Physiology of pregnancy: clinical anaesthetic implications

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Key points

In the parturient:

Decreased functional residual capacity results in the faster onset of hypoxaemia during periods of apnoea.

Blood loss of 1.5 litres or more can occur without any change in cardiovascular parameters.

Aortocaval compression occurs in every parturient and may be asymptomatic.

All patients should be considered to have a 'full stomach' from 16 weeks gestational age to 48 h post-partum.

The incidence of difficult intubation is increased—intubation difficulty may increase further over the course of labour and delivery.

Pregnancy causes anatomical and physiological changes that have implications for the anaesthetist not only for intrapartum management but also when surgery is required incidentally to pregnancy. These adaptations primarily occur, so that the metabolic demands of the growing fetus may be met.

Cardiovascular

Physiological changes occur very early in pregnancy, leading to an overall hyperdynamic circulation. These early hormonal effects lead to the primary event of peripheral vasodilatation which causes a decrease in the systemic vascular resistance (SVR). This occurs as early as 8 weeks of gestation.[1]

If arterial pressure (AP) is to be maintained which is essential for an effective uteroplacental functioning unit, then the cardiac output (CO) has to be increased.

$$AP = CO\,(HR \times SV) \times SVR$$

This is initially achieved by increasing stroke volume (SV), but as pregnancy progresses, the increase in SV plateaus and there is an increase in heart rate.

The increase in SV occurs secondary to an increase in both end-diastolic volume (EDV) and ventricular muscle wall mass. Increased pre-load and EDV is a result of the increased blood volume which is progressive from 6 to 8 weeks gestation to a maximum volume at 32 weeks. There is an overall increase of up to 2000 ml in blood volume compared with the non-pregnant individual. As a result of this, the pregnant patient compensates well for blood loss (Table 1). By the time the classical symptoms and signs of hypovolaemia such as tachycardia, hypotension, and oliguria are evident, more than 1500 ml may have already been lost.[2]

Despite an increased CO, there is an early transient decrease in AP, resulting in a widened pulse pressure and a reduced mean arterial pressure. This activates the renin–angiotensin system leading to retention of water and sodium and ultimately an increase in plasma volume.

While the increase in plasma volume is in the region of 40–50%, the increase in red blood cell mass is only 20% resulting in the dilutional physiological anaemia of pregnancy. Central venous pressure and pulmonary capillary wedge pressure are unchanged.

The heart is physiologically dilated and displaced in both cephalad and lateral directions. A normal pregnancy ECG may have 15–20° left axis deviation and T waves may be inverted in lateral leads and lead III mimicking left ventricular hypertrophy and other structural disease.[3]

It must be remembered however that incipient cardiac disease is an important cause of maternal death in the UK. Many of the initial presenting symptoms and signs may be 'soft' and wrongly attributed to the physiological changes of pregnancy.

A high index of suspicion should be maintained and if there is any doubt, further investigations and cardiology referral should be considered.[4]

Anatomically, the iliac veins join to form the inferior vena cava at a level corresponding to the L4/5 interspace. Once the uterus is at this level, inferior vena cava compression may occur. By the time enlarging uterus approaches the level of the umbilicus, corresponding to 20 weeks in a singleton pregnancy, the mechanical effects of the enlarging uterus can cause compression of both the inferior vena cava and the descending aorta in the supine position. The combination of these leads to a reduced venous return and decreased CO.

By 38–40 weeks gestational age, there is a 25–30% decrease in CO when turning from the lateral to the supine position. As the uteroplacental circulation possesses no autoregulation properties, this causes a decreased uterine blood flow and reduced placental perfusion. Aortocaval

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Table 1 The effects of blood loss in pregnancy

% blood loss	Actual blood loss (ml)	Abnormal clinical findings
15–20	1200–1500	None
20–25	1500–2000	Respiratory rate 14–20 Heart rate ↑ 100–120 Systolic AP slight ↓
>25%	>2000	Respiratory rate 20–30 Heart rate ↑↑ >120 AP ↓ Restless Oliguria

compression can therefore lead to maternal hypotension and a subsequent fetal acidaemia. The maternal compensatory mechanisms for aortocaval compression comprise an increase in sympathetic tone, causing vasoconstriction and tachycardia and diversion of blood flow from the lower limbs through the vertebral plexus and the azygos veins to reach the right heart. In 10% of parturients, this is inadequate to maintain AP in the supine position and hypotension may be severe enough for the mother to lose consciousness. Even if the mother is asymptomatic, uterine blood flow may still be compromised.

Peripheral vasodilatation facilitates venepuncture and i.v. cannulation. Epidural veins become dilated with increased risk of intravascular injection—'bloody tap' during epidural anaesthesia. This is exacerbated during uterine contractions as ~500 ml of blood is expelled from the uterus into the maternal circulation.

I.V. and inhalation anaesthetic agents, causing a reduction in SV and CO, and neuroaxial block, causing sympathetic block further increase the risk of supine hypotension. Whenever possible, pregnant patients should adopt a full lateral position. When the supine position is required, they should be tilted to the left or have a wedge inserted under their right hip.

In the event of cardiac arrest and cardiopulmonary resuscitation, if left lateral tilt is adopted then it must be with the parturient on a firm, flat surface to facilitate effective chest compressions. If this cannot be achieved then the supine position must be adopted with manual uterine displacement.[5]

Labour and delivery further increase the cardiac workload by pain and auto-transfusion. Those parturients with decreased cardiac reserve are at particular risk of ventricular failure and pulmonary oedema in the second stage of labour and early post-partum period. Regional analgesia should be used early in labour and gradually reduced post-partum.

Haematological changes

Changes in the coagulation system produce a hypercoagulable state to facilitate clotting at the time of placental separation and prevent bleeding during pregnancy. There is a 10-fold risk of venous thromboembolic disease during pregnancy and a 25-fold increase in the post-partum period. All clotting factors except XI and XIII increase; there is a decrease in natural anticoagulants and a reduction in fibrinolytic activity.[6] All pregnant women should routinely undergo a thromboembolic risk assessment in the antenatal period and again on admission to hospital with appropriate thromboprophylaxis prescribed. As low molecular weight heparins (LMWHs) are being used increasingly in the antenatal period, it is essential that the anaesthetist is aware of this and importantly the time the last dose was administered as regional block should not be performed within 12 h of a prophylactic dose of LMWH.[7]

Platelet production increases, but the platelet count decreases due to increased destruction and haemodilution occurring maximally in the third trimester. The changes that occur are not usually reflected in standard clotting screens.

Most platelet counts remain within normal limits and the results of a platelet count are not essential before regional anaesthesia in an otherwise healthy parturient.

However, in severe preeclampsia, the platelet count can decrease rapidly, potentially exposing the parturient to an increased risk of an epidural haematoma.

For the group of patients in whom the disease is considered severe enough for the Collaborative Eclampsia Trial regimen of magnesium sulphate[8] to be instituted, a recent platelet count (within 6 h) should be performed both before siting an epidural and removing the epidural catheter.

There is no absolute platelet level that is predictive for development of a neuraxial haematoma; both the number and function of platelets are important.

Formal laboratory-based tests of platelet aggregation take too long to be of use in the acute clinical situation. Thromboelastography (TEG) is a point-of-care bedside test which provides information about global haemostatic function. TEG measures the coagulation process from the initial fibrin formation to platelet interaction and clot strengthening to fibrinolysis. The maximum amplitude (MA) represents platelet function. Most anaesthetists will not provide regional anaesthesia in the presence of thrombocytopenia and an abnormal TEG.[9]

The leucocyte count is normally elevated during pregnancy (14 000 mm^3). This may increase further during labour and delivery and is not indicative of evolving sepsis. Pregnant patients are however predisposed to the development of sepsis as it is a state of altered immune competence (allowing for paternal antigens in feto-placental tissue).

Respiratory

Oxygen requirements and carbon dioxide production increase 60% during pregnancy. Anatomical and physiological changes occur to meet the metabolic demands of mother and fetus. There is an early increase in the tidal volume which gives rise to a maximal increase in minute ventilation of 45% by the second trimester. There is a minimal increase in respiratory rate.[10]

The driving force for this is progesterone which lowers the carbon dioxide response threshold of the respiratory centre.

As the uterus expands, the diaphragm gets pushed in a cephalad direction. The functional residual capacity (FRC) is decreased by 20% in the upright position and up to 30% in the supine position (Table 2). The increase in ventilation leads to decreased arterial carbon dioxide tensions with an average Pa_{CO_2} of 4 kPa at term. This can reduce further in active labour. Ordinarily, this would lead to a respiratory alkalosis, but a compensatory increase in renal bicarbonate excretion and resulting decrease in serum bicarbonate occurs (HCO_3 18 mEq litre^{-1}) to minimize this.

Physiological breathlessness of pregnancy is experienced by the majority of pregnant women, but it can also be the presenting symptom of serious underlying respiratory or cardiac disease. Features suggestive of more sinister pathology include breathlessness of sudden onset or associated with chest pain, orthopnoea, and paroxysmal nocturnal dyspnoea.

The increase in oxygen consumption and decreased FRC mean that parturients become hypoxaemic very quickly during episodes of apnoea, despite careful preoxygenation. Increased minute ventilation and a reduced FRC facilitates gas exchange at the alveolar level resulting in increased rate of uptake of inhalation agents and more rapid changes in depth of anaesthesia. When ventilating a parturient, the lower levels and also the equivalent gradients between end-tidal CO_2 and Pa_{CO_2} must be remembered. The lack of gradient is attributed to the reduction in alveolar dead space (increased blood perfusion from an increase in maternal CO). Excessive hyperventilation can lead to severe alkalosis and a left shift of the oxygen dissociation curve resulting in reduced oxygen transfer to the fetus.

Anatomically, swelling and friability of the nasopharyngeal and oropharyngeal tissue occurs secondary to capillary engorgement. The parturients' airway can become compromised and tracheal intubation more difficult. Intubation prediction with Mallampati class is still commonly used but has been shown to have a low positive predictive value. It can be useful when used in conjunction with other difficult airway predictors. The course of labour can change the Mallampati score, with the biggest increase in Mallampati 3 and 4 grades occurring between the first and second stages of labour.[11] This in conjunction with enlarged breasts and increasing obesity in the pregnant population can make laryngoscopy more difficult and short-handle laryngoscopes and smaller diameter tracheal tubes may be required. The nasopharyngeal approach should be avoided because of the increased risk of epistaxis.

Table 2 Changes in cardiorespiratory variables with pregnancy

Cardiorespiratory variable	Alteration in pregnancy
Functional residual capacity: FRC	↓ 30%
Forced expiratory volume in 1 s: FEV1	→ unchanged
FEV1/FVC	→ unchanged
Tidal volume	↑ 45%
Minute volume	↑ 20–50%
Respiratory rate	→ ↑small increase
Cardiac output	↑
Stroke volume	↑
Heart rate	→↑ small increase

Central and peripheral nervous system

Altered anatomy and responses to pain and pharmacotherapy occur as pregnancy progresses. Increases in venous pressure below the gravid uterus cause blood to flow through the path of least resistance and as such is diverted through the epidural plexus which becomes engorged (Table 2). The epidural space is bound and a compensatory decrease in cerebrospinal fluid volume occurs. This in addition to enhanced neural susceptibility to local anaesthetics and a higher apical level of the thoracic kyphosis result in a 25% reduction in the dose requirement for spinal and epidural anaesthesia, with a more rapid onset and longer duration of action when compared with the non-pregnant state. Parturients are also more susceptible to drugs acting on the central nervous system with a decrease in MAC of 30% of inhalation anaesthetic agents.

Hepatic

With regard to standard liver function tests, serum albumin, transaminases (AST and ALT), and bilirubin levels are generally lower than in the non-pregnant state. Serum alkaline phosphatase (ALP), however, may be physiologically elevated, particularly in the third trimester due to placental production of ALP at the brush border membranes of the syncytiotrophoblast. ALP is produced in the bones, kidneys, and small intestine in addition to the liver and placenta. In the parturient, elevated levels could also be caused by HELLP syndrome (haemolysis, elevated liver enzymes, and low platelets), intrahepatic cholestasis, malignancy, and primary liver or bone disease.[12]

Plasma cholinesterase activity reduces from the 10th week of pregnancy to a maximal reduction on the third postpartum day where levels may be 33% less than the non-pregnant state. This is partly due to the haemodilution effect and partly due to reduced synthesis by the liver. This is usually insignificant in the fit parturient, so drug doses do not need to be adjusted. Activity has to be reduced by 50% for there to be increased sensitivity to succinylcholine. Caution however should be undertaken if the parturient has HELLP syndrome as it has been shown that more than 60% of these patients have pseudocholinesterase activity below the level of normal.[13]

Gastrointestinal

As pregnancy progresses, the stomach is increasingly displaced upwards by the gravid uterus leading to altered axis and increased intragastric pressure. This combined with decreased oesophageal sphincter tone leads to the symptoms of heartburn in pregnancy, essentially the cephalad passage of acidic gastric content. In the non-labouring term parturient, gastric emptying itself is not delayed. In the labouring patient in whom there may be the additive effects from anxiety and pain of labour, gastric emptying is delayed. Gastric emptying is also delayed in women who have received opiates by any route, including the epidural or subarachnoid route.

This results in an increased risk of aspiration. The incidence of aspiration, leading to Mendelson's syndrome (acid aspiration leading to an inflammatory response of the lung parenchyma causing a chemical pneumonia), is declining. Oral intake in normal labour is a controversial subject.

The safest and most effective way of aspiration prophylaxis is the effective use of regional anaesthesia. For all patients from 16 weeks gestational age, antacid premedication should be considered. Histamine H2-receptor antagonists used in combination with sodium citrate increase the mean pH and decreases the percentage of patients with a gastric pH <2.5 required to cause a chemical pneumonitis.

If general anaesthesia is necessary, after preoxygenation, a rapid sequence induction technique with cricoid pressure should be used and the airway secured with a cuffed tracheal tube.

Gastrointestinal effects return to the pre-pregnancy state 24–48 h post-partum.

Renal

There is an increase in renal blood flow of 50% leading to an increase in renal size and a raised glomerular filtration rate from 100 to 150 ml min^{-1} by the second trimester with resulting increased clearance of urea, creatinine, and drugs.

Serum urea and creatinine levels are 40% less than in the non-pregnant individual; hence, results with levels at the upper end of the 'normal range' indicate decreased renal function in pregnancy.

The increased GRF exceeds the capacity of reabsorption within the distal tubules, leading to increased urine levels of glucose and protein.

The upper 'normal limit 'of urinary proteins is 300 mg day^{-1}, double that accepted as normal in the non-pregnant state.[14]

The actions of aldosterone are enhanced leading to increased water absorption, causing an increase in the volume of distribution and increased elimination half-life of certain drugs, including thiopental.

Primary renal disease is uncommon, but deterioration in renal function is seen in more common disorders of pregnancy such as preeclampsia. Renal impairment warrants careful anaesthetic approach with strict management of fluid balance, diabetic control, and adjustment of drug doses and regime.

Endocrine

The thyroid gland can increase in size by almost 20% during pregnancy which can affect patients with pre-existing goitres. Increasing levels of human chorionic gonadotropin (Hcg) stimulate thyroid-stimulating receptors (TSH) in the anterior pituitary as the α subunits of TSH and Hcg are identical. This leads to a transient hyperthyroidism and hyperemesis gravidarum.

Most of the cases of true hyperthyroidism in pregnancy are due to Graves' disease which complicates about one in 500 pregnancies. A parturient with thyrotoxicosis requires careful airway evaluation, ECG, invasive cardiovascular monitoring, correction of hydration, electrolyte and glucose abnormalities, and avoidance of sympathetic stimulation. Provision of care should be in a critical care setting with continued post-partum monitoring (http://health-7.com/Textbook%20of%20Endocrinology/CHAPTER%2020%20-%20ENDOCRINE%20CHANGES%20IN%20PREGNANCY).

Pregnancy is a diabetogenic state of relative insulin resistance and compensatory increased insulin synthesis and secretion. Hyperplasia of the b-cells in the islets of Langerhans occurs. Fetal insulin levels are independent of maternal insulin production but dependent on the maternal glucose load and hence the glucose available for placental transfer. Poor maternal glucose control can result in macrosomia in the fetus and neonatal hypoglycaemia after delivery.

Declaration of interest

None declared.

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Please see multiple choice questions 17–20.