

Section 1

Basic science, epidemiology and service organization

Chapter

1

Physiology of pregnancy

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Introduction

Maternal physiology undergoes complex changes during pregnancy in order to enable the female reproductive system to nurture and adapt to the fetus and placenta. The changes are predominantly either secondary to hormonal responses to female sex hormones or physical adaptations to increasing fetal size. The definition and detailed understanding of the normal physiological changes occurring in the antepartum, intrapartum and postpartum periods of pregnancy are crucial to recognize pathophysiological deviations as a result of disease and anaesthesia. Even though the changes are in fact quite widespread, this chapter will focus on some of the key physiological systems that are of direct relevance to the anaesthetist's management of a pregnant woman during the peripartum period.

Haematological system

Antepartum period

Pregnancy and the neonatal period result in significant changes in the haematological system with an associated increased risk for the development of complications, such as anaemia, thromboembolism and consumptive coagulopathies. Most haematological parameters are progressively altered during pregnancy and are reflected in laboratory investigations. Blood and plasma volumes increase, resulting in an adaptive hypervolaemia. An increase of 30–45% in the blood volume occurs, with changes starting at 6–8 weeks and peaking at 28–34 weeks, approximately 1.5 L higher than the prepregnant state. The increased blood volume is accompanied by increases in red cell mass secondary to increased erythropoiesis stimulated by high circulating levels of renal erythropoietin (Epo). The changes in erythropoiesis begin by week 10 and progressively accelerate through the second and

third trimesters and are accompanied by erythroid hyperplasia of the bone marrow and an increase in the reticulocyte counts. While the early increases in erythropoietin may be due to the decreased oxygen-carrying capacity, in the last two trimesters, the increase is thought to be induced by progesterone, prolactin and human placental lactogen. Pregnancy-induced physiological changes are also responsible for a rise in red blood cell 2,3 diphosphoglycerate (2,3-DPG) levels leading to a gradual rightward shift of the maternal oxygen–haemoglobin dissociation curve, with improved oxygen transfer from mother to fetus. Red cell parameters like the mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC) remain relatively stable in the absence of iron deficiency anaemia.

Circulating oestrogen and progesterone act directly on the kidney, inducing the release of renin with activation of the aldosterone–renin–angiotensin mechanism resulting in Na^+ retention and an associated increase in total body water. The resultant increase in plasma volume (~45%) is relatively greater than accompanying increases in red cell mass (~33%). The consequent haemodilution causes decreases in haematocrit (33–39% at term) and haemoglobin concentrations (~150 g/L prepregnancy to ~120 g/L in the third trimester) leading to physiological anaemia of pregnancy. White cell counts can increase by ~8% from the second month of pregnancy, predominantly due to an oestrogen-induced neutrophilia. While T- and B-lymphocyte counts do not change, their function is suppressed leading to increased susceptibility to infections. Platelet levels generally remain within the normal range during pregnancy. There is some evidence of increased production and increased consumption. Gestational thrombocytopenia is a physiological condition that occurs in a small number of parturients.

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Hypervolaemia and the ensuing haemodilution can cause significant changes in other plasma components as well (plasma proteins, electrolytes, lipids, enzymes, serum iron etc.). Total plasma protein is reduced by 10–14%, particularly during the first trimester. Despite an absolute increase in serum albumin concentrations, the relative decrease due to haemodilution results in decreased oncotic pressure, contributing to oedema, which is further aggravated by increased venous hydrostatic pressure in the third trimester. The albumin-to-globulin ratio decreases due to absolute and relative increases in globulin concentrations. Increases in fibrinogen levels of 50–80% are reported in pregnancy, which, together with elevations in serum globulins, cause progressive elevations in the erythrocyte sedimentation rate (ESR) in pregnancy. A combination of hypervolaemia and effects of alterations in the respiratory system (low CO₂ levels) result in a decrease of serum electrolyte levels with reduced plasma osmolarity. Increases in serum lipids (40–60% at term), particularly cholesterol and phospholipids, occur due to increased fetal and placental demands. With poor iron supplementation, serum iron and ferritin levels decrease. Reduction of serum ferritin – a more precise indicator of reticuloendothelial iron stores – peaks in the second trimester in parallel with the rapid expansion in maternal red blood cell mass. An increase in serum alkaline phosphatase is a common finding and is usually attributed to increased placental production.

Pregnancy induces a hypercoagulable state with an increased risk of thrombosis and coagulopathies due to an intrinsic activation of the coagulation system in the uteroplacental circulation. The majority of the coagulation factors are elevated, particularly Factors I, VII, VIII, X, XII, prekallikrein and the von Willebrand factor (vWF). Activated partial thromboplastin time (APTT) and prothrombin time (PT) decrease after mid pregnancy, while the bleeding time remains normal. The overall effect on the coagulation system during pregnancy is an increase in thrombin generation due to increased activity of procoagulant proteins and suppression of the fibrinolytic system. The resultant hypercoagulable state facilitates and stabilizes clot formation. Haematological changes occurring in pregnancy are summarized in Table 1.1 below.

The physiological changes in the haematological and haemostatic system during pregnancy are essential to meet the demands of the fetus and protect against intrapartum blood loss. An understanding

Table 1.1 The most significant haematological changes in pregnancy

Physiological anaemia
Neutrophilia
Mild thrombocytopenia
Increased procoagulant factors
Diminished fibrinolysis

of the normal physiological process is vital, given the influence of these changing parameters on the interpretation of laboratory investigations and the increased susceptibility to thromboembolism and coagulopathies. The haematological changes revert to prepregnancy status at 2 weeks post partum.

Intrapartum and postpartum phases

Maternal adaptations in the haematological system during the intrapartum phase of the pregnancy are primarily aligned to coping with and minimizing the impact of significant blood loss associated with the delivery of the fetus. The efficacy of this adaptation is reflected in the ability to withstand losses of up to 1000 mL of blood (~500 mL in a normal vaginal delivery; up to ~ 1000 mL for a caesarian section or normal twin delivery) with minimal resultant effects on the blood and pulse pressures estimated to be around half the extra blood volume acquired antepartum.

A stress-induced increase in erythropoiesis coupled with muscular exertion and dehydration result in haemoconcentration and mild increases in haemoglobin levels in the peripartum period. The stress response also contributes to neutrophilia and increased WBC counts that could confound or mask the diagnosis of infection. Some authors have documented a physiological increase in white cell counts of up to 30 000 mm³ in the postpartum period.

An enhancement of the hypercoagulable state of pregnancy and activation of the clotting cascades and platelets ensures a more stringent control on the blood losses in the peripartum phase. In order to minimize blood losses from the endometrial placental separation site, fibrinolytic activity decreases during partus, promoting clot formation. Placental and decidual tissue factor, a membrane bound protein that initiates coagulation, increases during labour, as does Factor VIII complex and Factor V. Prothrombin time decreases, particularly in the final stages of labour.

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The reduction of fibrinolytic inhibitor levels following placental detachment results in normal fibrinolytic activity 48 h after the delivery. By week 6 post partum, the haemostatic system returns to the pre-pregnant state. These changes in the pro- and anti-coagulation systems account for the marked increase in the risks of venous thrombosis in women during this period.

The cardiovascular system

Physiological changes in pregnancy

The increased metabolic demands of the mother and fetus during pregnancy result in a range of physiologically significant, but reversible adaptive changes in the maternal cardiovascular system. In most instances, the increased demands on the maternal cardiovascular system are met adequately by the ensuing physiological adaptations. If, however, there is underlying maternal cardiovascular compromise due to disease, or the normal physiological haemodynamic changes fail to occur, the adverse effects on the uteroplacental circulation could result in fetal and maternal disease.

Most cardiovascular and haemodynamic changes are initiated in the early stages of pregnancy due to high circulatory levels of the vasoactive reproductive hormones oestrogen, progesterone and prostaglandins (PGE1 and PGE2). The resulting vasodilation and reduction in systemic and pulmonary vascular resistance (~20%) cause a fall in systolic and diastolic blood pressures triggering reflex increases in the stroke volume (~25–30%) and heart rate (~10–20), and increases in cardiac output by approximately 30–50% of the prepregnancy states. Changes in heart rate and stroke volume are detected as early as 5 weeks and 8 weeks, respectively. Stroke volume peaks around 16–24 weeks and decreases in the last trimester to reach prepregnancy values by term. The increased cardiac outputs are facilitated by physiological hypertrophy and dilatation of the left ventricles and, together with increases in total blood volume, plasma volume and red cell mass, aid in increasing the capacity of the maternal cardiovascular system to effectively respond to the increased demands imposed by the fetal and uteroplacental circulations. A further increase in cardiac output may occur during labour in response to the sympathetic and catecholamine drives.

Maternal blood volume increase starts as early as 6 weeks' gestation and progressively rises through

pregnancy peaking at 30% at 28–32 weeks of gestation. Increases in the total volume are consequent to increases in plasma volumes and red blood cell volumes. While changes in the blood volume during pregnancy are mediated primarily by hormonal effects, vasoactive mediators like nitric oxide are largely responsible for the vasodilatation that is commonly seen within the maternal circulation. This combination of increased circulating volume and vasodilatation will result in an increase in stroke volume and cardiac output. While much of the increased cardiac output is redistributed in the utero-placental circuit, organs like the mammary glands, skin, uterus and kidneys also have increased perfusion. Uterine blood flow increases from ~50 mL/min at 10 weeks' gestation to 500–600 mL/min at term. The elasticity of the uterine spiral arteries is severely compromised, resulting in permanent dilatation and unresponsiveness to circulating vasopressor agents and the autonomic nervous system. The resulting pooling of uterine blood aids in the maintenance of the uteroplacental blood circulation.

Arterial and venous blood pressures during pregnancy do not show increases, despite the significant perturbations in blood volume and cardiac output. Inferior vena caval compression, particularly post 20 weeks of gestation, may result in decreases in cardiac output and placental perfusion and cause maternal hypotension. Positional changes in blood pressure are more evident in diastolic pressures, with average decreases of 10–15 mmHg, while systolic blood pressures remain constant. Consequent to these changes the pulse pressure increases in the third trimester.

Some of the physiological changes in pregnancy may also be reflected in an electrocardiogram (ECG) and need to be defined in order to be differentiated

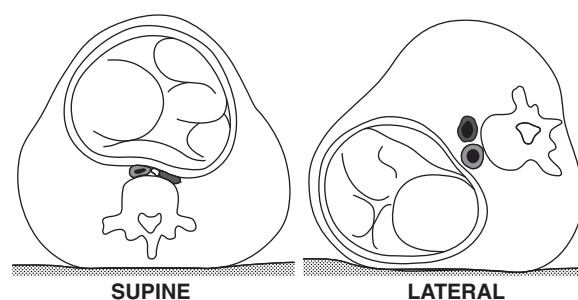


Figure 1.1 The relationship between the gravid uterus and the IVC in the supine and lateral positions. For the colour version, please refer to the plate section.

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Table 1.2 Summary of key cardiovascular changes in pregnancy

Parameter	Change
Stroke volume	+30%
Heart rate	+15–20%
SVR	–5% (approximately)
SBP	–10 mmHg
DBP	–15–20 mmHg
MAP	–15–20 mmHg
Oxygen consumption	+20%
Cardiac output	+50–70% (increase is more dramatic in late pregnancy)

from pathological changes. Diaphragmatic elevation due to increased uterine size causes a deviation of the position of the heart to the left. A 15° left axis deviation may be seen with Q waves in leads III and AVF. Unspecific ST changes and inverted T waves in lead III may also occur.

Intrapartum period

The stress-induced release of catecholamines and an increased sympathetic drive during labour and delivery of the fetus result in significant haemodynamic and cardiovascular perturbations. A significant increase occurs in cardiac output as a result of the additional circulatory load secondary to each uterine contraction (approximately 300–500 mL). Cardiac output rises progressively throughout labour, peaking immediately after delivery. Rises in systolic and diastolic blood pressure occur during the contractions. Heart rate changes in the intrapartum period are variable, although SVR remains constant. Arrhythmias may occur in subjects with pre-existing cardiac diseases and occasionally in subjects with no previous cardiac disease in response to these changes. These arrhythmias include sinus tachycardia/bradycardia, supraventricular tachycardia and premature ventricular/atrial and nodal contractions.

Postpartum period

While blood loss during delivery can be significant (up to 10% (500 mL) with vaginal deliveries and 15–30% with caesarean sections), the compensatory increase in stroke volume and therefore cardiac output seen in early pregnancy could last for up to 2 hours after delivery of the fetus. The cardiac

output continues to decline by a further 30% over 2 weeks, reaching prepregnant values by 6–12 weeks in most cases.

The respiratory system

Antepartum period

The increased demands of pregnancy require an associated expansion in the efficacy of tissue oxygenation, and maternal alterations during pregnancy are designed to accommodate this. A 30–50% increase in the minute ventilation is achieved through a series of hormonal and biochemical changes, ensuring enhanced oxygen availability and more efficient carbon dioxide removal. In addition to hormonal effects, several mechanical factors influence respiratory function.

The progressive enlargement of the gravid uterus causes progressive cranial displacement and alterations in the movement of the diaphragm. The increased intra-abdominal pressures lead to a flaring of the lower thorax and an increase in the thoracic circumference by ~ 6 cm. The hormonal and biochemical effects on respiration may occur through either central effects on the respiratory centre or via direct local effects in the respiratory smooth muscles. Increasing levels of serum progesterone, a known respiratory stimulant, are primarily responsible for these changes, aided by high circulating levels of oestradiol and prostaglandins. The mechanism of action is postulated to be a progesterone-induced enhanced sensitivity to CO₂ (up to 60% by 20 weeks), a lowering of the carbon dioxide thresholds in the respiratory centre and a consequent increase in minute ventilation. The consequent reduction in maternal PaCO₂ facilitates a greater carbon dioxide pressure gradient (PaCO₂) between the maternal and fetal circulations resulting in a more efficient transfer via the placental circulation. In addition, progesterone-induced relaxation of the bronchial and tracheal smooth musculature results in decreased airway resistance and increased respiratory air volumes in pregnancy, often causing symptoms attributed to asthma to lessen in pregnancy. The increased respiratory rate and increased minute ventilation result in a fall in PaCO₂ (to ~ 4.1 kPa, 31 mmHg) by the end of the first trimester. A small increase in PaO₂ (to ~ 14 kPa, 105 mmHg) is also observed during the third trimester. Nearer to term however, the inability of increases in cardiac output to fully compensate for the increased oxygen demand results in a small

reduction in PaO₂ to less than 13.5 kPa (101 mmHg). The changes in PaO₂ alluded to above, however, are too small to have any important consequences on maternal or fetal physiology. O₂ consumption and CO₂ production increase by 60% of prepregnant values at term.

Changes in respiratory volume become apparent at around 20 weeks' gestation and progress throughout the pregnancy. A 30–40% increase in tidal volume (V_t) is accompanied by an increased inspiratory reserve volume (IRV) and decreases in expiratory reserve volume (ERV, 20–30%), residual volume (RV, ~20%) and functional residual capacity (FRC, 20%). The decrease in FRC as a result of decreases in ERV and RV could make parturients more prone to respiratory collapse in the supine position. The vital capacity (VC), forced expiratory volume in 1 second (FEV1) and the FEV1/VC ratios remain unchanged during pregnancy. An increase in the physiological dead space up to a volume of ~60 mL may occur. The reduction in FRC by approximately 20% and an increase in minute ventilation by 30–50% have major implications for changes to alveolar gas compositions (anaesthetic agents as well as PaO₂) in response to changes in alveolar ventilation. This includes a faster rise in the concentration of anaesthetic agents during induction of anaesthesia and a faster fall in PaO₂ in response to upper airway obstruction or central respiratory depression.

Airflow is mainly determined by bronchial smooth muscle tone and the degree of congestion in the bronchial capillaries, particularly in the smaller airways.

The net effect on airway resistance is probably determined by the balance between factors enhancing bronchoconstriction (e.g. PFG2a, decreased RV and decreased PaCO₂) and those enhancing bronchodilation (PGE₂ and progesterone). In the small airways (< 1 mm), airway closure in pregnancy occurs above the FRC nearer term with a higher tendency for closure in the supine position. This may result in an alteration in PaO₂ due to ventilation–perfusion (V/Q) mismatch in the lung bases.

Diffusing capacity, a measure of the ease with which gas transfers across the pulmonary membrane, may show an increase in early pregnancy, although the changes are not deemed to be clinically significant.

Changes in the intrapartum and postpartum periods

The specific changes during these phases will largely be dependent on the effect of pain, anxiety, airway congestion and posture on alveolar ventilation, air-flow resistance and arterial PaCO₂ levels along the lines described above. As the size of the gravid uterus gets smaller, the FRC and minute ventilation are returned to prepregnant values over the first few weeks after delivery.

Acid–base regulation in pregnancy

Pregnancy induces a state of respiratory alkalosis and a left shift of the oxyhaemoglobin dissociation curve. The respiratory alkalosis drives CO₂ transfer from the fetus to the mother by increasing the arterial CO₂ pressure gradient between the maternal and fetal circulations. Increased renal excretion of bicarbonate metabolically compensates for the respiratory alkalosis, with maternal pH levels at the higher end of normal values (pH 7.4–7.45). Changes are stable throughout pregnancy until the onset of labour. Maternal hyperventilation associated with labour results in an acute left shift of the oxyhaemoglobin dissociation curve. The resultant increase in the affinity of maternal haemoglobin for oxygen compromises oxygen delivery to the fetus. In addition, prolonged, painful labour results in increases in the basic metabolic rates and oxygen demand, which cannot be compensated by further increases in cardiac output. Effective administration of regional anaesthesia could prevent further exacerbations in BMR and hyperventilation and serve to minimize potentially detrimental effects on the fetus.

Table 1.3 Changes in lung function tests during the late stages (third trimester) of pregnancy

Respiratory rate	Unchanged
FEV1	Unchanged
PEFR	Unchanged
Minute volume/ventilation	Increased by 30–50%
Tidal volume	Increased by 30–50%
FVC	Unchanged
FEV1/FVC	Unchanged
Maximum mid-expiratory flow rate (forced expiratory flow rate 25–75)	Unchanged
Functional residual volume	Decreased by 18%

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Oxygen–haemoglobin dissociation curve in pregnancy

The oxygen dissociation curve demonstrates the equilibrium between the partial pressure of oxygen in the blood (P_{aO_2}) and the saturation of haemoglobin with oxygen. The sigmoid nature of the curve dictates that once the plateau stage has been reached, large changes in oxygen partial pressures are required to make relatively small differences in percentage haemoglobin saturation (SaO_2). The left/right shift in the position of the curve is determined by the affinity of haemoglobin for oxygen, with a shift to the right implying lowered affinity, and vice versa. The affinity is expressed by the P_{50} values, i.e. the oxygen tension at 50% haemoglobin saturation. The normal adult P_{50} (at pH 7.4, 37 °C) is 26 mmHg (3.4 kPa). Throughout pregnancy there is a gradual rightward shift of the curve due to a progressive increase in P_{50} . At term, the P_{50} is approximately 30 mmHg, resulting in decreased haemoglobin affinity and therefore increased oxygen transfer to the fetus. These changes are mediated by increases in 2,3-DPG levels seen throughout pregnancy. The median concentration of red cell 2,3-DPG in the first trimester of pregnancy is approximately 16.1 $\mu\text{mol/gHb}$ and this may increase to a level of approximately 17.0 $\mu\text{mol/gHb}$ by the end of the third trimester. Red cell 2,3-DPG levels decrease rapidly during the postpartum period. These changes in 2,3-DPG levels and the consequent reduction in oxygen affinity may partially compensate for the physiological anaemia seen during pregnancy.

The gastrointestinal system

Anatomical and physiological alterations in the maternal gastrointestinal and hepatic systems during pregnancy are essential to support the increased nutritional demands of the fetus. The changes are primarily due to either mechanical changes imposed by the growing fetus and/or hormonal effects of progesterone and oestrogen. Appetite and food consumption are increased during pregnancy, although variations can occur in the food types desired, with avoidance of certain items and cravings for others. Although the basis for these changes is unclear, a combination of hormonal changes (oestrogens and progesterone), insulin/glucagon levels and alterations in taste etc. are postulated to have a role to play.

A combination of increased abdominal pressure due to the growing fetus and a progesterone-induced

decrease in the lower oesophageal sphincter tone result in gastro-oesophageal reflux in as many as 80% of term parturients. Most of the clinical changes occur in the third trimester at about 36 weeks. The flattening of the hemidiaphragm could result in the reduction of the normally acute gastro-oesophageal angle, thereby contributing to the reflux. The alterations in lower oesophageal sphincter tone are also primarily responsible for heartburn in pregnancy. Although a progesterone-induced decreased gastric tone can result in delayed gastric emptying and increased gastric volumes during pregnancy, the effects are more significant during labour. The effects may be exaggerated due to the administration of opiate analgesics and general anaesthetics, thereby increasing the risk of vomiting and aspiration pneumonia on induction of general anaesthesia. Preventive measures include administration of H_2 blockers, neutralization of gastric contents and rapid sequence induction with cricoid pressure.

Similarly, a progesterone-induced decrease in smooth muscle tone and motility can also occur in pregnancy, prolonging intestinal transit times, particularly during late pregnancy. Histological changes in the intestinal villi show villus hypertrophy and increased absorptive capacity to cope with corresponding increases in demand. Together with the increased absorptive surface, decreased motility allows for increased absorption of fluids and nutrients, including amino acids, glucose, sodium chloride and water. Iron absorption in the duodenum increases twofold by the third trimester. Calcium absorption is enhanced primarily due to increased levels of 1,25-dihydroxy-vitamin D. All pregnancy-associated changes to the gastrointestinal system are thought to revert to normal by 48 hours post partum.

The hepatic system

Pregnancy-associated changes in the hepatic system are primarily related to the effects of oestrogens on liver metabolism. The enlarging uterus displaces the liver superiorly, posteriorly and anteriorly. Small but significant increases in the plasma concentrations of all liver enzymes, including gamma-GT, ALT, AST and LDH are demonstrable in pregnancy. In most patients, however, these changes do not imply liver dysfunction and are clinically insignificant. These small increases in liver enzymes and the presence of some of the clinical signs – usually attributed to liver disease, such as spider naevi and palmar erythema, in

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otherwise normal pregnancies may render the diagnosis of liver disease more challenging in pregnant women. The placenta is a rich source of alkaline phosphatase and consequently plasma concentrations of alkaline phosphatase may be increased almost threefold in the late stages of pregnancy. Pregnant women also have a slightly greater tendency to develop gall stones due to a progesterone-induced reduction in cholecystokinin release and a reduced contractile response of the gall bladder, resulting in biliary stasis. Plasma cholinesterase levels may be almost 25% lower in the third trimester due to reduced hepatic synthesis and, theoretically, this reduction may prolong the duration of action of succinylcholine. Even though these differences are not clinically important in the majority of women who receive suxamethonium, a small group of women with increased succinylcholine sensitivity (who are heterozygote for an abnormal cholinesterase gene) may show prolonged neuromuscular block following the administration of suxamethonium during pregnancy.

Renal system

As a result of an increase in blood volume, stroke volume and cardiac renal blood flow, and renal plasma flow and glomerular filtration rate are increased in pregnancy. In fact, renal plasma flow and GFR may be 40–65% greater in a pregnant woman at term when compared to her prepregnant values. This is reflected by an increased clearance of urea, creatinine, urate and excretion of bicarbonate, resulting in a corresponding reduction in the plasma levels of these solutes. Through increased activity of the renin-angiotensin-aldosterone axis and the effects of circulating progesterone, increased free water retention is seen and this leads to a reduction in plasma osmolality. It has been shown that plasma osmolality starts to decline soon after conception and reaches a value almost 10 mosmol/kg lower than preconception values by the 10th week of pregnancy, changing very little after this. Glycosuria can be observed in 40% of parturients secondary to increased filtration (due to raised GFR) and the filtered load of glucose exceeding the tubular maximum for glucose.

Urinary tract infections are also more common in pregnant patients due to urinary stasis from progesterone-mediated ureteric smooth muscle relaxation and the direct effects of the gravid uterus on the bladder. Finally the changes in the ECF volume and GFR may alter the volume of distribution and

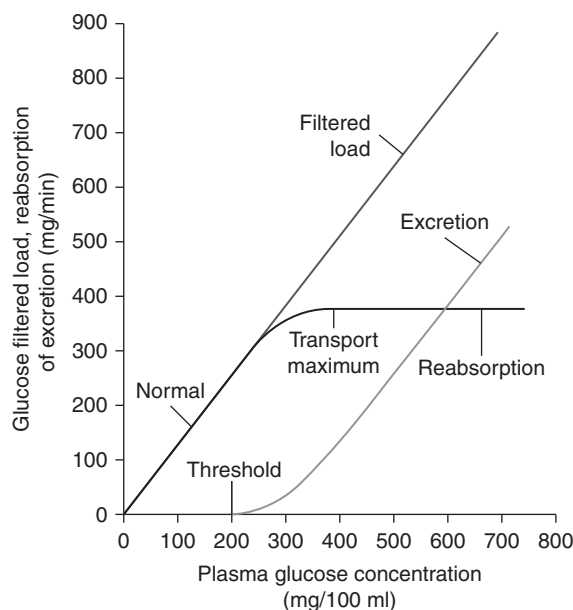


Figure 1.2 Relationship between filtered/reabsorbed glucose levels and the inability of the renal tubules to indefinitely reabsorb all the filtered glucose due to saturation of the relevant transport systems. When the filtered load exceeds the tubular transport systems, glucose will appear in the urine – renal glycosuria.

clearance of some drugs that are of considerable importance to anaesthetists. For example, although some studies show conflicting results, it is generally seen that the plasma concentrations of anticonvulsant drugs may be decreased considerably in the third trimester of pregnancy. A combination of factors including changes to protein binding, increased GFR and expansion of plasma volume may account for these observed changes in the pharmacokinetics of some of the common drugs used in clinical practice

Endocrine system

Pregnancy is frequently associated with increased insulin production and increased insulin resistance. These changes are brought about largely through the effects of human placental lactogen (HPL), which is also known as the human chorionic somatomammotropin (HCS). HCS is a polypeptide placental hormone that is secreted by the syncytiotrophoblast of the developing embryo. Structurally and functionally HCS mimics the effects of human growth hormone and modifies the metabolic state of the mother during pregnancy. The changes brought about by the actions of HCS facilitate the constant and uninterrupted supply of glucose and other energy substrates to the

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Table 1.4 Changes in GFR in pregnancy

Normal adult female	106 to 132 mL/min
Trimester one	131 to 166 mL/min
Trimester two	135 to 170 mL/min
Trimester three	117 to 182 mL/min

growing fetus. HPL has anti-insulin properties and consequently relative hyperglycaemia and impaired glucose tolerance is common in pregnancy. Approximately 6% of pregnancies are complicated by maternal diabetes mellitus (80% of which are gestational). Maternal hyperglycaemia can result in fetal hyperglycaemia, which is usually accompanied by fetal hyperinsulinism. This results in large fetal sizes (macrosomia), which may have considerable implications for delivery and hypoglycaemia during the immediate peripartum periods. In addition to the above, pregnancy is also associated with an increase in the production of prolactin, parathyroid hormone and the adrenal cortical hormones, such as cortisol and aldosterone.

Key points

1. The complex changes in maternal physiology are predominantly secondary to hormonal responses to female sex hormones or physical adaptations to increasing fetal size.
2. Significant changes in the haematological system increase the risk for development of anaemia, thromboembolism and consumptive coagulopathies.
3. Cardiovascular adaptations occur early, with an increase in stroke volume and heart rate and a reduction in SVR, PVR and blood pressure.
4. The respiratory system undergoes significant changes to improve efficacy of tissue oxygenation.

5. Acid–base regulation changes alter normal non-pregnant parameters.
6. Gastrointestinal, hepatic, endocrine and renal physiology undergoes significant alterations to support the development of the fetus.

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Chapter 2

Placental physiology

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Introduction

The placenta is an organ that connects a developing fetus to the uterine wall for exchange of oxygen, nutrients, antibodies and hormones between the mother and fetus. It is required for the removal of waste products. The development of the placenta is essential for normal fetal growth, development, and the maintenance of a healthy pregnancy.

Embryological development

The placenta begins to develop upon implantation of a blastocyst into the maternal endometrium, leading to rapid proliferation and differentiation of trophoblasts. This leads to the formation of two layers: the cytotrophoblast and syncytiotrophoblast. As the blastocyst implants in the uterine lining, vacuoles and lacunae form within the syncytiotrophoblast. This network of lacunae eventually become the intervillous spaces. The cytotrophoblast erodes deeper into the endometrial tissues leading to formation of chorionic villi, which will cover the entire surface of the chorionic sac. Transformation of the narrow spiral arteries into wide uteroplacental arteries also takes place, due to invasion of cytotrophoblasts into the vascular smooth muscle and endothelial cells. The maternal endometrium undergoes various changes, known collectively as the decidual reaction, forming the decidua, which is shed at delivery.

Anatomical structure

The placenta is discoid in shape with a diameter of 15 to 25 cm. A full-term placenta is approximately 2–3 cm thick and weighs about 500–600 g. The growth of the placenta roughly parallels that of the expanding uterus and covers approximately 15 to 30% of the internal surface of the uterus. It consists of two components: a fetal and a maternal portion.

The fetal component of the placenta is formed by the wall of the chorion (chorionic plate). The villi that arise from it project into the intervillous spaces which contain maternal blood. The maternal component of the placenta, on the other hand, is formed by the decidua basalis, which is the endometrium, deep into the fetal component of the placenta. The two components are held together by the cytotrophoblastic shell. Wedge-shaped areas of decidual tissues, known as placental septa, form as the villi invade the decidua, leading to grooves when viewed from the maternal side of the placenta. Cotyledons are easily recognizable bulging areas that are covered by a thin layer of decidua basalis. These areas of irregular convexities within the fetal part of the placenta result from the formation of the placental septa. These septa contain two or more stem villi and their branches. Anastomoses are formed between the dilated spiral arteries from the decidua and endometrial veins. These anastomoses result in the formation of sinusoids which drain into the lacunar network, establishing the uteroplacental circulation (see Figures 2.1 and 2.2).

Placental circulation

The placenta receives the highest blood flow of any fetal organ (40% of fetal cardiac output). The maternal and fetal circulations are separated by a placental membrane consisting of fetal tissue.

Maternal placental circulation

Maternal blood fills the intervillous space through 80 to 100 spiral arteries in the decidua. Remodelling of these arteries causes them to be wider and less convoluted, and this in turn increases maternal blood flow to the placenta. This pulsatile flow of blood bathes the fetal villi with oxygenated blood. The pressure from the arteries forces the blood deep

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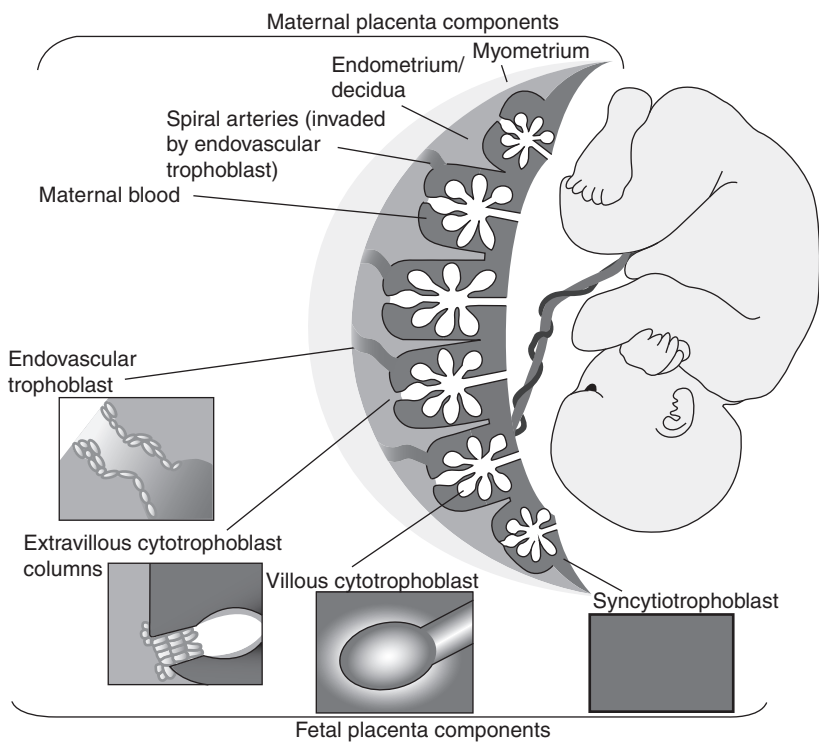


Figure 2.1 Anatomical structure of the placenta.

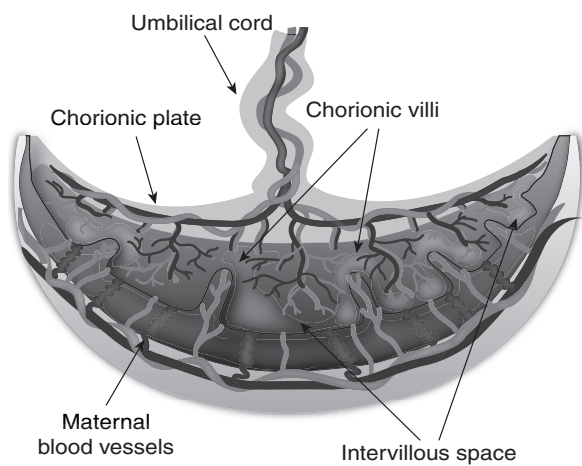


Figure 2.2 Structure of the placenta. For the colour version, please refer to the plate section.

into the intervillous spaces to allow gas and metabolic exchange. As the pressure decreases, the deoxygenated maternal blood re-enters the circulation through the endometrial veins. There is a total of approximately 150 mL of blood within the intervillous

spaces of a mature placenta. It is replenished about three to four times a minute and is affected by uterine contractions.

Placental membrane

This membrane separates the maternal and fetal blood. In the first four months of pregnancy, it consists of four layers: the endothelial lining of the fetal vessels, the connective tissue of the villus, the cytotrophoblast layer and the syncytiotrophoblast layer. This gradually thins out to permit closer contact between the fetal endothelium and the syncytial membrane, allowing greater exchange of compounds between mother and fetus. Although also called a ‘barrier’, this is a misnomer, as many substances pass through freely.

Fetal placental circulation

Deoxygenated fetal blood leaves the fetus through umbilical arteries to the placenta. The umbilical arteries then branch radially, forming the chorionic arteries at the junction of the umbilical cord and the placenta; these arteries further branch into cotyledon