Pregnancy causes a two- to three-fold increase in the requirement for iron, not only for haemoglobin synthesis but also for for the foetus and the production of certain enzymes. There is a 10- to 20-fold increase in folate requirements and a two-fold increase in the requirement for vitamin B12.

Changes in the coagulation system during pregnancy produce a physiological hypercoagulable state (in preparation for haemostasis following delivery).[3](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R03) The concentrations of certain clotting factors, particularly VIII, IX and X, are increased. Fibrinogen levels rise significantly by up to 50% and fibrinolytic activity is decreased. Concentrations of endogenous anticoagulants such as antithrombin and protein S decrease. Thus pregnancy alters the balance within the coagulation system in favour of clotting, predisposing the pregnant and postpartum woman to venous thrombosis. This increased risk is present from the first trimester and for at least 12 weeks following delivery. *In vitro* tests of coagulation [activated partial thromboplastin time (APTT), prothrombin time (PT) and thrombin time (TT)] remain normal in the absence of anticoagulants or a coagulopathy.

Venous stasis in the lower limbs is associated with venodilation and decreased flow, which is more marked on the left. This is due to compression of the left iliac vein by the left iliac artery and the ovarian artery. On the right, the iliac artery does not cross the vein.

 [:](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/)

Cardiac changes

Changes in the cardiovascular system in pregnancy are profound and begin early in pregnancy, such that by eight weeks’ gestation, the cardiac output has already increased by 20%. The primary event is probably peripheral vasodilatation. This is mediated by endothelium-dependent factors, including nitric oxide synthesis, upregulated by oestradiol and possibly vasodilatory prostaglandins (PGI2). Peripheral vasodilation leads to a 25–30% fall in systemic vascular resistance, and to compensate for this, cardiac output increases by around 40% during pregnancy. This is achieved predominantly via an increase in stroke volume, but also to a lesser extent, an increase in heart rate. The maximum cardiac output is found at about 20–28 weeks’ gestation. There is a minimal fall at term.

An increase in stroke volume is possible due to the early increase in ventricular wall muscle mass and end-diastolic volume (but not end-diastolic pressure) seen in pregnancy. The heart is physiologically dilated and myocardial contractility is increased. Although stroke volume declines towards term, the increase in maternal heart rate (10–20 bpm) is maintained, thus preserving the increased cardiac output. Blood pressure decreases in the first and second trimesters but increases to non-pregnant levels in the third trimester

There is a profound effect of maternal position towards term upon the haemodynamic profile of both the mother and foetus. In the supine position, pressure of the gravid uterus on the inferior vena cava (IVC) causes a reduction in venous return to the heart and a consequent fall in stroke volume and cardiac output. Turning from the lateral to the supine position may result in a 25% reduction in cardiac output. Pregnant women should therefore be nursed in the left or right lateral position wherever possible. If the woman has to be kept on her back, the pelvis should be rotated so that the uterus drops to the side and off the IVC, and cardiac output and uteroplacental blood flow are optimised. Reduced cardiac output is associated with a reduction in uterine blood flow and therefore in placental perfusion, which could compromise the foetus.

Although both blood volume and stroke volume increase in pregnancy, pulmonary capillary wedge pressure and central venous pressure do not increase significantly. Pulmonary vascular resistance (PVR), like systemic vascular resistance (SVR), decreases significantly in normal pregnancy. Although there is no increase in pulmonary capillary wedge pressure (PCWP), serum colloid osmotic pressure is reduced by 10–15%. The colloid osmotic pressure/pulmonary capillary wedge pressure gradient is reduced by about 30%, making pregnant women particularly susceptible to pulmonary oedema. Pulmonary oedema will be precipitated if there is either an increase in cardiac pre-load (such as infusion of fluids) or increased pulmonary capillary permeability (such as in pre-eclampsia) or both.

Labour is associated with further increases in cardiac output (15% in the first stage and 50% in the second stage) Uterine contractions lead to an auto-transfusion of 300–500 ml of blood back into the circulation and the sympathetic response to pain and anxiety further elevate the heart rate and blood pressure. Cardiac output is increased between contractions but more so during contractions.

Following delivery there is an immediate rise in cardiac output due to relief of the inferior vena cava obstruction and contraction of the uterus, which empties blood into the systemic circulation. Cardiac output increases by 60–80%, followed by a rapid decline to pre-labour values within about one hour of delivery. Transfer of fluid from the extravascular space increases venous return and stroke volume further.

Those women with cardiovascular compromise are therefore most at risk of pulmorary oedema during the second stage of labour and the immediate postpartum period. Cardiac output has nearly returned to normal (pre-pregnancy values) two weeks after delivery, although some pathological changes (e.g. hypertension in pre-eclampsia) may take much longer.

The above physiological changes lead to changes on cardiovascular examination that may be misinterpreted as pathological by those unfamiliar with pregnancy. Changes may include a bounding or collapsing pulse and an ejection systolic murmur, present in over 90% of pregnant women. The murmur may be loud and audible all over the precordium, with the first heart sound loud and possibly sometimes a third heart sound. There may be ectopic beats and peripheral oedema.

Normal findings on ECG in pregnancy that may partly relate to changes in the position of the heart include:

* atrial and ventricular ectopics
* Q wave (small) and inverted T wave in lead III
* ST-segment depression and T-wave inversion in the inferior and lateral leads
* left-axis shift of QRS.

 [:](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/)

Adaptive changes in renal vasculature

The primary adaptive mechanism in pregnancy is a marked fall in systemic vascular resistance (SVR) occurring by week six of gestation. The 40% fall in SVR also affects the renal vasculature.[4](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R04) Despite a major increase in plasma volume during pregnancy, the massive decrease in SVR creates a state of arterial under-filling because 85% of the volume resides in the venous circulation.[5](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R05) This arterial under-filling state is unique to pregnancy. The fall in SVR is combined with increased renal blood flow and this is in contrast to other states of arterial under-filling, such as cirrhosis, sepsis or arterio-venous fistulas.[3](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R03),[6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/%22%20%5Cl%20%22R06)

Relaxin, a peptide hormone produced by the corpus luteum, decidua and placenta, plays an important role in the regulation of haemodynamic and water metabolism during pregnancy. Serum concentrations of relaxin, already elevated in the luteal phase of the menstrual cycle, rise after conception to a peak at the end of the first trimester and fall to an intermediate value throughout the second and third trimester. Relaxin stimulates the formation of endothelin, which in turn mediates vasodilation of renal arteries via nitric oxide (NO) synthesis.[7](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R07)

Despite activation of the renin–angiotensin–aldosterone (RAA) system in early pregnancy, a simultaneous relative resistance to angiotensin II develops, counterbalancing the vasoconstrictive effect and allowing profound vasodilatation.[8](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R08) This insensitivity to angiotensin II may be explained by the effects of progesterone and vascular endothelial growth factormediated prostacyclin production, as well as modifications in the angiotensin I receptors during pregnancy.[9](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R09) The vascular refractoriness to angiotensin II may also be shared by other vasoconstrictors such as adrenergic agonists and arginine vasopressin (AVP).[10](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R10) It is possible that in the second half of pregnancy, the placental vasodilatators are more important in the maintenance of the vasodilatatory state.[6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R06)

 [:](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/)

Changes in renal anatomy and function

As a consequence of renal vasodilatation, renal plasma flow and glomerular filtration rate (GFR) both increase, compared to non-pregnant levels, by 40–65 and 50–85%, respectively. In addition, the increase in plasma volume causes decreased oncotic pressure in the glomeruli, with a subsequent rise in GFR.[11](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R11) Vascular resistance decreases in both the renal afferent and efferent arterioles and therefore, despite the massive increase in renal plasma flow, glomerular hydrostatic pressure remains stable, avoiding the development of glomerular hypertension. As the GFR rises, both serum creatinine and urea concentrations decrease to mean values of about 44.2 μmol/l and 3.2 mmol/l, respectively.

The increased renal blood flow leads to an increase in renal size of 1–1.5 cm, reaching the maximal size by mid-pregnancy. The kidney, pelvis and calyceal systems dilate due to mechanical compressive forces on the ureters. Progesterone, which reduces ureteral tone, peristalsis and contraction pressure, mediates these anatomical changes.[11](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R11) The increase in renal size is associated with an increase in renal vasculature, interstitial volume and urinary dead space. There is also dilation of the ureters, renal pelvis and calyces, leading to physiological hydronephrosis in over 80% of women.[12](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R12) There is often a right-sided predominance of hydronephrosis due to the anatomical circumstances of the right ureter crossing the iliac and ovarian vessels at an angle before entering the pelvis. Urinary stasis in the dilated collecting system predisposes pregnant women with asymptomatic bacteriuria to pyelonephritis.[12](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R12)

There are also alterations in the tubular handling of wastes and nutrients. As in the non-pregnant state, glucose is freely filtered in the glomerulus. During pregnancy, the reabsorption of glucose in the proximal and collecting tubule is less effective, with variable excretion. About 90% of pregnant women with normal blood glucose levels excrete 1–10 g of glucose per day. Due to the increases in both GFR and glomerular capillary permeability to albumin, the fractional excretion of protein may increase up to 300 mg/day and protein excretion also increases. In normal pregnancies the total protein concentration in urine does not increase above the upper normal limit. Uric acid excretion also increases due to increased GFR and/or decreased tubular reabsorption.[11](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R11)

Arterial under-filling in pregnancy leads to the stimulation of arterial baroreceptors, activating the RAA and the sympathetic nervous systems. This results in a non-osmotic release of AVP from the hypothalamus. These changes lead to sodium and water retention in the kidneys and create a hypervolaemic, hypoosmolar state characteristic of pregnancy.[6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R16) Extracellular volume increases by 30–50% and plasma volume by 30–40%. Maternal blood volume increases by 45% to approximately 1 200 to 1 600 ml above non-pregnant values. By the late third trimester the plasma volume increases by more than 50–60%, with a lower increase in red blood cell mass, and therefore plasma osmolality falls by 10 mosmol/kg. The increase in plasma volume plays a critical role in maintaining circulating blood volume, blood pressure and uteroplacental perfusion during pregnancy.[13](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R13)

Activation of the RAA system leads to increased plasma levels of aldosterone and subsequent salt and water retention in the distal tubule and collecting duct. In addition to the increased renin production by the kidneys, ovaries and uteroplacental unit produce an inactive precursor protein of renin in early pregnancy.[14](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R14) The placenta also produces oestrogens that stimulate the synthesis of angiotensinogen by the liver, resulting in proportionally increased levels of aldosterone compared to renin. Plasma levels of aldosterone correlate well with those of oestrogens and rise progressively during pregnancy. The increase in aldosterone is responsible for the increase in plasma volume during pregnancy.[13](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R13) Progesterone, which is a potent aldosterone antagonist, allows natriuresis despite the sodium-retaining properties of aldosterone. The rise in GFR also increases distal sodium delivery, allowing excretion of excess sodium. Progesterone has antikaliuretic effects and therefore excretion of potassium is kept constant throughout pregnancy due to changes in tubular reabsorption, and total body potassium increases during pregnancy.[6](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R06),[15](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/%22%20%5Cl%20%22R15)

Hypothalamic AVP release increases early in pregnancy as a result of increased relaxin levels. AVP mediates an increase in water reabsorption via aquaporin 2 channels in the collecting duct. The threshold for hypothalamic secretion of AVP and the threshold for thirst is reset to a lower plasma osmolality level, creating the hypo-osmolar state characteristic of pregnancy. These changes are mediated by human chorionic gonadotropin (hCG) and relaxin.[11](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R11),[16](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R16)

In middle and late pregnancy there is a four-fold increase in vasopressinase, an aminopeptidase produced by the placenta. These changes enhance the metabolic clearance of vasopressin and regulate the levels of active AVP. In conditions of increased placental production of vasopressinase, such as pre-eclampsia or twin pregnancies, a transient diabetes insipidus may develop.[17](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R17) As a consequence of this volume expansion, the secretion of atrial natriuretic peptides increases by 40% in the third trimester, and rises further during the first week postpartum. The levels of natriuretic peptides are higher in pregnant women with chronic hypertension and pre-eclampsia.[18](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4928162/#R18)

Respiratory changes

There is a significant increase in oxygen demand during normal pregnancy. This is due to a 15% increase in the metabolic rate and a 20% increased consumption of oxygen. There is a 40–50% increase in minute ventilation, mostly due to an increase in tidal volume, rather than in the respiratory rate. This maternal hyperventilation causes arterial pO2 to increase and arterial pCO2 to fall