

# Physiology of pregnancy

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## Abstract

During pregnancy, maternal physiology undergoes continual adaptation. These often interlinked changes occur in all body systems and are affected by the hormonal influences of the placenta and the mechanical adaptations required to accommodate the developing fetus. These important physiological changes can potentially lead to decompensation in parturients with pre-existing co-morbidities. They may also unmask asymptomatic pre-pregnancy disease. A sound knowledge of the expected maternal changes are essential to enable accurate interpretation of physiological and laboratory parameters. This allows for the implementation of robust care planning with the aim of reducing potential complications.

**Keywords** Obstetrics; physiology; pregnancy

**Royal College of Anaesthetists CPD Matrix:** 1A01, 2A09, 2B06

## Introduction

Maternal physiology undergoes continual adaptation during pregnancy. The changes are present in all body systems and are driven by the hormonal influences of the placenta and the mechanical adaptations required to accommodate a growing fetus. Knowledge of these changes is essential for safe anaesthetic practice.

## Cardiovascular

Most cardiovascular changes occur early in pregnancy. Vascular smooth muscle relaxation occurs in response to increased circulating levels of progesterone, oestrogen and prostaglandins, leading to a reduction in systemic and pulmonary vascular resistance. Cardiac output gradually increases, eventually by up to 30–50% during the third trimester. The increase in cardiac output is as a result of an increase in heart rate and stroke volume, secondary to ventricular hypertrophy and increased end diastolic volume. Increases in stroke volume peak at around weeks 16–24.

Blood pressure at term is usually maintained, although there may be a transient reduction earlier in pregnancy with a widening of pulse pressure as diastolic pressure is more significantly affected than systolic. Parturients may also develop murmurs during pregnancy, these can be flow murmurs as a result of

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## Learning objectives

After reading this article, you should be able to:

- describe the physiological changes that occur in each body system throughout pregnancy
- understand how these physiological changes may affect clinical practice
- appreciate the changes in laboratory and monitoring parameters for different body systems throughout pregnancy

the increased cardiac output or tricuspid and mitral regurgitant murmurs due to dilatation of these valves.

As pregnancy progresses, diaphragmatic elevation leads to displacement of the heart upwards and to the left. This can result in ECG changes including leftward axis deviation and T wave inversion in the lateral leads and lead III. These changes do not, in themselves, have clinical significance but may mask further changes secondary to pathological processes. The increase in heart rate necessary to maintain the increased cardiac output may present as sinus tachycardia and may predispose to tachyarrhythmias.

Aortocaval compression by the gravid uterus in the supine position can lead to profound hypotension. This is widely reported to occur from 20 weeks' gestation onwards. Compression of the inferior vena cava produces a reduction in venous return and, therefore, cardiac output. The resultant increase in sympathetic tone causes vasoconstriction and diversion of blood flow through the vertebral and azygos veins, allowing maintenance of blood pressure. However, this adaptive mechanism is not present in up to 10% of parturients and those who have sympathetic blockade as a result of neuraxial anaesthesia.

Regardless of the parturient's ability to compensate for aortocaval compression, there can still be significant compromise of utero-placental perfusion. To prevent this, the uterus can be displaced by positioning the parturient with a left lateral tilt or, if this is not feasible, by manual displacement of the uterus.

## Respiratory

The alterations in maternal respiratory physiology occur as a result of hormonal and biochemical effects on the central respiratory centre, via local effects on the respiratory smooth muscle or by mechanical effects of the growing fetus.

Circulating progesterone stimulates the respiratory centre, leading to an increase in minute ventilation, primarily by an increase in tidal volume (by ~ 40%) and by an increase in respiratory rate (by ~ 15%). The resulting increase in alveolar ventilation can produce a decrease in arterial partial pressures of carbon dioxide (PaCO<sub>2</sub>) and, consequently, a leftward shift of the oxygen haemoglobin dissociation curve. However, maternal levels of 2,3-DPG also increase throughout pregnancy, which leads to the overall rightward shift in the oxygen dissociation curve, facilitating oxygen transfer to the fetus. The increased minute ventilation results in a respiratory alkalosis that is partially compensated by increased renal bicarbonate excretion. Parturients therefore usually have a serum pH at the upper end of the normal range.

### Lung volume changes by term

| Lung volume  | Effect at term compared to pre-pregnancy |
|--|--|
| Expiratory reserve volume  | Decrease 20–30%                          |
| Functional residual capacity   | Decrease 20%                             |
| Tidal volume   | Increase 30–40%                          |
| Residual volume  | Decrease 20%                             |
| Vital capacity (VC)/Forced expiratory volume in 1 second (FEV <sub>1</sub> ) | Unchanged                                |

**Table 1**

A small increase in PaO<sub>2</sub> occurs during the third trimester (to ~14 kPa); however as the parturient approaches term, the increase in cardiac output is unable to keep up with the increased oxygen demands of the gravid uterus and fetus, and the PaO<sub>2</sub> falls (to <13.5 kPa). By term there is a 60% increase in CO<sub>2</sub> production and oxygen consumption.

During labour there is a further increase in respiratory rate which results in an acute fall in PaCO<sub>2</sub>. This increases the affinity of maternal haemoglobin for oxygen and, combined with an increase in metabolic rate and oxygen consumption, can compromise oxygen delivery to the fetus.

Expected changes to lung volumes at end term are shown in Table 1.

The presence of the gravid uterus can have a 'splinting effect' on the diaphragm. This is initially compensated for by increases in the transverse and anterior-posterior diameters of the chest, facilitated by increased ligamentous laxity which allows flaring of the lower rib cage. However, inspiration remains largely a function of diaphragmatic movement and, by term, functional residual capacity (FRC) is reduced by approximately 20%. This,

combined with greater oxygen consumption, renders parturients more prone to desaturation during induction of general anaesthesia. Airway management in obstetrics can also be more complex due to anatomical issues (enlarged breasts and an increase in chest wall diameter), mucosal oedema, dilation of small vessels and increased mucosal friability. A more difficult laryngoscopy view, compounded by rapid desaturation and urgency of the surgery results in a challenging environment.

The importance of optimum pre-oxygenation and positioning is essential prior to embarking on general anaesthesia.

The concomitant increase in minute volume and decrease in FRC, speeds up the 'wash-in' of volatile anaesthetic agents. Adequate alveolar concentrations are therefore achieved more quickly on institution of inhalational anaesthesia.

The balance between bronchodilatation (effected by PGE<sub>2</sub> and progesterone) and bronchoconstriction (effected by PFG<sub>2a</sub>, decreased RV and decreased PaCO<sub>2</sub>) determines airway resistance.

Diffusing capacity may increase in early pregnancy although this is not clinically significant.

### Haematological

The peripartum period sees wide spread adaptations in the haematological system with a marked increase in risks including anaemia, thromboembolism and consumptive coagulopathies. See Table 2.

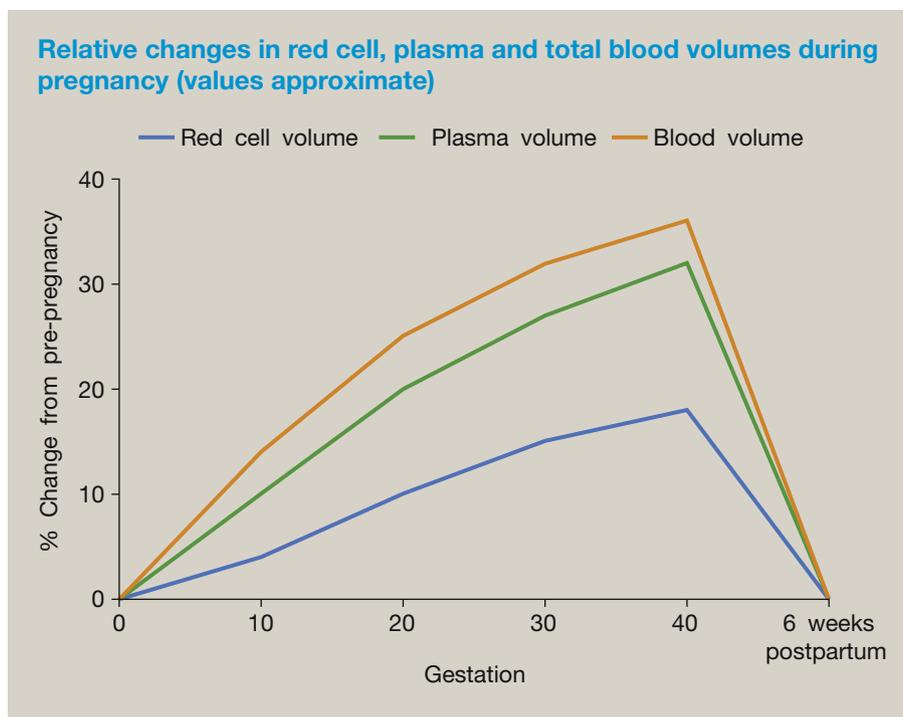
Increased secretion of aldosterone (by activation of the renin–angiotensin axis) results in an increase in total body water and, consequently, plasma volume. Erythropoiesis also increases by around 30%. These changes are illustrated in Figure 1. The resulting dilution of red cell mass (physiological anaemia of pregnancy) is reflected by a reduction in haematocrit.

During labour, each contraction 'squeezes' blood back into the circulation. After delivery, approximately 500 ml of blood is returned into the circulation. While most parturients tolerate this without adverse effect, it can contribute to decompensation in

### Alterations in the haematological system at term pregnancy

| Increased   | Unchanged                                     | Decreased                               |
|---|---|---|
| Blood volume 30–45%   | Mean corpuscular haemoglobin concentration    | Haematocrit 35–45%                      |
| Plasma volume 45%   | Lymphocyte/T-cell (although function reduced) | Plasma protein 10–14%                   |
| Red cell mass 33%   | Bleeding time                                 | Plasma oncotic pressure (haemodilution) |
| White cell count 8%   |   | Antithrombin III                        |
| Clotting factors (I, VII, VIII, X, XII, prekallikrein, von Willebrand factor, thrombin) |   | Platelets                               |
| Activated partial thromboplastin time, prothrombin time                                 |   |   |
| Fibrinogen levels 50–80%  |   |   |
| Renal erythropoietin/Reticulocyte count   |   |   |
| RBC 2,3-diphosphoglycerate (rightward shift in oxygen-haemoglobin dissociation curve)   |   |   |
| Serum albumin concentration   |   |   |
| Venous hydrostatic pressure   |   |   |
| Erythrocyte sedimentation ratio   |   |   |
| Serum lipids 40–60%   |   |   |

**Table 2**



**Figure 1**

those with existing cardiac disease. Plasma volume has been demonstrated to revert to that of pre-pregnancy within 6 days of delivery.

All clotting factors excluding factors XI and XIII increase throughout pregnancy with a corresponding decrease in anticoagulant proteins such as protein S and antithrombin III. Although protective against post partum haemorrhage, it confers a greater risk of thromboembolic complications. Parturients with pre-existing procoagulant pathologies require careful management with appropriately dosed low-molecular weight heparin (LMWH). The risk of thromboembolic complications is highest within the first 6 weeks postpartum.

The platelet count decreases in pregnancy, as a result of consumption and the increased plasma volume although production actually increases. Platelet counts are usually maintained within the normal laboratory reference range but a mild thrombocytopenia mainly in the third trimester has been described. Function is usually preserved.

The white cell count also increases during pregnancy and, more significantly, in labour. This is primarily due to an increase in the neutrophil count and is stimulated by oestrogen. This physiological neutrophilia can complicate decision making regarding treatment of sepsis and suitability for regional anaesthesia in labour. Immunological function (both B and T lymphocytes) is suppressed leading to an overall increase in susceptibility to infection.

## Renal

Renal blood flow and, therefore, the glomerular filtration rate are increased by 50% owing to the proportional increase in cardiac output. Serum urea and creatinine can be 40% lower than pre-pregnant values.

Urinary protein and glucose levels are increased as renal absorption of these molecules (and others such as bicarbonate and some electrolytes) is outpaced by the increase in glomerular filtration. The increased bicarbonate loss contributes to compensation of the respiratory alkalosis driven by increased minute ventilation.

Relaxation of ureteric smooth muscle can lead to urinary stasis. This, combined with external obstructive pressure from the fetus, confers an increased propensity to urinary tract infection during pregnancy.

The increase in plasma volume will increase the volume of distribution of some drugs (particularly those which are more highly water-soluble, such as thiopentone) – this may have an impact on their eventual clearance.

## Neurological

The nervous system exhibits increased sensitivity to both general and local anaesthetic agents. The minimum alveolar concentration (MAC) value of several volatile anaesthetic agents has been demonstrated to decrease during pregnancy. The MAC value of sevoflurane is reported to decrease by approximately 30%. Although uterine relaxation is an undesired effect when using volatile anaesthetic agents, these concerns must be balanced against the need to provide adequate anaesthesia. The obstetric populations continue to be over-represented in cases of accidental awareness as evidenced by the results of 5th National Audit Project.

Local anaesthetic agents can cause a more profound and prolonged block that is independent of the route of administration. When performing neuraxial anaesthesia, the volume of local anaesthetic required is reduced due to reduction in epidural volume as a result of engorgement of the epidural veins. Risk of extensive cephalad spread leading to high or total spinal block is

## Summary of physiological changes of pregnancy

### Neurological

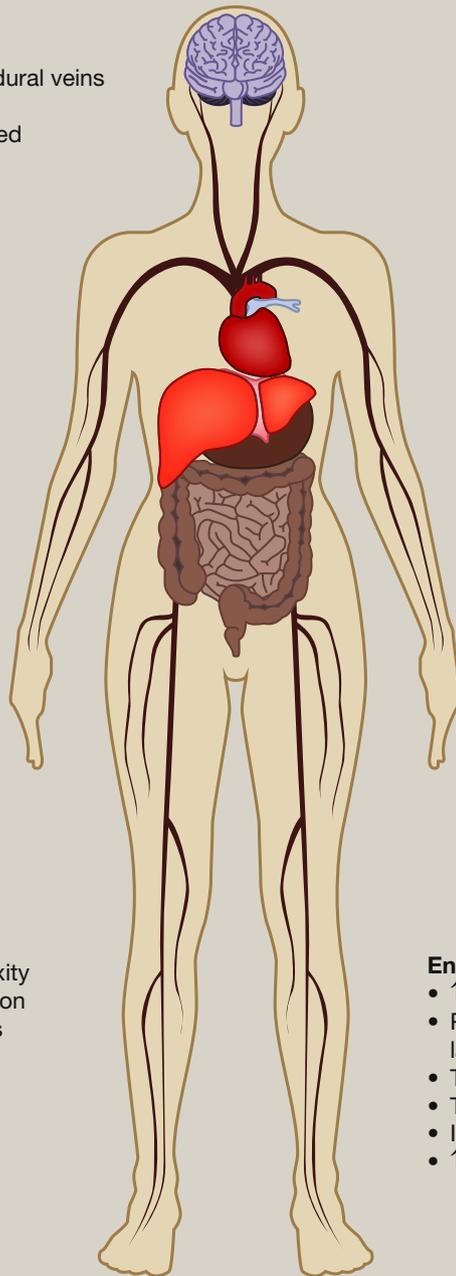
- ↑ CSF pressure
- Engorgement of epidural veins
- ↓ MAC
- ↓ LA volumes required

### Respiratory

- ↑ MV ( ↑TV and ↑RR)
- ↓ PaCO<sub>2</sub>
- ↑ PaO<sub>2</sub>
- ↓ FRC

### Musculoskeletal

- ↑ Ligamentous laxity
- ↑ Risk of dislocation
- ↑ Lumbar lordosis



### Cardiac

- ↑ CO
- ↑ SV
- ↑ HR
- Left ventricular hypertrophy
- Regurgitant murmurs
- ↓ SVR

### Gastrointestinal

- ↓ Lower oesophageal sphincter tone
- Reflux
- ↑ Risk of aspiration
- Liver enzymes (AST, ALT, GGT) ↓
- ↑ ALP

### Renal

- ↑ Renal blood flow
- ↑ GFR
- ↓ Plasma urea and creatinine
- ↑ Urinary protein and glucose
- ↑ Risk of UTI

### Endocrine

- ↑ Progesterone and oestrogen
- Placenta secretes relaxin, human placental lactogen and human chorionic gonadotrophin
- Thyroid hyperplasia
- Transient hyperthyroidism
- Insulin resistance
- ↑ Cortisol secretion by adrenal glands

ALP, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate transaminase; CO, cardiac output; CSF, cerebrospinal fluid; FRC, functional residual capacity; GFR, glomerular filtration rate; GGT,  $\gamma$ -glutamyl transferase; HR, heart rate; LA, local anaesthetic; MAC, minimum alveolar concentration; MV, minute volume; SV, stroke volume; SVR, systemic vascular resistance; UTI, urinary tract infection.

Figure 2

increased in this population. A suggested dose reduction of 25–30% is described.

Venous engorgement within the epidural space confers an increased risk of intravascular injection, particularly during contractions, when the venous pressure in the epidural veins reaches its peak.

### Gastrointestinal

Lower oesophageal sphincter smooth muscle relaxation and upward displacement of the stomach by the gravid uterus contribute to the increased incidence of reflux during pregnancy. Although gastric transit is unaffected, there remains an increased

risk of aspiration. Fear, pain and analgesics in labour can compound gastric stasis further increasing this risk. The risk of aspiration is thought to revert to that of pre-pregnancy within 24–48 hours post delivery.

Muscular relaxation also occurs within the gallbladder during pregnancy, leading to biliary stasis and increased risk of gallstone formation. This is thought to be mediated by progesterone and its inhibitory action on cholecystokinin release. Plasma levels of most hepatic enzymes (specifically gamma GT, the transaminases (ALT and AST) and bilirubin) typically decrease during pregnancy, and alternative laboratory ranges have been suggested for obstetric patients. Spider naevi and palmar erythema may occur without clinically significant liver disease.

The placenta produces additional alkaline phosphatase (ALP) causing the serum level to rise. Plasma cholinesterase levels decline from the 10th week of pregnancy onwards, reaching a nadir in the days following delivery. Parturients have a high volume of distribution with only a small reduction in plasma cholinesterase, therefore suxamethonium has a similar duration of action as in the pre-pregnant state. However, those parturients with an unrecognized abnormal copy of the gene encoding plasma cholinesterase may have an increased duration of neuromuscular block.

Plasma protein production decreases and this may have an effect on the free concentrations of drugs, which are usually highly protein bound.

## Endocrine

Many of the physiological adaptations of pregnancy are due to increased circulating reproductive hormones including oestrogen and progesterone. Additionally, the placenta secretes hormones such as relaxin, human placental lactogen (HPL) and human chorionic gonadotrophin which contribute to changes within several body systems.

The thyroid gland undergoes follicular hyperplasia and increases in size. Thyroid stimulating hormone (TSH) receptors can be stimulated by B-HCG (as this shares a structural similarity with TSH) which then leads to a transient hyperthyroidism.

Insulin resistance, secondary to placental secretion of HPL, can result in gestational diabetes. While glucose readily crosses the placenta, insulin does not and the fetus must produce its own. As a result, babies of diabetic mothers tend to have higher birth weights (macrosomia) and may develop hypoglycaemia following delivery.

Secretion of corticosteroid hormones by the zona fasciculata of the adrenal gland is increased. The resulting increase in cortisol can further contribute to the development of insulin resistance and can also produce changes in skin pigmentation.

## Musculoskeletal

Gestational weight gain, with a change in posture required to accommodate the growing fetus, alters the loading pattern on joints and other musculoskeletal structures. For example, lumbar lordosis becomes increasingly exaggerated as pregnancy progresses. In some parturients, these changes can cause significant pain.

The hormones relaxin and oestrogen contribute to increased ligamentous laxity, particularly in the pelvis. This enables the fetus to be accommodated but can contribute to musculoskeletal pain during pregnancy. Parturients predisposed to joint instability have an increased risk of subluxation or dislocation. It is important to take particular care when positioning these at risk parturients following neuraxial anaesthesia.

## Conclusion

The adaptive changes that occur in pregnancy affect all of the body's systems and are summarized in [Figure 2](#). Knowledge of the expected physiological changes is essential to enable recognition of pathology, anticipation of possible complications and modification of anaesthesia to ensure safe obstetric practice. ◆

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## FURTHER READING

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