D: Diffuse or localized presence of endometrial tissue within the myometrium. If localized to one large area it is known as an adenomyoma.

A: Unknown. ? Direct invasion by overlying endometrium. ? Metaplastic change of tissue surrounding myometrial vessels giving rise to endometrial stroma and glandular tissue. ? Migration of decidua (the endometrium becomes deciduous during pregnancy) with uterine contractions during labour.

A/R: Endometriosis, fibroids, long period of secondary subfertility, multiparity, ↑ age.

E: Unknown, underestimated as diagnosis is based on histopathology. Occurs in 20–40 % of hysterectomy specimens.

H: 30 % asymptomatic.
Menstrual problems: menorrhagia, dysmenorrhoea (premenstrual and menstrual, peaking in later stages), ↑ frequency, spotting. **Others**: deep dyspareunia. Subfertility.
Symptoms regress after menopause as lesions are oestrogen dependent.

E: **Bimanual:** uterus (?↑ size, premenstrual and menstrual tenderness).

P: **Macro:** diffuse enlargement of uterus, thickened walls (posterior > anterior), absence of pseudocapsule formation around lesions (as seen in fibroids).
Micro: endometrial tissue within myometrium (stroma > glandular tissue). Proliferative cyclical variations seen in more mature tissue.

I: **Diagnostic:** transvaginal USS or MRI, hysteroscopy and histology of endometrial biopsy.
Exclusion of other causes: *Bloods*: FBC (↓ Hb), clotting screen. *Urine*: β-hCG (exclude pregnancy). *Others*: cervical smear (exclude cancer), laparoscopy (exclude endometriosis).

M: Treat symptomatic cases only.
Medical:
1 antifibrinolytics (tranexamic acid);
2 NSAIDs (mefenamic acid—helps with pain and bleeding);
3 GnRH agonists (buserelin);
4 IUS (Mirena);
5 COC;
6 progesterone (e.g. norethisterone).
Surgical (if medical treatment unsuccessful): abdominal hysterectomy with preservation of ovaries. If adenomyoma present can use local excision of lesion.

C: Anaemia. Malignant change to adenocarcinoma (rare).

P: Adenomyosis rarely responds to hormonal therapy, so most women will eventually require a hysterectomy to control symptoms.

Amenorrhoea

D: Absence of menstruation. Primary amenorrhoea is failure to establish menstruation. Secondary amenorrhoea is absence of menstruation for $\geq$6 consecutive months in a woman who has previously established regular menses.

A: **Primary (5 %):**

1 *Constitutional delay*: most common cause of primary.

2 *Obstructive*: imperforate hymen, transverse vaginal septum, absent or non-functioning uterus.

3 *Hormonal*: Kallmann's syndrome, weight loss, hyperprolactinoma.

4 *Congenital*: Androgen insensitivity syndrome, Turner's syndrome, gonadal agenesis, CAH.

5 *Others*: ovarian failure (e.g. chemotherapy/radiotherapy), pituitary tumour.

Secondary (95 %):

1 *Pregnancy*: most common cause of secondary amenorrhoea and should always be considered first.

2 *Ovary* (60 % of pathological causes): PCOS (35 %), premature ovarian failure (25 %).

3 *Pituitary* (20 %): hyperprolactinoma (17 %), hypopituitarism, Sheehan's syndrome, trauma, tumour, post OCP insensitivity.

4 *Hypothalamus*: hypothalamic hypogonadism (extreme exercise, $\downarrow$ weight, e.g. anorexia nervosa, idiopathic or chronic illness may result in thalamic suppression).

5 *Uterus* (rare): Asherman's syndrome, tuberculous endometritis.

6 *Others*: endocrine (thyroid disease, Cushing's).

A/R: n/a.

E: Not uncommon.

H: Assess LMP, menarche, previous menstrual history, contraception now and previously, possibility of pregnancy, weight loss, exercise, hirsuitism, galactorrhoea, vision, thyroid symptoms, climacteric symptoms and last smear date.

E: May be unremarkable.
Primary: delayed puberty, signs of underlying causes, e.g. imperforate hymen.
Secondary: signs of underlying cause, e.g. low weight, signs of PCOS.

P: n/a.

I: Tailor according to history and examination. Consider: *Bloods*: FSH, LH estradiol, androgens, prolactin, TFTs, SHBG. *Urine*: β-hCG (exclude pregnancy). *Others*: Anterior pituitary function tests, pelvic USS, visual fields, X-ray pituitary fossa. In primary amenorrhoea chromosomal studies may be indicated.

M: Depends on underlying cause.

C: Long-standing amenorrhoea can lead to osteoporosis and menopausal symptoms and signs.

P: Depends on underlying cause.

D: The presence of amniotic fluid in the maternal circulation.

A: Appears to be a combination of increased amniotic fluid pressure and a defect near the placental site allowing access into the maternal circulation.

A/R: Multiparity, uterine hyperstimulation (oxytocin use), rapid labour, caesarean section, increased maternal age.

E: 1 in 80 000 pregnancies.

H: Sudden-onset dyspnoea, often pink frothy sputum. ? Loss of consciousness.

E: **Output failure**: tachycardia, hypotension, cold sweaty peripheries, cyanosis, raised JVP.
Cardiac arrest: pulseless, no respiratory effort.
Seizures.
Coagulation failure: petechial skin haemorrhage, bleeding at puncture sites.

P: Poorly understood (lack of human data). Recently established register for all cases.
Amniotic fluid thought to cause severe transient pulmonary artery spasm and ↑ pulmonary arterial pressure, with resultant hypoxia leading to myocardial and pulmonary capillary damage and left ventricular failure. Activation of coagulation cascade → leakage of intravascular fluid to intra-alveolar and interstitial spaces.

I: *Bloods*: FBC, U&E, LFT, ABG, cross-match 6 units.

M: CPR (if required).
High flow oxygen ± intubation, IPPV.
Insert two large-bore cannulae, take blood sample, IV fluids (crystalloid/colloid).
Use cross-matched blood if needed.
Fresh frozen plasma (if fibrinogen low).
Consider delivery.
Transfer to ITU.
Treat ARDS/ARF.

C: Cardiorespiratory arrest, DIC, left ventricular failure, haemorrhage, pulmonary oedema, ARDS, ARF, uterine atony, convulsions.

P: 80 % maternal mortality.

Anaemia in pregnancy

D: Haemoglobin level < 10.4 g/dL.

A: Most common cause is iron deficiency, but all other causes of anaemia must be considered.
Microcytic: iron deficiency, thalassaemia.
Macrocytic: *Megaloblastic*: folate/B_{12} deficiency (unlikely to be B_{12} deficiency as severe deficiency causes infertility). *Non-megaloblastic*: excessive alcohol, hypothyroidism, pregnancy itself, haemolysis.
Normocytic: haemorrhage (APH, PPH), haemolysis, anaemia of chronic disease, hydraemia of pregnancy (caused by dilution).

A/R: **Iron deficiency:** vegetarian/vegan diet, multiparity, previous menorrhagia.
Thalassaemia: family history, Mediterranean/Asian origin.
Folate deficiency: drugs (e.g. anticonvulsants), small bowel disease, malnutrition, haemolysis (e.g. sickle cell anaemia), malaria (in Africa).

E: Depends on population. ↑ Incidence seen in areas of ethnic minority (because of poor diet and ↑ incidence of haemoglobinopathies).

H: Asymptomatic (common), fatigue, dyspnoea, palpitations.

E: **General**: pallor, pale mucous membranes, ↑ capillary refill time, oedema. Signs of underlying cause may be present, e.g. mild jaundice in haemolysis.

P: ↓ Hb level is normal in pregnancy (a slight ↓ is associated with ↑ weight and well-being of fetus) as plasma volume expands at a greater rate than red cell volume causing dilution (especially with multiple pregnancy). Iron deficiency is more common in pregnancy as a result of ↑ iron demands secondary to ↑ red cell mass, new tissue formation (e.g. myometrium) and fetal demands. Lactation also ↑ demand for iron, and is associated with a higher incidence of anaemia in the post-partum period.

I: **Initial:** FBC, peripheral blood film, and MCV.
If ↓ Hb and ↓ MCV: serum iron, ferritin and total iron-binding capacity (TIBC). If normal consider Hb electrophoresis (exclude thalassaemia).
If ↓ Hb, ↓ MCV: serum iron, ferritin, TIBC, B_{12}, folate and red cell folate (exclude mixed picture). Tailor further tests according to clinical presentation.
If ↓ Hb and ↑ MCV: serum B_{12}, folate and red cell folate. If normal consider TFTs, LFTs, etc.

M: Treat underlying cause.
Iron deficiency: for anaemia detected early and Hb > 6.5 give oral $FeSO_4$ 60 mg/day. If < 4 weeks to delivery, anaemia severe or compliance problems give intramuscular iron. Blood transfusion is reserved for extreme circumstances. Avoid iron in thalassaemia and sickle cell anaemia.
Folate deficiency: oral folic acid supplement.

C: ↑ Susceptibility to complications of haemorrhage, SE of iron therapy (constipation, nausea—less well-tolerated in first trimester). ↑ Maternal mortality (5 ×), IUGR and stillbirth (6 ×).

P: Iron deficiency responds well to treatment.

D: X-linked recessive condition resulting in failure of testosterone to cause normal masculinization in the male (46 XY karyotype) leading to female phenotype with absent uterus. Complete or partial, depending on the amount of receptor function.

A: Mutation (deletions, insertions and point mutations) of the androgen receptor (*AR*) gene on the long arm of the X chromosome causing loss of function (receptor loss/altered substrate-binding affinity). Sometimes ↓ activity of enzyme converting testosterone to dihydrotestosterone or the testosterone receptor missing—testosterone produced in normal amounts but receptor-mediated events do not occur.

A/R: Family history (e.g. infertile unmarried aunt); male genotype.

E: 1 in 20 400 live males.

H: Amenorrhoea; lack of pubic and axillary hair; ? abnormal external genitalia.

E: Female appearance and voice; lack of pubic and axillary hair.
Complete: female external genitalia with normal breast development (testosterone converted to estradiol), labia, clitoris, and vaginal introitus.
Partial: variable phenotype from mildly virilized female to mildly undervirilized male external genitalia; absent uterus; ? testes palpable in the abdomen or groin.

P: Histology of the testes: normal testicular structure, ↓ sperm numbers post puberty. Testes produce normal amounts of müllerian-inhibiting factor (MIF) which causes regression of müllerian duct therefore absent fallopian tubes, uterus, or an upper vagina. Variable anatomical deviations may occur, from clitoromegaly, without other external anomalies, to hypospadias.

I: **Karyotyping:** *Bloods*: testosterone ↑; negative progesterone challenge; can measure dihydrotestosterone, dihydroepiandrosterone (DHEA), androstenedione, and their precursors, 17-hydroxypregnenolone and 17-hydroxyprogesterone (eliminate error). Rule out pregnancy/other causes amenorrhoea. *USS*: absence of uterus, location of testes.

M: **Medical:** oestrogen replacement therapy after the development of secondary sexual characteristics and removal of gonads. Combination with progesterone controversial.
Surgical: removal of gonads after the development of secondary sexual characteristics; vaginal lengthening procedures. Cosmetic procedures for masculinized genitalia.
Other: psychological support. Parental genetic counselling (risk of recurrence). Support groups.

C: Testicular malignancy (therefore orchidectomy recommended); infertility; extreme psychological trauma; osteoporosis; symptoms of oestrogen deficiency.

P: Good provided that adequate care and support is available.

Asherman's syndrome

D: Presence of intrauterine adhesions, which partially or completely occlude the uterine cavity, following instrumentation or infection.

A: Damage to the endometrium involving the basal layer, which leads to fibrosis and adhesion formation.

A/R: Endometrial resection (diathermy/laser ablation); excessive curettage (following miscarriage, therapeutic abortion, post-partum haemorrhage); surgery (myomectomy, caesarean section); endometritis (especially tuberculous and schistosomiasis infection).

E: Up to 20 % prevalence following ERPC (includes mild cases).

H: Women may present with abnormal menstruation (secondary amenorrhoea or hypomenorrhoea). Previous uterine instrumentation/infection. Dysmenorrhoea.

E: No physical signs.

P: Intrauterine adhesions/synechiae. Varying degree of uterine cavity occlusion.

I: *Bloods*: weekly progesterone (ovulatory range does not correspond with menstruation). *Other*: progestogen challenge test (no menstruation occurs). Hysterosalpingogram. Hysteroscopy.

M: Insert a large IUCD *or* hysteroscopic adhesiolysis + IUCD (1 week), antibiotic coverage, high-dose oestrogen (21 days) and a progestogen (10 days) to induce endometrial proliferation.

C: Infertility. Pregnancy complications: premature rupture of membranes, preterm labour, fetal hypoxia and caesarean hysterectomy (if pregnancy occurs).

P: 50 % likelihood of subsequent infertility in more severe cases.

D: Atrophy of the vagina and vulva with thinning of the epithelium.

A: ↓ In circulating oestrogen levels.

A/R: Prior to menarche, prolonged lactation, postmenopausal.

E: Postmenopausal women mostly affected. Common cause of postmenopausal bleeding.

H: Bloodstained, sometimes purulent, vaginal discharge. Vaginal dryness and dyspareunia. Superimposed infection with Gram-positive cocci or Gram-negative bacilli can worsen symptoms.

E: **Pelvic:** *Speculum*: thin pale inflamed vaginal wall with loss of rugal folds. Petechial haemorrhages and occasionally ecchymoses.

P: ↓ Stimulatory effects of oestrogen result in a loss of glycogen in the epithelial cells and a decrease in vaginal acidity, which results in ↑ risk of superimposed infection.

I: **Exclude malignancy:** cervical smear, HVS (exclude superimposed infection), USS (usually transvaginal, but transabdominal if vagina too tight. Endometrial thickness assessed), hysteroscopy.

M: Vaginal pH and epithelium must be restored.
Medical: 1 Dienestrol cream topically. Applied once a day at night for 1 week, followed by monthly application to prevent atrophy.
2 Systemic HRT in postmenopausal women.

C: Increased frequency of UTI resulting from atrophy of lower urinary tract, psychosexual problems resulting from dyspareunia, infection, side-effects from excessive absorption of topical oestrogen.

P: Treatment successful in majority of patients.