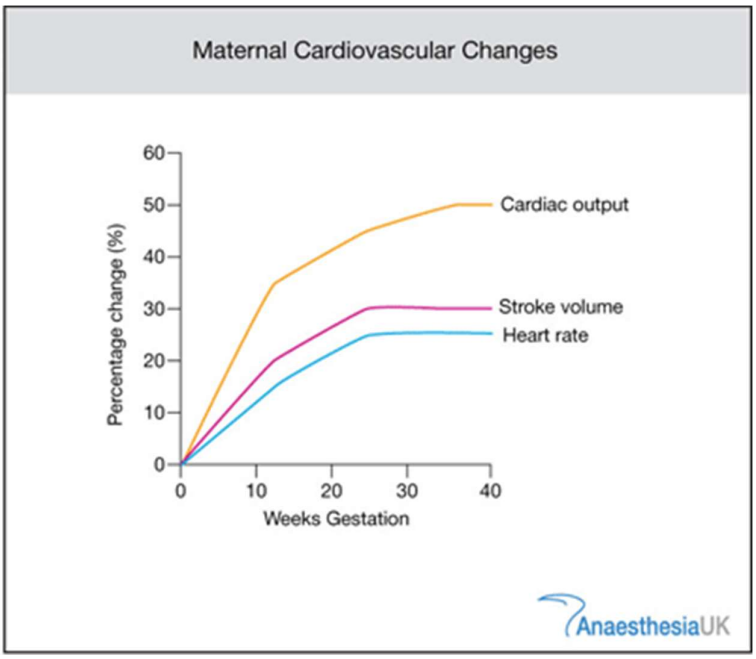
Physiological changes of pregnancy

Maternal physiological changes occur in order to meet the increasing metabolic demands of the foetus and prepare the mother for delivery.

Systems

Cardiovascular



Cardiac output increases by up to 50% by the third trimester. Stroke volume increases by 35% predominately because of the increased blood volume. The increase in circulating oestrogen and progesterone causes vasodilatation and a fall in peripheral vascular resistance. Heart rate increases by 15 – 25% as a result.

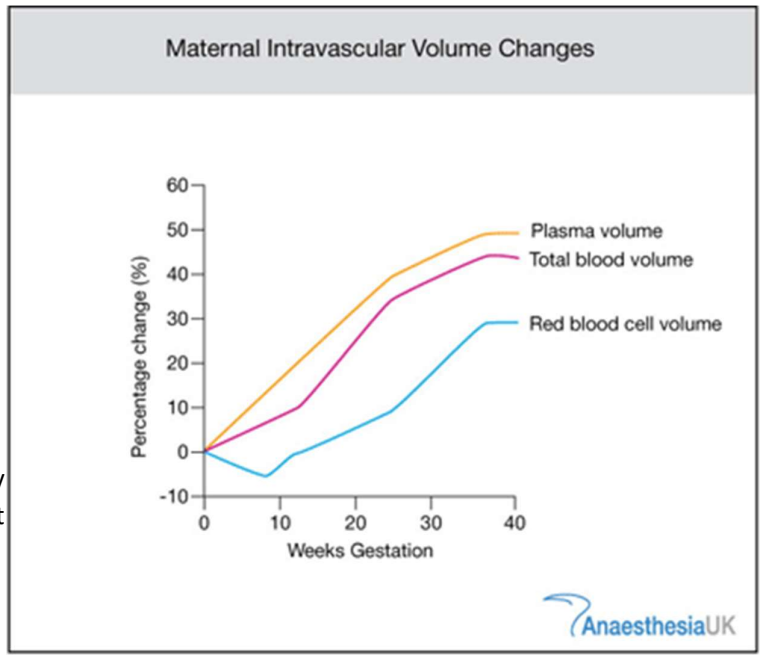
Left ventricular hypertrophy and dilatation facilitate this change in cardiac output but contractility remains unchanged. Together with the upward displacement of the diaphragm, the apex is moved anterior and to the left. These changes may result in ECG findings of left axis deviation, depressed ST segments and inversion or flattening of the T-wave in lead III.

Aortocaval Compression

From mid-pregnancy the enlarging uterus compresses both the inferior vena cava and the lower aorta when the patient lies supine. Compression of the inferior vena cava reduces venous return to the heart leading to a fall in pre-load and cardiac output. The fall in blood pressure may be severe enough for the mother to lose consciousness. Compression of the aorta may lead to a reduction in uteroplacental and renal blood flow. During the last trimester, maternal kidney function is markedly lower in the supine than in the lateral position. Furthermore, foetal transplacental gas exchange may be compromised. For these reasons no woman should lie supine in late pregnancy. Most unanaesthetised women are capable of compensating for the resultant decrease in stroke volume by increasing systemic vascular resistance and heart rate. Blood from the lower limbs may return through the paravertebral and azygos systems.
General anaesthesia, subarachnoid and epidural blocks abolish the sympathetic response and

increase the risk of supine hypotension. During Caesarean section and for other situations requiring a supine position, the uterus should be displaced (usually to the left) by placing a rigid wedge under the hip and/or tilting the table.

Haematology



Blood Volume increases progressively from 6-8 weeks gestation and reaches a maximum at approximately 32-34 weeks with little change thereafter. The plasma volume increases by 45% mediated by progesterone and oestrogen acting on the kidneys initiating renin-angiotensin and aldosterone pathways. Total body water increases secondary to renal sodium retention. Most of the added volume is accounted for by an increased capacity of the uterine, breast, renal, striated muscle and cutaneous vascular systems, with no evidence of circulatory overload in the healthy parturient. Renal erythropoietin increases red cell mass by 20-30% which is a smaller rise than the plasma volume, resulting in haemodilution and a decrease in haemoglobin concentration from 15 g/dl to 12 g/dl. This is termed the physiological anaemia of pregnancy. Supplemental intake of iron and folic acid help to restore haemoglobin levels. The blood volume returns to normal 10-14 days post partum.
The increased blood volume reduces the impact of maternal blood loss at delivery. An "autotransfusion" of blood from the contracting uterus compensates for the typical losses of 300-500 ml for vaginal births and 750-1000 ml for a Caesarean section. This can however delay the onset of the classical signs and symptoms of hypovolaemia. The increased blood volume also facilitates maternal and foetal exchanges of respiratory gases, nutrients and metabolites.

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

Coagulation

Pregnancy affects the normal balance between intravascular coagulation and fibrinolysis, inducing a hypercoagulable state. With the exception of FXI and FXIII, plasma concentrations of all clotting factors and fibrinogen increase. Coagulation - classical model : AUK
Increased levels of antithrombin III and fibrin degradation products reflect enhanced fibrinolysis.

Platelet production is increased but the platelet count falls because of dilution and consumption. Platelet function remains normal.
None of these changes are reflected in routine coagulation screens which are essentially normal. Thromboelastometry may be useful in pre-eclampsia and HELLP syndrome (haemolysis, elevated liver enzymes, low platelets). The maximum amplitude is closely related to platelet count (and function) and falls steeply when the count is below 100 x 109/l.

After delivery fibrinolysis is reduced and coagulation increased. The protection against postpartum haemorrhage is offset by the increased risk of thromboembolic complications, which remains a common source of morbidity and mortality in pregnancy.

Respiratory

Changes in the respiratory system are of great significance to the anaesthetist and may be categorised as anatomical and physiological. Reports in the literature suggest failure to intubate the trachea is 7 - 10 times more common in the term parturient compared with non-pregnant patients.

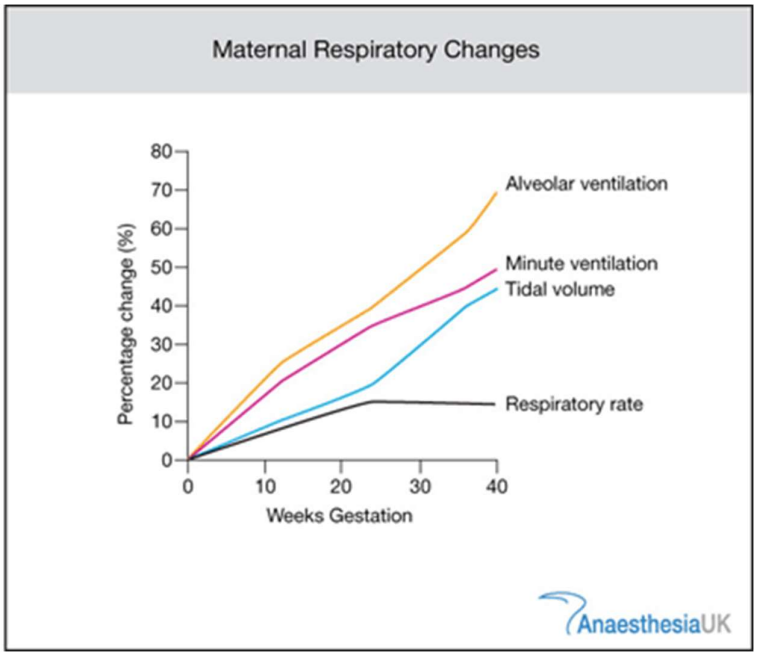
Anatomical changes

Hormonal changes to the mucosal vasculature of the respiratory tract lead to capillary engorgement and oedema of the upper airway down to the pharynx, false cords, glottis and arytenoids. This can be exacerbated by fluid overload or oedema associated with pregnancy-induced hypertension (PIH) or pre-eclampsia. These changes may lead to upper airway obstruction and bleeding making mask anaesthesia and tracheal intubation more difficult. A smaller diameter endotracheal tube may be required. The increase in chest diameter and enlarged breasts can make laryngoscopy with a standard Macintosh blade more difficult.

The diaphragm is progressively displaced cranially by the gravid uterus causing 4 cm elevation. Hormonal changes loosen ligaments so that total lung capacity decreases only slightly because of compensatory increases in the transverse and antero-posterior diameters of the chest, as well as flaring of the ribs. Despite the upward displacement, the diaphragm moves with greater excursions during breathing in the pregnant than in the non-pregnant state. In fact, breathing is more diaphragmatic than thoracic during gestation, an advantage during supine positioning and high regional blockade.
From the middle of the second trimester, expiratory reserve volume, residual volume and functional residual volume are progressively decreased, by approximately 20% at term. The inspiratory reserve volume is increased but vital capacity, total lung volume and FEV1 remain unchanged. Spirometry - Anaesthesia UK
The reduced functional residual capacity causes airway closure in 50 % of parturients at term in the supine position. Most importantly, pre-oxygenation is less effective in the term parturient due to increased oxygen consumption and the decreased functional residual capacity leading to a rapid falls in arterial oxygen tension.
Lung compliance is relatively unaffected, but chest wall compliance is reduced, especially in the lithotomy position.

Physiological changes

Increased progesterone levels mediate many of the physiological changes in the respiratory system. Airway resistance is reduced due to the progesterone-mediated bronchial and tracheal smooth muscle relaxation. Progesterone-mediated hypersensitivity to CO2 increases the respiratory rate by 15% and the tidal volume by 40%. Since dead space remains unchanged, alveolar ventilation is about 70% higher at the end of gestation. Consequently, there is a fall in arterial and alveolar carbon dioxide tensions with a PaCO2 that plateaus at 4.1 kPa by the end of the first trimester. The development of alkalosis is forestalled by compensatory decreases in serum bicarbonate. PaO2 rises to 14 kPa during the third trimester but then falls to <13.5 kPa at term because the increased cardiac output is unable to compensate for the increased oxygen consumption. This can increase the alveolar arterial oxygen gradient. Oxygen consumption and carbon dioxide production are increased by 60 % above non-pregnant values at term.



Gastrointestinal

Aspiration of gastric contents is an important cause of maternal morbidity and mortality in association with general anaesthesia. Heartburn can affect up to 80% of woman at term and the supine position may exacerbate the reflux. There is no evidence of delayed gastric emptying during pregnancy itself, however labour is associated with increased gastric volumes and delayed emptying. This is exacerbated by the administration of opioids.

The enlarging uterus displaces the gastric axis and causes a gradual cephalad displacement of stomach and intestines. These mechanical forces lead to increased intragastric pressures as well as a change in the angle of the gastroesophageal junction, which in turn tends toward greater oesophageal reflux.

Relaxation of the lower oesophageal sphincter has been described, but the upper oesophageal sphincter is not affected by progesterone as it is formed from striated muscle. Induction of general anaesthesia reduces upper oesophageal sphincter tone, increasing the risk of aspiration.

Parturients should be considered to have a "full stomach" with increased risk of aspiration during most of gestation.

In the UK, it is common practice to premedicate woman at risk of undergoing a caesarean section with an H2 receptor block such as ranitine and a prokinetic agent such as metoclopramide. For patients requiring a general anaesthetic, sodium citrate is given to neutralize gastric acid prior to a rapid sequence induction.

Hepatic

Changes in liver function such as high normal or elevated levels of GGT, ALT, AST and LDH are clinically insignificant. Plasma concentrations of ALP are increased up to 3 times normal, as a result of placental production.
Clinical signs of liver disease such as spider naevi and palmar erythema may occur during normal pregnancy, making the diagnosis of liver disease more difficult.

Plasma cholinesterase levels fall by 25% at term and a further 8% three days postpartum prolonging neuromuscular blockade after the administration of suxamethonium. Clinically this is rarely significant. Protein synthesis is reduced by approximately 25% and pregnant females heterozygous for an abnormal cholinesterase gene may show suxamethonium sensitivity.

The pregnant patient is more inclined to develop gallstones as hormonal changes suppress the release of cholecystokinin and reduce the contractile response of the gallbladder.

Renal Physiology

The increased blood volume and cardiac output cause the renal plasma flow and glomerular filtration rate (GFR) to increase progressively during pregnancy and both are 50-60% higher at term. The increased clearance of urea, creatinine, urate and excretion of bicarbonate results in lower plasma levels than in the non-pregnant population.

Mild glycosuria and/or proteinuria can occur in normal pregnancy because the increase in GFR may overwhelm the renal tubules ability to reabsorb glucose and protein.

Plasma osmolality falls because of water retention secondary to increased the activity of progesterone and renin-angiotensin-aldosterone pathways. The volume of distribution and excretion of certain drugs may be increased and therefore dose adjustments required.
Pregnant women are more prone to urinary tract infections because of progesterone-mediated ureteric smooth muscle relaxation.
After the 12th week of gestation, the enlarging uterus can compress the ureters as they cross the pelvic brim and cause further dilatation by obstructing flow.

Endocrine

In spite of increased insulin production, pregnancy is associated with insulin resistance caused predominantly by human placental lactogen. This facilitates placental glucose transfer and any carbohydrate load will cause a greater than normal increase in plasma glucose. The foetus relies on its own production of insulin, as maternal insulin does not cross the placenta.
Approximately 6% of pregnancies are complicated by maternal diabetes mellitus (80% of which are gestational).
Maternal hyperglycaemia can result in foetal hyperglycaemia with secondary foetal hyperinsulinism and neonatal hypoglycaemia. Insulin is the main 'growth hormone' of the fetus and therefore infants of diabetic mothers are often macrosomic (> 4,000 g), resulting in an increase in assisted deliveries and caesarean sections.

Drug handling

Pregnancy and the early puerperium alters the response to anaesthetic and adjuvant drugs. This most commonly manifests as a reduction in dosages for both regional and general anaesthesia.

Regional Anaesthesia

From the late first trimester to the early puerperium, a smaller dose of local anaesthetic is required to obtain the desired level of spinal or extradural blockade. Physical spread of the solution can be increased by changes in the lumbar lordosis and in the volume and density of the CSF. Cephalad spread is not related to the degree of weight gain during pregnancy, but is greater in twin compared with singleton pregnancies, perhaps due to an effect on intra-abdominal pressure, as discussed or through a progesterone-mediated increase in neuronal sensitivity. During the last months of gestation, approximately two-thirds of the normal dose is adequate. This altered response subsides progressively in the early postpartum period.

Factors affecting intrathecal spread of local anaesthetics

Characteristics of the injected solution

Baricity
Volume/dose/concentration
Temperature of injectate
Viscosity
Additives

Clinical technique

Patient position
Level of injection
Needle type/alignment

Intrathecal catheters
Fluid currents
Epidural injection

Patient characteristics

Age
Height
Weight
Sex
Intra-abdominal pressure
Spinal anatomy
Lumbosacral cerebrospinal fluid volume
Pregnancy

Intrathecal drug spread - BMJ
Spinal anaesthetic spread

General Anaesthesia

Anaesthetists must recognise the risk of maternal awareness between induction of general anaesthesia and delivery of the infant. The desire to minimize neonatal depression must be balanced against the risk of maternal awareness.
Induction and changes in depth of inhalation anaesthesia occur with greater rapidity in pregnant women than in non-pregnant subjects. Pregnancy enhances anaesthetic uptake in two ways. The increase in resting ventilation delivers more agent into the alveoli per unit time, while the reduction in functional residual capacity favours rapid replacement of lung gas with the inspired agent. In addition, there is a reduction in anaesthetic requirements, with a fall in the minimum alveolar concentrations (MAC) of halogenated vapours. When measured in ewes MAC was 25-40% lower in gravid as compared with non-pregnant animals.

References:

(i) Changes in maternal physiology during pregnancy CEACCP, Jun 2003; 3: 65 - 68. Bernhard H Heidemann and John H McClure

(ii) Physiological Changes Associated with Pregnancy - Updates in Anaesthesia

(iii) PFA vs TEG in the parturient - PubMed

(iv) Intrathecal drug spread - BJA