CHANGES IN MATERNAL PHYSIOLOGY DURING PREGNANCY

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Medical Terms

Gestation	Period between conception and birth
Pregesterone/Oestrogen	Female hormones
Erythropoietin	Hormone secreted to increase the numbers of red blood cells
Trimester	A period of 3 months - during pregnancy there are three trimesters
Gravid	Pregnant - "Gravid uterus" means pregnant uterus
FEV^1	Forced Expiratory Volume in 1 minute
FRC	Functional Residual Capacity - *see Update in Anaesthesia (2000) 12;42*
Parturient	A patient who is about to or is giving birth
Palmar erythema	Reddening of the palm of the hand

Maternal physiology undergoes many changes during pregnancy. These changes, which are largely secondary to the effects of progesterone and oestrogen, begin as early as 4 weeks gestation and are progressive. In the first 12 weeks of pregnancy progesterone and oestrogen are produced predominately by the ovary and thereafter by the placenta. These changes both enable the fetus and placenta to grow and prepare the mother and baby for childbirth.

Haematological

Red cell mass, white cell count and platelet production are all increased during pregnancy. The rising white cell count during pregnancy, which peaks after delivery, can make diagnosis of infection difficult. Platelet production is increased, but platelet consumption increases more, causing the platelet count to fall to low normal values. Renal erythropoietin production increases leading to a 20% increase in red cell mass.

Increased concentrations of progesterone and oestrogen directly act on the kidney causing the release of renin. This activates the aldosterone-renin-angiotensin mechanism leading to renal sodium retention and an increase in total body water. Plasma volume increases by 45% and as this increase is relatively greater than the increase in red cell mass, maternal haemoglobin concentrations falls from 150 g per litre pre-pregnancy to 120 g per litre during the 3rd trimester (Figue 1). *This is termed physiological anaemia of pregnancy.*

The increased circulating volume offers protection for mother and fetus from the effects of haemorrhage at delivery. Knowledge of this is important for the anaesthetist as it can delay the onset of classic signs and symptoms of hypovolaemia. It is very easy to be misled into thinking that, even in the presence of considerable volume loss, it does not need replacement. This is wrong, it being essential to replace the measured loss, and to be aware that more volume may have been lost than the blood pressure and pulse might indicate. By two weeks post partum the haematological changes have mostly reverted to pre-pregnancy status.

Cardiovascular

Oestrogen and progesterone mediated relaxation of vascular smooth muscle in pregnancy cause vasodilatation reducing the peripheral vascular resistance by 20%. Consequently systolic and diastolic blood pressures fall. A reflex increase in heart rate by 25% together with a 25% increase in stroke volume, results in a 50% increase in cardiac output. During labour cardiac output may increase further by up to 45%. Cardiac contractility remains unchanged. The rise in cardiac output is facilitated by anatomical changes, namely left ventricular hypertrophy and dilatation.

In the supine position the gravid uterus can compress the inferior vena cava. This will reduce venous return to the heart resulting in a decrease of cardiac output, maternal blood pressure and placental perfusion. The descending aorta can also be compressed by the uterus causing a reduction in uterine blood flow. Aortocaval compression must be considered as a cause of maternal hypotension from the end of the 1st trimester onwards, though it typically occurs after 20 weeks gestation.

Figure 1: Respiratory changes
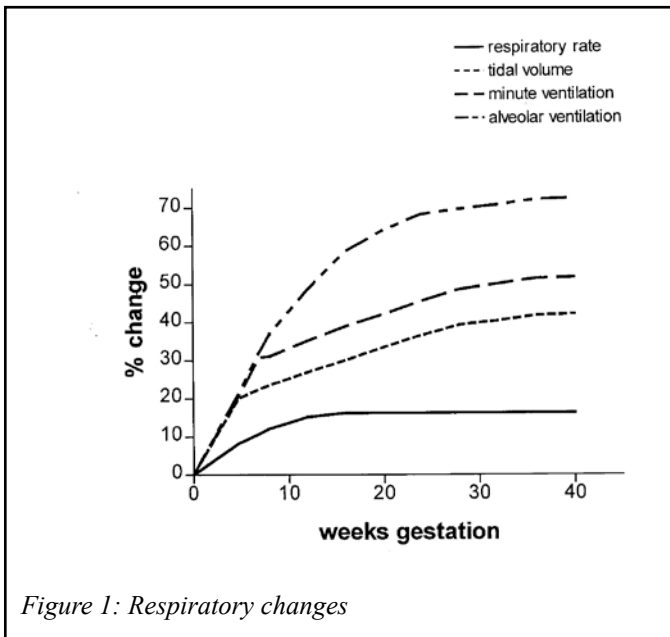
The maternal compensatory mechanism for aortocaval compression comprises of an increase in sympathetic tone causing vasoconstriction and tachycardia and diversion of blood flow from the lower limbs through the vertebral plexus and the azygos veins to reach the right heart. In 10% of parturients this is inadequate to maintain blood pressure in the supine position and hypotension may be severe enough for the mother to lose consciousness. Obstetricians and anaesthetists should be aware that fetal hypoxia due to aortocaval compression may occur in the asymptomatic mother. Intravenous and inhalational anaesthetic agents, causing a reduction in stroke volume and cardiac output, and neuroaxial blockade (spinal/epidural), causing sympathetic blockade, increase the risk of supine hypotension. Whenever possible pregnant patients should adopt a full lateral position. When supine position is required they should be tilted to the left or have a wedge inserted under their right hip.

Coagulation

Plasma levels of fibrinogen and all clotting factors, except XI and XIII, gradually increase during pregnancy inducing a hypercoagulable state. An increase in fibrinolysis is reflected in increased concentrations of antithrombin III, plasminogen, and fibrin degradation products. Platelet activity and consumption are both increased but platelet function remains normal in pregnancy. None of these changes are reflected in a routine clotting screen, which will show values around normal. Platelet function, as assessed by thromboelastography, remains normal while the platelet count is greater than 100×10^9 per litre. A platelet count of greater than 80×10^9 per litre is regarded as safe for the use of neuroaxial blockade by many. Thromboembolic complications remain a common source of morbidity and mortality associated with pregnancy.
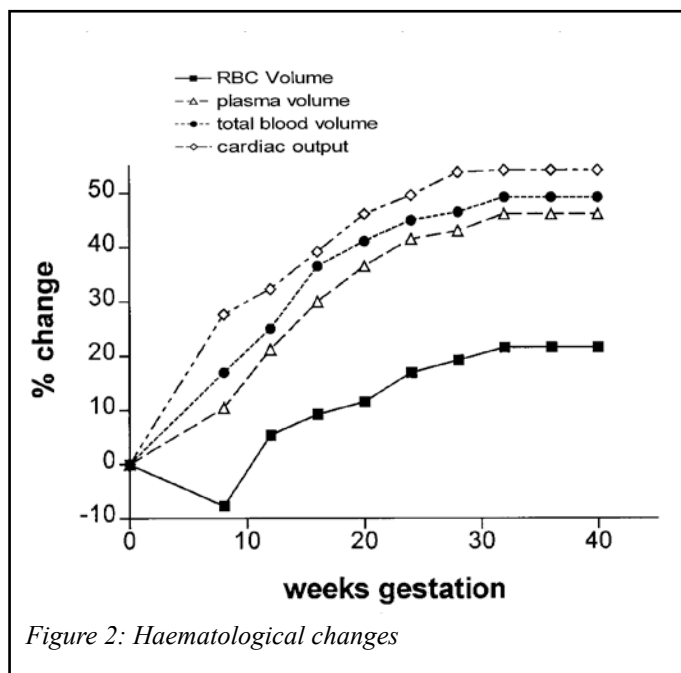
Respiratory System

Changes in the respiratory system may be categorised as anatomical and physiological. The anatomical changes make upper airway obstruction and bleeding more likely during mask anaesthesia and may make tracheal intubation more difficult. There is approximately a 7-fold increase in failed intubations in parturients at term. The anatomical changes include capillary engorgement and oedema of the upper airway, pharynx, false cords, glottis and arytenoids. There is also an increase in chest diameter, to allow increased minute ventilation, and an enlargement of the breasts, which can make laryngoscopy with a standard Macintosh blade more difficult.

The gravid uterus progressively displaces the diaphragm cranially reducing diaphragmatic movement in late pregnancy, particularly in the supine position. Inspiratory reserve volume is increased but vital capacity, total lung volume and FEV1 remain unchanged. A decrease in both residual and expiratory reserve volumes causes a 20% reduction in functional residual capacity, which in turn 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 - 5min is the standard recommendation. Some of the changes to respiratory physiology are illustrated in Figure 2.

Bronchial and tracheal smooth muscle relaxation are a result of increased progesterone concentrations. This often causes the symptoms of asthma to lessen in pregnancy. $PaCO_2$ falls and then levels off at 4.1kPa (31mmHg) by the end of the first trimester. This is caused by a 10% increase in the respiratory rate, secondary to progesterone mediated hypersensitivity to CO_2, and an increase in alveolar and minute ventilation, secondary to increased respiratory rate and tidal volume. PaO_2 rises to 14 kPa (105mmHg) during the 3rd trimester but then falls to less than 13.5 kPa (101mmHg) 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 dependant airways. At term (40 weeks gestation), oxygen consumption and carbon dioxide production are increased by 60% above non-pregnant values.

Renal

As a result of the changes in the cardiovascular system, renal plasma flow and glomerular filtration rate increase in pregnancy. This results in an increase in urea, creatinine and urate clearance and excretion of bicarbonate causing plasma concentrations to be less than in the non-pregnant population. The activities of renin-angiotensin, aldosterone

Figure 2: Haematological changes

Pre-oxygentation for the **3-5 full minutes** by the clock is vital:

- Mothers destaurate more quickly than the non-pregnant patient

- The airway is narrower because of venous engorgement possible oedema

- Intubation is more difficult may take longer

and progesterone are increased leading to increased water retention and a decreased plasma osmolality. Glycosuria can be observed in 40% of parturients secondary to reduced reabsorption of glucose. Urinary tract infections are more common in pregnant patients due to urinary stasis from progesterone mediated ureteric smooth muscle relaxation.

The 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 and may have prolonged action.

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 P50 from 3.5 kPa to 4 kPa (26-30mmHg). 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 becomes prolonged and is also painful, basic metabolic rate increases and O_2 extraction does as well. Under these circumstance there will be less O_2 available to the fetus, as cardiac output cannot be further increased to match the increased O_2 demand. In this situation regional analgesia is useful as it prevents the increase in BMR and further hyperventilation secondary to the pain. Effective regional analgesia largely abolishes the detrimental effects of a painful labour on the fetus.

Hepatic
Plasma concentrations of γ-GT, ALT, AST, and LDH are high normal or slightly elevated and clinical signs of liver

Table 1: Ventilation in pregnancy and labour			
	pregnancy	**labour**	**Non-pregnant**
respiratory rate [per min]	15	22 - 70	12
tidal volume [ml]	480 - 680	650 - 2000	450
PaCO$_2$ [kPa] (mmHg)	4.1 (31)	2 - 2.7 (15-20)	5.3 (40)
PaO$_2$ [kPa] (mmHg)	14 (105)	13.5 - 14.4 (101-108)	13.3 (100)

Table 2: Renal function		
plasma level	**non-pregnant**	**pregnant**
creatinine [μmol per litre]	73	50 - 73
urea [mmol per litre]	4.3	2.3 - 4.3
urate [mmol per litre]	0.2 - 0.35	0.15 - 0.35
bicarbonate [mmol per litre]	22 - 26	18 - 26

disease like spider naevi and palmar erythema may occur during normal pregnancy making diagnosis of liver disease during pregnancy more difficult. Plasma concentrations of alkaline phosphatase are increased 3-fold as a result of placental production. Pregnant patients are more likely to develop gall-stones as increased progesterone concentrations cause a decrease in cholecystokinin release and a reduction of the contractile response to cholecystokinin. Succinylcholine may lead to prolonged neuromuscular blockade secondary to a 25% fall in plasma cholinesterase concentrations at term and a further 8% fall three days postpartum (post delivery). This is compounded by an increased volume of distribution at term but not usually clinically significant. Never the less, standard or increased doses of succinylcholine are recommended in pregnancy. Succinylcholine sensitivity in females who are heterozygote for an abnormal cholinesterase gene may be unmasked due to a 25% decrease in hepatic protein synthesis in pregnancy.

Gastro-intestinal System

Increased intra-abdominal pressure by the gravid uterus, displacement of the gastric axis and progesterone mediated reduction in lower oesophageal sphincter tone cause gastro-oesophageal reflux in as many as 80% of term parturients. Whilst pregnancy does not seem to cause increased gastric volumes and delayed gastric emptying, both of these are features of labour. The administraion of opioids for labour analgesia further accentuates this. Pregnant women are therefore at risk of developing Mendelson's syndrome (aspiration pneumonitis) especially on induction of general anaesthesia, which reduces upper oesophageal sphincter pressure. Strategies for the prevention of this may include the administration of H_2 blocking drugs, neutralization of gastric contents with non-particulate antacids, e.g. sodium citrate, and the use of a rapid sequence induction with cricoid pressure, when administering general anaesthesia to pregnant women. At 24 - 48 hours postpartum the changes in the gastro-intestinal system are thought to have reverted to normal.

Endocrine

In the non-diabetic pregnant woman carbohydrate loads will cause a greater than normal increase in plasma glucose levels facilitating placental glucose transfer. This is due to increased insulin resistance caused by placental hormones (mainly human placental lactogen). Insulin production is also increased during pregnancy.

Maternal hyperglycaemia in diabetic pregnant women induces an increase in fetal insulin production, as insulin does not cross the placenta. Neonatal hypoglycaemia may follow as the carbohydrate load falls immediately after birth. Since insulin also acts as a growth hormone maternal diabetes is associated with fetal macrosomia.

Acknowledgement

Further reading

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