Physiologic Changes During Normal Pregnancy and Delivery

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KEYWORDS
- Pregnancy • Physiology • Hemodynamic changes • Cardiocirculatory • Labor and delivery

KEY POINTS
- The major adaptations of the maternal cardiovascular system that progress throughout gestation may unmask previously unrecognized heart disease and result in significant morbidity and mortality.
- Most of these changes are almost fully reversed in the weeks and months after delivery.
- Hemodynamic changes during pregnancy include increased blood volume, cardiac output (CO), and maternal heart rate; decreased arterial blood pressure; decreased systemic vascular resistance.
- CO increases up to 30% in the first stage of labor, primarily because of increased stroke volume; maternal pushing efforts in the second stage of labor can increase CO by as much as 50%.

INTRODUCTION
Soon after conception, the maternal cardiovascular system undergoes major adaptations that progress throughout gestation. In conjunction with the increased circulatory burden of pregnancy, these changes may unmask previously unrecognized heart disease and result in significant morbidity and mortality. Most of these changes are almost fully reversed in the weeks and months after delivery.

HEMODYNAMIC CHANGES DURING PREGNANCY

Blood Volume
Blood volume increases significantly during pregnancy. The increase starts at around 6 weeks’ gestation and reaches a maximal volume of 4700 to 5200 mL by 32 weeks’ gestation. A rapid increase is typically noted until midpregnancy, with a slower increase thereafter (Fig. 1). Overall, a continuous blood volume increase of about 45% (1200–1600 mL), or a mean recorded blood volume ranging from 73 to 96 mL/kg greater than nonpregnant values is typical. In addition to blood volume expansion, there is redistribution of fluid during pregnancy. Studies of pregnant women in their third trimester have shown increases of interstitial and plasma volume, with more extracellular fluid volume in the intravascular space in pregnant versus nonpregnant women. In twins, the increase in blood volume after 20 weeks parallels that in singletons, but at a 20% higher volume (Fig. 2).

This increase in blood volume during pregnancy has important clinical implications. Normal fetal growth and birthweight are directly correlated with the degree of plasma volume expansion. In contrast, pathologic conditions like intrauterine growth restriction and small for gestational age newborns, as well as preeclampsia, have been...
associated with reduced blood volume expansion. In cases of concomitant maternal cardiac disease, rapid decompensation may result. An accumulation of approximately 900 mmol of sodium is seen in normal pregnancy, which leads to water accumulation.

Additional changes include increased production of red blood cells leading to a significant increase of 17% to 40% (250 mL–450 mL) in red blood cell mass. Progesterone, placental chorionic somatomammotropin, and perhaps prolactin are responsible for the increased erythropoiesis. The increased production, in turn, increases maternal demand for iron by 500 mg during pregnancy. In addition, increased pregnancy levels of 2,3-diphosphoglycerate lead to enhanced fetal oxygen transfer. Despite the increase in red cell mass, plasma volume increases are greater and more rapid, such that hemoglobin concentrations decrease during pregnancy. This phenomenon has been called the physiologic anemia of pregnancy. Hemoglobin and hematocrit levels can be as low as 11 to 12 g/dL and 33% to 38%, respectively. Oral iron supplementation helps mitigate this decrease in maternal hemoglobin.

Mechanisms of hypervolemia in pregnancy
Although sodium and water retention physiologically protect a pregnant woman from potential hemodynamic instability caused by blood loss at delivery, the specific mechanisms responsible for the hypervolemia remain unclear. Many different factors, including steroid hormones and nitric oxide, act simultaneously to alter maternal fluid balance and increase plasma volume.

Estrogen promotes sodium retention both by direct renal action and by increased hepatic production of angiotensinogen (renin substrate). Estrogen stimulates increased renal renin production, in addition to production in the uterus and liver. Increased renin stimulates aldosterone secretion, which in turn increases total body water.

Other hormones responsible for increased total body water include deoxycorticosterone, prostaglandins, prolactin, placental lactogen, growth hormone, and adrenocorticotropic hormone. Increased ureteral pressure secondary to mechanical obstruction may also contribute to sodium retention. However, a fetus is not essential for the development of hypervolemia. A 50% increase in volume has been reported in patients with hydatidiform moles.

Atrial natriuretic peptide and brain natriuretic peptide
Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) are peptide hormones that play important roles in volume homeostasis during pregnancy. ANP is released primarily by the atria in response to atrial stretching from volume expansion. ANP is a peripheral vasodilator and a diuretic hormone. Genetically altered mice lacking the ANP-receptor show chronically increased plasma volume, hypertension, and cardiac hypertrophy. In early pregnancy, volume expansion contributes to increased ANP release, increased stroke volume, and peripheral vasodilation. ANP levels increase throughout pregnancy and increase further after delivery, implicating its role in postpartum diuresis. Patients with preeclampsia have relative volume depletion and endothelial
cell injury, but ANP levels are higher than in women without pre eclampsia. This finding suggests that the hemodynamic changes with pre eclampsia are more complex. In pre eclamptic women, the degree of ANP and BNP increase has been correlated with the severity of maternal left ventricular dysfunction.

BNP is a peptide similar to ANP and is produced by the cardiac ventricles. Its actions are similar to those of ANP in that it leads to decreased systemic vascular resistance and increased diuresis, thereby increasing cardiac output (CO). In addition to its role in the complex milieu of maternal fluid homeostasis, a link between BNP and myometrial quiescence has also been shown. At least 2 reports have found production of BNP in chorionic membranes with measurable levels in amniotic fluid. Furthermore, BNP was shown to inhibit contractions in preterm (but not term) human myometrium, thereby implicating a broader role for the peptide that extends beyond the mitigation of volume expansion.

**CO**

CO is calculated as the product of stroke volume and heart rate (HR), and can be considered a measure of the functional capacity of the heart. Numerous studies have shown that CO increases as much as 50% in pregnancy. CO begins to increase during the first trimester, and peaks between 25 and 35 weeks’ gestation. The increase in CO early in pregnancy is mostly caused by stroke volume. As pregnancy advances, HR increases and becomes a more dominant factor in increasing CO. Stroke volume increases gradually until the end of the second trimester and then remains constant.

CO fluctuates with changes in maternal position. Compression of the inferior vena cava by the enlarged gravid uterus in the supine position results in decreased venous return to the heart and significant decrease in CO. Evaluation of hemodynamic changes in twin gestations shows a significantly greater increase in CO compared with singletons (approximately 15% at 24 weeks).

**Techniques to measure CO in pregnancy**

CO may be calculated by invasive heart catheterization using the Fick method, dye dilution, or thermodilution, or noninvasively with thoracic electric bioimpedance (impedance cardiography) and echocardiography. Although assessment of CO by thermodilution remains the gold standard, the technique requires insertion of a pulmonary artery catheter, which precludes its use in most pregnant patients. More recently, M-mode echocardiography and Doppler studies have been shown to correlate well with thermodilution, and are frequently used to assess CO during pregnancy.

**HR**

Maternal HR increases as early as 5 weeks’ gestation to a maximal increase of 15 to 20 beats per minute at by 32 weeks’ gestation (Figs. 5 and 6, Table 1). The magnitude of the increase is greater in twin gestations. Maternal HR decreases slightly with a change from the supine to the left lateral position. Note that the increase in HR is gradual with a peak at the third trimester such that maternal tachycardia is primarily responsible for maintaining CO late in pregnancy.

**Blood Pressure**

Arterial blood pressure (BP) decreases as early as 7 weeks’ gestation. The decrease in BP reaches a nadir by midpregnancy, when the BP starts a gradual increase, returning to or exceeding prepregnancy levels by term (see Fig. 5, Table 1). Several issues related to BP during pregnancy are important. First, reliable measurement of diastolic pressure has been complicated by the absence of a fifth Korotkoff sound in some women. This absence may be related to the hyperdynamic state of maternal circulation, which may cause the fifth Korotkoff sound to be heard even after...
complete deflation of the cuff. However, the fifth Korotkoff sound can be heard in most pregnant women and is more accurate than the fourth sound, compared with results obtained from invasive BP measurements. The diastolic BP measured with the use of the fourth sound is 5 to 13 mm Hg higher than that measured using the fifth sound and may lead to an erroneous conclusion. The use of the fifth sound is therefore recommended for the measurement of diastolic BP during gestation. The use of automated cuff measurement of BP may avoid many operator-dependent biases associated with measurement of BP by auscultation. A second important issue is the patient’s position, which may greatly influence levels of recorded BP during pregnancy. In general, BPs, both systolic and diastolic, are approximately 16 mm Hg higher in the sitting position than in the recumbent position. After midpregnancy, because of potential vena caval occlusion in the recumbent position, BP may be measured in the lateral position. In either case, consistency in position during successive BP measurements is critical for accurate determination of BP trends. Both increasing maternal age and parity seem to be associated with higher systolic and diastolic BPs during pregnancy.

Chronic hypertension in pregnancy is defined as a maternal BP greater than or equal to 140/90 mm Hg diagnosed before 20 weeks’ gestation. A decrease in CO caused by a change in posture is typically followed by a compensatory increase in

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**Fig. 4.** Venocaval compression of the inferior vena cava and abdominal aorta by the gravid uterus can lead to reduced venous return and thus to decreased CO. (From Elkayam U, Gleicher N. Diagnosis and management of maternal and fetal heart disease, 3rd Edition. 1998; New York, Wiley-Liss; with permission.)

**Fig. 5.** Potential mechanisms of hypervolemia during pregnancy.

**Fig. 6.** Alteration in stroke volume and HR during pregnancy. Stroke volume increases during the first half of gestation, with a slight decrease thereafter until term. A mild increase in HR begins in early pregnancy continues until term. (Adapted from Robson SC, Hunter S, Boys RJ, et al. Serial study of factors influencing changes in cardiac output during human pregnancy. Am J Physiol 1989;256:H1060; with permission.)
peripheral resistance, with no overall significant change in systemic BP or HR. However, a significant increase in HR with a decrease in BP is sometimes noted, resulting in symptoms such as weakness, lightheadedness, nausea, dizziness, and even syncope. This phenomenon occurs in 0.5% to 11.2% of pregnancies, and is described as the supine hypotensive syndrome of pregnancy. Symptoms usually resolve quickly with appropriate maternal positioning.

Systemic Vascular Resistance

A significant decrease in systemic vascular resistance (SVR) occurs during pregnancy (see Table 1), with concomitant decrease in BP (primarily the diastolic component) and a widened pulse pressure. These changes begin as early as 5 weeks’ gestation, and result from a variety of factors including the vasodilatory effects of progesterone and prostaglandin, as well as the contribution of the low-resistance flow of the uteroplacental unit. An approximate 10% decrease in SVR has been shown to occur in the first trimester, with a nadir of about 35% less than baseline at 20 weeks’ gestation. Thereafter, SVR remains constant until around 32 weeks, with a small increase noted from week 32 to term. As SVR decreases, vascular compliance increases.

Differing mechanisms related to the decreased SVR in pregnancy have been studied. Estrogen, progesterone, prostaglandins, and prolactin play a role in SVR reduction. Furthermore, prostacyclin attenuates the vasoconstrictor effect of angiotensin II described during pregnancy. Resistance to the pressor effect of angiotensin and noradrenaline may also contribute to a decreased SVR.

Recent evidence suggests that nitric oxide (NO) may also be related to gestational vasodilation. Nitric oxide is produced from L-arginine and is a potent endothelium-derived relaxing factor. Increased production of NO in pregnancy acts to maintain vascular relaxation, in part to counteract the vasoconstrictive effects of thromboxane. NO targets guanylate cyclase, leading to increased formation of cyclic guanosine monophosphate (cGMP). The cGMP, in turn, helps maintain dephosphorylated myosin light chains, thus causing relaxed vascular smooth muscle. Doppler studies in pregnant women treated with NO donors showed decreased peripheral resistance and pulsatility indices in women treated with glyceryl trinitrate. Similar results were shown in a study of isosorbide dinitrate infusion in the second trimester. Thus, it seems that NO plays a key role in maternal vascular dynamics and SVR.

Another important hormone in the regulation of SVR in pregnancy is relaxin. Relaxin is a heterodimer of 2 peptide chains, with peak levels in the first trimester and at delivery. In addition to its effects on SVR, in pregnant women relaxin contributes to changes in connective tissue composition, myometrial activity, and labor. Relaxin causes reduced arterial load by decreasing SVR and reduced plasma osmolality. The net effect is an increase in CO. Recent reports have shown relaxin expression in myocardial muscle, where its production attenuates endothelial-derived vasoconstrictors. Thus, relaxin is essential for SVR and osmoregulatory changes in early and mid-pregnancy and likely plays a role in the transition of the maternal cardiovascular system from the nonpregnant to the pregnant state. At term, relaxin helps soften the maternal pubic symphysis to help facilitate delivery.

### Table 1
Circulatory changes during normal pregnancy

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Changes at Various Times (wk)</th>
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<tr>
<td></td>
<td>5</td>
</tr>
<tr>
<td>HR</td>
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<tr>
<td>Systolic blood pressure</td>
<td>↔</td>
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<tr>
<td>Diastolic blood pressure</td>
<td>↔</td>
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<tr>
<td>Stroke volume</td>
<td>↑</td>
</tr>
<tr>
<td>CO</td>
<td>↑</td>
</tr>
<tr>
<td>Systemic vascular resistance</td>
<td>↓</td>
</tr>
<tr>
<td>Left ventricular ejection fraction</td>
<td>↑</td>
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</tbody>
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↑, ≤5%; ↑↑, 6–10%; ↑↑↑, 11–15%; ↑↑↑↑, 16–20%; ↑↑↑↑↑, 21–30%; ↑↑↑↑↑↑, >30%; ↑↑↑↑↑↑↑, >40%.

Effect of the Gravid Uterus on the Circulation

The gravid uterus causes femoral vein and inferior vena caval obstruction in up to 90% of women. These effects can be relieved with a lateral recumbent position (see Fig. 4). In addition, paravertebral and collateral circulation facilitate venous return from the legs and the pelvic organs limited by a compressed inferior vena cava. Various studies have shown that the enlarged uterus also compresses the arterial system. Angiography has shown compression and reduced flow in the aorta and iliac vessels and other smaller vessels (right renal artery, ovarian artery, lumbar artery).

Other Changes in Blood Flow

Along with the changes described earlier for maternal BP, CO, and HR, many other organs have changes in blood flow during normal pregnancy. These changes are summarized in Table 2. The effect of pregnancy on coronary blood flow is still unknown. However, an increase caused by the augmentation in CO is likely.

Oxygen Consumption

Oxygen consumption, commonly estimated by measurement of oxygen extracted by the lungs over a given time period, reflects the rate of the body’s metabolism. In pregnancy, there is a progressive increase in resting oxygen consumption, with a peak increase of 20% to 30% near term. However, in early gestation, there is a rapid increase in CO that is proportionally greater than the increase in oxygen consumption to ensure a well-oxygenated blood supply during organogenesis.

The continuous increase in oxygen consumption in the later phases of pregnancy, when CO increase is slow and small, results in a widening of the arterial venous oxygen difference to nonpregnant levels. The arterial venous oxygen difference is, therefore, small in early pregnancy, increases gradually throughout pregnancy, and reaches nonpregnant levels in the later part of gestation.

Functional and Anatomic Cardiac Changes During Pregnancy

Ventricular wall muscle mass and end-diastolic volume increase in pregnancy, although end-systolic volume and end-diastolic pressure remain unchanged. Because this increases cardiac compliance, a physiologically dilated maternal heart results, without a decrease in ejection fraction (see Table 1). Using invasive hemodynamic monitoring with a pulmonary artery catheter at 36 to 38 weeks of gestation, no difference was shown in the level of left ventricular filling pressure and left ventricular stroke work index compared with 11 to 13 weeks postpartum.

Overall, left ventricular systolic function improves early in pregnancy and progresses gradually until 20 weeks’ gestation. Because left ventricular systolic function directly correlates with changes in SVR, improvement in systolic function is most likely caused by left ventricular afterload reduction.

CARDIOCIRCULATORY CHANGES DURING LABOR AND DELIVERY

Women with cardiac disease require close monitoring during labor and delivery. Uterine contractions alone can transfer 300 to 500 mL of blood from the uterus to the general circulation and lead to significant circulatory stress.

Effects on CO

CO increases up to 30% in the first stage of labor primarily because of increased stroke volume. Maternal pushing efforts in the second stage of labor can increase CO by as

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Changes in regional blood flow during normal pregnancy</th>
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<tbody>
<tr>
<td>Organ</td>
<td>Change</td>
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<td>Uterus</td>
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<tr>
<td>Kidneys</td>
<td>Increased</td>
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<td>Liver</td>
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<td>Brain</td>
<td>Unchanged</td>
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<tr>
<td>Breast</td>
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Abbreviation: GFR, glomerular filtration rate.
much as 50%. Laboring in the left lateral decubitus position or with epidural anesthesia reduces, but does not eliminate, this increase.\textsuperscript{166,167}

Compression of the uterus with contractions results in an increase in circulating blood volume and venous return to the heart, with concomitant increase in stroke volume. Pulmonary arterial venous oxygen difference also increases with contractions, corroborating a flow of blood from the maternal uterine vascular bed into the systemic circulation.\textsuperscript{168} Pain and anxiety leads to increased sympathetic tone with increased BP and HR, which also contributes to the increased CO.\textsuperscript{161,163}

### Effects on Maternal HR

In contrast with CO, the effects of contractions on maternal HR seem to be more variable. The observed differences in reported HR responses to uterine contractions relate to differences in maternal position and pain control during labor, as well as individual variation.\textsuperscript{163,165–172}

### Effects on Maternal BP

Both systolic and diastolic BPs increase with uterine contractions,\textsuperscript{161–165,173,174} and this increase seems to precede a contraction by up to 8 seconds. The maximal increase occurs in the second stage of labor. Because peripheral resistance changes only slightly during labor, the increase in BP is attributed to increased CO.\textsuperscript{163} As expected, the hemodynamic effects of uterine contractions are less pronounced in the left lateral recumbent position.\textsuperscript{171} Oxygen consumption increases about 3-fold during uterine contractions, with its mean value increasing gradually to levels 100% higher than those before labor.\textsuperscript{175,176}

### Effects of Maternal Anesthesia

With local anesthesia, tachycardia may develop during the second stage of labor, which can be additive to the effect of uterine contractions. Both the systolic and diastolic BPs show a mild gradual increase during the first stage of labor and a significant increase during the second stage. These changes are associated with a progressive increase in stroke volume toward a peak immediately following delivery. In contrast, regional anesthesia is not associated with a significant change in HR or BP. Many patients with regional anesthesia have transient hypotension early on, which can be mitigated with preinduction volume load. Unlike local anesthesia, stroke volume with regional anesthesia remains constant throughout labor but increases rapidly after delivery. Mean blood loss does not seem to be affected by type of anesthesia at delivery.\textsuperscript{164}

In patients with underlying cardiac disease, anesthesia during labor and delivery can pose unique challenges. Continuous lumbar epidural anesthesia with or without local anesthetics or narcotics, is frequently optimal. Limited sympathetic blockade and its effects on preload and afterload can be helpful in patients with mitral valve lesions. In patients with more complex lesions, anesthesia options must be considered on a case-by-case basis using a multidisciplinary approach.

### HEMODYNAMIC EFFECTS OF CESAREAN SECTION

Transient maternal hypotension can occur in up to 30% of women undergoing regional anesthesia for cesarean section,\textsuperscript{74} but most women undergoing cesarean section under epidural anesthesia remain stable hemodynamically. BP typically declines moderately after anesthesia induction, but then remains constant. In addition, HR, CO, and stroke volume remain constant. Following delivery, CO increases about 25% more than baseline, with a stable HR. In contrast, cesarean section under spinal anesthesia is associated with significant cardiovascular changes and should be used with extreme caution in patients with heart disease.\textsuperscript{177–180}

Hemodynamic fluctuations during cesarean section were less with thiopental, nitrous oxide, and succinylcholine anesthesia.\textsuperscript{178} Thus, balanced anesthesia with thiopental, nitrous oxide, and succinylcholine, or epidural anesthesia without epinephrine, are preferred in patients with limited cardiac reserves.

### HEMODYNAMIC CHANGES POSTPARTUM

A 60% to 80% increase in CO occurs immediately after delivery, followed by a rapid decrease within 10 minutes to values approaching normal 1 hour postpartum. In addition, SVR decreases.\textsuperscript{163,164,178,181,182} This high output state is likely caused by the transfer of blood from the uterus into the systemic circulation (autotransfusion) in conjunction with improved venous return caused by decreased vena caval compression and the rapid mobilization of extracellular fluid. Placental separation in the third stage of labor does not seem to cause any further hemodynamic changes. These changes are summarized in Fig. 7.

Even though childbirth can result in a mean blood loss of 1000 mL or more, patients are protected by the significant blood volume expansion.
during pregnancy. In women with postpartum hemorrhage, stroke volume decreases and HR increases, whereas BP and CO remain stable.\textsuperscript{183} Equally important, levels of ANP and BNP increase postpartum. Both ANP and BNP have potent diuretic effects, and help mediate the diuresis noted in the early postpartum period.\textsuperscript{184}

**REFERENCES**

Hemodynamics and Pregnancy


