

ANTENATAL OBSTETRIC COMPLICATIONS

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OVERVIEW

There are a variety of maternal and fetal complications which can arise during pregnancy. Some of these 'minor' conditions arise because the physiological changes of pregnancy exacerbate many irritating symptoms that in the normal non-pregnant state would not require specific treatment. While these problems are not dangerous to the mother, they can be extremely troublesome and incapacitating. Some of the more major fetal and maternal complications are discussed in detail in other chapters. Here we discuss common complications, including malpresentation, Rhesus disease and abnormalities of amniotic fluid production.

'Minor' complications of pregnancy

Musculoskeletal problems

Backache

Backache is extremely common in pregnancy and is caused by:

- hormone induced laxity of spinal ligaments;
- a shifting in the centre of gravity as the uterus grows;
- additional weight gain;

which cause an exaggerated lumbar lordosis. Pregnancy can exacerbate the symptoms of a prolapsed intervertebral disc, occasionally leading to complete immobility. Advice should include maintenance of correct posture, avoiding lifting heavy objects (including children), avoiding high heels, regular physiotherapy and simple analgesia (paracetamol or paracetamol-codeine combinations).

Symphysis pubis dysfunction

This is an excruciatingly painful condition most common in the third trimester, although it can occur at any time during pregnancy. The symphysis pubis joint becomes 'loose', causing the two halves of the pelvis to rub on one another when walking or moving. The condition improves after delivery and the management revolves around simple analgesia. Under a physiotherapist's direction, a low stability belt may be worn.

Carpal tunnel syndrome

Compression neuropathies occur in pregnancy due to increased soft-tissue swelling. The most common of these is carpal tunnel syndrome. The median nerve, where it passes through the fibrous canal at the wrist before entering the hand, is most susceptible to compression. The symptoms include numbness, tingling and weakness of the thumb and forefinger, and often quite severe pain at night. Simple analgesia and splinting of the affected hand usually help, although there is no realistic prospect of cure until after delivery. Surgical decompression is very rarely performed in pregnancy.

Gastrointestinal symptoms

Constipation

Constipation is common in pregnancy and usually results from a combination of hormonal and mechanical factors that slow gut motility. Concomitantly administered iron tablets may exacerbate the condition. Women should be given clear explanations, reassurance and advice regarding the adoption of a high-fibre diet. Medications are best avoided but if necessary, mild (non-stimulant) laxatives, such as lactulose, may be suggested.

Hyperemesis gravidarum

Nausea and vomiting in pregnancy are extremely common; 70–80 per cent of women experience these symptoms early in their pregnancy and approximately 35 per cent of all pregnant patients are absent from work on at least one occasion through nausea and vomiting. Although the symptoms are often most pronounced in the first trimester, they by no means are confined to it. Similarly, despite common usage of the term ‘morning sickness’, in only a minority of cases are the symptoms solely confined to the morning. Nausea and vomiting in pregnancy tends to be mild and self-limited and is not associated with adverse pregnancy outcome.

Hyperemesis gravidarum, however, is a severe, intractable form of nausea and vomiting that affects 0.3–2.0 per cent of pregnancies. It causes imbalances of fluid and electrolytes, disturbs nutritional intake and metabolism, causes physical and psychological debilitation and is associated with adverse pregnancy outcome, including an increased risk of preterm birth and low birthweight babies. The aetiology is unknown and various putative mechanisms have been proposed including an association with high levels of serum human chorionic gonadotrophin (hCG), oestrogen and thyroxine. The likely cause is multifactorial. Severe cases of hyperemesis gravidarum cause malnutrition and vitamin deficiencies, including Wernicke’s encephalopathy, and intractable retching predisposes to oesophageal trauma and Mallory–Weiss tears. Treatment includes fluid replacement and thiamine supplementation. Antiemetics such as phenothiazines are safe and are commonly prescribed. Other proposed treatments including the administration of corticosteroids have not yet been adequately proven and remain empirical.

Gastroesophageal reflux

This is very common. Altered structure and function of the normal physiological barriers to reflux, namely the weight effect of the pregnant uterus and hormonally induced relaxation of the oesophageal sphincter, explain the extremely high incidence in the pregnant population. For the majority of patients, lifestyle modifications such as smoking cessation, frequent light meals and lying with the head propped up at night are helpful. When these prove insufficient to control symptoms, medications can be added in a stepwise fashion starting with simple antacids. Histamine-2 receptor antagonists and proton pump inhibitors can be used if more simple measures fail although their safety record in pregnancy is less certain. Severe, refractory dyspeptic symptoms warrant gastroenterology referral just in case a stomach ulcer or hiatus hernia is being overlooked.

Haemorrhoids

Several factors conspire to render haemorrhoids more common during pregnancy including the effects of circulating progesterone on the vasculature, pressure on the superior rectal veins by the gravid uterus and increased circulating volume. A conservative approach is usually advocated including local anaesthetic/anti-irritant creams and a high-fibre diet. Never overlook the ‘warning’ symptoms of tenesmus, mucus, blood mixed with stool and back passage discomfort that may suggest rectal carcinoma; a rectal digital examination should be carried out if these symptoms are suggested.

Varicose veins

Varicose veins may appear for the first time in pregnancy or pre-existing veins may become worse. They are thought to be due to the relaxant effect of progesterone on vascular smooth muscle and the dependent venous stasis caused by the weight of the pregnant uterus on the inferior vena cava.

Varicose veins of the legs may be symptomatically improved with support stockings, avoidance of standing for prolonged periods and simple analgesia. Thrombophlebitis may occur in a large varicose vein, more commonly after delivery. A large superficial varicose vein may bleed profusely if traumatized; the leg must be elevated and direct pressure applied. Vulval and vaginal varicosities are uncommon but

symptomatically troublesome; trauma at the time of delivery (episiotomy, tear, instrumental delivery) may also cause considerable bleeding.

Oedema

This is common, occurring to some degree in approximately 80 per cent of all pregnancies. There is generalized soft-tissue swelling and increased capillary permeability, which allows intravascular fluid to leak into the extravascular compartment. The fingers, toes and ankles are usually worst affected and the symptoms are aggravated by hot weather. Oedema is best dealt with by frequent periods of rest with leg elevation; occasionally, support stockings are indicated. Excessively swollen fingers may necessitate removal of rings and jewellery before they get stuck. It is important to remember that generalized (rather than lower limb) oedema may be a feature of pre-eclampsia, so remember to check the woman's blood pressure and urine for protein. More rarely, severe oedema may suggest underlying cardiac impairment or nephrotic syndrome.

Other common 'minor' disorders:

- Itching
- Urinary incontinence
- Nose bleeds
- Thrush (vaginal candidiasis)
- Headache
- Fainting
- Breast soreness
- Tiredness
- Altered taste sensation
- Insomnia
- Leg cramps
- Striae gravidarum and chloasma.

Problems due to abnormalities of the pelvic organs

Fibroids (leiomyomata)

Fibroids are compact masses of smooth muscle that lie in the cavity of the uterus (submucous), within the uterine muscle (intramural) or on the outside

surface of the uterus (subserous). They may enlarge in pregnancy, and in so doing present problems later on in pregnancy or at delivery (Figure 8.1). A large fibroid at the cervix or in the lower uterine segment may prevent descent of the presenting part and obstruct vaginal delivery.

Red degeneration is one of the most common complications of fibroids in pregnancy. As it grows, the fibroid may become ischaemic; this manifests clinically as acute pain, tenderness over the fibroid and frequent vomiting. If these symptoms are severe, uterine contractions may be precipitated, causing miscarriage or preterm labour. Red fibroid degeneration requires treatment in hospital, with potent analgesics (usually opiates and intravenous fluids). The symptoms usually settle within a few days. The differential diagnosis of red degeneration includes acute appendicitis, pyelonephritis/urinary tract infection, ovarian cyst accident and placental abruption.

A subserous pedunculated fibroid may tort in the same way that a large ovarian cyst can. When this happens, acute abdominal pain and tenderness may make the two difficult to distinguish from one another. In this scenario, a pertinent history followed by an ultrasound scan (transvaginal in the first trimester, transabdominal in the second and third) will aid the diagnosis.

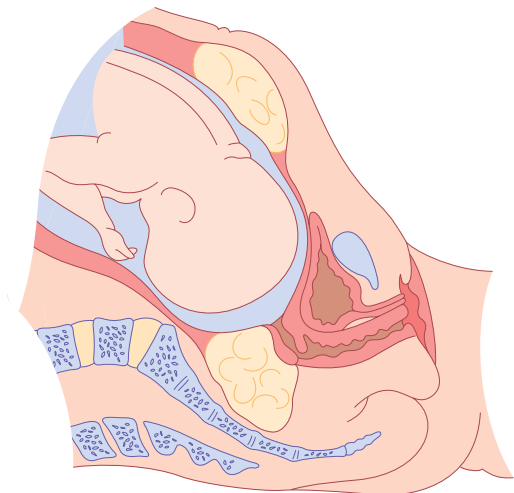


Figure 8.1 Fibroids complicating pregnancy. The tumour in the anterior wall of the uterus has been drawn up out of the pelvis as the lower segment was formed, but the fibroid arising from the cervix remains in the pelvis and will obstruct labour

Retroversion of the uterus

Fifteen per cent of women have a retroverted uterus. In pregnancy, the uterus grows and a retroverted uterus will normally 'flip' out of the pelvis and begin to fill the abdominal cavity, as an anteverted uterus would. In a small proportion of cases, the uterus remains in retroversion and eventually fills up the entire pelvic cavity; as it does so, the base of the bladder and the urethra are stretched. Retention of urine may occur, classically at 12–14 weeks, and this is not only very painful but may also cause long-term bladder damage if the bladder becomes over-distended. In this situation, catheterization is essential until the position of the uterus has changed.

Congenital uterine anomalies

The shape of the uterus is embryologically determined by the fusion of the Mullerian ducts. Abnormalities of fusion may give rise to anything from a subseptate uterus through to a bicornuate uterus and even (very rarely) to a double uterus with two cervixes. These findings are often discovered incidentally at the time of a pelvic operation such as a laparoscopy, or an ultrasound scan.

The problems associated with bicornuate uterus are:

- miscarriage;
- preterm labour;
- preterm prelabour rupture of membranes (PPROM);
- abnormalities of lie and presentation;
- higher Caesarean section rate.

Ovarian cysts in pregnancy

Ovarian cysts are common in pregnant women; fortunately, the incidence of malignancy is uncommon in women of childbearing age. The most common types of pathological ovarian cyst are serous cysts and benign teratomas. Physiological cysts of the corpus luteum may grow to several centimetres but rarely require treatment, therefore asymptomatic cysts may be followed up by clinical and ultrasound examination, but large cysts (for example, dermoids) may require surgery in pregnancy.

Surgery is usually postponed until the late second or early third trimester, when there is the potential that if the baby were delivered, it would be able to survive.

The major problems are of large (>8 cm) ovarian cysts in pregnancy, which may undergo torsion, haemorrhage or rupture, causing acute abdominal pain. The resulting pain and inflammation may lead to a miscarriage or preterm labour. Symptomatic cysts, most commonly due to torsion, will require an emergency laparotomy and ovarian cystectomy or even oophorectomy if the cyst is torted. A full assessment must include a family history of ovarian or breast malignancy, tumour markers (although these are of limited value in pregnancy) and detailed ultrasound investigation of both ovaries. Surgery in the late second and third trimester of pregnancy is normally performed through a midline or paramedian incision; a low transverse suprapubic incision would not allow access to the ovary, as it is drawn upwards in later pregnancy.

Cervical cancer

Cervical abnormalities are much more difficult to deal with in pregnancy, partly because the cervix itself is more difficult to visualize at colposcopy, and also because biopsy may cause considerable bleeding. Cervical carcinoma most commonly arises in poor attenders for cervical screening. The disease is commonly asymptomatic in early stages, but later stage presentation includes vaginal bleeding (especially postcoital). Examination may reveal a friable or ulcerated lesion with bleeding and purulent discharge. The prospect of cervical carcinoma in pregnancy leads to complex ethical and moral dilemmas concerning whether the pregnancy must be terminated (depending on the stage it has reached) to facilitate either surgical treatment (radical hysterectomy) or chemotherapy. Cervical cancer is dealt with in greater detail in Chapter 14, premalignant and malignant disease of the cervix in *Gynaecology by Ten Teachers*, 19th edition.

Urinary tract infection

Urinary tract infections (UTIs) are common in pregnancy. Eight per cent of women have asymptomatic bacteriuria; if this is untreated, it may progress to UTI or even pyelonephritis, with the attendant associations of low birth weight and preterm delivery.

The predisposing factors are:

- history of recurrent cystitis;
- renal tract abnormalities: duplex system, scarred kidneys, ureteric damage and stones;

- diabetes;
- bladder emptying problems, for example multiple sclerosis.

The symptoms of UTI may be different in pregnancy; it occasionally presents as low back pain and general malaise with flu-like symptoms. The classic presentation of frequency, dysuria and haematuria is not often seen. On examination, tachycardia, pyrexia, dehydration and loin tenderness may be present. Investigations should include a full blood count and midstream specimen of urine (MSU) sent for urgent microscopy, culture and sensitivities. If there is a strong clinical suspicion of UTI, treatment with antibiotics should start immediately. The woman should drink plenty of clear fluids and take a simple analgesic, such as paracetamol.

The most common organism for UTI is *Escherichia coli*; less commonly implicated are streptococci, *Proteus*, *Pseudomonas* and *Klebsiella*. If more than 10⁵ organisms are present at culture, this confirms a diagnosis of UTI. The commonly reported 'heavy mixed growth' is often associated with UTI symptoms and may be treated, or the MSU repeated after a week, depending on the clinical scenario. The first-line antibiotic for UTI is amoxicillin or oral cephalosporins.

Pyelonephritis is characterized by dehydration, a very high temperature (>38.5°C), systemic disturbance and occasionally shock. This requires urgent and aggressive treatment including intravenous fluids, opiate analgesia and intravenous antibiotics (such as cephalosporins or gentamicin). In addition, renal function should be determined, with at least baseline urea and electrolytes, and the baby must be monitored with cardiotocography (CTG). Recurrent UTIs in pregnancy require MSU specimens to be sent to the microbiology laboratory at each antenatal visit, and low-dose prophylactic oral antibiotics may be prescribed. Investigation should take place after delivery, unless frank haematuria or other symptoms suggest that an urgent diagnosis is essential. Investigations might include a renal ultrasound scan, renal DMSA function scan, creatinine clearance, intravenous urogram and cystoscopy.

Abdominal pain in pregnancy

Abdominal pain is one of the most common minor disorders of pregnancy; the problem is in

distinguishing pathological from 'physiological' pains. There are many possibilities to exclude. Furthermore, the anatomical and physiological changes of pregnancy may alter 'classical' presenting symptoms and signs making clinical diagnosis challenging. The causes listed in Table 8.1 are not exhaustive, but cover most possible diagnoses. The crucial point is that certain conditions are potentially

Table 8.1 Causes of abdominal pain in pregnancy

Pregnancy-caused (obstetric) conditions	
Early pregnancy (<24 weeks)	
	Ligament stretching
	Miscarriage
	Ectopic pregnancy
	Acute urinary retention due to retroverted gravid uterus
Later pregnancy (>24 weeks)	
	Labour
	Placental abruption
	HELLP syndrome
	Uterine rupture
	Chorioamnionitis
Pregnancy-unrelated conditions	
Uterine/ovarian causes	
	Torsion or degeneration of fibroid
	Ovarian cyst accident
Urinary tract disorders	
	Urinary tract infection (acute cystitis and acute pyelonephritis)
	Renal colic
Gastrointestinal disorders	
	Medical gastric/duodenal ulcer
	Acute appendicitis
	Acute pancreatitis
	Acute gastroenteritis
	Intestinal obstruction or perforation
Medical causes	
	Sickle cell disease (abdominal crisis)
	Diabetic ketoacidosis
	Acute intermittent porphyria
	Pneumonia (especially lower lobe)
	Pulmonary embolus
	Malaria

dangerous or debilitating (e.g. acute appendicitis) and may be masked by the altered anatomy and physiology of pregnancy. Obstetricians may therefore have to perform x-rays and arrange invasive assessments to make a diagnosis.

Venous thromboembolism

Venous thromboembolic disease (VTE) is the most common cause of direct maternal death in the UK. In the most recent triennium, there were 41 fatalities, giving a maternal mortality rate of 1.94 per 100 000 – more than twice that of the next most common cause (pre-eclampsia).

Pregnancy is a hypercoagulable state because of an alteration in the thrombotic and fibrinolytic systems. There is an increase in clotting factors VIII, IX, X and fibrinogen levels, and a reduction in protein S and anti-thrombin (AT) III concentrations (see Chapter 3, Physiological changes in pregnancy). The net result of these changes is thought to be an evolutionary response to reduce the likelihood of haemorrhage following delivery.

These physiological changes predispose a woman to thromboembolism and this is further exacerbated by venous stasis in the lower limbs due to the weight of the gravid uterus placing pressure on the inferior vena cava in late pregnancy and immobility, particularly in the puerperium.

Pregnancy is associated with a 6–10-fold increase in the risk of venous thromboembolic disease compared to the non-pregnant situation. Without thromboprophylaxis, the incidence of non-fatal pulmonary embolism (PE) and deep vein thrombosis (DVT) in pregnancy is about 0.1 per cent in developed countries, this increases following delivery to around 1–2 per cent and is further increased following emergency Caesarean section.

Thrombophilia

Some women are predisposed to thrombosis through changes in the coagulation/fibrinolytic system that may be inherited or acquired. There is growing evidence that both heritable and acquired thrombophilias are associated with a range of adverse pregnancy outcomes particularly recurrent fetal loss. The major hereditary forms of thrombophilia

Risk factors for thromboembolic disease

Pre-existing

- Maternal age (>35 years)
- Thrombophilia
- Obesity (>80 kg)
- Previous thromboembolism
- Severe varicose veins
- Smoking
- Malignancy

Specific to pregnancy

- Multiple gestation
- Pre-eclampsia
- Grand multiparity
- Caesarean section, especially if emergency
- Damage to the pelvic veins
- Sepsis
- Prolonged bed rest

currently recognized include: deficiencies of the endogenous anticoagulants protein C, protein S and AT III; abnormalities of procoagulant factors, factor V Leiden (caused by a mutation in the factor V gene) and the prothrombin mutation G20210A. It seems probable that there are still some thrombophilias not yet discovered or described. Heritable thrombophilias are present in at least 15 per cent of Western populations.

Acquired thrombophilia is most commonly associated with antiphospholipid syndrome (APS). APS is the combination of lupus anticoagulant with or without anti-cardiolipin antibodies, with a history of recurrent miscarriage and/or thrombosis. It may (or, more commonly, may not) be associated with other autoantibody disorders, such as systemic lupus erythematosus (SLE).

If thrombophilic disorders are taken together, more than 50 per cent of women with pregnancy-related VTE will have a thrombophilia. It is therefore vital that women with a history of thrombotic events are screened for thrombophilia. The presence of thrombophilia, with a history of thrombotic episode(s), means that prophylaxis should be considered for pregnancy.

Diagnosis of acute venous thromboembolism

Clinical diagnosis of VTE is unreliable, therefore women who are suspected of having a DVT or PE should be investigated promptly.

Deep vein thrombosis

The most common symptoms are pain in the calf with varying degrees of redness or swelling. Women's legs are often swollen during pregnancy; therefore unilateral symptoms should ring alarm bells. The signs are few, except that often the calf is tender to gentle touch. It is mandatory to ask about symptoms of PE (see next section), as a woman with PE might present initially with a DVT.

Compression ultrasound has a high sensitivity and specificity in diagnosing proximal thrombosis in the non-pregnant woman and should be the first investigation used in a suspected DVT. Calf veins are often poorly visualized, however, it is known that a thrombus confined purely to the calf veins with no extension is very unlikely to give rise to a PE.

Venography is invasive, requiring the injection of contrast medium and the use of x-rays. It does, however, allow excellent visualization of veins both below and above the knee.

Pulmonary embolus

It is crucial to recognize PE, as missing the diagnosis could have fatal implications. The most common presentation is of mild breathlessness, or inspiratory chest pain, in a woman who is not cyanosed but may be slightly tachycardic (>90 bpm) with a mild pyrexia (37.5°C). Rarely, massive PE may present with sudden cardiorespiratory collapse (see Chapter 16, Obstetric emergencies).

If PE is suspected, initial electrocardiogram (ECG), chest x-ray and arterial blood gases should be performed to exclude other respiratory diagnoses. However, these investigations are insufficient on their own to exclude or diagnose PE and it may be sensible to investigate the lower limbs for evidence of DVT by ultrasound and if positive treat with a presumptive diagnosis of PE. If all the tests are normal but a high clinical suspicion of PE remains, a ventilation perfusion (V/Q) scan or computed tomography pulmonary angiogram (CTPA) should be performed. In both cases the radiation to the fetus is below the threshold considered safe.

D-dimer is now commonly used as a screening test for thromboembolic disease in non-pregnant women,

in whom it has a high negative predictive value. Outwith pregnancy, a low level of D-dimer suggests the absence of a DVT or PE, and no further objective tests are necessary, while an increased level of D-dimer suggests that thrombosis may be present and an objective diagnostic test for DVT and/or PE should be performed. In pregnancy, however, D-dimer can be elevated due to the physiological changes in the coagulation system, limiting its clinical usefulness as a screening test in this situation.

Treatment of VTE

Warfarin is given orally and prolongs the prothrombin time (PT). Warfarin is rarely recommended for use in pregnancy (exceptions include women with mechanical heart valves) as it crosses the placenta and can cause limb and facial defects in the first trimester and fetal intracerebral haemorrhage in the second and third trimesters.

Low molecular weight heparins (LMWHs) are now the treatment of choice. They do not cross the placenta and have been shown to be at least as safe and effective as unfractionated heparin (UFH) in the treatment of VTE with lower and fewer haemorrhagic complications in the initial treatment of non-pregnant subjects. In addition, LMWH is safe and easy to administer. Women are taught to inject themselves and can continue on this treatment for the duration of their pregnancy.

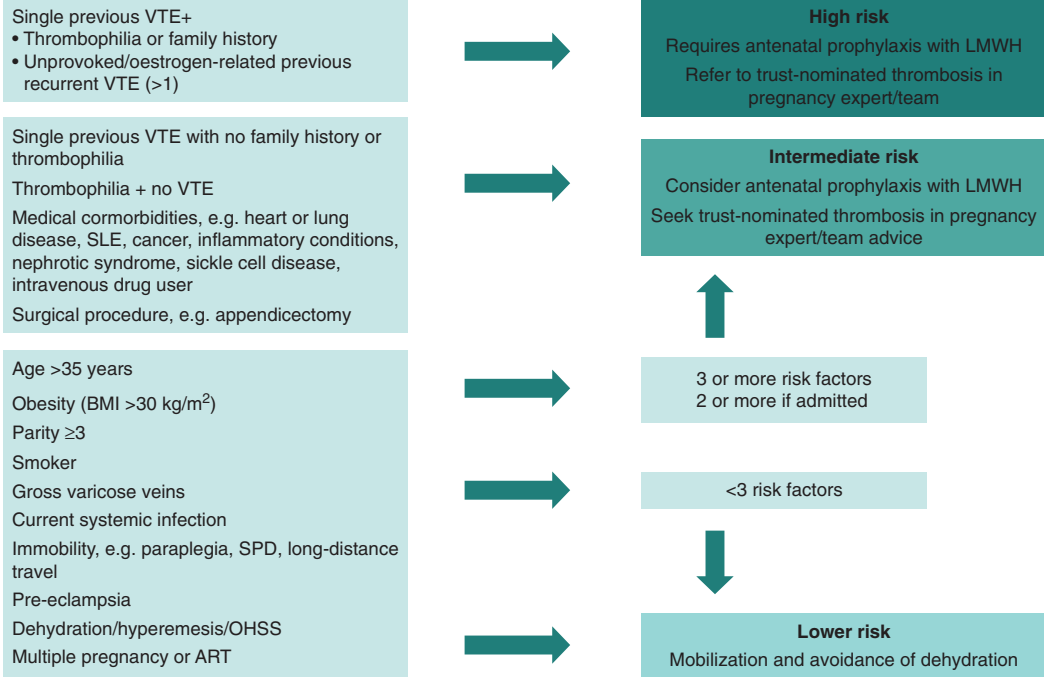
Following delivery, women can choose to convert to warfarin (with the need for stabilization of the doses initially and frequent checks of the international normalized ratio (INR) or remain on LMWH. Both warfarin and LMWH are safe in women who are breastfeeding.

Graduated elastic stockings should be used for the initial treatment of DVT and should be worn for two years following a DVT to prevent post phlebotic syndrome.

Prevention of VTE in pregnancy and postpartum

The Royal College of Obstetricians and Gynaecologists have recently released updated guidelines on the prevention of thrombosis and embolism in pregnancy and the puerperium (Green-top Guideline No. 37, November 2009) and these are summarized in Figure 8.2.

Antenatal thromboprophylaxis risk assessment and management



Postnatal thromboprophylaxis risk assessment and management

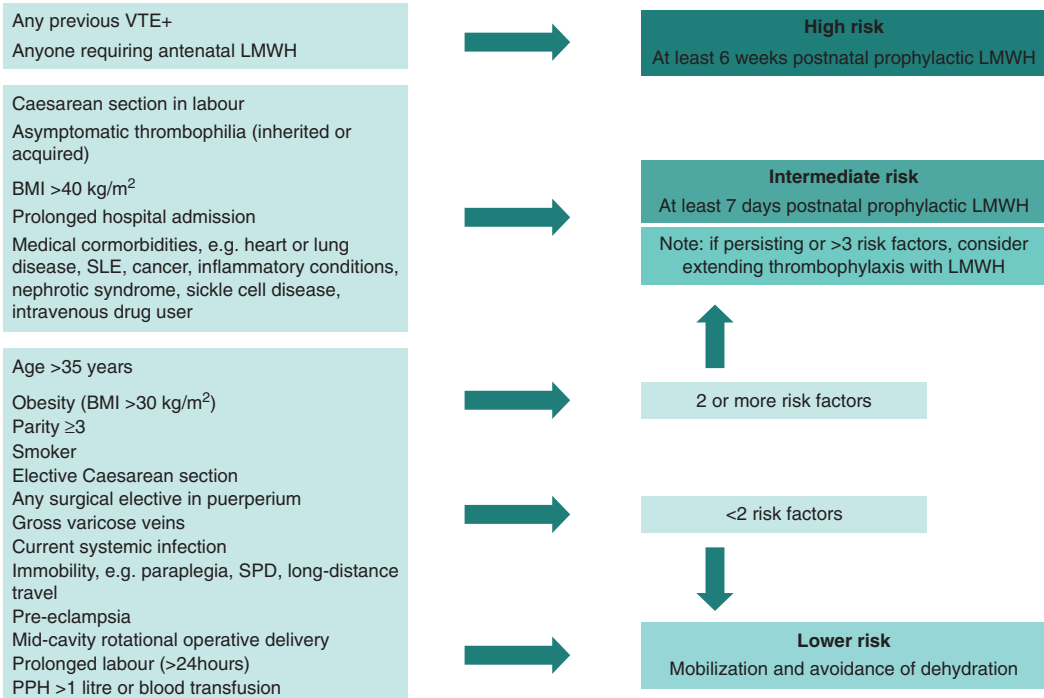


Figure 8.2 Obstetric thromboprophylaxis – risk assessment and management.

Key points



- Screening for thrombophilias should be carried out in those with a strong family or personal history of VTE.
- Rapid treatment of suspected VTE in pregnancy should be commenced while awaiting diagnosis.
- LMWHs are now the treatment of choice.
- Graduated compression stockings should be fitted and worn for two years to reduce the incidence of post thrombotic syndrome.

Substance abuse in pregnancy

Approximately one-third of adults who access drug services are women of reproductive age. There are approximately 6000 births to problem drug users in the UK each year (about 1 per cent of all deliveries). Multidisciplinary care is often necessary to optimize outcomes because the financial, psychological, social and domestic problems associated with drug misuse are often greater than the physical and medical concerns.

Opioids, especially heroin, remain the most commonly used drugs in the UK, although many drug users take combinations of drugs that often include cocaine or crack cocaine. Most problem drug users smoke tobacco and are heavy users of alcohol and cannabis. Taking drugs in combination greatly increases the unpredictability of their effect on the user. Intravenous injection of drugs also puts drug users at greater risk of infection with blood-borne viruses (hepatitis B and C and HIV). Many drug users live in disadvantaged communities in conditions of poverty and social exclusion. Many have had poor parenting experiences, poor education and significant mental health problems. The aims of management are to stabilize the mother's drug-taking habits and ensure contact with social/care workers and psychiatric/drug liaison services as appropriate.

It is important not to try to reduce the opiate dose too rapidly in pregnancy, as this can easily precipitate acute withdrawal in both the mother and fetus; the principle is to administer the lowest effective dose of methadone liquid in three divided doses every day.

Screening for infections such as hepatitis B and human immunodeficiency virus (HIV) is routinely offered in the UK. In many cases,

Problems frequently encountered amongst drug addicts

- Social problems: housing, crime, other children in care or abused.
- Co-existent addictions: alcohol and smoking.
- Malnutrition: especially iron, vitamins B and C.
- Risk of viral infections, e.g. human immunodeficiency virus (HIV) or hepatitis B.
- Specific fetal and neonatal risks (Table 8.2).

Table 8.2 The effects of some drugs of abuse on the fetus and neonate

Drug	Fetal and neonatal risk
Tobacco	Fetal growth restriction
Placental abruption	Fetal growth restriction
Alcohol	Fetal alcohol syndrome (FAS)
Opiates	Pre-term labour Neonatal withdrawal syndrome
Cocaine and derivatives	Placental abruption Fetal growth restriction Pre-term labour

multidisciplinary case conferences should be held to make arrangements and decisions for when the baby is delivered.

Alcohol

There is much debate about what is a 'safe' dose of alcohol during pregnancy. What is likely is that an intake of less than 100 g per week (approximately two drinks per day, e.g. two medium glasses of wine or one pint of beer) is not associated with any adverse effects. Doses greater than this have been related to fetal growth restriction (FGR). Massive doses, in excess of 2 g/kg of body weight (17 drinks per day), have been associated with fetal alcohol syndrome. However, the syndrome is not seen consistently in infants born to women who are heavy consumers of alcohol, and occurs only in approximately 30–33 per cent of children born to women who drink about 2 g/kg of

body weight per day (equivalent to approximately 18 units of alcoholic drink per day). The differing susceptibility of fetuses to the syndrome is thought to be multifactorial and reflects the interplay of genetic factors, social deprivation, nutritional deficiencies, tobacco and other drug abuse, along with alcohol consumption.

If alcohol abuse is suspected, it may be necessary to involve social workers and arrange for formal psychiatric/addiction assessment. It is extremely difficult to 'test' for alcohol abuse, as even markers such as mean corpuscular volume and gamma GT are not reliable in pregnancy. Malnutrition is very likely in heavy alcohol abuse and requires (in addition to a change in basic diet) B vitamin supplements and iron; the problem is that the majority of such patients not only do not take their medicines but also default antenatal appointments.

Smoking and pregnancy

Smoking acutely reduces placental perfusion. Overall perinatal mortality is increased, babies are smaller at delivery and there is a higher risk of antepartum haemorrhage in smokers compared with non-smokers. It is estimated that a baby will weigh less than its target weight by a multiple of 15g times the average number of cigarettes a woman smokes per day; smoking fewer than five cigarettes per day has a barely discernible obstetric effect and quitting by 15 weeks gestation reduces the risk as much as quitting before pregnancy. Consequently, all women should be counselled regarding smoking cessation at their booking visit.

Oligohydramnios and polyhydramnios

Amniotic fluid is produced almost exclusively from fetal urine from the second trimester onwards. It serves a vital function in protecting the developing baby from pressure or trauma, allowing limb movement, hence normal postural development, and permitting the fetal lungs to expand and develop through breathing.

Oligohydramnios

Too little amniotic fluid (oligohydramnios) is commonly defined as amniotic fluid index <5th

centile for gestation. The amniotic fluid index (AFI) is an ultrasound estimation of amniotic fluid derived by adding together the deepest vertical pool in four quadrants of the abdomen. The AFI (in cm) is therefore associated with some degree of error. In general, however, it is possible to differentiate subjectively on ultrasound between 'too much', 'too little' and 'normal looking'.

Oligohydramnios may be suspected antenatally following a history of clear fluid leaking from the vagina; this may represent PPRM (see Chapter 11, Late miscarriage and early birth). Clinically, on abdominal palpation, the fetal poles may be very obviously felt and 'hard', with a small for dates uterus. The possible causes of oligohydramnios and anhydramnios (no amniotic fluid) are described in the box.

The fetal prognosis depends on the cause of oligohydramnios, but both pulmonary hypoplasia and limb deformities (contractures, talipes) are common to severe early-onset (<24 weeks) oligohydramnios. Renal agenesis and bilateral multicystic kidneys carry a lethal prognosis, as life after birth is impossible without functioning kidneys. In this situation, the fetal lungs would probably be hypoplastic; this may also be true of severe urinary tract obstruction. Oligohydramnios due to FGR/uteroplacental insufficiency is usually of a less severe degree and less commonly causes limb and lung problems.

Polyhydramnios

Polyhydramnios is the term given to an excess of amniotic fluid, i.e. AFI >95th centile for gestation on ultrasound estimation. It may present as severe abdominal swelling and discomfort. On examination, the abdomen will appear distended out of proportion to the woman's gestation (increased SFH). Furthermore, the abdomen may be tense and tender and the fetal poles will be hard to palpate. The condition may be caused by maternal, placental or fetal conditions.

Maternal

- Diabetes

Placental

- Chorioangioma
- Arterio-venous fistula

Possible causes of oligohydramnios and anhydramnios

Too little production	Diagnosed by
Renal agenesis	Ultrasound: no renal tissue, no bladder
Multicystic kidneys	Ultrasound: enlarged kidneys with multiple cysts, no visible bladder
Urinary tract abnormality/ obstruction	Ultrasound: kidneys may be present, but urinary tract dilatation
FGR and placental insufficiency	Clinical: reduced SFH, reduced fetal movements, possibly abnormal CTG Ultrasound: FGR, abnormal fetal Dopplers
Maternal drugs (e.g NSAIDs)	Withholding NSAIDs may allow amniotic fluid to re-accumulate

Post-dates pregnancy

Leakage	Diagnosed by
PPROM	Speculum examination: pool of amniotic fluid on posterior blade

NSAIDs, non-steroidal anti-inflammatory drugs; SFH, symphysis–fundal height.

Fetal

- Multiple gestation (in monochorionic twins, it may be twin-to-twin transfusion syndrome)
- Idiopathic
- Oesophageal atresia/tracheo-oesophageal fistula
- Duodenal atresia
- Neuromuscular fetal condition (preventing swallowing)
- Anencephaly.

The management of polyhydramnios is directed towards establishing the cause (hence determining fetal prognosis), relieving the discomfort of the mother (if necessary by amniodrainage), and assessing the risk of preterm labour due to uterine over-distension. The last-mentioned may require assessment of cervical length by ultrasound. If prior to 24 weeks, following amniotic fluid drainage, the cervical length is less than 25 mm, consideration might be given to cervical suture insertion.

Polyhydramnios due to maternal diabetes needs urgent investigation, as it often suggests high maternal blood glucose levels. In this context, polyhydramnios should correct itself when the mother's glycaemic control is optimized.

Twin-to-twin transfusion syndrome is a rare cause of acute polyhydramnios in the recipient

sac of monochorionic twins. It is associated with oligohydramnios and a small baby in the other sac. The condition may be rapidly fatal for both twins; amniodrainage and removal by laser of the placental vascular connections are two therapeutic modalities employed in dealing with this condition. This is discussed further in Chapter 9, Twins and higher multiple gestations.

Fetal malpresentation at term

Malpresentation is a presentation that is not cephalic. Breech presentation is the most commonly encountered malpresentation and occurs in 3–4 per cent of term pregnancies, but is more common at earlier gestations. Similarly, oblique and transverse positions are not uncommon antenatally. They only become a problem if the baby (or first presenting baby in a multiple gestation) is not cephalic by 37 weeks.

Breech presentation

There are three types of breech: the most common is extended (frank) breech (Figure 8.3a); less common is a flexed (complete) breech (Figure 8.3b); and least common is footling breech, in which a foot presents at the cervix (Figure 8.3c). Cord and foot prolapse are risks in this situation.

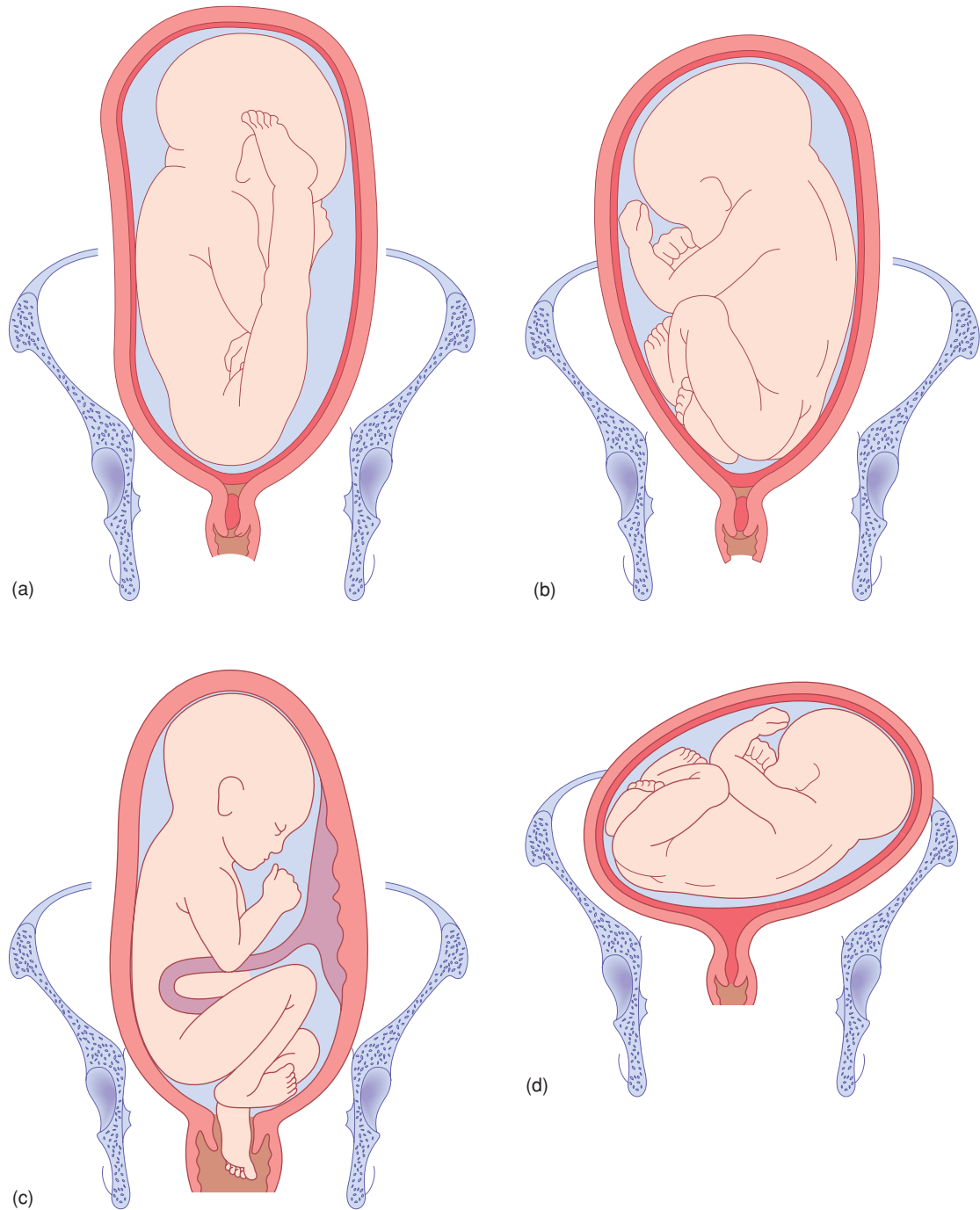
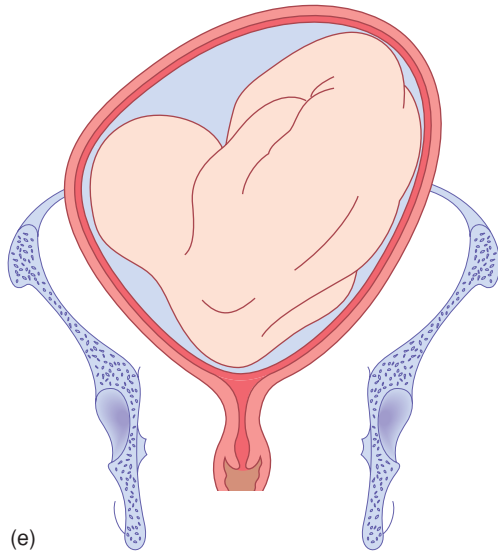


Figure 8.3 (a) Frank breech (also known as extended breech) presentation with extension of the legs. (b) Breech presentation with flexion of the legs. (c) Footling breech presentation. (d) Transverse lie. (e) Oblique lie



(e)

Figure 8.3 (continued)

Predisposing factors for breech presentation

Maternal

- Fibroids
- Congenital uterine abnormalities, e.g. bicornuate uterus
- Uterine surgery

Fetal/placental

- Multiple gestation
- Prematurity
- Placenta praevia
- Abnormality, e.g. anencephaly or hydrocephalus
- Fetal neuromuscular condition
- Oligohydramnios
- Polyhydramnios

Antenatal management of breech presentation

If a breech presentation is clinically suspected at or after 36 weeks, this should be confirmed by ultrasound scan. The scan should document fetal biometry, amniotic fluid volume, the placental site and the position of the fetal legs. The scan should also look for any anomalies previously undetected.

The three management options available at this point should be discussed with the woman. These are external cephalic version (ECV), vaginal breech delivery and elective Caesarean section.

External cephalic version

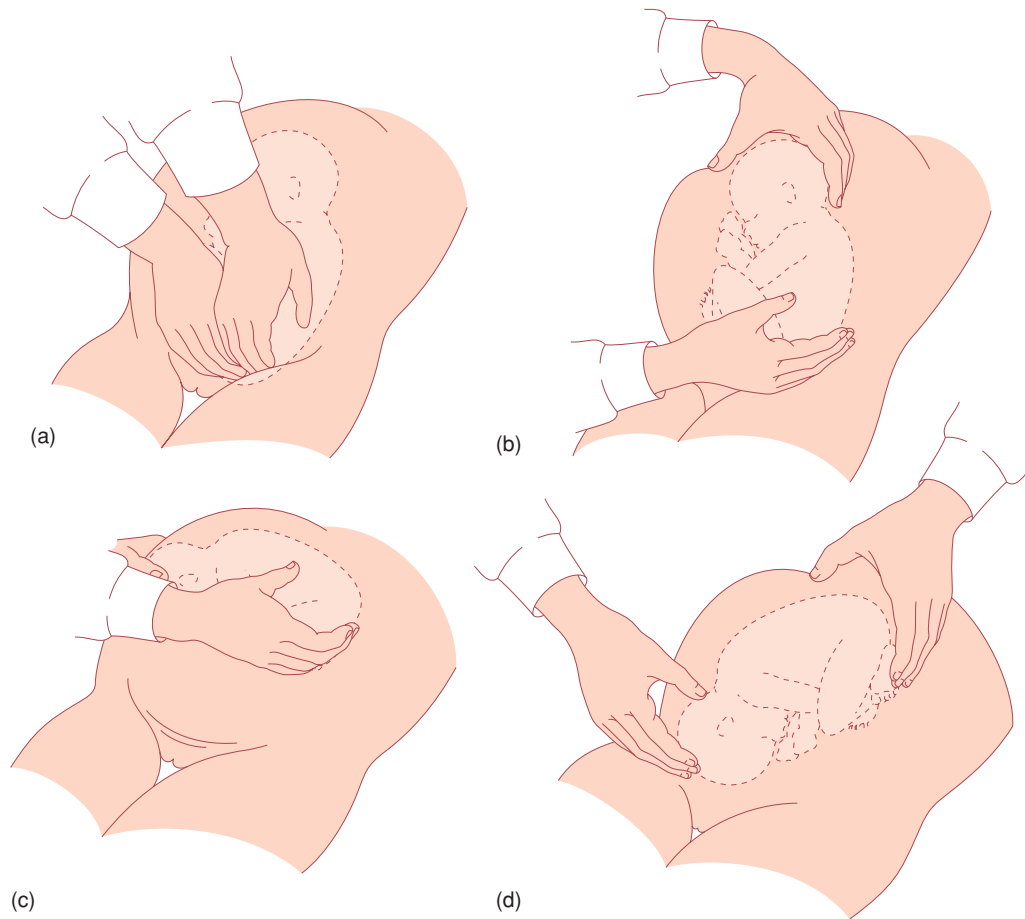
ECV is a relatively straightforward and safe technique and has been shown to reduce the number of Caesarean sections due to breech presentations. Success rates vary according to the experience of the operator but in most units are around 50 per cent (and are higher in multiparous women who tend to have more lax abdominal musculature).

The procedure is performed at or after 37 completed weeks by an experienced obstetrician at or near delivery facilities. ECV should be performed with a tocolytic (e.g. nifedipine) as this has been shown to improve the success rate. The woman is laid flat with a left lateral tilt having ensured that she has emptied her bladder and is comfortable. With ultrasound guidance, the breech is elevated from the pelvis and one hand is used to manipulate this upward in the direction of a forward role, while the other hand applies gentle pressure to flex the fetal head and bring it down to the maternal pelvis (Figure 8.4).

The procedure can be mildly uncomfortable for the mother and should last no more than 10 minutes. If the procedure fails, or becomes difficult, it is abandoned. A fetal heart rate trace must be performed before and after the procedure and it is important to administer anti-D if the woman is Rhesus-negative.

Contraindications to ECV

- Fetal abnormality (e.g. hydrocephalus)
- Placenta praevia
- Oligohydramnios or polyhydramnios
- History of antepartum haemorrhage
- Previous Caesarean or myomectomy scar on the uterus
- Multiple gestation
- Pre-eclampsia or hypertension
- Plan to deliver by Caesarean section anyway



Figures 8.4 External cephalic version. (a) The breech is disengaged from the pelvic inlet. (b) Version is usually performed in the direction that increases flexion of the fetus and makes it do a forward somersault. (c) On completion of version, the head is often not engaged for a time. (d) The fetal heart rate should be checked after the external version has been completed

Risks of ECV

- Placental abruption
- Premature rupture of the membranes
- Cord accident
- Transplacental haemorrhage (remember anti-D administration to Rhesus-negative women)
- Fetal bradycardia

Mode of delivery

If ECV fails, or is contraindicated, and Caesarean section is not indicated for other reasons, then women

should be counselled regarding elective Caesarean section and planned vaginally delivery. A recent large multicentre trial (the Term Breech Trial) confirmed that planned vaginal delivery of a breech presentation is associated with a 3 per cent increased risk of death or serious morbidity to the baby. Although this trial did not evaluate long-term outcomes for child or mother, it has led to the recommendation that the best method of delivering a term breech singleton is by planned Caesarean section. Despite this, either by choice or as a result of precipitous labour, a small proportion of women with breech presentations will deliver vaginally. It therefore remains important that clinicians and hospitals are prepared for vaginal breech delivery.

Prerequisites for vaginal breech delivery

Feto-maternal:

- The presentation should be either extended (hips flexed, knees extended) or flexed (hips flexed, knees flexed but feet not below the fetal buttocks).
- There should be no evidence of feto-pelvic disproportion with a pelvis clinically thought to be adequate and an estimated fetal weight of <3500 g (ultrasound or clinical measurement).
- There should be no evidence of hyperextension of the fetal head, and fetal abnormalities that would preclude safe vaginal delivery (e.g. severe hydrocephalus) should be excluded.

Management of labour:

- Fetal well-being and progress of labour should be carefully monitored.
- An epidural analgesia is not essential but may be advantageous; it can prevent pushing before full dilatation.
- Fetal blood sampling from the buttocks provides an accurate assessment of the acid-base status (when the fetal heart rate trace is suspect).
- There should be an operator experienced in delivering breech babies available in the hospital.

Although much emphasis is placed on adequate case selection prior to labour, a survey of outcome of the undiagnosed breech in labour managed by experienced medical staff showed that safe vaginal delivery can be achieved.

Technique

Breech delivery epitomizes the position of 'masterly inactivity' (hands-off). Problems are more likely to arise when the obstetrician tries to speed up the process (by pulling on the baby).

Delivery of the buttocks

In most circumstances, full dilatation and descent of the breech will have occurred naturally. When the buttocks become visible and begin to distend the perineum, preparations for the delivery are made. The buttocks will lie in the anterior–posterior diameter. Once the anterior buttock is delivered and the anus is

seen over the fourchette (and no sooner than this), an episiotomy can be cut.

Delivery of the legs and lower body

If the legs are flexed, they will deliver spontaneously. If extended, they may need to be delivered using Pinard's manoeuvre. This entails using a finger to flex the leg at the knee and then extend at the hip, first anteriorly then posteriorly. With contractions and maternal effort, the lower body will be delivered. Usually a loop of cord is drawn down to ensure that it is not too short.

Delivery of the shoulders

The baby will be lying with the shoulders in the transverse diameter of the pelvic mid-cavity. As the anterior shoulder rotates into the anterior–posterior diameter, the spine or the scapula will become visible. At this point, a finger gently placed above the shoulder will help to deliver the arm. As the posterior arm/shoulder reaches the pelvic floor, it too will rotate anteriorly (in the opposite direction). Once the spine becomes visible, delivery of the second arm will follow. This can be imagined as a 'rocking boat' with one side moving upwards and then the other. Loveset's manoeuvre essentially copies these natural movements (Figure 8.5). However, it is unnecessary and meddlesome to do routinely (one risks pulling the shoulders down but leaving the arms higher up, alongside the head).

Delivery of the head

The head is delivered using the Mauriceau–Smellie–Veit manoeuvre: the baby lies on the obstetrician's arm with downward traction being levelled on the head via a finger in the mouth and one on each maxilla (Figure 8.6). Delivery occurs with first downward and then upward movement (as with instrumental deliveries). If this manoeuvre proves difficult, forceps need to be applied. An assistant holds the baby's body aloft while the forceps are applied in the usual manner (Figure 8.7).

Complications

The greatest fear with a vaginal breech is that the baby will get 'stuck'. Interference in the natural process by the inappropriate use of oxytocic agents or by trying to pull the baby out (breech extraction) will (paradoxically) increase the risk of obstruction occurring. When delay occurs, particularly with

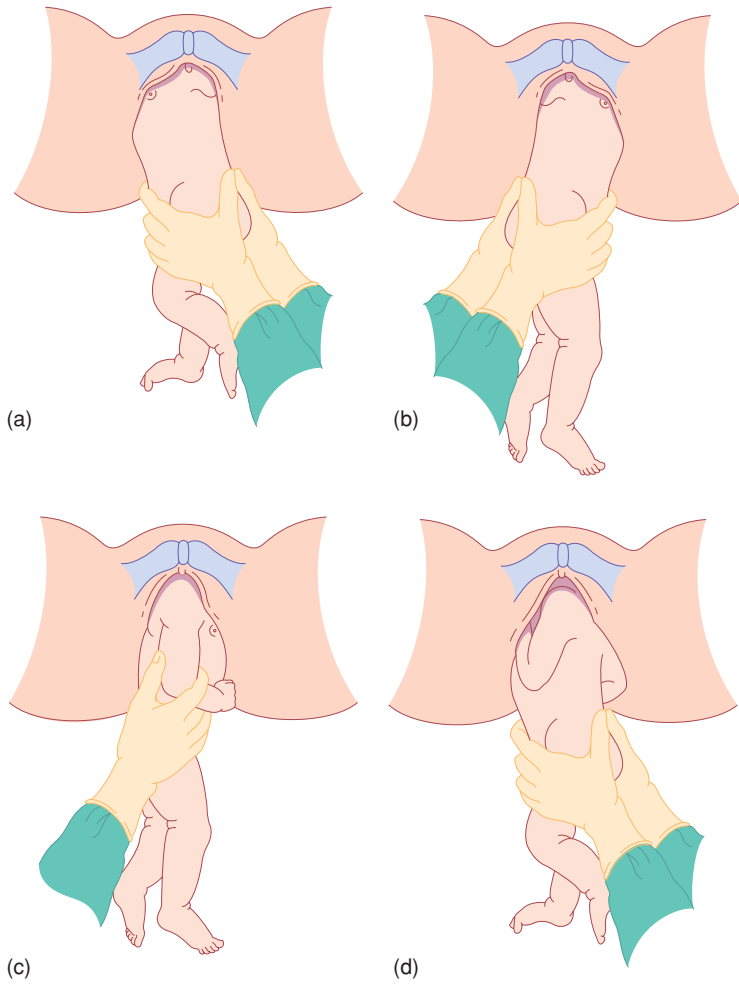


Figure 8.5 Loveset's manoeuvre.

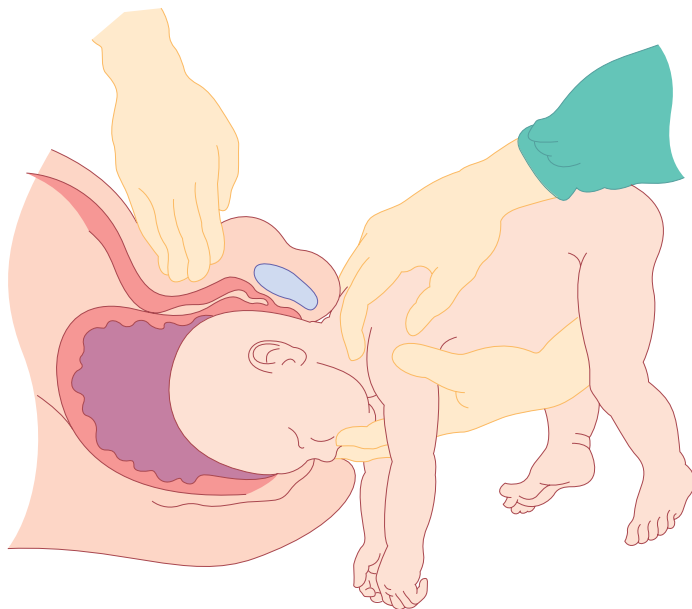


Figure 8.6 Mauriceau–Smellie–Veit manoeuvre for delivery of the head

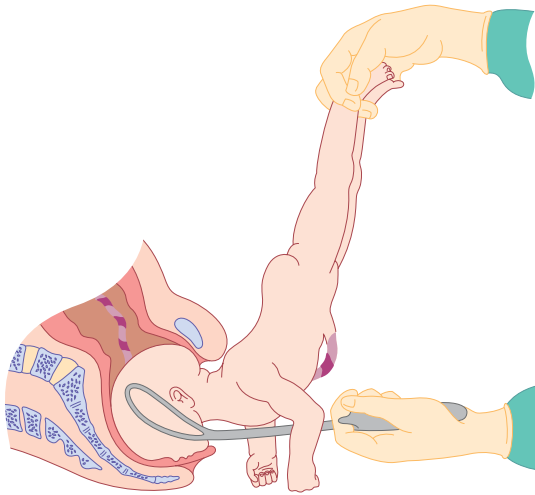


Figure 8.7 Delivery of the aftercoming head with forceps

delivery of the shoulders or head, the presence of an experienced obstetrician will reduce the risk of death or serious injury.

Key points

Breech presentation

- ECV should be offered at 36–37 weeks in selected women.
- Elective Caesarean section is safer than vaginal delivery for a baby presenting by the breech at or close to term.
- Planned or unexpected vaginal breech deliveries should be attended by experienced clinicians.

Other fetal malpresentations

A transverse lie occurs when the fetal long axis lies perpendicular to that of the maternal long axis and classically results in a shoulder presentation (see Figure 8.3d). An oblique lie occurs when the long axis of the fetal body crosses the long axis of the maternal body at an angle close to 45 degrees (see Figure 8.3e).

Any woman presenting at term with a transverse or oblique lie is at potential risk of cord prolapse following spontaneous rupture of the membranes, and prolapse of the hand, shoulder or foot once in labour. In most cases, the woman is multiparous with a lax uterus and

abdominal wall musculature, and gentle version of the baby's head in the clinic or on the ward will restore the presentation to cephalic. If this does not occur, or the lie is unstable (alternating between transverse, oblique and longitudinal), it is important to think of possible uterine or fetal causes of this (see the box describing predisposing factors for breech presentation).

The diagnosis of transverse or oblique lie might be suspected by abdominal inspection: the abdomen often appears asymmetrical. The SFH may be less than expected, and on palpation the fetal head or buttocks may be in the iliac fossa. Palpation over the pelvic brim will reveal an 'empty' pelvis.

It goes without saying that a woman in labour with the baby's lie anything other than longitudinal will not be able to deliver vaginally; this is one situation in which if Caesarean section is not performed both the mother and baby are at considerable risk of morbidity and mortality. The only exception to this is for exceptionally preterm or small babies, where vaginal delivery may occur irrespective of lie or presentation.

A woman with an unstable lie at term should be admitted to the antenatal ward. The normal plan would be to deliver by Caesarean section if the presentation is not cephalic in early labour or if spontaneous rupture of the membranes occurs. In a multiparous woman, an unstable lie will often correct itself in early labour (as long as the membranes are intact).

Post-term pregnancy

A pregnancy that has extended to or beyond 42 weeks gestation is defined as a prolonged or post-term pregnancy. Accurate dating remains essential for the correct diagnosis and should ideally involve a first-trimester ultrasound estimation of crown–rump length.

Post-term pregnancy affects approximately 10 per cent of all pregnancies and the aetiology is unknown. Post-term pregnancy is associated with increased risks to both the fetus and the mother an increased risk of stillbirth and perinatal death, an increased risk of prolonged labour and an increased risk of Caesarean section.

Fetal surveillance and induction of labour are two strategies employed that may reduce the risk of adverse outcome. Unfortunately, there are no

known tests that can accurately predict fetal outcome post-term; an ultrasound scan may give temporary reassurance if the amniotic fluid and fetal growth are normal. Similarly, a CTG should be performed at and after 42 weeks.

Immediate induction of labour or delivery post-dates should take place if:

- there is reduced amniotic fluid on scan;
- fetal growth is reduced;
- there are reduced fetal movements;
- the CTG is not perfect;
- the mother is hypertensive or suffers a significant medical condition.

Induction of labour is discussed further in Chapter 14, Labour.

When counselling the parents regarding waiting for labour to start naturally after 42 weeks, it is important that the woman is aware that no test can guarantee the safety of her baby, and that perinatal mortality is increased (at least two-fold) beyond 42 weeks. A labour induced post-term is more likely to require Caesarean section; this may partly be due to the reluctance of the uterus to contract properly, and the possible compromise of the baby leading to abnormal CTG.

Antepartum haemorrhage

This is defined as vaginal bleeding from 24 weeks to delivery of the baby. The causes are placental or local.

Placental causes

- Placental abruption
- Placenta praevia
- Vasa praevia

Local causes

- Cervicitis
- Cervical ectropion
- Cervical carcinoma
- Vaginal trauma
- Vaginal infection

The incidence of antepartum haemorrhage is 3 per cent. It is estimated that 1 per cent is attributable to placenta praevia, 1 per cent is attributable to placental abruption and the remaining 1 per cent is from other causes. Placental causes are obviously the most worrying, as potentially the mother's and/or fetus' life is in danger. However, any antepartum haemorrhage must always be taken seriously, and any woman presenting with a history of fresh vaginal bleeding must be investigated promptly and properly. The key question is whether the bleeding is placental, and is compromising the mother and/or fetus, or whether it has a less significant cause. A pale, tachycardic woman looking anxious with a painful, firm abdomen, underwear soaked in fresh blood and reduced fetal movements needs emergency assessment and management for a possible placental abruption (see Chapter 16, Obstetric emergencies). A woman having had a small postcoital bleed with no systemic signs or symptoms represents a different end of the spectrum.

History

- How much bleeding?
- Triggering factors (e.g. postcoital bleed).
- Associated with pain or contractions?
- Is the baby moving?
- Last cervical smear (date/normal or abnormal)?

Examination

- Pulse, blood pressure.
- Is the uterus soft or tender and firm?
- Fetal heart auscultation/CTG.
- Speculum vaginal examination, with particular importance placed on visualizing the cervix (having established that placenta is not a praevia, preferably using a portable ultrasound machine).

Investigations

- Depending on the degree of bleeding, full blood count, clotting and, if suspected praevia/abruption, crossmatch six units of blood.

- Ultrasound (fetal size, presentation, amniotic fluid, placental position and morphology).

Placental abruption

The premature separation of the placenta is termed 'abruption'. The bleeding is maternal and/or fetal and abruption is acutely dangerous for both the mother and fetus (Figures 8.8 and 8.9; see Chapter 10, Pre-eclampsia and other disorders of placentation and Chapter 16, Obstetric emergencies).

Placenta praevia

A placenta covering or encroaching on the cervical os may be associated with bleeding, either provoked or

spontaneous. The bleeding is from the maternal not fetal circulation and is more likely to compromise the mother than the fetus (Figure 8.10).

Risk factors for placenta praevia

- Multiple gestation
- Previous Caesarean section
- Uterine structural anomaly
- Assisted conception

Vasa praevia

Vasa praevia is present when fetal vessels traverse the fetal membranes over the internal cervical os. These vessels may be from either a velamentous insertion of the umbilical cord or may be joining an accessory (succenturiate) placental lobe to the main disk of the placenta. The diagnosis is usually suspected when either spontaneous or artificial rupture of the membranes is accompanied by painless fresh vaginal bleeding

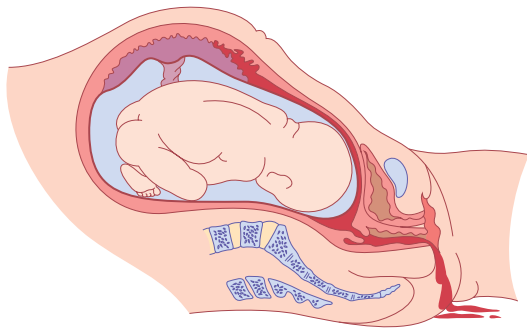


Figure 8.8 Placental abruption with revealed haemorrhage

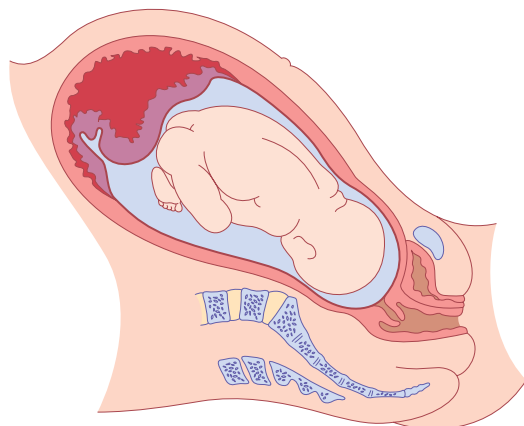


Figure 8.9 Placental abruption with concealed haemorrhage

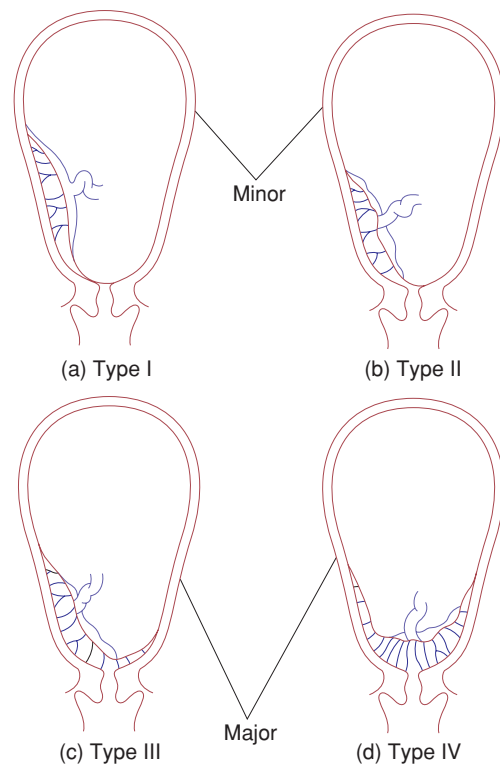


Figure 8.10 Classification of placenta praevia

from rupture of the fetal vessels. This condition is associated with a very high perinatal mortality from fetal exsanguination. If the baby is still alive once the diagnosis is suspected, the immediate course of action is delivery by emergency Caesarean section.

Key points



- Placenta praevia is most dangerous for the mother.
- Placental abruption is more dangerous for the fetus than the mother.
- Vasa praevia is not dangerous for the mother but is nearly always fatal for the baby.

Further management

If there is minimal bleeding and the cause is clearly local vaginal bleeding, symptomatic management may be given (for example, antifungal preparations for candidiasis), as long as there is reasonable certainty that cervical carcinoma is excluded by smear history and direct visualization of the cervix. Placental causes of bleeding are a major concern. A large-gauge intravenous cannula is sited, blood sent for full blood count, clotting and crossmatch, and appropriate fetal and maternal monitoring instituted. If there is major fetal or maternal compromise, decisions may have to be made about immediate delivery irrespective of gestation. Emergency management is described in Chapter 16, Obstetric emergencies. If bleeding settles, the ongoing management depends on the underlying cause. If the cause was a suspected placental abruption, the woman must be admitted for 48 hours as the risk of rebleeding is high within this time frame. Steroids should be administered if the gestation is less than 34 weeks. Rhesus status is important: if the mother is Rhesus negative, send a Kleihauer test (to determine whether any, or how much, fetal blood has leaked into the maternal circulation) and administer anti-D. The ongoing management of placenta praevia is more contentious. Many clinicians favour retaining major placenta praevias in hospital until delivery.

Rhesus iso-immunization

Blood group is defined in two ways. First, there is the ABO group, allowing four different permutations of

blood group (O, A, B, AB). Second, there is the rhesus system, which consists of C, D and E antigens. The importance of these blood group systems is that a mismatch between the fetus and mother can mean that when fetal red cells pass across to the maternal circulation, as they do to a greater or lesser extent during pregnancy, sensitization of the maternal immune system to these fetal 'foreign' red blood cells may occur and subsequently give rise to haemolytic disease of the fetus and newborn (HDFN).

The Rhesus system is the one most commonly associated with severe haemolytic disease.

The aetiology of Rhesus disease

The Rhesus system is coded on two adjacent genes, which sit within chromosome one. One gene codes for antigen polypeptides C/c and E/e while the other codes for the D polypeptide (Rhesus antigen). Note that the d (little d) antigen has not been identified so it may be that women who are D negative lack the antigen altogether, as opposed to those with c (little c) or e (little e), where c is the allelic antigen of C and e is the allelic antigen of E. Antigen expression is usually dominant, whereas those who have a negative phenotype are either homozygous for the recessive allele or have a deletion of that gene (Figure 8.11). In practice, only anti-D and anti-c regularly cause HDFN. Anti-D is much more common than anti-c and is therefore the focus of this discussion.

Occurrence of HDFN as a result of Rhesus isoimmunization involves three key stages (see Figure 8.12). First, a Rhesus negative mother must conceive a baby who has inherited the Rhesus positive phenotype from the father. Second, fetal cells must gain access to the maternal circulation in a sufficient volume to provoke a maternal antibody response. Finally, maternal antibodies must gain transplacental access and cause immune destruction of red cells in the fetus. Rhesus disease does not affect a first pregnancy as the primary response is usually weak and consists primarily of IgM antibodies that do not cross the placenta. Thereafter IgG antibodies are produced and these can cross the placenta. Rhesus antigens are well expressed by the fetus from as early as 30 days gestation so in a subsequent pregnancy, when maternal resensitization occurs (Rhesus-positive red cells pass from the baby to the maternal circulation; Figure 8.12), IgG antibodies cross from the mother to the fetal circulation. If these antibodies

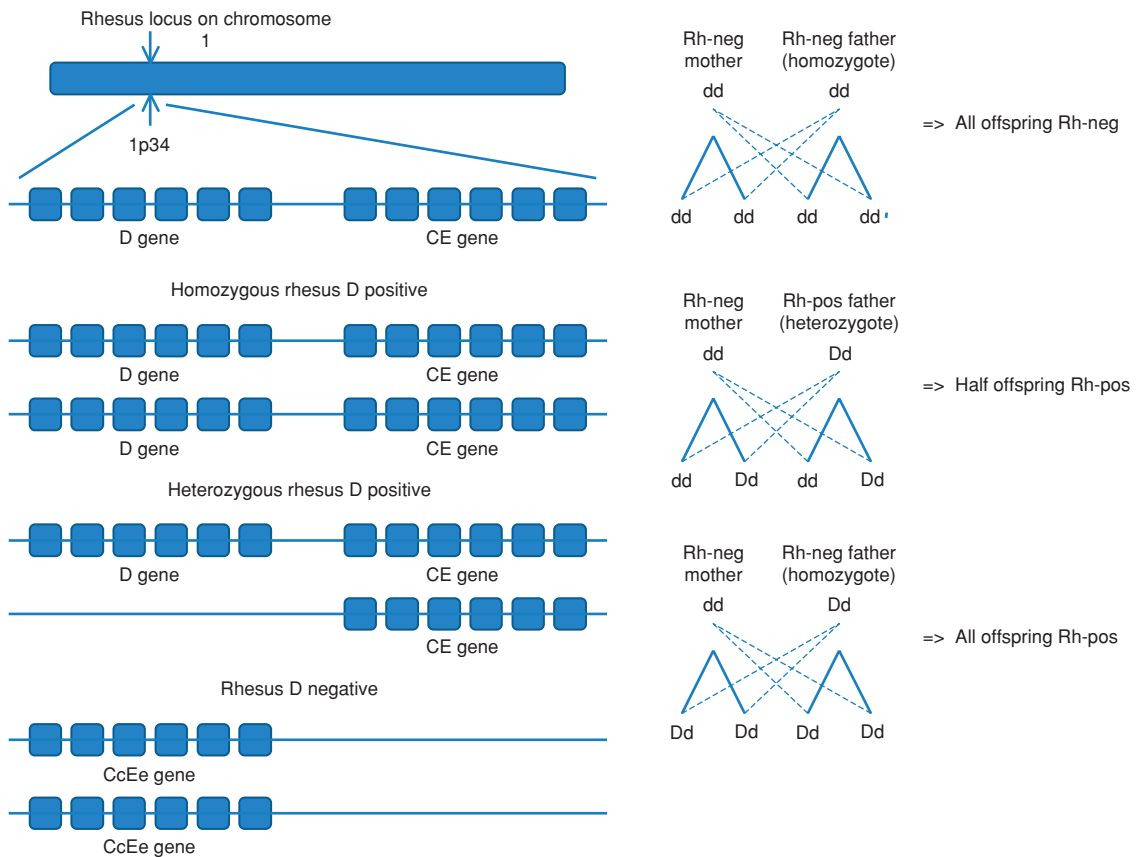


Figure 8.11 The parental genotype determinants of Rhesus group

are present in sufficient quantities, fetal haemolysis may occur, leading to such severe anaemia that the fetus may die unless a transfusion is performed. It is for this reason that Rhesus-negative women have frequent antibody checks in pregnancy; an increasing titre of atypical antibodies may suggest an impending problem.

Potential sensitizing events for Rhesus disease

- Miscarriage
- Termination of pregnancy
- Antepartum haemorrhage
- Invasive prenatal testing (chorion villus sampling, amniocentesis and cordocentesis)
- Delivery

Prevalence of Rhesus disease

The prevalence of D Rhesus negativity is 15 per cent in the Caucasian population, but lower in all other ethnic groups. It is very uncommon in Orientals. Rhesus disease is most common in countries where anti-D prophylaxis is not widespread, such as the Middle East and Russia.

Preventing Rhesus iso-immunization

The process of iso-immunization can be 'nipped in the bud' by the intramuscular administration of anti-D immunoglobulins to a mother, preferably within 72 hours of exposure to fetal red cells. Anti-D immunoglobulins 'mop up' any circulating rhesus-positive cells before an immune response is excited in the mother. The practical implications of this are that anti-D immunoglobulin must be

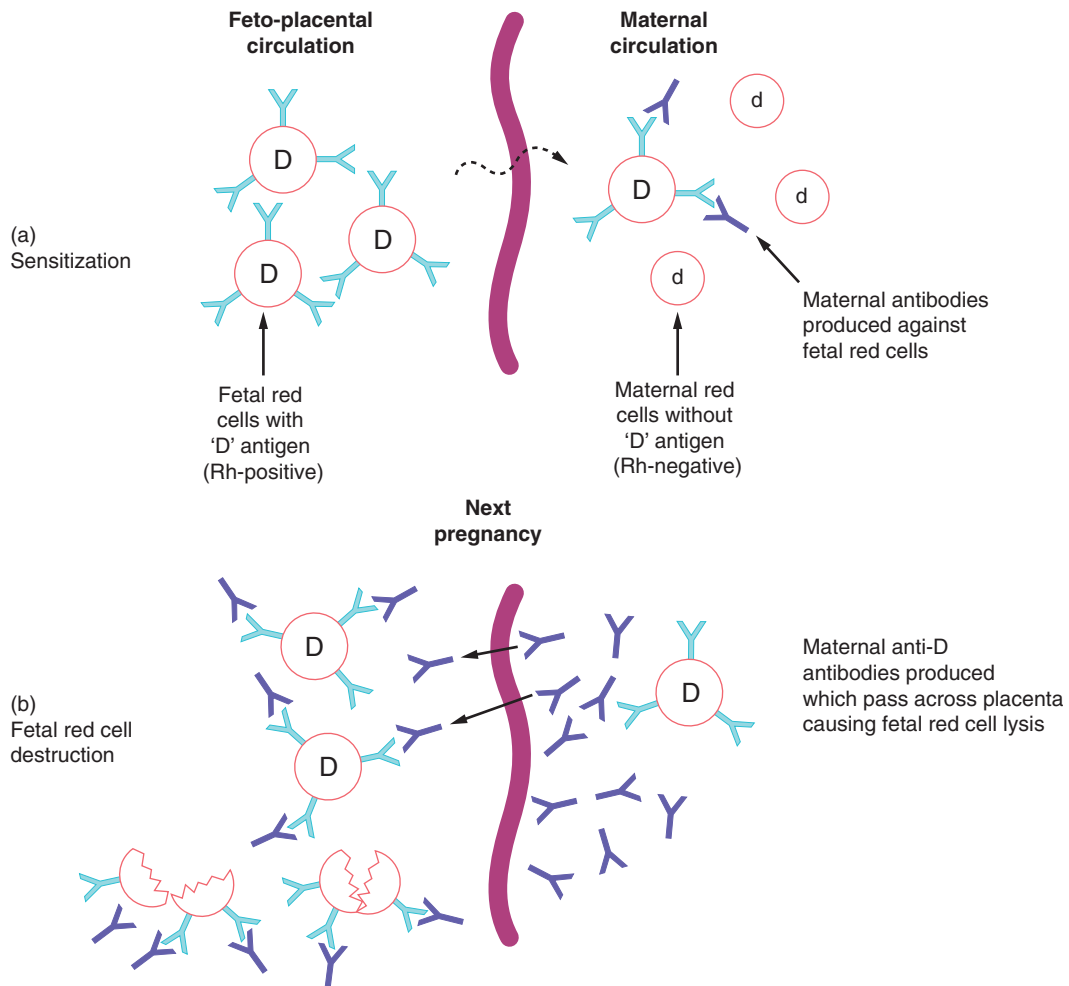


Figure 8.12 The mechanism of rhesus sensitization (a) and fetal red cell destruction (b)

given intramuscularly as soon as possible after any potentially sensitizing event. It is normal practice to administer anti-D after any of these events; the exact dose is determined by the gestation at which sensitization has occurred and the size of the fetomaternal haemorrhage.

In the first trimester of pregnancy, because the volume of fetal blood is so small, it is unlikely that sensitization would occur, and a 'standard' dose of anti-D (the exact dose varies from country to country) is given; this will more than cover even the largest fetomaternal transfusion. In the second and third trimesters, fetal blood volume is greater and because there is a possibility of a fetomaternal transfusion of several millilitres, a larger dose is given and a Kleihauer test performed.

A Kleihauer is a test of maternal blood to determine the proportion of fetal cells present (relying on their ability to resist denaturation by alcohol or acid); it will allow calculation of the amount of extra anti-D immunoglobulin required should a large transfusion have occurred.

In many countries, Rhesus-negative women are given anti-D at 28 and/or 34 weeks routinely. This is based on the finding that a small number of Rhesus-negative women become sensitized during pregnancy despite the administration of anti-D at delivery and without a clinically obvious sensitizing event. The likelihood is that a small fetomaternal haemorrhage occurs without any obvious clinical signs; therefore, prophylactic anti-D would reduce the risk of iso-immunization from this event.

Signs of fetal anaemia

Note: Clinical and ultrasound features of fetal anaemia do not usually become evident unless fetal haemoglobin is more than 5 g/dL less than the mean for gestation. Usually, features are not obvious unless the fetal haemoglobin is less than 6 g/dL.

- Polyhydramnios.
- Enlarged fetal heart.
- Ascites and pericardial effusions.
- Hyperdynamic fetal circulation (can be detected by Doppler ultrasound by measuring increased velocities in the middle cerebral artery or aorta).
- Reduced fetal movements.
- Abnormal CTG with reduced variability, eventually a 'sinusoidal' trace.

The management of Rhesus disease in a sensitized woman

Once a woman who is D Rhesus negative has been sensitized to the D Rhesus antigen, no amount of anti-D will ever turn the clock back. In a subsequent pregnancy, close surveillance is required. Rhesus disease gets worse with successive pregnancies, so it is important to note the severity of the disease in previous pregnancies. The management depends on the clinical scenario.

- The father of the next baby is D Rhesus negative. In this situation, there is no risk that the baby will be D Rhesus positive and therefore there is no chance of Rhesus disease.
- The father of the next baby is D Rhesus positive. He may be heterozygous and in this situation determining the paternal phenotype is useful in anticipating the likely fetal phenotype and, thus, the potential for development of HDFN. However, it is important to bear in mind that there are issues regarding paternal testing, and assuming paternity runs the risk of false prediction. Notwithstanding this issue, paternal blood grouping is frequently used and often useful.
- In a sensitized woman, if the father is D Rhesus positive or unknown, standard management involves monitoring antibody levels every 2–4 weeks from booking. Antibody levels or quantity can be described using the titre or by using

IU (international units) as a standard quantification method. The titre simply refers to the number of times a sample has been diluted before the amount of antibody becomes undetectable; titre of 2, 4, 8, 16, 32, 64, 128, etc. Each time a sample is tested, it should be checked in parallel with the previous sample to ensure the detection of significant changes in the antibody level. It has been found that titrations of anti-D do not correlate well with the development of HDFN, and that the standard quantification method (IU/mL) gives more clinically relevant levels.

Anti-D level	Outcome
<4 IU/mL	HDFN unlikely
4–15 IU/mL	Moderate risk of HDFN
>15 IU/mL	High risk of hydrops fetalis

- If antibody levels rise, the baby should be examined for signs of anaemia. In the past, the bilirubin concentration of amniotic fluid was determined optically to give an indirect measure of fetal haemolysis. This involved an invasive procedure with the attendant risks of miscarriage/preterm labour and further boosting of the alloimmune response. In the last decade, middle cerebral artery (MCA) Dopplers (peak velocity measurement) have been shown to correlate reliably with fetal anaemia. In practice, this means that the use of invasive tests to monitor disease progression (once a critical antibody level has been reached) have been replaced by non-invasive assessment using MCA Doppler. There is now substantial data to support the use of peak MCA velocity as a correlate of fetal anaemia. The sensitivity is reported at 100 per cent with a false positive rate of 12 per cent (see figure 6.17 in Chapter 6, Antenatal imaging and assessment of fetal well-being).
- A fetus with raised MCA Dopplers has a high probability of anaemia. These cases are not common and the treatment should be in, or guided by, tertiary fetal medicine centres. Treatment options include delivery or fetal blood transfusion. Delivery of the fetus is an option if the fetus is sufficiently mature. However, delivery

of an anaemic, rapidly haemolysing premature baby is a significant risk and should not be undertaken lightly. Delivery must take place in a unit where adequate neonatal support and expertise is available and generally delivery should not be before 36–37 weeks of gestation unless there are specific reasons, such as special difficulty with fetal transfusion.

- Fetal blood transfusion is life saving in a severely anaemic fetus that is too premature for delivery to be contemplated. The aim is to restore haemoglobin levels, reversing or preventing hydrops or death. A side effect is that transfusion will also suppress fetal erythropoiesis, which reduces the concentration of antigen positive cells available for haemolysis. Blood can be transfused into a fetus in various ways depending on the gestation, the site of the cord insertion and the clinical situation.
- Routes of administration:
 - into the umbilical vein at the point of the cord insertion (ideally through the placenta and not through the amniotic sac);
 - into the intrahepatic vein;
 - into the peritoneal cavity (not as effective but some blood is absorbed and this may be the only option, for example in low gestations);
 - into the fetal heart.

Once a decision has been made that the fetus is severely anaemic and requires a blood transfusion, the invasive procedure aims to first take a sample to confirm the anaemia and then infuse the blood during a single puncture.

- Transfused blood is:
 - RhD negative;
 - crossmatched with a maternal sample;
 - densely packed (Hb usually around 30 g/L) so that small volumes are used;
 - white cell depleted and irradiated;
 - screened for infection including CMV.

At delivery

If the baby is known to be anaemic or has had multiple transfusions, a neonatologist must be present at delivery should exchange transfusion be required.

Blood must therefore always be ready for the delivery. All babies born to Rhesus-negative women should have cord blood taken at delivery for a blood count, blood group and indirect Coomb's test.

Key points



D Rhesus disease

- Rhesus disease gets worse with successive pregnancies.
- If the father of the fetus is Rhesus negative, the fetus cannot be Rhesus positive.
- If the father of the fetus is Rhesus positive, he may be a heterozygote (50 per cent likelihood that the baby is D Rhesus positive) or a homozygote (100 per cent likelihood).
- Anti-D is given only as prophylaxis and is useless once sensitization has occurred.
- Prenatal diagnosis for karyotype, or attempts at determining fetal blood group by invasive testing (e.g. chorion villus sampling), may make the antibody levels higher in women who are already sensitized.

ABO

ABO blood group iso-immunization may occur when the mother is blood group O and the baby is blood group A or B. Anti-A and anti-B antibodies are present in the maternal circulation naturally, usually secondary to sensitization against A or B substances in food or bacteria. This means that ABO incompatibility may occur in a first pregnancy. In this situation, anti-A or anti-B antibodies may pass to the fetal circulation, causing fetal haemolysis and anaemia. However, most anti-A and anti-B are mainly IgM and do not cross the placenta. In addition, A and B antigens are not fully developed in the fetus. Therefore ABO incompatibility generally causes only mild haemolytic disease of the baby, but may sometimes explain unexpected jaundice in an otherwise healthy term infant.

Additional reading

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TWINS AND HIGHER MULTIPLE GESTATIONS

Griffith Jones

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OVERVIEW

In 1–2 per cent of pregnancies, there is more than one fetus. The chances of miscarriage, fetal abnormalities, poor fetal growth, preterm delivery and intrauterine or neonatal death are considerably higher in twin than in singleton pregnancies. In about two-thirds of twins the fetuses are non-identical, or dizygotic, and in one-third they are identical, or monozygotic. In all dizygotic pregnancies there are two functionally separate placentae (dichorionic). In two-thirds of monozygotic pregnancies there are vascular communications within the two placental circulations (monochorionic) and in the other one-third of cases there is dichorionic placentation. Monochorionic, compared to dichorionic, twins have a much higher risk of abnormalities and death. The maternal risks are also increased in multiple gestations, including adverse symptoms such as nausea and vomiting, tiredness and discomfort, and the risk of serious complications, including hypertensive and thromboembolic disease, and antepartum and postpartum haemorrhage.

Definitions

In general terms, multiple pregnancies consist of two or more fetuses. There are rare exceptions to this, such as twin gestations made up of a singleton viable fetus and a complete mole. Twins make up the vast majority (nearly 99 per cent) of multiple gestations. Pregnancies with three or more fetuses are referred to as ‘higher multiples’.

Prevalence

Risk factors for multiple gestations include assisted reproduction techniques (both ovulation induction and *in vitro* fertilization (IVF)), increasing maternal age, high parity, black race and maternal family history.

In the UK, twins currently account for approximately 1.5 per cent of all pregnancies, up from 1 per cent in 1984.

Since the mid-1980s, the incidence of multiple pregnancy has been increasing. Two related and overlapping trends are contributors to this. Delay in childbearing results in increased maternal age at conception. The increased use of infertility treatments, also often by older women, is another factor.

Traditionally, the expected incidence was calculated using Hellin’s rule. Using this rule, twins were expected in 1 in 80 pregnancies, triplets in 1 in 80² and so on. Based upon the number of births in the UK in 2007, 9555 twins would have been predicted. In fact, 11 573 were delivered, 21 per cent higher than expected. The figures for triplets are similar; 119 sets may have been expected but in actuality 149 were delivered. Now seen in just over 1 in 5000 UK pregnancies, this represents a 25 per cent excess over expected; however, these figures for triplets have actually fallen dramatically since the late 1990s. At that time, the Human Fertilisation and Embryology Authority placed restrictions on fertility centres, limiting the number of embryos that could