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ANATOMICAL AND PHYSIOLOGICAL CHANGES DURING PREGNANCY

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ABSTRACT

Pregnant women undergo profound anatomical and physiological changes so that they can cope with the increased physical and metabolic demands of their pregnancies. The cardiovascular, respiratory, hematological, renal, gastrointestinal and endocrine systems all undergo important physiological alterations and adaptations needed to allow development of the fetus and to allow the mother and fetus to survive the demands of childbirth. Such alterations in anatomy and physiology may cause difficulties in interpreting signs, symptoms, and biochemical investigations, making the clinical assessment of a pregnant woman inevitably confusing but challenging. Understanding these changes is important for every practicing obstetrician, as the pathological deviations from the normal physiological alterations may not be clear-cut until an adverse outcome has resulted. Only with a sound knowledge of the physiology and anatomy changes can the care of an obstetric parturient be safely optimized for a better maternal and fetal outcome.

KEYWORDS: Anatomical, physiological, pregnancy.

INTRODUCTION

Pregnant women undergo anatomical and physiological changes that are not only important for coping with the increased metabolic demands of the pregnancy, but also to meet the developmental needs of the fetus and to allow mother and fetus to survive the demands of childbirth. Understanding these changes is essential for all clinicians looking after pregnant women as a clinical assessment of a pregnant woman can be confusing and challenging.[1]

Treatment background

Changes in the Hematological System Maternal blood volume increases during pregnancy, and this involves an increase in plasma volume as well as in red cell and white cell volumes.1 The plasma volume increases by 40–50%, whereas the red cell volume increases by only 15–20%, which causes a "physiological anemia of pregnancy" (normal hemoglobin 12 g/dL; hematocrit 35). Because of this hemodilution, blood viscosity decreases by approximately 20%. The exact mechanism of this increase in plasma volume is unknown. However, several mediators such as renin–angiotensin–aldosterone, atrial natriuretic peptide, estrogen, progesterone, and nitric oxide may be involved.[2]

The most likely hypothesis attributes the increase to an "underfill" state caused by initial vasodilation, which stimulates hormones such as renin, angiotensin, and aldosterone to cause fluid retention. Alternatively, some have proposed an "overfill" state characterized by an early increase in sodium retention (due to an increase in mineralocorticoids) that leads to fluid retention, causing an increase in blood volume, followed subsequently by vasodilation. Blood volume increases further during labor, as uterine contractions squeeze blood out of the intervillous space and into the central circulation. After delivery, involution of the uterus and termination of placental circulation causes an autotransfusion of approximately 500 mL of blood.[3]

Levels of clotting factors I, VII, VIII, IX, X, and XII and fibrinogen are elevated during pregnancy as well. Platelet production is increased, thrombopoietin levels are increased, and platelet aggregation measured in vitro is likewise increased; indices of platelet destruction are also increased. The overall effect of these changes is variable, but prospective observations have reported a statistically significant fall in platelet count as pregnancy progresses, with 7.6% of women having a count less than 150,000 and 1% less than 100,000 at term.[4]

Endogenous anticoagulants, such as protein S, are decreased in normal pregnancy and there is acquired resistance to activated protein C during pregnancy, adding to the prothrombotic state. Fibrinolysis is impaired in normal pregnancy due to placentally derived plasminogen activator inhibitor (PAI) but returns to normal following delivery of the placenta. Overall indices of coagulation indicate that normal pregnancy is a hypercoagulable state.[5]

Pregnancy causes a two- to three-fold increase in the requirement for iron, not only for hemoglobin synthesis but also for the fetus 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 hemostasis following delivery).

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 favor 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.[6]

Increased blood volume and enhanced coagulation serve several important functions:
(1) the increased circulatory needs of the enlarging uterus and growing fetus and placenta are met and
(2) the parturient is protected from bleeding at the time of delivery.[7] Anesthesiologists should consider the enlarged blood volume when making decisions on fluid and blood replacement in the peripartum period. Parturients become hypercoagulable as gestation progresses and are at increased risk of thromboembolism. After a rapid mobilization and diuresis of some fluid in the first few postpartum days, blood volume slowly returns to normal over 8 weeks.[8]

Table 1

Changes in electrocardiogram and cardiac auscultation during pregnancy

Changes in cardiac auscultation	Changes in electrocardiogram
Loud S_1	Shortened PR and QT interval
Ejection systolic murmur	Shifted QRS axis
S_3 and S_4 (no clinical significance)	Rightwards (1st trimester)
	Leftwards (3rd trimester)
	ST segment depression
	Isoelectric low-voltage T waves in both precordial and limb leads

Changes in the Cardiovascular System

An increase in cardiac output is one of the most important changes in pregnancy. Cardiac output increases by 30–40% during pregnancy, and the maximum increase is attained around 24 weeks' gestation.[9] The increase in heart rate occurs first (by the end of the first month of pregnancy) and plateaus at an increase of 10–15 beats per minute by 28–32 weeks' gestation. Stroke volume increases by mid first trimester and progressively increases through the second trimester. Echocardiography demonstrates increases in end-diastolic chamber size and total left ventricular wall thickness but no change in end-systolic volume, so ejection fraction is increased. Cardiac output can vary depending on the uterine size and maternal position at the time of measurement. The enlarged gravid uterus can cause aortocaval compression and reduced cardiac filling while the pregnant woman is in the supine position[10], leading to an underestimation of cardiac function. Normal pregnant women exhibit a marked increase in femoral venous and inferior vena cava pressures. Collateral vessels maintain atrial filling but lead to engorgement of veins, including the epidural venous (Batson's) plexus.[11] Filling pressures (CVP, pulmonary capillary wedge pressure, LV end-diastolic pressure) do not change despite the increased cardiac dimensions, due to myocardial remodeling during gestation.

Systemic vascular resistance is decreased by approximately 20%. Blood pressure never increases in normal pregnancy, and systolic and diastolic blood pressures decreased by approximately 8 and 20%, respectively, on average.[12] Pregnancy hormones (estradiol and progesterone), prostacyclin, and nitric oxide all may play a role in the reduction in blood

pressure observed despite an increase in cardiac output. Cardiac output increases further during labor, up to 50% higher than pre-labor values, although effective analgesia can attenuate some of this increase. In the immediate postpartum period, cardiac output increases maximally and can rise 80% above pre-labor values and approximately 150% above nonpregnant measurements. An increase in stroke volume as well as in heart rate maintains the increased cardiac output. The heart is displaced to the left and upward during pregnancy because of the progressive elevation of the diaphragm by the gravid uterus.

The electrocardiogram of normal parturients may include:
(1) sinus tachycardia or benign dysrhythmias,
(2) depressed ST segments and flattened T waves,
(3) left axis deviation, and
(4) left ventricular hypertrophy.[13]

Auscultation frequently reveals a systolic murmur of tricuspid or mitral regurgitation and a third or fourth heart sound. Cardiac output, heart rate, and stroke volume decrease to pre-labor values 24–72 h postpartum and return to nonpregnant levels within 6–8 weeks after delivery.[14]

Changes in renal anatomy and function

As a consequence of renal vasodilatation, renal plasma flow and glomerular filtration rate (GFR) both increases, 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 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.[15]

The increased renal blood flow leads to an increase in the 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.[16] 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.[17] 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.

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.[18]

Respiratory system

Major physiological and anatomical changes occur in the respiratory system during pregnancy due to a combination of both hormonal and mechanical factors. Dyspnoea is a common complaint in pregnancy affecting over half of the women at some stage. Difficult intubation is said to be very much more common in the pregnant patient at term. Firstly, due to increased breast size, insertion of the laryngoscope may be difficult (a laryngoscope with an angled blade may be useful).[19]

Secondly, airway mucosal edema (which tends to be even worse in the presence of pre-eclampsia) may make the view at laryngoscopy poor. It is recommended that a smaller size endotracheal tube is used. Nasal congestion can occur and nasal intubation is not recommended as it can result in trauma to the airways. Hyperventilation occurs which is due both to an increase in tidal volume (40%) and a lesser increase in respiratory rate (15%). This results in a slight drop in the partial pressure of carbon dioxide (to approximately 32 mmHg or 4.3 kPa) resulting in a mild respiratory alkalosis (pH 7.44) Both the metabolic demands of the fetus and the increased work of breathing result in increased oxygen consumption (up to 60% during labor). Functional residual capacity decreases by about 20% (decreasing even further in the supine position). The above changes in the respiratory system warrant a heightened awareness of the following factors when performing general anesthesia. Difficult

intubation and a need for a range of ETT sizes. 2. Pre-oxygenation is essential due to rapid de-saturation owing to increased O2 consumption and a reduction in FRC. Maintenance of the 'normal' lowered levels of arterial PCO2 during mechanical ventilation.[20]

Table 2

Changes in respiratory mechanics during pregnancy

Parameter	Change during pregnancy
Expiratory reserve volume	↓ 25%
Residual volume	↓ 15%
Functional residual capacity	↓ 20%
Tidal volume	↑ 45%
Inspiratory reserve volume	↑ 5%
Inspiratory capacity	↑ 15%
Vital capacity	No change
Total lung capacity	↓ 5%
FEV_1	No change
FEV_1/FVC	No change
Closing capacity	No change

FEV_1: Forced expiratory volume in 1 s; FVC: Forced vital capacity; ↓:Decreased by; ↑:Increased by

Gastric Function

In the first trimester, hormonal changes may result in 'morning sicknesses. The most extreme form of this is labeled 'hyper-emesis gravidarum' and occasionally warrants admission to the hospital for iv fluid resuscitations. In pregnancy, there is a relaxation of the lower oesophageal sphincter and an increase in intragastric pressure due to the expanding uterus.

As a result of this, the symptoms of heartburn and reflux are common in pregnancy affecting up to 70% of women. There is also an increased risk of gastric regurgitation and aspiration during induction of general anesthesia in the later stages of pregnancy. Pregnancy itself does not prolong gastric emptying time but labor pain and any opioids administered for the pain will do so. Due to the combination of factors above,[21] a rapid sequence induction is considered mandatory when inducing general anesthesia in the third trimester and for 48 hours after delivery.

Musculoskeletal system

The placenta produces relaxin, a hormone that causes widespread relaxation of ligaments. This results in widening and increased mobility of the pubis and sacroiliac joints to allow passage of the fetus through the birth canal. Pain relating to these joints may occur during the

later stages of pregnancy. Due to the enlarging uterus, there is a compensatory increase in the lumbar lordosis.[22]

As a result, backache is a common complaint during pregnancy. Back pain in the post-partum period is also very common and although there is no evidence that epidurals cause it, they are often blamed.

Neurological System

The minimal alveolar concentration (MAC) of volatile anesthetics decreases during pregnancy. This may be secondary to the high levels of progesterone and possibly an increase in B endorphin levels.[23]

There is a similar increase in sensitivity to opioids, sedatives, and local anesthetics. The effects of local anesthetic drugs, when used for neuraxial anesthesia and analgesia, are also enhanced secondary to mechanical factors within the epidural and subarachnoid space. As mentioned earlier, compression of the inferior vena cava results in diversion of blood through the vertebral venous plexus that lies within the epidural space. This causes the epidural veins to engorge and the volume of the epidural and sub-arachnoid space to decrease.[24]

Therefore, an identical volume of local anesthetic will spread more extensively in the pregnant than in the non-pregnant state. Cannulation of an epidural vein when performing epidural insertion (‘a bloody tap’) is also more common. The constituents of cerebral spinal fluid (CSF) do not change during pregnancy but its volume is reduced due to compression from the epidural veins in the epidural space. The pressure of the CSF is therefore increased. Between contractions, the pressure may be around 28 mm Hg but during painful contractions, it may rise to as much as 70mmHg. It is therefore probably safer not to advance an epidural or spinal needle during contractions for risk of puncturing the dura and expulsion of CSF at high pressure.[25]

Changes in the Endocrine System

Thyroid-binding globulin is increased in pregnancy, but free T3 and T4 are normal. Adrenal cortical hyperplasia leads to increases in both free and total cortisol in pregnancy. Fasting blood sugar is lower in pregnant than nonpregnant women, but tolerance to a glucose load may be somewhat impaired due to the actions of placental lactogen, producing a mild

diabetogenic state. Occasionally, this progresses to gestational diabetes. Glucose responses return to normal promptly after delivery of the placenta.[26]

Changes in the Dermatological System

Hyperpigmentation of certain parts of the body such as the face, neck, and midline of the abdomen is not uncommon during pregnancy. Melanocyte-stimulating hormone is responsible for this change.[27]

Changes in Mammary

Tissue Enlargement of the breasts is typical and may complicate the use of a conventional laryngoscope during induction of general anesthesia. A short-handled laryngoscope may facilitate easier instrumentation of the airway.[28]

Changes in the Ocular System

Intraocular pressure has been shown to decrease during pregnancy; this is related to (1) increased progesterone levels, (2) the presence of relaxing, and (3) decreased the production of aqueous humor due to increased secretion of human chorionic gonadotropin. Changes in intraocular pressure in parturients may produce visual disturbances as well as contact lens intolerance.[29]

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