Changes in maternal physiology during pregnancy

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Maternal physiology undergoes many changes during pregnancy. These are largely secondary to the effects of progesterone and oestrogen which are produced predominantly by the ovary in the first 12 weeks of pregnancy and thereafter are produced by the placenta. These changes both enable the fetus and placenta to grow and prepare the mother and baby for childbirth

Cardiovascular and haematological

Cardiovascular and haematological changes begin as early as 4 weeks' gestation and are progressive. During pregnancy the plasma volume increases by 45%. This increase is mediated by a direct action of progesterone and oestrogen on the kidney causing the release of renin and thus an activation of the aldosterone renin-angiotensin mechanism. This leads to renal sodium retention and an increase in total body water.

Through an increase in renal erythropoietin production, red cell mass increases by 20%. As the increase in red cell mass is relatively smaller than that of plasma volume, the haemoglobin falls from 150 g litre^{-1} pre-pregnancy to 120 g litre^{-1} during the third trimester (Fig. 1). This is termed the physiological anaemia of pregnancy. At two weeks' post partum, the blood volume has returned to pre-pregnancy levels. The increased circulating volume offers protection for mother and fetus from the effects of haemorrhage at delivery but it can delay the onset of the classical signs and symptoms of hypovolaemia.

The white cell count rises throughout pregnancy and peaks after delivery, making diagnosis of infection more difficult.

Increased levels of circulating oestrogen and progesterone cause vasodilatation and a consequent fall in peripheral vascular resistance by 20%. As a result, systolic and diastolic blood pressure fall and there is a reflex increase in heart rate of 25%. Stroke volume is increased by 25% and together with that in heart rate, increases cardiac output by 50% by the third trimester. During labour, cardiac output may increase by up to a further 45%. Left ventricular hypertrophy and dilatation facilitate this change in cardiac output but contractility remains unchanged.

The enlarging uterus can compress both the inferior vena cava and descending aorta in the supine position. Compression of the vena cava reduces venous return and results in decreased cardiac output, blood pressure and hence placental perfusion. Compression of the descending aorta also leads to a reduction in uterine blood flow. This may cause fetal distress. Aortocaval compression typically occurs after 20 weeks' gestation but must be considered as a cause of maternal hypotension from the end of the first trimester onwards. To compensate for the effects of aortocaval compression, there is firstly an increase in sympathetic tone causing vasoconstriction and tachycardia. Secondly,

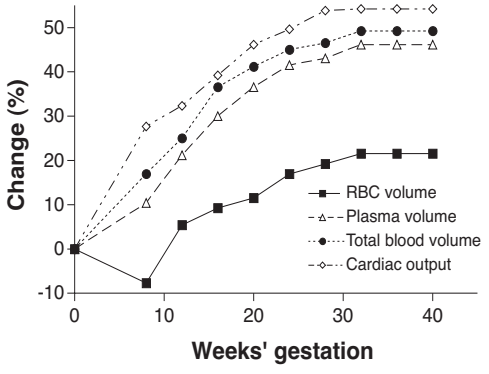

Fig. 1 Haematological changes.

Key points

Difficult intubation is more common in pregnancy.

Desaturation is more rapid in pregnant women.

Mendelson's syndrome may result from aspiration secondary to impaired lower oesophageal sphincter competence and reduced upper oesophageal sphincter tone.

General anaesthesia and neuraxial blockade may unmask aortocaval compression.

The clinical signs of hypovolaemia may be masked.

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blood from the lower limbs may flow through the vertebral plexus and the azygos veins to reach the right heart. In 10% of parturients, these mechanisms are inadequate to maintain blood pressure in the supine position. The fall in blood pressure may be severe enough for the mother to loose consciousness. However, fetal hypoxia may occur in the asymptomatic mother. Induction of general anaesthesia and neuraxial blockade abolish this sympathetic response and increase the risk of supine hypotension. Therefore, all pregnant patients should either be tilted to the left or have a wedge inserted under their right hip when being positioned supine and the full lateral position adopted whenever possible.

Coagulation

Pregnancy induces a hypercoagulable state. Plasma concentrations of fibrinogen and all clotting factors, except XI and XIII, gradually increase. Although there is an increase in platelet production, the platelet count falls because of increased platelet activity and consumption. Platelet function remains normal in pregnancy. An increase in fibrinolysis is reflected in increased concentrations of antithrombin III, plasminogen and fibrin degradation products. None of these changes are reflected in a routine clotting screen, which will show values around normal. Thromboelastography is useful in assessing coagulation and is increasingly used in transplantation and vascular surgery. It provides useful information on platelet function and clot stability which may become abnormal in late pregnancy and pre-eclampsia. In thromboelastography, the maximum amplitude is closely related to the platelet count and falls steeply when the platelet count is $< 100\ 000\ mm^{-3}$. The coagulation index from thromboelastography tends to be at the higher end of normal in normal pregnancy reflecting the hypercoagulable state. In mild pre-eclampsia, the coagulation index rises further but in severe pre-eclampsia with a platelet count $< 100\ 000\ mm^{-3}$ it falls to below normal limits. Thromboembolic complications remain a common source of morbidity and mortality associated with pregnancy.

Respiratory system

Changes in the respiratory system may be categorised as anatomical and physiological. Anatomical changes include capillary engorgement and oedema of the upper airway down to the pharynx, false cords, glottis and arytenoids. These changes are important to the anaesthetist as oedema in the airway makes upper airway obstruction and bleeding more likely during mask anaesthesia and may make tracheal intubation more difficult. A smaller diameter endotracheal tube may be required. The diaphragm is progressively displaced cranially by the gravid uterus. An increase in the diameter of the chest ensures that minute ventilation rises during pregnancy. However, diaphragmatic movement is reduced in late pregnancy, particularly in the supine position. There is also a 20% reduction in functional residual capacity due decreases in both residual and expiratory reserve volumes. The inspiratory reserve volume is increased but vital capacity, total lung volume and FEV_1 remain unchanged.

The increase in chest diameter and enlarged breasts can make laryngoscopy with a standard Macintosh blade more difficult. Reports in the literature suggest failure to intubate the trachea is 7 times more common in the term parturient compared to non-pregnant patients. The reduced functional residual capacity causes airway closure in 50% of parturients at term in the supine position. Thus, pre-oxygenation is less effective in the term parturient and desaturation is likely to occur much faster than in the non-pregnant patient. A pre-oxygenation period of 3–5 min is the standard recommendation. Some of the changes to respiratory physiology are illustrated in Figure 2.

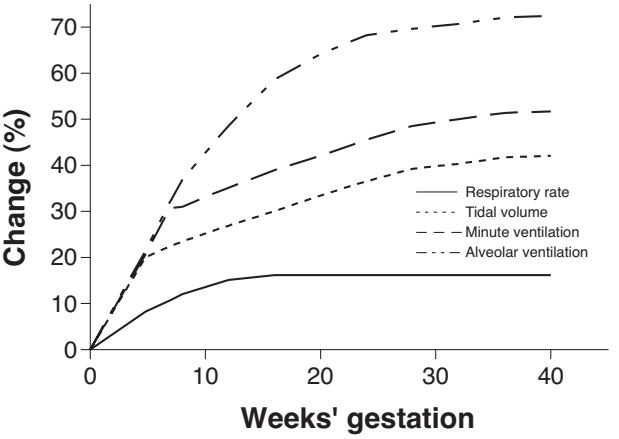

Fig. 2 Respiratory changes.

Table 1 Ventilation in pregnancy and labour

	Pregnancy	Labour	Non-pregnant
Respiratory rate (min^{-1})	15	22–70	12
Tidal volume (ml)	480–680	650–-2000	450
$PaCO_2$ (kPa)	4.1	2–2.7	5.3
PaO_2 (kPa)	14	13.5–14.4	13.3

Many of the physiological changes in the respiratory system are mediated by increased progesterone levels, such as bronchial and tracheal smooth muscle relaxation. Progesterone-mediated hypersensitivity to CO_2 increases the respiratory rate by 10%. The increases in respiratory rate and tidal volumes result in increases in both alveolar and minute ventilation. Consequently, there is a fall in P_aCO_2 that plateaus at 4.1 kPa by the end of the first trimester. P_aO_2 rises to 14 kPa during the third trimester but then falls to < 13.5 kPa at term because increased oxygen consumption is no longer fully compensated for by the rise in cardiac output. Thus, the alveolar arterial oxygen gradient increases. In some parturients, this may be worsened by aortocaval compression and closure of dependent airways. At term, oxygen consumption and carbon dioxide production are increased by 60% above non-pregnant values.

Renal

As might be expected from the increase in cardiac output, renal plasma flow and glomerular filtration rate during pregnancy increase. Urea, creatinine, urate clearance and excretion of bicarbonate are increased causing plasma concentrations to be less than in the non-pregnant population. The activities of renin-angiotensin, aldosterone and progesterone are increased leading to water retention and a decreased plasma osmolality. The re-absorption of glucose falls and glycosuria is present in 40% of parturients. Progesterone-mediated ureteric smooth muscle relaxation can lead to urinary stasis making pregnant women prone to urinary tract infections. These changes in renal physiology increase the volume of distribution for drugs and those that are renally excreted may have to be given in higher than normal dosages.

Acid–base regulation

Increased minute ventilation leads to a decrease in $PaCO_2$ producing a respiratory alkalosis and a left shift of the oxyhaemoglobin dissociation curve. A 30% increase in 2,3-DPG has the opposite effect on the oxyhaemoglobin dissociation curve with an increase of the P_{50} from 3.5 kPa to 4 kPa. The respiratory alkalosis is compensated by increased renal bicarbonate excretion so that plasma hydrogen ion concentrations remain essentially unchanged.

Pain in labour causes maternal hyperventilation associated with an acute left shift of the oxyhaemoglobin dissociation curve. This increases the affinity of maternal haemoglobin for oxygen and consequently oxygen delivery to the fetus decreases. If labour is particularly painful and prolonged, the increase in oxygen consumption and basic metabolic rate can result in lactic acidosis, a right shift of the oxyhaemoglobin dissociation curve and a decrease in maternal oxygen uptake. The above can be largely abolished by the institution of effective regional analgesia.

Table 2 Renal function

Plasma concentration	Non-pregnant	Pregnant
Creatinine (μmol litre^{-1})	73	50–73
Urea (mmol litre^{-1})	4.3	2.3–4.3
Urate (mmol litre^{-1})	0.2–0.35	0.15–0.35
Bicarbonate (mmol litre^{-1})	22–26	18–26

Hepatic

The changes in liver function in normal pregnancy tend not to have clinically significant effects but may make diagnosis of liver disease during pregnancy more difficult. The levels of γ-GT, ALT, AST, and LDH are high, normal or slightly elevated and clinical signs of liver disease like spider naevi and palmar erythema may occur during normal pregnancy. Plasma concentrations of alkaline phosphatase are increased 3-fold as a result of placental production. Increased progesterone concentrations cause a decrease in cholecystokinin release as well as a reduction of the contractile response to cholecystokinin. Thus the pregnant patient is more likely to develop gallstones. At term, plasma cholinesterase falls by 25% and a further 8% three days' postpartum. This, together with an increased volume of distribution at term, means there may be a prolongation of neuromuscular blockade after administration of succinylcholine. This is not usually clinically significant. Standard or increased doses of succinylcholine are recommended in pregnancy and should be calculated according to the current BMI. However, protein synthesis by the liver is decreased by about 25% and pregnancy may unmask succinylcholine sensitivity in females that are heterozygote for an abnormal cholinesterase gene.

Gastro-intestinal system

Changes in the gastro-intestinal system are relevant to the anaesthetist, particularly when general anaesthesia is required. Heartburn during pregnancy is very common and as many as 80% suffer from reflux at term, aggravated by the supine position. This is partly due to increased intra-abdominal pressure

by the gravid uterus and displacement of the gastric axis. Additionally, there is a progesterone-mediated reduction in lower oesophageal sphincter tone. Upper oesophageal sphincter pressure is not affected by progesterone as it is formed from striated muscle. There is no evidence that pregnancy itself is associated with delayed gastric emptying. However, labour causes both delayed gastric emptying and an increase in gastric volume. If opioids are administered these changes are made worse. Induction of anaesthesia reduces upper oesophageal sphincter pressure and, combined with an incompetent lower oesophageal sphincter, predisposes pregnant women to aspiration. Pneumonitis may result (Mendelson's syndrome). In the UK, it is accepted practice to administer an H_2 blocking drug, neutralise gastric contents with sodium citrate and to use a rapid sequence induction with cricoid pressure, when administering general anaesthesia to pregnant women. The gastro-intestinal system is considered to return to normal 24–48 h post partum.

Endocrine

Insulin production rises during pregnancy but is accompanied by increased insulin resistance caused by placental hormones (mainly human placental lactogen). Therefore, any carbohydrate load will cause a greater than normal increase in plasma glucose concentrations. This facilitates placental glucose transfer. As insulin does not cross the placenta, the fetus relies on its own production of insulin. Poorly controlled maternal diabetes is associated with fetal macrosomia. Maternal hyperglycaemia causes increases in fetal insulin and this can result in neonatal hypoglycaemia as the carbohydrate load falls immediately after birth.

Acknowledgement

The figures and tables are taken and modified by permission from *The Simpson Handbook of Obstetric Anaesthesia* by Dr A S Buchan and Dr G H Sharwood-Smith.

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See multiple choice questions 45–49.