Physiological Changes In Pregnancy

Pregnancy is associated with normal physiological changes that assist fetal survival as well as preparation for labour. It is important to know what 'normal' parameters of change are in order to diagnose and manage common medical problems of pregnancy, such as hypertension, gestational diabetes, anaemia and hyperthyroidism.

As a result of normal physiological change, normal ranges for certain blood tests are different in pregnancy, and women may have different susceptibility to medication. [1]

See separate Antenatal Care and Common Problems in Pregnancy articles.

Endocrine system (non-reproductive) changes [2]

See also separate Gestational Diabetes article.

Pituitary hormones

- FSH/LH fall to extremely low levels due to the high levels of oestrogen and progesterone.
- ACTH and melanocyte-stimulating hormone increase.
- Prolactin levels increase.
- Pituitary growth hormone (GH) levels fall but overall serum levels increase due to placental production.
- Oxytocin levels increase to a peak at term.
- ADH levels are unchanged.

Thyroid and parathyroid gland

- Thyroxine-binding globulin (TBG) concentrations rise due to increased oestrogen levels.
- T4 and T3 increase over the first half of pregnancy but there is a normal to slightly decreased amount of free hormone due to increased TBG-binding. Normal ranges are slightly reduced in the second and third trimester.
- TSH production is stimulated after the first trimester, although in healthy individuals this is not usually significant. A large rise in TSH is likely to indicate iodine deficiency or subclinical hypothyroidism.
- Women are relatively iodine-deficient in pregnancy; the World Health Organization (WHO) recommends an increased intake during this time. [3, 4] Where iodised salt is unavailable, supplements are recommended. If iodine levels are maintained in pregnancy, the thyroid gland should stay the same size and any increase be investigated. It will be larger in the presence of iodine deficiency.
- Although fetal need for calcium is high, maternal serum calcium levels are maintained in pregnancy by increased intestinal absorption. There is also increased excretion in the urine, as a result of which pregnant women are at increased risk of renal stones.
- Colecalciferol (vitamin D3) is converted to its active metabolite, 1,25-dihydroxycolecalciferol, by placental 1α-hydroxylase. Serum levels rise and are responsible for the increased intestinal absorption of calcium.

Adrenal gland and pancreas

- Cortisol levels increase in pregnancy, which favours lipogenesis and fat storage.
- Insulin response also increases so blood sugar should remain normal or low.
- Peripheral insulin resistance increases after early stages of pregnancy due to increased production of hormones such as cortisol, prolactin, progesterone and human placental lactogen.
- The combination of insulin resistance and relatively low glucose promotes the use of fat for energy, preserving glucose and amino acids for the fetus.
- Gestational diabetes is thought to reflect a pronounced insulin resistance of this sort.
- HbA1c is not considered suitable for use in pregnancy, as normal range changes and suitable reference ranges have not been established. [5]

Cardiovascular system changes [2]

- There is peripheral vasodilation.
- Cardiac output increases by 20% by week 8, and then further up to 40% increase, maximal at week 20-28. In labour there is further increase in cardiac output and then a huge increase immediately after delivery, followed by return to normal within around an hour.
- Contributing to the increased cardiac output are increased stroke volume and an increase in heart rate of 10-20 beats per minute.
- Blood pressure is lower than normal in the first two trimesters but returns to normal in the third.
- Venous return in the inferior vena cava can be compromised in late pregnancy if a woman lies flat on her back due to pressure from the uterus, resulting in reduced stroke volume and cardiac output. This is relieved by lying in the left lateral position. Reduced cardiac output can compromise fetal blood supply.
There is an increased risk of pulmonary oedema if there is an increase in blood volume, or increased pulmonary capillary permeability secondary to pre-eclampsia. The highest risk time is the second stage of labour or immediate postpartum period when cardiac output is high. Changes on examination and ECG below are caused by the physiological changes described above.

Cardiac examination in pregnancy
- There may be a bounding or collapsing pulse.
- Many women have a third heart sound after mid-pregnancy.
- Diastolic murmurs should be considered potentially pathological.
- Systolic flow murmurs are common.

ECG changes considered normal in pregnancy
- Left axis deviation.
- Small Q waves and inverted T wave in lead III.
- ST depression and inversion or flattening of the T wave in inferior and lateral leads.
- Atrial and ventricular ectopics.

Respiratory system changes[^2][^6]
- Tidal volume increases by about 200 ml, increasing vital capacity and decreasing residual volume. In later stages of pregnancy, splinting of the diaphragm may occur with some decrease in tidal volume. Respiratory rate does not alter significantly.
- Increased oxygen consumption (by approximately 20%) and increased metabolic rate cause increased oxygen demand.
- State of compensated respiratory alkalosis - arterial pCO\textsubscript{2} drops, arterial pO\textsubscript{2} rises and decrease in bicarbonate prevents pH change. Lower maternal pCO\textsubscript{2} facilitates oxygen/carbon dioxide transfer to/from the fetus.
- Many women complain of feeling short of breath in pregnancy without hypoxia or explanatory pathology. The mechanism of this is not fully understood.

Alimentary system changes
- Nausea and vomiting are common in early pregnancy.
- Appetite is usually increased, sometimes with specific cravings.
- Progesterone causes relaxation of the lower oesophageal sphincter and increased reflux, making many women prone to heartburn. Pressure on the stomach from the enlarging uterus further contributes to this in later pregnancy.
- Gastrointestinal motility is reduced and transit time is consequently longer. This allows increased nutrient absorption. Constipation is common.
- The gallbladder may dilate and empty less completely. Pregnancy also predisposes to the precipitation of cholesterol gallstones.
- Gums become spongy, friable and prone to bleeding. Good dental care is important.
Urinary tract changes\[6\]
- The increased blood volume and cardiac output during pregnancy cause a 50-60% increase in renal blood flow and glomerular filtration rate (GFR). This causes an increased excretion and reduced blood levels of urea, creatinine, urate and bicarbonate.
- Mild glycosuria and/or proteinuria may occur because the increase in GFR may exceed the ability of the renal tubules to reabsorb glucose and protein.
- Increased water retention causes a reduction of plasma osmolality.
- The smooth muscle of the renal pelvis and ureter become relaxed and dilated, kidneys increase in length and ureters become longer, more curved and with an increase in residual urine volume.
- Bladder smooth muscle also relaxes, increasing capacity and risk of urinary tract infection.
- The enlarging uterus may put pressure on the ureters.
- 2-10% of women have asymptomatic bacteriuria in pregnancy and if untreated up to 30% may develop acute pyelonephritis.\[7\]

Haematological changes\[2, 6\]
- Plasma volume increases over the course of pregnancy by about 50%. Dilutional anaemia is caused by the rise in plasma volume. Elevated erythropoietin levels increase the total red cell mass by the end of the second trimester but haemoglobin concentrations never reach pre-pregnancy levels.
- Usually mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentration (MCHC) are unaffected.
- A modest leucocytosis is observed.
- A normal pregnancy creates a demand for about 1000 mg of additional iron. This equates to 60 mg elemental iron or 300 mg ferrous sulfate per day.
- Serum iron falls during pregnancy whilst transferrin and total iron binding capacity rise.
- Levels of some clotting factors (VII, VIII, IX and X) and fibrinogen increase whilst fibrinolytic activity decreases. These changes protect from haemorrhage at delivery but also make pregnancy a hypercoagulable state with increased risk of thromboembolism. See separate Venous Thromboembolism in Pregnancy article.
- One study found that during early pregnancy: antithrombin activity remained unchanged, protein S activity decreased significantly and there was a potentially biologically significant increase in protein C activity.\[8\] See separate Thrombophilia article.
- Serum albumin decreases.

Metabolic changes
- The basal metabolic rate increases slowly over the course of pregnancy, by 15-20%.
- It is thought that energy requirement does not increase significantly during the first or second trimesters, increasing by around 200 kcal per day in the third.\[9\]
- Active energy expenditure tends to fall over pregnancy.
- Recommended normal weight gain in pregnancy is 11.4 to 15.9 kg for a woman of normal body mass index (BMI).\[10\] Around 5 kg is the fetus, placenta, membranes and amniotic fluid and the rest is maternal stores of fat and protein and increased intra- and extra-vascular volume. Weight is no longer monitored in pregnancy as it does not affect outcome and is affected by a number of factors.

Skin changes
- Hyperpigmentation of the umbilicus, nipples, abdominal midline (linea nigra) and face (melasma (chloasma)) are common due to the hormonal changes of pregnancy.
- Hyperdynamic circulation and high levels of oestrogen may cause spider naevi and palmar erythema.
- Striae gravidarum (‘stretch marks’) are common.

Musculoskeletal changes
- Increased ligamental laxity caused by increased levels of relaxin contribute to back pain and pubic symphysis dysfunction.
- Shift in posture with exaggerated lumbar lordosis leading to the typical gait of late pregnancy.

Interpreting blood test results in pregnancy
<table>
<thead>
<tr>
<th>Test</th>
<th>Trend in normal pregnancy (compared to non-pregnant state)</th>
<th>Pregnancy normal values (ALWAYS USE LOCAL REFERENCE RANGES)</th>
<th>Abnormalities and possible interpretations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin</td>
<td>Decreased</td>
<td>10.5-13.5 g/dL</td>
<td>Consider dilutional anaemia of pregnancy.</td>
</tr>
<tr>
<td>White cell count</td>
<td>Increased</td>
<td>8-18 x 10^9/L</td>
<td>Always consider in the light of the patient's clinical status. Can make infection more difficult to diagnose.</td>
</tr>
<tr>
<td>Platelets</td>
<td>Unchanged/slightly increased</td>
<td>200-600 x 10^9/L</td>
<td>Always consider in the light of the patient's clinical status. In practice a pregnant woman is not considered thrombocytopenic unless the platelet count is below 100 x 10^9/L. [2]</td>
</tr>
<tr>
<td>Sodium</td>
<td>Slightly decreased</td>
<td>132-140 mmol/L</td>
<td>Always consider in the light of the patient's clinical status.</td>
</tr>
<tr>
<td>Potassium</td>
<td>Slightly decreased</td>
<td>3.2-4.6 mmol/L</td>
<td>Always consider in the light of the patient's clinical status.</td>
</tr>
<tr>
<td>Urea</td>
<td>Decreased</td>
<td>1.0-3.8 mmol/L</td>
<td>Increased in dehydration, hyperemesis, late stages of pre-eclampsia and renal impairment.</td>
</tr>
<tr>
<td>Creatinine</td>
<td>Decreased</td>
<td>40 - 80 μmol/L</td>
<td>Increased in renal impairment and the late stages of pre-eclampsia.</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>Unchanged</td>
<td>3.0-5.0 mmol/L</td>
<td>Increased in gestational diabetes.</td>
</tr>
<tr>
<td>Total calcium</td>
<td>Decreased</td>
<td>2.0-2.4 mmol/L</td>
<td>Increased in primary hyperparathyroidism. (Total serum calcium decreased due to reduced serum albumin secondary to haemodilution) but ionised calcium unchanged in pregnancy.)</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Unchanged</td>
<td>0.6-0.8 mmol/L</td>
<td>Decreased if there is vomiting or hyperemesis gravidarum.</td>
</tr>
<tr>
<td>Albumin</td>
<td>Decreased</td>
<td>24-31 g/L</td>
<td>Decreased further if there is malnutrition, recurrent vomiting or hyperemesis gravidarum.</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>Decreased</td>
<td>3-14 μmol/L</td>
<td>Increased in obstetric cholestasis, HELLP syndrome, the late stages of pre-eclampsia, acute fatty liver, viral hepatitis. See separate Jaundice in Pregnancy article.</td>
</tr>
<tr>
<td>ALT</td>
<td>Unchanged/slightly decreased</td>
<td>1-30 U/L</td>
<td>As for bilirubin.</td>
</tr>
<tr>
<td>AST</td>
<td>Unchanged/slightly decreased</td>
<td>1-21 U/L</td>
<td>As for bilirubin.</td>
</tr>
<tr>
<td>ALP</td>
<td>Increased</td>
<td>125-250 U/L</td>
<td>Increased further in metabolic bone disorders or rare pregnancy-associated conditions - eg, chronic histiocytic intervillositis.</td>
</tr>
<tr>
<td>TSH</td>
<td>Slight decrease in the first trimester, normal in the second trimester, slightly raised in the last trimester</td>
<td>0.1-4.0 IU/L</td>
<td>Less than 0.05 in Graves’ disease or hyperemesis gravidarum.</td>
</tr>
<tr>
<td>fT4</td>
<td>Unchanged</td>
<td>10-25 pmoL</td>
<td>Increased in Graves’ disease or hyperemesis gravidarum.</td>
</tr>
<tr>
<td>fT3</td>
<td>Unchanged</td>
<td>3.5-6 pmoL</td>
<td>Increased in Graves’ disease or hyperemesis gravidarum.</td>
</tr>
</tbody>
</table>

Further reading & references


3. Iodine supplementation in pregnant and lactating women; World Health Organization (WHO)


6. Physiological changes of pregnancy; Anaesthesia UK


9. Weight management before, during and after pregnancy; NICE Public Health Guideline (July 2010)


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Peer Reviewer: Dr John Cox

Document ID: 740 (v27)

Last Checked: 20/06/2016

Next Review: 19/06/2021

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