipid syndrome, she would also be recommended thromboprophylaxis throughout the pregnancy and postnatal period.

There is as yet no proven benefit from progesterone in women with recurrent miscarriage. Psychological support should be given with regular reassurance ultrasound scans in the first trimester. There is some evidence that shows repeated ultrasound scans for reassurance alone improve the outcome after recurrent miscarriage.

! Causes of recurrent miscarriage

- Parental chromosome abnormality (3–5 per cent, e.g. balanced translocation)
- Antiphospholipid syndrome
- Other thrombophilia (e.g. activated protein C resistance)
- Uterine abnormality (intracavity fibroids, uterine septum)
- Uncontrolled diabetes or hypothyroidism
- Bacterial vaginosis (usually associated with second-trimester loss)
- Cervical weakness ('incompetence', second-trimester loss only)

KEY POINTS

- Only a minority of women with recurrent miscarriage will have a cause identified.
- Aspirin and heparin are effective in women with antiphospholipid syndrome.
- Reassurance ultrasound scans and support may improve outcome for women with recurrent loss.

CASE 15: PELVIC PAIN

History

A 29-year-old woman presents with lower abdominal pain for 4 years occurring with her periods. She takes paracetamol and ibuprofen and goes to bed with a hot water bottle for up to 2 days every month. For the last 18 months pain has also occurred in between periods.

The pain is dull and constant across the lower abdomen. Her periods are regular and there is no menorrhagia, intermenstrual or postcoital bleeding. There is no other significant medical history.

She has been married for 2 years and has deep dyspareunia which makes her interrupt intercourse. She does not use any contraception, as they are keen to start a family. She has never been pregnant in the past.

Examination

There is generalized lower-abdominal tenderness, particularly in the suprapubic area but no masses are palpable. Speculum examination is unremarkable. On bimanual palpation the uterus is axial and fixed with cervical excitation. The Pouch of Douglas is very tender and contains a mass. The adnexae are both tender but no adnexal masses are palpable.

INVESTIGATIONS

Transvaginal ultrasound scan is shown in Fig. 15.1.
The findings at laparoscopy are shown in Fig. 15.2.



Figure 15.1 Transvaginal ultrasound scan showing transverse view of the Pouch of Douglas.



Figure 15.2 Findings at laparoscopy (see colour insert).

Questions

- What is the diagnosis?
- How would you further manage this woman?

ANSWER 15

The history of dysmenorrhoea and dyspareunia is classic for endometriosis, and the ultrasound examination ('kissing cysts') and laparoscopy images show bilateral endometriomas ('chocolate cysts'), a complication of this disease.

Endometriosis is a common condition where active endometrial glands and stroma are located outside the endometrial cavity. Endometriomas develop as ectopic endometrial tissue on the ovary produces blood, which builds up into an encapsulated cyst with each consecutive menstrual cycle.

Endometriosis is benign but carries a high physical and psychological morbidity due to the clinical features:

- pelvic pain
- dysmenorrhoea
- dyspareunia
- infertility.

Examination findings include tenderness or a pelvic mass, and may include palpable nodules in the rectovaginal septum and a fixed retroverted uterus secondary to adhesions (the 'frozen pelvis').

Diagnosis is made at laparoscopy, although ultrasound features such as these ovarian cysts containing 'ground-glass' echoes can be suggestive.

Management

The mainstay of management for endometriosis is surgical, with ablation or excision of endometriotic deposits by laparoscopy. In this case there are bilateral endometriotic cysts that need to be removed laparoscopically by incision and drainage and either cautery to or stripping of the cyst capsules. Surgical treatment should relieve the dyspareunia and dysmenorrhoea and may improve fertility in more severe disease.

Medical suppression of endometriosis is possible with the contraceptive pill or gonadotrophin-releasing hormone analogues, which inhibit ovulation and hence prevent stimulation of endometrial deposits by oestrogen. However these are ineffective for endometriomas. The levonorgestrel-releasing intrauterine device has also been used to suppress endometriosis and reduce symptoms.

KEY POINTS

- Endometriosis classically presents with dysmenorrhoea, dyspareunia and infertility.
- Endometriosis is often diagnosed years after symptoms start.
- Surgical excision is the mainstay of treatment.

CASE 16: INFERTILITY

History

A 31-year-old woman and her 34-year-old partner are referred by the general practitioner because of primary infertility. They have been trying to conceive for over 2 years. The woman has regular menstrual periods, bleeding for 4 days every 28–30 days. Her periods are not heavy and have never been painful. There is no intermenstrual bleeding or discharge and no postcoital bleeding. She has never been diagnosed with any sexually transmitted infections.

The last smear was normal 1 year ago. She is a non-smoker and drinks alcohol very occasionally.

The partner's only previous medical history was an appendectomy and a course of anti-*Helicobacter* therapy after he developed epigastric pain and was diagnosed with the infection. He previously smoked 20 cigarettes per day and drank up to 28 units of alcohol per week but has now stopped smoking and significantly reduced his alcohol intake. He works as buyer for a retail company.

The couple has intercourse 1–4 times per week and there is no reported sexual dysfunction or pain on intercourse. They both deny recreational drug use.

Examination

On examination the woman has a body mass index of 23 kg/m². There is no hirsutism or acne. There are no signs of thyroid disease. The abdomen is soft and non-tender. Speculum and bimanual palpation are unremarkable. Genital examination of the partner is also normal.

INVESTIGATIONS

		<i>Normal range</i>
Follicle-stimulating hormone (day 3)	4.2 IU/L	Day 2–5 1–11 IU/L
Luteinizing hormone (day 3)	2.7 IU/L	Day 2–5 0.5–14.5 IU/L
Day 21 progesterone	45 nmol/L	
Prolactin	374 mu/L	90–520 mu/L
Testosterone	2.0 nmol/L	0.8–3.1 nmol/L
Semen analysis		
Volume	4 mL	2–5 mL
Count	63 million/mL	>20 million/mL
Normal forms	22 per cent	>15 per cent normal shape
Motility	53 per cent progressively mobile	>50 per cent progressively mobile
Rubella antibody: immune Chlamydia: negative A hysterosalpingogram is shown in Fig. 16.1 .		

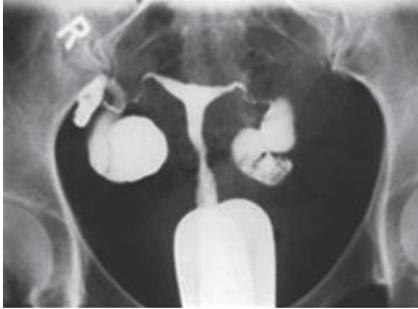


Figure 16.1 Hysterosalpingogram.

Questions

- How do you interpret the investigation results?
- Are any further investigations necessary?
- How would you manage this couple?

ANSWER 16

Day 21 progesterone above 30 nmol/L confirms ovulation, and this is supported by normal follicle-stimulating hormone (FSH), luteinizing hormone (LH) and prolactin. Normal testosterone suggests that polycystic ovaries is an unlikely diagnosis.

The semen analysis is normal, and therefore any male factor aetiology is unlikely. Rubella immunity should always be confirmed.

The hysterosalpingogram shows fill of contrast medium into both uterine tubes but no spill, suggesting tubal obstruction as the cause of the fertility problem.

Further investigation

Tubal blockage on hysterosalpingogram can sometimes be due to tubal spasm, and therefore a laparoscopy and dye is needed to confirm the pathology and also to determine a cause such as adhesions from previous infection or possibly endometriosis (although the history does not support this diagnosis).

Management

If the tubes are found at dye test to be patent, then this would suggest that it is feasible to attempt pregnancy with in utero insemination. However if blocked tubes are confirmed then in vitro fertilization (IVF) is indicated. Abnormal tubes are usually removed prior to IVF, as success rates for pregnancy are better and ectopic pregnancy rate reduced after bilateral salpingectomy.

General advice should be given to take folic acid 400 mg daily to reduce the risk of neural tube defects, and to the partner to minimize his alcohol intake.

In this case the laparoscopy showed bilateral hydrosalpinges and adhesions as well as perihepatic 'violin-string' adhesions. These findings are consistent with previous infection with chlamydia (or more rarely gonorrhoea). It is not unusual to find such severe pelvic adhesions even when there has never been a clear clinical history of pelvic infection or sexually transmitted infection. Although the infection may be long ago, it is sensible to treat both the woman and her partner with a course of antibiotics for pelvic inflammatory disease.

KEY POINTS

- Infertility may be due to anovulation, tubal or endometrial/uterine pathology as well as male factors.
- Up to 30 per cent of infertile couples have more than one factor causing infertility.
- Tubal obstruction on hysterosalpingogram is not always confirmed at laparoscopy.

CASE 17: HEAVY PERIODS

History

A 39-year-old woman complains of increasingly long and heavy periods over the last 5 years. Previously she bled for 4 days but now bleeding lasts up to 10 days. The periods still occur every 28 days. She experiences intermenstrual bleeding between most periods but no postcoital bleeding.

The periods were never painful previously but in recent months have become extremely painful with intermittent cramps. She has had four normal deliveries and had a laparoscopic sterilization after her last child. Her smear tests have always been normal, the most recent being 4 months ago. She has never had any previous irregular bleeding or any other gynaecological problems.

Examination

The abdomen is soft and non-tender with no palpable masses. Speculum examination shows a normal cervix. On bimanual palpation the uterus is bulky (approximately 8-week size), mobile and anteverted. There are no adnexal masses.

INVESTIGATIONS

		<i>Normal range</i>
Haemoglobin	9.2 g/dL	11.7–15.7 g/dL
Mean cell volume	75 fL	80–99 fL
White cell count	$4.5 \times 10^9/L$	$3.5–11 \times 10^9/L$
Platelets	$198 \times 10^9/L$	$150–440 \times 10^9/L$

Findings at hysteroscopy are shown in Fig. 17.1.



Figure 17.1 Hysteroscopy (see colour insert).

Questions

- What is the diagnosis?
- What further preoperative non-invasive investigation might have allowed the same diagnosis?
- How would you manage this patient and counsel her about the management and its potential risks?

ANSWER 17

The hysteroscopy shows a submucosal fibroid. Ultrasound scan would have provided a preoperative diagnosis too. At hysteroscopy a submucosal fibroid appears as a solid, pale, smooth,

relatively immobile (unless pedunculated) structure, whereas a polyp appears pink, fleshy and highly mobile. Submucosal fibroids are a common cause of menorrhagia and can cause, as in this case, intermenstrual bleeding. The cramp-like pain occurs as the uterus tries to expel the fibroid. In some cases this eventually occurs with the fibroid becoming pedunculated and extending through to the vagina on a pedicle.

Management

The management is by hysteroscopic (transcervical) resection of the fibroid (TCRF). This can be performed as a day case under general anaesthetic (or even local anaesthetic if the fibroid is small). The important points in counselling the patient are as follows.

- *Description of the procedure:* the procedure involves stretching (dilatation) of the cervix and insertion of an endoscope into the uterus (hysteroscopy) to view the fibroid. The fibroid is 'shaved' away with a hot wire loop (diathermy). Fluid is circulated through the uterine cavity to enhance the view and allow cooling.
- What are the risks?
- Bleeding: it is rare to bleed heavily but in the extreme situation blood transfusion could be required, or even a hysterectomy to control the loss
- Infection
- Fluid overload: during the procedure, irrigation fluid is absorbed into the circulation. Excessive absorption can cause breathing difficulties (pulmonary oedema) and the need for hospital admission
- Uterine perforation: rarely the hysteroscope perforates the wall of the uterus, and if this occurs or is suspected then laparoscopy is needed immediately to confirm it, secure any bleeding and check for damage to surrounding bowel or bladder.
- *What to expect afterwards:* most women experience bleeding, discharge and passing of 'debris' for up to 2 weeks after the procedure.

KEY POINTS

- Ultrasound is critical in the diagnosis of menorrhagia.
- Submucosal fibroids are more likely to cause menorrhagia than those that are intramural or subserous.
- Transcervical resection of fibroids is a relatively simple procedure but is associated with important risks.

CASE 18: URINARY INCONTINENCE

History

A 61-year-old woman complains of involuntary loss of urine. She has noticed it gradually over the last 10 years and has finally decided to see her general practitioner about it after hearing a programme on the radio about treatment for incontinence. The leaking is generally of small amounts and she wears a pad all the time. It tends to occur when she cannot get to the toilet in time. She never leaks on coughing or sneezing. She suffers urgency, particularly when she comes home after being out and is about to come into the house. She also has frequency, passing urine every hour during the day and getting up two or three times each night.

Due to the incontinence she tries not to drink much and usually has two cups of tea first thing in the morning, coffee mid-morning and a further cup of tea mid-afternoon. Other than that she drinks one glass of squash per day and has one glass of wine at night.

She is a non-smoker. She has had two uncomplicated vaginal deliveries. Her periods stopped at the age of 54 years. There is no other gynaecological or medical history of note.

Examination

Abdominal examination is normal. On vaginal examination there is minimal uterovaginal descent and no anterior or posterior vaginal wall prolapse.

INVESTIGATIONS

Midstream urinalysis: protein negative, blood negative, leucocytes negative, nitrites negative
Urodynamics: the first urge to void was reported at 150 mL bladder filling. Involuntary detrusor contractions were noted while the patient was attempting to inhibit micturition. There was no loss of urine with coughing.

Questions

- What is the diagnosis?
- How would you advise and manage this patient?

ANSWER 18

The diagnosis is of urge urinary incontinence and overactive bladder syndrome (OAB), defined as urgency that occurs with or without urge incontinence (UI) and usually with frequency and nocturia. This was formerly referred to as detrusor instability. In this condition the bladder contracts involuntarily without the normal trigger to void caused by bladder filling. This results in involuntary loss of urine that is embarrassing and often impacts enormously on women's lives, as they are constantly aware of needing to void and where the nearest toilet might be.

Urodynamic investigation with filling and voiding cystometry is helpful (as in this case) in confirming the diagnosis by showing spontaneous detrusor contractions during bladder filling.

It is important to exclude other causes of such symptoms (such as urinary tract infection or a bladder tumour) with urine microscopy.

Management

- *Conservative:*
 - The woman should be advised that both caffeine and alcohol are bladder stimulants and are likely to worsen symptoms so should be minimized. She should take a normal fluid intake per day but avoid drinks after about 7 pm to limit nocturia.
 - Bladder retraining for 6 weeks, involving a 'drill' restricting voiding to increasing intervals should be taught.
- *Medical treatment:*
 - If lifestyle advice and bladder retraining fail then anticholinergic medication such as oxybutynin, tolterodine, fesoterodine or darifenacin should be commenced. The associated side effects to be warned of include dry eyes, dry mouth and constipation. Mirabegron is a beta-3-adrenoceptor agonist, which may be used if anticholinergics fail.
 - The effects of treatment should be monitored using one of the validated incontinence-specific quality-of-life scales.

KEY POINTS

- Overactive bladder syndrome is associated with urgency, frequency and urge incontinence.
- Conservative measures are bladder retraining and caffeine avoidance.
- Medical treatment is with anticholinergics.

CASE 19: ABSENT PERIODS

History

An 18-year-old woman presents with an absence of periods for 6 months. This has occurred twice before in the past but on both occasions menstruation returned so she was not too concerned. Her periods started at the age of 12 years and were initially regular. She has no medical history of note and denies any medication. She is currently in her first year at university. She runs most days and reports a 'healthy' diet avoiding carbohydrate foods and meat. She is the oldest of three siblings and her parents separated when she was 12 years. She has minimal contact with her father and lives mainly with her mother who she says she gets on well with. She has had a boyfriend in the past but has veered away from any sexual relationships.

Examination

The woman is tall and thin with a body mass index (BMI) of 15.5 kg/m². There is evidence of fine downy hair growth on her arms. Heart rate is 86/min and blood pressure 100/65 mmHg. Abdominal examination reveals no scars or masses, and genital examination is not performed.

INVESTIGATIONS

		<i>Normal range</i>
Follicle-stimulating hormone	1.0 IU/L	Day 2–5 1–11 IU/L
Luteinizing hormone	0.8 IU/L	Day 2–5 0.5–14.5 IU/L
Oestradiol	52 pmol/L	70–600 pmol/L
Prolactin	630 mu/L	90–520 mu/L
Testosterone	1.6 nmol/L	0.8–3.1 nmol/L

Transabdominal ultrasound report: the uterus is anteverted and measures 41 × 33 × 19 mm. The endometrium appears thin and regular measuring 2.3 mm. The right ovary contains a few tiny follicles and the ovarian volume is 4.3 cm³. The left ovary has no visible follicles and measures 3.8 cm³. No dominant follicle or corpus luteum is visualized on either ovary.

Questions

- What is the diagnosis?
- How would you further investigate and manage this woman?

ANSWER 19

The woman has evidence of hypogonadotrophic hypogonadism – she has low oestradiol levels associated with low gonadotrophin stimulation from the anterior pituitary. This may be due to various pituitary or hypothalamic causes, but in this case clearly relates to anorexia nervosa and possibly excessive exercise. The raised prolactin is consistent with stress and does not need to be investigated further. At a BMI below 18 kg/m², menstruation tends to cease, returning once the BMI increases again.

The ultrasound shows a small uterus, very thin inactive endometrium and immature ovaries with minimal follicular activity, all of which are typical findings in anorexia nervosa.

The previous episodes of amenorrhoea probably occurred when her dietary intake was very low and it may be that starting at university may have increased her stress levels with the consequence of worsening her anorexia.

Further investigation

- Full blood count, liver and renal function should all be monitored as these are affected in severe disease.
- A bone scan should be arranged to check for bone density – hypo-oestrogenism as a result of anorexia is likely to induce early-onset osteoporosis and fractures.
- Psychological assessment is also important to guide appropriate treatment.

Management

Encouraging the woman to eat a more normal diet and to avoid exercising is the ideal management, but anorexia is a chronic disease that is often refractory to treatment. Explanation that her periods will return if she increases her BMI may possibly encourage her to put on weight.

The combined oral contraceptive pill should be prescribed in the meantime, which will prevent osteoporosis and bring on periods, albeit pharmacologically induced.

Referral to a specialist eating disorders unit is vital in addressing the long-term problem for this woman. Commonly, eating disorders arise out of childhood difficulties and family or group therapy should be considered.

If the investigations suggest renal or hepatic impairment then inpatient management is likely to be necessary.

KEY POINTS
<ul style="list-style-type: none">• Menstruation usually ceases when BMI is less than 18 kg/m².• Amenorrhoeic anorexic women need oestrogen replacement to protect them from osteoporosis.• Anorexia is often refractory to treatment.

CASE 20: ABDOMINAL AND BACK PAIN

History

An 83-year-old woman complains of a dragging sensation in the lower abdomen and lower back pain when standing or walking. It has been present for some years but she can now only stand for a short time before feeling uncomfortable. It is not noticeable at night. She has had four vaginal deliveries. She had her menopause at 52 years and took hormone-replacement therapy for several years for vasomotor symptoms. She has not had any postmenopausal bleeding and has not had a smear for several years.

She is generally constipated and sometimes finds she can only defecate by placing her fingers into the vagina and compressing a ‘bulge’ she can feel. She has mild frequency and gets up twice most nights to pass urine. There is no dysuria or haematuria. Occasionally she does not get to the toilet in time and leaks a small amount of urine, but this does not worry her unduly.

Medically she is very well and does not take any medications regularly. She lives alone and does her own shopping and housework.

Examination

On examination she appears well. Blood pressure and heart rate are normal. She is of average build. The abdomen is soft and non-tender. There is a loss of vulval anatomy consistent with atrophic changes. On examination in the supine position there is a mild prolapse. On standing, the cervix is felt at the level of the introitus. There is a large posterior wall prolapse and a minimal anterior wall prolapse.

Questions

- What is the diagnosis for her discomfort and pain?
- How could the prolapse be more thoroughly assessed?
- How would you manage this patient?

ANSWER 20

The diagnosis is of second-degree uterovaginal prolapse with rectocele. Prolapse is traditionally categorized according to the level of descent of the cervix in relation to the introitus:

- first degree: descent within the vagina
- second degree: descent to the introitus
- third degree: descent of the cervix outside the vagina
- procidentia: complete eversion of the vagina outside the introitus.

A more thorough assessment using the Pelvic Organ Prolapse Quantification (POP-Q) System is now standard practice. It is a validated tool to quantify, describe and stage pelvic support. The hymen is used as the main reference point with measurements taken (and recorded on a grid) from six defined reference points plus three further measurements, with positive or negative numbers assigned according to whether the reference points are located above or below the hymen.

Common presenting symptoms are of ‘something coming down’, a ‘lump’ or a dragging sensation. Symptoms are always worse on standing or walking because of the effect of gravity. Prolapse is more common in women who are parous, have had long or traumatic deliveries, have a chronic cough or constipation. However it may occur in any woman, even if she is nulliparous, as it relates to collagen strength.

Management

Initial management involves treating the constipation with dietary manipulation and laxatives. This may relieve some of the symptoms and is also important to prevent recurrence if surgery is to be performed.

Pelvic floor exercises are helpful for mild prolapse and to preserve the integrity of repair postoperatively, though in this case they are unlikely to make any significant difference to the presenting symptoms. If surgery is not wanted then she can try a ring pessary to hold up the prolapse, which can work extremely well and only needs replacing every 6 months.

Although she is 83 this woman has no medical problems and should be offered definitive prolapse surgery which for her involves vaginal hysterectomy and posterior vaginal wall repair (colporrhaphy). As there is no abdominal incision involved, recovery is quick and she would expect to be in hospital for around 3 days.

KEY POINTS

- Prolapse incidence increases with age, parity, constipation and chronic cough.
- Conservative management with a ring pessary, or surgical prolapse repair may be appropriate.
- Relief of exacerbating factors is important to prevent symptoms worsening or to maintain the integrity of the repair.

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