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Maternal Physiological Changes During Pregnancy, Labor, and the Postpartum Period

Parturients undergo remarkable changes during pregnancy, labor, and the immediate postpartum period that can directly affect anesthetic techniques; hence a broad knowledge of these changes is essential for optimum management of these women.

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).[2] 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

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renin–angiotensin–aldosterone, atrial natriuretic peptide, estrogen, progesterone, and nitric oxide may be involved. 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.[3] Alternatively, some have proposed an "overfill" state characterized by an early increase in sodium retention (due to an increase in mineralcorticoids) 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 intervillious 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.

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,[4] 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.[5] 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.[6]

Clinical Implications

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. 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.

Changes in the Cardiovascular System

An increase in cardiac output is one of the most important changes of pregnancy. *Cardiac output increases by 30–40% during pregnancy, and the maximum increase is attained around 24 weeks' gestation.*[7] 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 (Fig. 1-1), leading to an underestimation of cardiac function. Normal pregnant women exhibit a marked increase in femoral venous and inferior vena caval pressures. Collateral vessels maintain atrial filling but lead to engorgement of veins, including the epidural venous (Batson's) plexus.

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 approximately 20%. Blood pressure never increases in normal pregnancy, and systolic and diastolic blood pressures decrease by approximately 8 and 20%, respectively, on average.[9] Pregnancy hormones (estradiol and progesterone), prostacyclin, and nitric

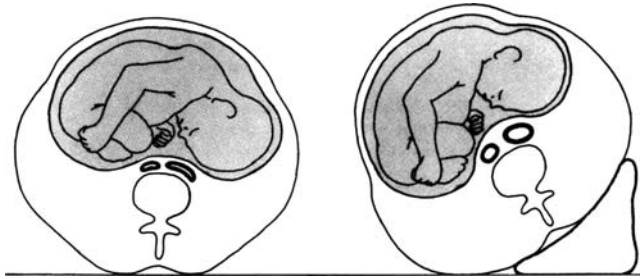

Figure 1–1. Aortocaval compression. (From Chestnut.[8] Used with permission from Elsevier.)

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. 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.[10]

Clinical Implications

An increased cardiac output might not be well tolerated by pregnant women with valvular heart disease (e.g., aortic or mitral stenosis) or coronary arterial disease. *Decompensation in*

myocardial function can develop at 24 weeks' gestation, during labor, and especially immediately after delivery.

Engorgement of the epidural venous plexus increases the risk of intravascular catheter placement in pregnant women; direct connection of the azygos system to the heart as well as brain also increases the risks of local anesthetic cardiovascular and central nervous system toxicity.

Changes in the Respiratory System

Changes in respiratory parameters start as early as the fourth week of gestation. Minute ventilation is increased at term by about 50% above nonpregnant values. The increase in minute ventilation is mainly due to an increase in tidal volume (40%) and, to a lesser extent, an increase in the respiratory rate (15%).[11] Alveolar ventilation is greatly increased as the tidal volume increases without any change in the ratio of dead space to tidal volume (V_D/V_T). At term PCO_2 is decreased to 32–35 mmHg, although renal excretion of bicarbonate keeps arterial pH normal. Increased progesterone concentrations during pregnancy likely stimulate increased respiration, even before an increase in metabolic rate.[12] Oxygen consumption and carbon dioxide production increase by approximately 60% over prepregnant values. PaO_2 is increased in early pregnancy due to a decrease in PCO_2.

Functional residual capacity, expiratory reserve volume, and residual volume are decreased at term (Fig. 1-2). These changes are related to the cephalad displacement of the diaphragm by the large gravid uterus. Inspiratory capacity increases somewhat because of increase in tidal volume and inspiratory reserve volume. Vital capacity is unchanged. Total lung capacity is only slightly reduced because chest circumference increases. Closing capacity (CC) does not change, but the reduction in FRC contributes to a tendency toward earlier desaturation, as lung volume more easily falls below CC.

Anatomic changes also accompany pregnancy. The respiratory mucous membranes become vascular, edematous, and friable. The voice may deepen and there is a progressive increase in the Mallampati score during gestation and labor.[13]

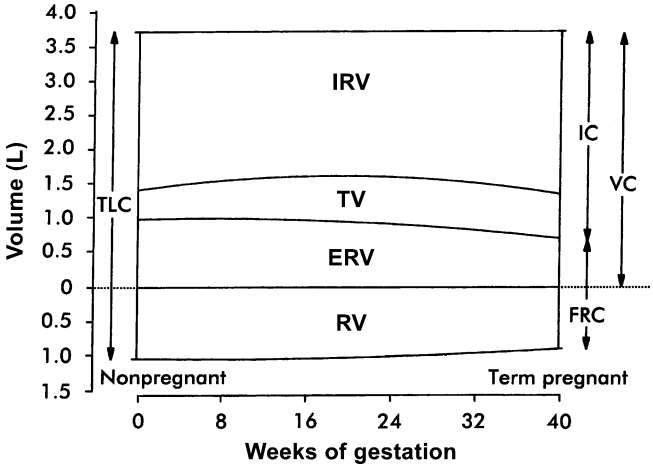

Figure 1–2. Pulmonary volume and capacity changes in pregnancy. (From Chestnut.[8] Used with permission from Elsevier.)

In labor, minute volume further increases in the absence of pain relief, and PCO_2 may decrease to 17 mmHg. Opioids somewhat attenuate this change, but epidural analgesia does so more completely. In the second stage, maternal expulsive efforts increase ventilation, even in the presence of effective regional analgesia.[14,15]

FRC changes return to normal 1–2 weeks postpartum, accompanying the reduction in uterine size. All other respiratory parameters return to nonpregnant values within 6–12 weeks postpartum.

Clinical Implications

Decreased FRC as well as increased oxygen consumption can cause a rapid development of maternal hypoxemia during apnea. Decreased FRC decreases the time for denitrogenation and speeds the uptake of inhaled anesthetics.

Because of the increased edema, vascularity, and friability of the mucous membrane, one should try to avoid nasal

intubation in pregnant women, and smaller endotracheal tubes should be used for oral intubation.

Maternal alkalosis associated with decreased $PaCO_2$ values due to hyperventilation as a result of labor pain can cause fetal acidosis because of (1) decreased uteroplacental perfusion due to uterine vasoconstriction and (2) shifting of the maternal oxygen dissociation curve to the left.

Changes in the Gastrointestinal System

The enlarging uterus displaces and disrupts the lower esophageal sphincter, and progesterone relaxes this high-pressure zone, causing a progressive increase in the incidence of heartburn (up to 80% at term). An increase in gastric pressure due to mechanical compression also contributes to heartburn. Despite the prevalence of this symptom, total acid production is decreased (although placental production of gastrin increases the total concentration of this hormone).

Gastric emptying is normal throughout pregnancy, as measured by acetaminophen absorption, ultrasound, dye-dilution, and radiographic techniques. Intestinal transit time is increased, leading to frequent complaints of constipation in pregnant women. Studies of gastric pH and volume in pregnant and nonpregnant women show no differences in the proportion of women meeting "at risk" criteria (pH <2.5, volume >25 ml[16]) for pulmonary aspiration of gastric contents.[8]

Labor fundamentally alters this pattern. Gastric emptying time is significantly slower during labor and hence gastric volume is increased. Opioids administered by any route will further increase the gastric emptying time. Studies demonstrate solid food in the stomachs of laboring women even after 18 h of fasting.[17] Gastric emptying remains abnormal on the first postpartum day but returns to normal on the second day.

Hepatic transaminases, bilirubin, and LDH are increased slightly in pregnancy. Alkaline phosphatase is markedly increased (2–4 fold), but due to placental production, not hepatic changes. *Serum cholinesterase activity is reduced 24% before delivery and reaches a nadir (33% reduction) on the third postpartum day*[14] (Fig. 1-3). Approximately 11% of post-

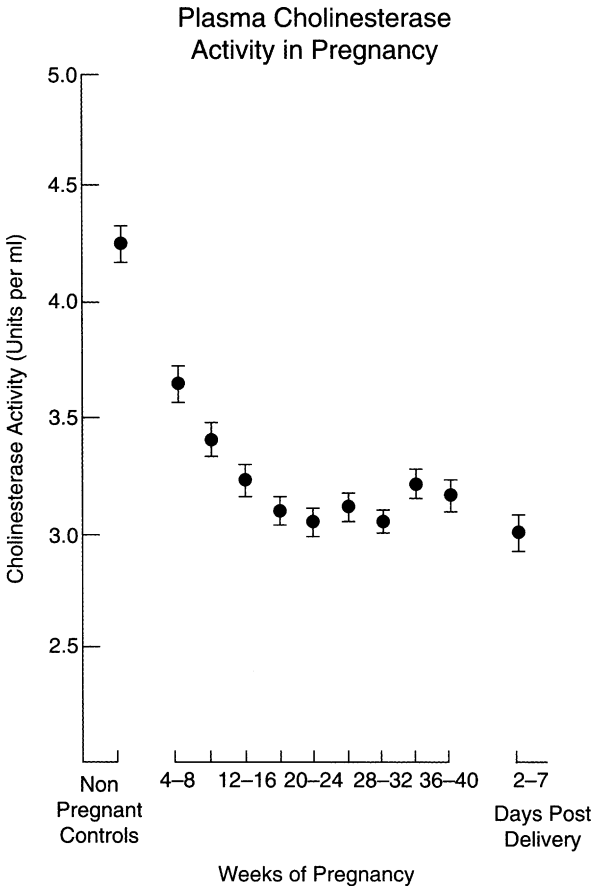

Figure 1–3. Plasma cholinesterase activity in pregnancy. (From Cohen.[18] Used with permission from Elsevier.)

partum women exhibit clinically deficient activity, manifest as an exaggerated response to normal doses of succinylcholine. *Even with this lower activity, normal dosing of succinylcholine for intubation is recommended when general anesthesia is required, though use of a peripheral nerve stimulator seems prudent.*

Gallbladder function and emptying are impaired during pregnancy, and there is evidence that pregnant women may be more prone to gallstones.

Clinical Implications

Pregnant women *in labor* should always be considered to have a full stomach irrespective of the time of their last meal. General anesthesia should be avoided when possible, and routine precautions (rapid sequence induction and endotracheal intubation) should be employed when general anesthesia is unavoidable. The routine use of nonparticulate antacid is important before cesarean section and before induction of regional anesthesia, and one should allow for proper mixing of the antacid and stomach contents. Pregnant women who are not in labor and who do not have other risk factors for aspiration may not require such treatment.

Changes in the Renal System

The glomerular filtration rate is increased during pregnancy because of increased renal plasma flow.[19] A rise in the filtration rate decreases plasma blood urea nitrogen (BUN) and creatinine concentrations by about 40–50%, to approximately 8–9 mg/dL and 0.5–0.6 mg/dL, respectively. Tubular reabsorption of sodium is increased. However, glucose and amino acids might not be absorbed as efficiently; hence glycosuria (up to 300 mg/day) and aminoaciduria may develop in normal gestation. The renal pelvis and ureters are dilated, and peristalsis is decreased. Physiological diuresis during the postpartum period occurs between the second and fifth days. The glomerular filtration rate and BUN concentration slowly return to nonpregnant values by the sixth postpartum week.

Clinical Implications

Normal nonpregnant values of BUN and Cr in parturients suggest abnormal kidney function.

Changes in the Central and Peripheral Nervous Systems

The central and peripheral nervous systems undergo significant changes during pregnancy. MAC is decreased by 25–40% during pregnancy.[20] Increased progesterone and endorphin concentrations during pregnancy have been implicated as a cause of this change. However, a few studies have shown that endorphin concentrations do not increase until the onset of active labor,[21] so this cannot explain early decreases in MAC. By injecting exogenous progesterone in oophorectomized rabbits, a decrease in MAC was observed when compared with control animals.[22]

A wider dermatomal spread of sensory anesthesia was observed in parturients following the use of epidural anesthesia as compared with nonpregnant age-matched controls.[23] The difference was explained by a reduction in epidural space volume caused by an engorged epidural venous plexus due to aortocaval compression. However, a subsequent report showed that this difference exists even during early pregnancy (8–12 weeks) when one might not expect any mechanical obstruction by the small gravid uterus,[24] and epidural venous engorgement later in pregnancy appears to reduce CSF volume, not epidural extravascular volume. The factors suggested were (1) compensated respiratory alkalosis of pregnancy, (2) reduced plasma and cerebrospinal fluid (CSF) protein levels during pregnancy, leading to increased free local anesthetic, and (3) pregnancy hormones. The latter is the most likely explanation, based on animal studies. An increased sensitivity to bupivacaine in isolated nerve fibers has been demonstrated (Fig. 1-4).[25]

It is possible that progesterone or one of its active metabolites is responsible for the observed increased sensitivity of the peripheral nervous system to anesthetics in parturients. This increased sensitivity was also observed in nerves from oophorectomized rabbits treated chronically with exogenous progesterone.[26] Interestingly, this phenomenon was not observed following acute exposure to progesterone.[27] In humans, enhanced sensitivity of peripheral nerves to local anesthetic has also been documented.[28]

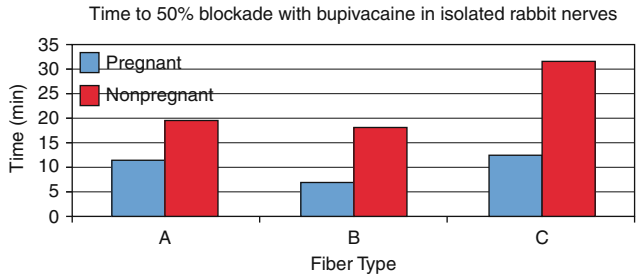

Figure 1–4. Increased sensitivity in nerves in pregnant vs. nonpregnant rabbits. (Data from Datta et al.[25])

Clinical Implications

Even though the exact mechanism of the increased sensitivity of the central nervous system and peripheral nervous system to general and local anesthetics is not known, in general, it is prudent to reduce the dose of anesthetics in pregnant women, at least on initial dosing.

Because of a paucity of data and uncertainty regarding the actual mechanisms underlying enhanced local anesthetic sensitivity in pregnancy, it is not known when these changes revert to their nonpregnant state. Spinal anesthetic sensitivity appears normal 24–48 h postpartum.

Changes in the Endocrine System

Thyroid-binding globulin is increased in pregnancy, but free T_3 and T_4 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.

Changes in the Musculoskeletal System

The hormone relaxin is responsible for both the generalized ligamentous relaxation and the softening of collagenous tissues. The lumbar spine demonstrates exaggerated lordosis, possibly complicating regional anesthesia. Stretching of the lateral femoral cutaneous nerve can occur, leading to sensory loss in the lateral thigh (meralgia paresthetica). This must be differentiated from neural injury due to childbirth or anesthesia. In addition, back pain frequently accompanies late pregnancy, and pregnant women must be counseled against relating this to regional anesthesia.

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.

Changes in Mammary Tissue

Enlargement of the breasts is typical and may complicate use of a conventional laryngoscope during induction of general anesthesia. A short-handled laryngoscope may facilitate easier instrumentation of the airway.[29]

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 relaxin, and (3) decreased 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.

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