Respiratory Physiology in Pregnancy

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This review discusses respiratory physiologic changes during normal pregnancy. Cardiovascular physiology is also reviewed, given the important interactions between the respiratory and cardiovascular systems in pregnancy. The combination of hormonal changes, mechanical effects of the enlarging uterus, and marked circulatory changes result in significant changes in pulmonary and cardiovascular physiology. These adaptations are necessary to meet the increased metabolic demands of the mother and fetus. It is important for the clinician to be familiar with the normal physiologic changes in pregnancy. Understanding these changes is critical in distinguishing the common dyspnea that occurs during normal pregnancy from pathophysiologic states associated with cardiopulmonary diseases seen in pregnancy,[1] and in anticipating disease worsening in pregnancy and the peripartum period in those women with cardiopulmonary disorders.

UPPER AIRWAY CHANGES IN PREGNANCY

There are significant changes to the mucosa of the nasopharynx and oropharynx during pregnancy. The mucosal changes in the upper airway include hyperemia, edema, leakage of plasma into the stroma, glandular hypersecretion, increased phagocytic activity, and increased mucopolysaccharide content.[2,3] All of these result in nasal congestion often called rhinitis of pregnancy. The clinical definition of rhinitis of pregnancy is "nasal congestion present during the last 6 or more weeks of pregnancy without other signs of respiratory tract infection and with no known allergic cause, disappearing completely within 2 weeks after delivery."[2] The incidence of rhinitis of pregnancy has been reported to be between 18% and 42%.[4–6] Nasal congestion is often noted early in the first trimester, peaks late in pregnancy, and disappears within 48 hours of delivery.[2,4] The etiology of rhinitis of pregnancy is not clear,[2] though increased blood volume and hormonal factors likely play a role. Blood volume changes are discussed later. Hormonal factors include estrogen and placental growth hormone. Nasal mucosal biopsies obtained during pregnancy and from women taking oral contraceptive medications have implicated estrogen as a cause.[3] However, other factors are likely involved, as estrogen levels are not higher in women who have rhinitis of pregnancy than in women who do not.[7] Placental growth hormone may contribute to rhinitis of pregnancy, as levels are significantly higher in patients with the syndrome.[2] Nonhormonal factors implicated in nasal congestion in pregnancy include smoking, nasal allergy, infections, and chronic use of topical vasoconstrictor medication.

Rhinitis of pregnancy has the potential to contribute to maternal-fetal complications. Nasal obstruction contributes to snoring and sleep-disordered breathing, both of which are associated with hypertension and preeclampsia and may

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contribute to intrauterine growth retardation, although the relationship between sleep-disordered breathing and intrauterine growth retardation is controversial.[2,8] Nasal congestion and resultant mouth breathing reduces concentrations of inhaled nitric oxide, primarily produced in the maxillary sinuses.[9] Nitric oxide is a potent mediator of pulmonary vascular tone, and reduced nitric oxide may contribute to the complications associated with snoring. The upper airway congestion and obstruction common in pregnancy may adversely affect the ability of air to pass through nasal and oral tubes.

Mallampati score, a common predictor of airway patency, has been shown to increase during the course of pregnancy.[10] Neck circumference has also been found to be increased with pregnancy,[11,12] and decreases in the postpartum period.[11]

Using acoustic reflectance measurements, oropharyngeal junction size is smaller in the seated position, and mean pharyngeal cross-sectional area is smaller in the supine, lateral, and seated position in pregnant women compared with nonpregnant controls.[11] In addition, there was a much larger drop in the size of the upper airway on laying down in pregnant women in their third trimester compared with nonpregnant controls in one study[13] but not in another.[11] Factors potentially affecting airway collapsibility in these patients include reduced lung volumes—leading to less caudal traction on the upper airway[14]—and fat infiltration of the upper airway. Functional residual capacity is reduced in pregnancy in the upright position with an additional reduction occurring in the supine position. Pregnant women may gain an average of 25 to 35 pounds (11–16 kg) during the course of pregnancy. However, in the study by Iczi and colleagues,[13] the drop in airway size between the seated and the supine position in the pregnant group did not appear to be related to body mass index, suggesting that other factors such as changes in functional residual capacity or changes in the upper airway related to interstitial fluid may play a role. Mean pharyngeal cross-sectional area increases significantly postpartum compared with intrapartum,[11] but it is not clear when or whether these changes return to preconception size. The measurements discussed here may be even more pronounced during sleep, with the loss of upper airway muscle dilation, but this theory needs to be tested further.

CHEST WALL CHANGES IN PREGNANCY

The thorax undergoes significant structural changes in pregnancy: The subcostal angle of the rib cage and the circumference of the lower chest wall increase and the diaphragm moves up.[15–18] These changes are necessary to accommodate the enlarging uterus and increasing maternal weight, but the changes occur early in pregnancy before the uterus is significantly enlarged.[15,18] Hormonal changes rather than the mechanical effects of the enlarging uterus cause relaxation of the ligamentous attachments of the lower ribs. Relaxin, the hormone responsible for relaxation of the pelvic ligaments, likely also causes relaxation of the lower rib-cage ligaments.[19] The subcostal angle progressively widens from 68.5° to 103.5° during pregnancy.[18] The anterior-posterior and transverse diameters of the chest wall each increase by 2 cm, resulting in an increase of 5 to 7 cm in the circumference of the lower rib cage. The anatomic changes of the chest wall peak at week 37. The chest wall configuration normalizes by 24 weeks postpartum but the subcostal angle remains about 20% wider than the baseline value.[15] The enlarging uterus causes the diaphragm to be displaced cephalad 4 cm in late pregnancy, but the increase in chest wall size mitigates any changes in lung volumes caused by the upward displacement of the diaphragm. The anatomic changes of the thorax with pregnancy are illustrated in **Fig. 1**.

RESPIRATORY MUSCLE FUNCTION

There is no significant change in respiratory muscle strength during pregnancy despite the cephalad displacement of the diaphragm and changes in the chest wall configuration. Maximal inspiratory and expiratory mouth pressures and maximum transdiaphragmatic pressure, measured as gastric pressure minus esophageal pressure, in late pregnancy and after delivery show no significant changes.[15,20] Despite the upward displacement of the diaphragm by the gravid uterus, diaphragm excursion actually increases by 2 cm compared with the nonpregnant state.[18,20] Increased diaphragmatic excursion and preserved respiratory muscle strength are important adaptations, given the increase in tidal volume and minute ventilation that accompanies pregnancy. Improved diaphragm mechanics in pregnancy are explained by an increased area of apposition of the diaphragm to the rib cage.[20]

LUNG FUNCTION IN PREGNANCY
Static Lung Function

Static lung function stays the same in pregnancy except for decreases in functional residual capacity (FRC) and its components: expiratory reserve volume (ERV) and residual volume (RV). FRC depends on 2 opposing forces: the elastic recoil of the lungs and the outward and downward
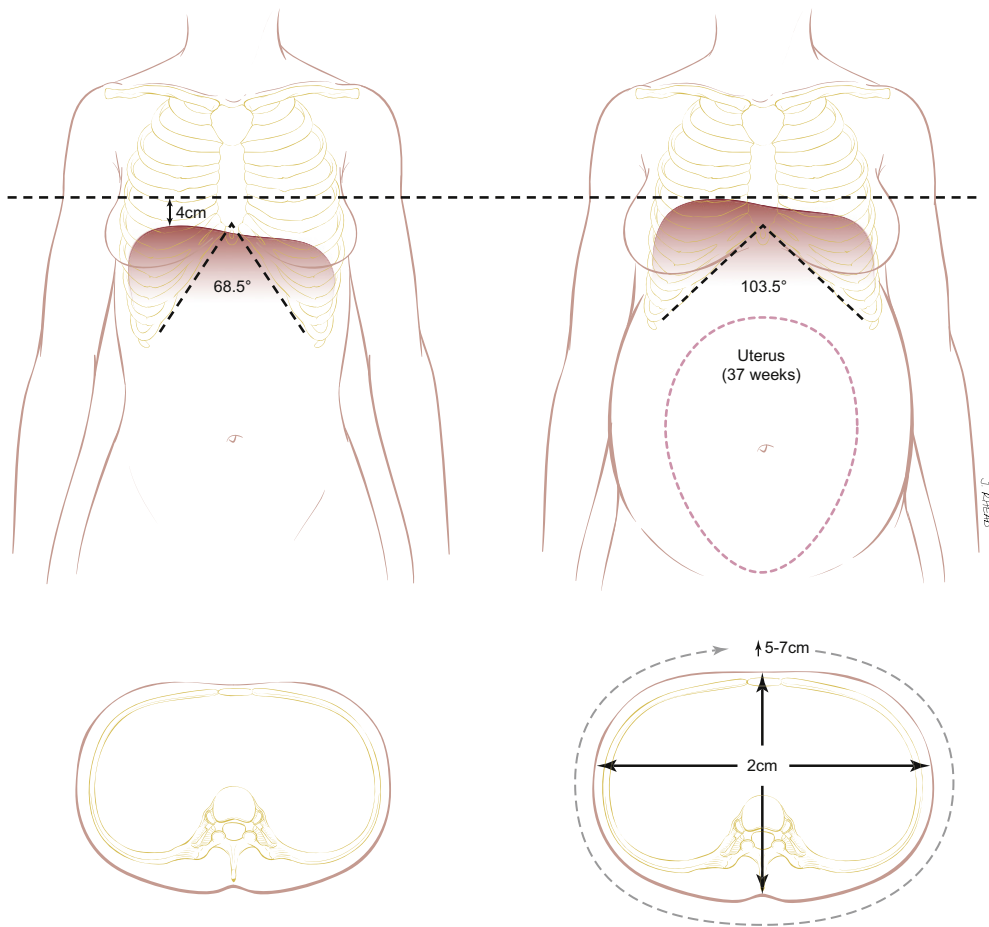
Fig. 1. Chest wall changes that occur during pregnancy. The subcostal angle increases, as does the anterior-posterior and transverse diameters of the chest wall and the chest wall circumference. These changes compensate for the 4-cm elevation of the diaphragm so that total lung capacity is not significantly reduced.

pull of the chest wall and abdominal contents. A reduction in FRC in pregnancy is expected given the 4-cm elevation of the diaphragm, decreased downward pull of the abdomen, and changes in chest wall configuration that decrease outward recoil.[17] As anticipated, chest wall compliance is decreased antepartum compared with postpartum.[21] Lung compliance is unaffected by pregnancy.[21,22]

Several studies have measured serial static lung volumes during pregnancy and after delivery.[23–27] The changes in lung function in pregnancy are illustrated in **Fig. 2**. FRC decreases by approximately 20% to 30% or 400 to 700 mL during pregnancy. FRC is composed of ERV, which decreases 15% to 20% or 200 to 300 mL, and RV, which decreases 20% to 25% or 200 to 400 mL. Significant reductions in FRC are noted at 6 months' gestation with a progressive decline as pregnancy continues.[23,28] At term, there is a further 25%

decrease in FRC in the supine position compared with sitting.[26]

Inspiratory capacity (IC), the maximum volume that can be inhaled from FRC, increases by 5% to 10% or 200 to 350 mL during pregnancy. Total lung capacity (TLC), the combination of FRC and IC, is unchanged or decreases minimally (less than 5%) at term.

Lung volume measurements can be made using inert gas techniques and by body plethysmography.[29] In patients without lung disease the 2 techniques produce similar results.[30] Garcia-Rio and colleagues[27] measured lung volumes by plethysmography and inert gas (helium dilution) techniques during pregnancy and postpartum. At 36 weeks of pregnancy there were significant differences in lung volumes between the 2 techniques. FRC measured by body plethysmography was decreased by 27% compared with postpartum whereas FRC measured by helium dilution
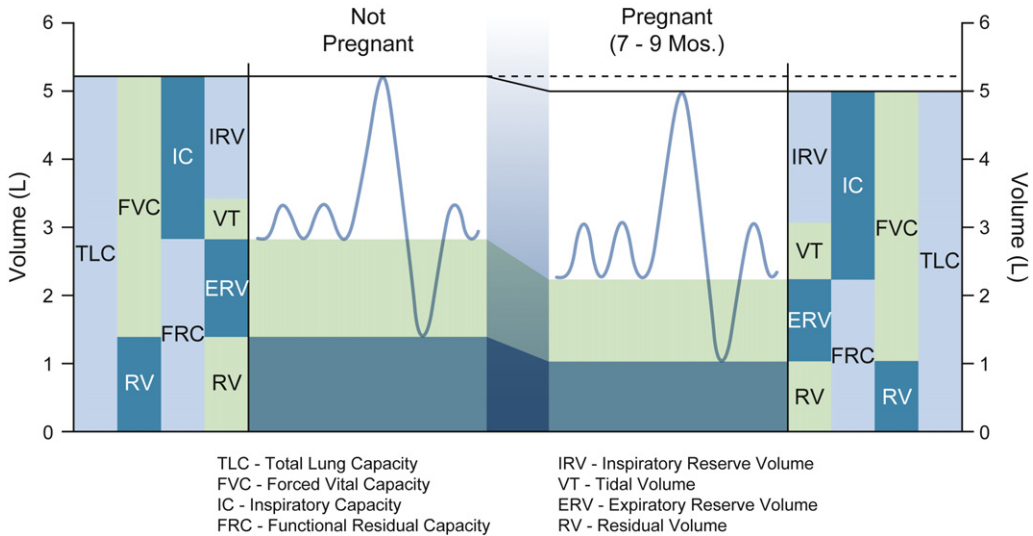
Fig. 2. Changes in lung volumes with pregnancy. The most significant changes are reductions in FRC and its subcomponents ERV and RV, and increases in IC and VT.

was decreased 38% compared with postpartum. FRC was larger by 18% or 350 mL when measured by plethysmography. The underestimation of lung volumes by inert gas technique has been attributed to airway closure during tidal breathing in late pregnancy.[27]

Both pregnancy and obesity are associated with an increase in abdominal mass, resulting in a reduction in FRC. However, significant differences are seen in other lung volumes between the 2 processes. Specifically, RV is decreased in pregnancy and increased in obesity.[31] The increase in RV in obesity is attributed to significant air trapping.[31]

Spirometry

Airflow mechanics during pregnancy have been extensively studied and are well characterized. Beginning with the classic study by Cugell in 1953, several investigators have measured lung function serially during pregnancy and after delivery.[23,25,27,32–36]

Routine spirometric measurements (forced expiratory volume in 1 second [FEV$_1$] and FEV$_1$/forced vital capacity [FVC] ratio) are not significantly different compared with nonpregnant values. FVC has been reported to be either minimally increased, decreased, or unchanged during pregnancy compared with the nonpregnant state; on average, there is no significant change.[23,25,27,32–36] The shape of the flow-volume curve and instantaneous flows that reflect larger airway caliber (peak expiratory flow) and smaller airway caliber (forced expiratory flow at 50% and 25% of vital capacity) are also unchanged.[35,37] Maximum breathing capacity,

also referred to as maximum voluntary ventilation, a measure of respiratory muscle strength and airway mechanics, is not significantly changed with pregnancy.[23,33]

The stability of spirometry during pregnancy suggests that there is no significant change in expiratory airflow resistance with pregnancy. Spirometry is also not significantly different in women with twin pregnancy as compared with singleton pregnancy.[38] Clinicians caring for pregnant patients should be alert to these findings: abnormal spirometry in a pregnant patient is likely not related to pregnancy and suggests respiratory disease.

Airway Resistance/Conductance

Several studies have addressed airway resistance and its reciprocal, airway conductance, during pregnancy.[22,32,34,39] Measurements of airway resistance and conductance quantify the ease with which air flows through the tracheobronchial tree for a given driving pressure. These parameters are primarily determined by the caliber of the large and medium-sized bronchi and because of this, lung volume is a key factor.[40] Investigators have found either a decrease in total pulmonary resistance[22,32] or no change[34,39] during pregnancy. The reduced or stable airway resistance indicates that there is no change in the caliber of the large and medium-sized airways in pregnancy despite factors that would be expected to increase airway resistance, including a reduction in FRC, reduced nasopharyngeal caliber due to upper airway congestion, and bronchoconstriction associated with the significant reduction in alveolar

P_{CO_2}. This outcome may be explained by hormonal changes during pregnancy. Specifically, progesterone and relaxin may have bronchodilatory effects that counterbalance the bronchoconstricting elements.[22,34]

Closing Volume

Measurement of closing volume provides a quantitative assessment of small airway closure.[41] Closing volume and closing capacity are often used synonymously, but technically, closing capacity equals closing volume plus RV. Airway closure occurs when pleural pressure exceeds airway pressure (ie, transpulmonary pressure is negative). Airway closure during tidal breathing occurs when the closing volume is greater than end-expiratory lung volume or closing capacity is greater than FRC. The closure of small airways with tidal breathing has important physiologic consequences, including a maldistribution of ventilation in relation to perfusion, and a resultant impairment of gas exchange and small airway injury from cyclic opening and closing of peripheral airways.[41] The single-breath nitrogen test is the most commonly used method for assessing closing volume.[41]

Closing volume has been extensively studied in pregnancy.[24,27,35,42–45] Given the significant reduction in end-expiratory lung volume and FRC and the increase in pleural pressure during pregnancy,[15] airway closure during tidal breathing was seen as an explanation for the mild decrease in oxygenation commonly seen in late pregnancy.[18,46] Studies of closing capacity in pregnancy have given conflicting results. Most studies indicate that closing volume and closing capacity do not change during pregnancy,[35,43,45] but one study that measured closing capacity at 2-month intervals during pregnancy noted a progressive, linear increase in closing capacity beginning in the second trimester.[24]

More important for gas exchange is the relationship between closing capacity and FRC. Here again, the studies are not consistent. Closing capacity has been reported to exceed FRC in up to 60% of patients in late pregnancy, especially in the supine position,[42,45] whereas others have reported this to be a rare finding.[35,43,44] The differences among studies may be explained by the large variability in closing volume measurements[47] or presence of other factors that affect closing volume such as smoking, asthma, obesity, and kyphoscoliosis.[48] Changes in closing capacity relative to FRC in late pregnancy likely cause a decrease in oxygenation, especially in the supine position, but the effect is likely small and not clinically important.[44]

Diffusing Capacity

The diffusing capacity for carbon monoxide (DL_{CO}) provides a quantitative measure of gas transfer in the lungs. The physiologic changes of pregnancy would be expected to have opposing effects on DL_{CO}. The increase in cardiac output and intravascular volume would be expected to recruit capillary surface area and increase DL_{CO} while the known reduction in hemoglobin concentration in pregnancy would be expected to decrease DL_{CO}. The most comprehensive study of DL_{CO} in pregnancy was performed by Milne and colleagues.[49] Diffusing capacity was measured monthly throughout pregnancy beginning in the first trimester and then 3 to 5 months postpartum. After correcting for alveolar volume and hemoglobin, DL_{CO} was highest in the first trimester, decreasing to a nadir at 24 to 27 weeks with no further reduction thereafter.[49] Alveolar volume measured by inert gas techniques was also significantly less after the first trimester.[49] Another study showed a similar reduction in DL_{CO} after the first trimester,[37] but this has not been a consistent finding.[50] When DL_{CO} is partitioned into its membrane and capillary blood volume components, the membrane component is either stable or slightly decreased while the capillary blood volume is unchanged.[37,50] Diffusing capacity increases with exercise in pregnancy just as it does in normal subjects,[51] indicating that pregnancy does not interfere with the ability to recruit pulmonary capillaries with exercise. Diffusing capacity does not increase when measured in the supine position as it does in nonpregnancy,[26] likely as a result of impaired venous return from the mechanical effects of the gravid uterus on the vena cava. Although most studies addressing DL_{CO} in pregnancy have methodological defects, pregnancy does not appear to cause a significant change in DL_{CO}.

VENTILATION AND GAS EXCHANGE

There is a significant increase in resting minute ventilation (V_E) during pregnancy. At term, V_E is increased by 20% to 50% compared with nonpregnant values.[15,23,25,28,52–55] The increase in V_E is associated with a 30% to 50% (from approximately 450 to 650 mL) increase in tidal volume with no change or only a small increase (1–2 breaths per minute) in respiratory rate. While V_E increases in all studies, the time course of the increase is variable. Some studies reveal a progressive increase throughout pregnancy[23,28] but most indicate that V_E rises sharply in the first 12 weeks with a minimal increase thereafter.[15,25,53,55]

The increase in tidal volume occurs without an increase in inspiratory time or the duration of the respiratory cycle, indicating that inspiratory flow is increased.[15,17,55]

The dead space to tidal volume ratio (V_D/V_T) in pregnancy is unchanged at approximately 30%.[17,56,57] Given the significant increase in tidal volume, this indicates that dead space ventilation is also increased. Studies of dead space ventilation in pregnancy have produced conflicting results.[56–58] Dead space ventilation would be expected to decrease in pregnancy because of the increases in cardiac output and perfusion to the lung apices. However, most studies indicate that there is an increase in dead space ventilation.[56,57] Anatomic dead space is unlikely to be altered by pregnancy, so an increase in alveolar dead space is the likely cause. The mechanism for the increase in alveolar dead space is not clear.

Hyperventilation in pregnancy is primarily caused by a progesterone effect augmented by an increased metabolic rate and increased CO_2 production. There is convincing evidence that progesterone is a respiratory stimulant. Increased ventilation occurs during the luteal phase of the menstrual cycle corresponding to increased plasma progesterone levels.[59] Exogenous progesterone administered to males causes increased minute ventilation and CO_2 chemosensitivity.[60,61] The mechanism by which progesterone causes an increase in ventilation is not completely understood, although progesterone decreases the threshold and increases the sensitivity of the central ventilatory chemoreflex response to CO_2.[59,62,63] Independent of its effect on CO_2 sensitivity, there is also evidence that progesterone, either alone or in combination with estradiol, stimulates central neural sites in the medulla oblongata, thalamus, and hypothalamus, involved in controlling ventilation.[59,62] Progesterone also has a direct effect on the carotid body so as to increase the peripheral ventilatory response to hypoxia. This effect is potentiated by estrogen.[64] In summary, progesterone and estradiol act synergistically to increase minute ventilation and reduce $Paco_2$ by multiple mechanisms.

The discordance between increasing progesterone after the first trimester and relative stability of minute ventilation has not been explained. Progesterone increases progressively during pregnancy. Most studies reveal a sharp increase in minute ventilation early in pregnancy and then only a minimal increase during the remainder of pregnancy.[15,25,53,55] There is a direct relationship between respiratory drive, quantified by mouth occlusion pressure ($P_{0.1}$), the pressure measured at the mouth 100 milliseconds following airway occlusion at FRC, and progesterone levels throughout pregnancy.[15] The lack of an association between $P_{0.1}$ and minute ventilation may be explained by increased respiratory impedance secondary to mechanical changes in the chest wall and abdomen.[15]

Dyspnea is a common complaint in healthy pregnant women. "Physiologic dyspnea" occurs in 60% to 70% of normal pregnant women by 30 weeks of gestation.[53,65,66] Women with physiologic dyspnea when compared with asymptomatic pregnant women have a higher $P_{0.1}$ and an increased ventilatory response to both CO_2 and hypoxia.[55] The increased minute ventilation and chemosensitivity are not explained by higher progesterone levels in patients with physiologic dyspnea compared with those without this symptom.[55] Physiologic dyspnea is likely related to an increased awareness of this augmented drive to breathe.[13]

The increased metabolic demands of the fetus, uterus, and maternal organs result in increased oxygen consumption (Vo_2), carbon dioxide production (Vco_2), and basal metabolic rate. Vo_2 and Vco_2 at term are approximately 20% and 35% greater, respectively, than nonpregnant values.[28,52,54,56,67–69] The respiratory exchange ratio (Vco_2/Vo_2) is unchanged or minimally increased with pregnancy.[52,54,56,69] The increase in V_E exceeds the increase in Vco_2 and Vo_2. The disproportionate increase in V_E leads to an increase in alveolar and arterial partial pressures of oxygen (PAo_2 and Pao_2) and a decrease in alveolar and arterial partial pressures of CO_2 ($PAco_2$ and $Paco_2$).

Normal arterial blood values in pregnancy at sea level are listed in **Table 1**. Templeton and Kelman[57] measured serial arterial blood gases in a cohort of healthy women throughout pregnancy and postpartum at sea level. Pao_2 was 106 mm Hg during the first trimester and decreased to 102 mm Hg near term. Pao_2 values during pregnancy were greater than those measured postpartum and in a control group (Pao_2 93–95 mm Hg). There was no change in the PAo_2-Pao_2 difference throughout pregnancy compared with the postpartum period or the control group. Other studies have also documented an increase in Pao_2 during pregnancy.[63,70,71]

The increased oxygen tension during pregnancy is an important adaptation that facilitates oxygen transfer across the placenta. Despite an increased oxygen tension, the combination of increased oxygen consumption and a lower reservoir of oxygen stores due to reduced functional residual capacity decreases maternal oxygen reserves. Pregnant women are more susceptible

Table 1
Arterial blood gas (ABG) changes in pregnancy (sea level)

		Pregnant State	
ABG Measurement	Nonpregnant State	First Trimester	Third Trimester
pH	7.40	7.42–7.46	7.43
P_aO_2 (mm Hg)	93	105–106	101–106
P_aCO_2 (mm Hg)	37	28–29	26–30
Serum HCO_3 (mEq/L)	23	18	17

Data from Refs.[44,57,63]

to the development of hypoxemia during periods of apnea, such as during endotracheal intubation.[72]

There is a significant reduction in Pa_{O_2} of approximately 10 mm Hg with changing from the sitting to the supine position in late pregnancy. This reduction has been attributed to closure of dependent airways and resultant ventilation/perfusion mismatch.[44,73]

Hyperventilation during pregnancy results in a significant reduction in Pa_{CO_2}. The Pa_{CO_2} decreases from a baseline value of 35 to 40 mm Hg to 27 to 34 mm Hg during pregnancy.[57,63,70,71] The reduction in Pa_{CO_2} is evident in the first trimester. Some studies reveal a progressive reduction in Pa_{CO_2} throughout pregnancy, reaching a nadir late in pregnancy.[28,63,70,71] Others show an initial reduction in Pa_{CO_2} that remains relatively stable throughout the remainder of pregnancy.[57] The persistently low Pa_{CO_2} results in a chronic respiratory alkalosis. Compensatory renal mechanisms excrete bicarbonate, reaching a nadir bicarbonate level of 18 to 22 mEq/L in late pregnancy.[63,70,71] pH is maintained at 7.42 to 7.46.[57,63,70,71] The chronic alkalosis stimulates 2,3-diphosphoglycerate synthesis causing a rightward shift of the oxyhemoglobin dissociation curve, which aids oxygen transfer across the placenta.[74]

CARDIOVASCULAR CHANGES IN PREGNANCY

Significant cardiovascular changes during the course of pregnancy affect respiratory physiology. These changes include increased plasma volume, increased cardiac output, and reduced vascular resistance. The adaptations begin early in pregnancy, and are critical in meeting the increasing metabolic demands of the mother and fetus and in tolerating the acute blood loss that occurs with childbirth. The cardiovascular changes with pregnancy are listed in **Table 2**.

Table 2
Hemodynamic changes in pregnancy

	Change with Pregnancy	
Measurement	% Change	(Absolute Change)
Cardiac output	30%–50% ↑	(2 L/min)
Heart rate	15%–20% ↑	(12 beats/min)
Stroke volume	20%–30% ↑	(18 mL)
Mean arterial pressure	0%–5% ↓	
Central venous pressure	No change	
Systemic vascular resistance	20%–30% ↓	(320 dyne·s/cm^5)
Left ventricular stroke work index	No change	
Mean pulmonary artery pressure	No change	
Pulmonary capillary wedge pressure	No change	
Pulmonary vascular resistance	30% ↓	(40 dyne·s/cm^5)

Data from Refs.[48,52,81,82]

Blood Volume Changes

Total body volume expansion occurs secondary to sodium and water retention during pregnancy. Total body volume expansion accounts for approximately 6 kg of the weight gained during pregnancy, and is distributed among the maternal extracellular and intracellular spaces, amniotic fluid, and the fetus.[17,75] Maternal blood volume increases progressively during pregnancy, peaking at a value approximately 40% greater than baseline by the third trimester. The increase in maternal plasma blood volume is physiologically important. Smaller increases in maternal plasma blood volume are associated with intrauterine growth retardation and poor fetal outcomes.[76]

The increase in plasma blood volume is best explained by the underfill hypothesis. Vasodilation of the maternal circulation and shunt-like effects created by the low-resistance uteroplacental circulation activate the renin-angiotensin system, and stimulate increased renal sodium reabsorption and water retention. Animal models suggest that the nitric oxide system is the main mediator of the primary peripheral vasodilation in pregnancy.[77] Hormonal factors also contribute to volume expansion and activation of the renin-angiotensin system[75,78,79] However, elevated levels of atrial natriuretic peptide early in pregnancy are not consistent with the underfill hypothesis.[80] The exact mechanism for volume homeostasis in normal pregnancy remains unexplained. The 40% increase (1.2 L on average) in maternal plasma blood volume exceeds the 20% to 30% increase in maternal red blood cell mass, resulting in hemodilution and the relative anemia of pregnancy.[76]

Cardiac Output

Cardiac output begins to increase as early as the fifth week of pregnancy and peaks at 30% to 50% (approximately 2 L per minute) above nonpregnant values at 25 to 32 weeks.[81–85] The increase in cardiac output is a result of a 20% increase in heart rate and a 20% to 30% increase in stroke volume. The increase in stroke volume is a consequence of an increase in preload, due to increased plasma volume and a 20% to 30% decrease in systemic vascular resistance with no significant change in ventricular contractility.[82–84,86] Studies that have used repeated echocardiograms during pregnancy have revealed no significant change in left ventricular ejection fraction, with increases in left ventricular mass and wall thickness as well as increases in all cardiac chamber dimensions.[83,84] Cardiac output may decrease slightly in the third trimester, but is highly dependent on body position. In late pregnancy, cardiac output in the supine position decreases by up to 30% compared with the left lateral decubitus position as a result of compression of the inferior vena cava by the gravid uterus and reduced venous return.[87]

Central Hemodynamic and Pulmonary Vascular Changes

In addition to the significant increase in cardiac output and reduction in systemic vascular resistance discussed earlier, right heart catheterization studies in normal pregnant women revealed no changes in central venous pressure and pulmonary capillary wedge pressure compared with nonpregnant values.[81,82] Mean pulmonary artery pressure is also unchanged during pregnancy.[81,82] Pulmonary artery pressures increase minimally with exercise but remain within the normal range.[81] Pulmonary vascular resistance significantly decreases during pregnancy, as would be expected given the stable mean pulmonary artery pressure and pulmonary wedge pressure as well as the increased cardiac output.

EXERCISE PHYSIOLOGY IN PREGNANCY

Moderate aerobic exercise during pregnancy appears to be safe for the mother and fetus, and may improve some pregnancy outcomes such as gestational diabetes and preeclampsia.[88–91] Most studies addressing the physiologic response to exercise in pregnancy used submaximal, constant load exercise protocols to avoid potential risk to the fetus.[52,56,67,69,89,92,93]

At moderate intensity of exercise, pregnant women respond differently to nonpregnant women. The increase in V_{O_2} for a given workload is greater.[68,69,92] However, V_{O_2} varies with the type of exercise. In pregnant subjects weight-bearing exercise, such as treadmill walking, is associated with a significantly higher V_{O_2} than is cycle ergometry compared with the difference between these 2 modes in nonpregnant controls.[52] When non–weight-bearing exercise is performed and V_{O_2} is adjusted for body weight (V_{O_2} expressed in mL O_2/kg/min), the V_{O_2} increases are similar for a given workload in pregnant and nonpregnant subjects.[89,92]

During pregnancy, minute ventilation (V_E) and alveolar ventilation (V_A) are higher at rest and the rate of increase with exercise is more rapid compared with the nongravid state. Both V_E and V_A increase 20% to 25% compared with nonpregnant values at submaximal work rates.[56,69,89,92] The increase in V_E exceeds the increase in V_{O_2},

resulting in an increase in the ventilatory equivalent for oxygen (V_E/V_{O_2}).

Cardiac output is higher for a given exercise level in pregnant subjects compared with nonpregnant subjects. This difference is primarily due to an increase in stroke volume.[67,92] The proportionally greater increase in cardiac output with exercise results in a reduction in the difference between the arterial and mixed venous oxygen content differences (C_{aO_2}–C_{vO_2}) compared with the nonpregnant state, leading to increased oxygen delivery to the fetus during maternal exercise.[67]

Few studies have performed symptom-limited maximal cardiopulmonary exercise tests in late pregnancy.[69,89] Maximal O_2 consumption has been noted to be reduced in sedentary pregnant women, but is associated with lower peak heart rates and may be partly due to effort. Maximal O_2 consumption is preserved in physically fit pregnant women but anaerobic working capacity may be reduced.

The fetus usually responds to submaximal maternal exercise with an increase in fetal heart rate. The fetal heart rate gradually returns to normal after the mother stops exercise.[89] Transient fetal bradycardia may develop with maximal exercise. The significance of fetal bradycardia with intense exercise is unclear. Prolonged submaximal exercise (greater than 30 minutes) in late pregnancy often results in a moderate reduction in maternal blood glucose concentration and may transiently reduce fetal glucose availability. Maternal core body temperature increases with moderate exercise, but generally less than 1.5°C.[89] The clinical significance of these changes is not clear, but moderate exercise does not appear to be associated with adverse effects to the mother or fetus.

RESPIRATORY PHYSIOLOGY IN LABOR, DELIVERY, AND POSTPARTUM

Hyperventilation, beyond the usual pregnancy-mediated increase in minute ventilation, is common during labor and delivery. Several factors interact to influence minute ventilation during labor and delivery. Pain, anxiety, and coached breathing techniques increase minute ventilation whereas narcotic analgesics have the opposite effect. The result is a wide variation in minute ventilation and breathing patterns, as illustrated by a study of 25 patients during labor that found tidal volumes ranging from 330 to 2250 mL and minute ventilation varying from 7 to 90 L per minute.[94] Pain control with narcotic analgesics minimizes labor-induced hyperventilation, suggesting that the main contributing factor for the hyperventilation is painful uterine contractions.[11] Hyperventilation during labor and delivery results in a reduction in alveolar CO_2 levels from 32 mm Hg during early labor to 26 mm Hg during the second stage.[95] The significant hyperventilation during labor and delivery and resultant hypocarbia can cause uterine vessel vasoconstriction and decreased placental perfusion, and may have deleterious effects in patients with marginal placental reserves.[43] Within 72 hours of delivery, the minute ventilation decreases halfway back toward the nonpregnant value and returns to baseline within a few weeks.[49,51]

The static lung volume changes that occur during pregnancy rapidly normalize after delivery with decompression of the diaphragm and lungs. FRC and RV return to baseline values within 48 hours.[20] The chest wall changes that occur during pregnancy normalize by 24 weeks postpartum, but the subcostal angle does not return to its prepregnancy value, remaining about 20% wider than baseline.[15]

CARDIOVASCULAR PHYSIOLOGY IN LABOR, DELIVERY, AND POSTPARTUM

Labor, delivery and the postpartum period are associated with significant cardiovascular changes. Cardiac output increases 10% to 15% above late pregnancy levels during early labor and by 50% during the second stage of labor.[87,96] The increase in cardiac output is caused by an increase in both heart rate and stroke volume. Factors contributing to the hemodynamic changes during labor include pain and anxiety with resultant increases in circulating catecholamines, and uterine contractions with resultant cyclic "autotransfusions" and increases in central blood volume and preload. Narcotic analgesics and regional anesthesia minimize the pain-mediated changes in cardiac output. Immediately postpartum there is a 60% to 80% increase in cardiac output and stroke volume relative to prelabor values, due to increased preload associated with "autotransfusion" of approximately 500 mL of blood that is no longer diverted to the uteroplacental vascular bed, and the relief of aortocaval compression with delivery.[82,91] Systolic and diastolic blood pressure and systemic vascular resistance increase during active labor, although the magnitude depends on the severity of maternal pain, anxiety, and the intensity of uterine contractions. It is important for the clinician to recognize that patients with underlying cardiac or pulmonary vascular disease may not be able to augment their

cardiac output in the peripartum period, resulting in decompensated heart failure.

There is conflicting information regarding the time course for the resolution of the cardiovascular physiologic changes after delivery. Most studies reveal a significant reduction in cardiac output and stroke volume by 2 weeks after delivery, with further reductions to near baseline values over 12 to 24 weeks.[77,79,81,97] However, another study indicated that cardiac output and stroke volume remained significantly elevated above prepregnancy values at 12 weeks postpartum.[98] Some of the cardiovascular changes resolve more slowly. Left ventricular wall thickness and mass remain significantly greater than nonpregnant controls at 24 weeks after delivery, suggesting an element of residual hypertrophy.[92]

SUMMARY

Significant anatomic and physiologic adaptations involving the respiratory and cardiac systems occur during pregnancy and are necessary to meet the increased metabolic demands of both the mother and the fetus. The prominent respiratory changes include: mechanical alterations to the chest wall and diaphragm to accommodate the enlarging uterus; a reduction in FRC and its components ERV and RV, with little or no change in TLC; and an increase in minute ventilation, resulting in reduced Pa_{CO_2} and chronic respiratory alkalosis. There is no significant change in spirometry, DL_{CO}, or oxygenation. The major cardiovascular changes include increased plasma blood volume, increased cardiac output, and a reduction in systemic vascular resistance. A basic knowledge of these expected changes will help health providers distinguish the common physiologic dyspnea from breathlessness caused by the various cardiopulmonary diseases that coexist with pregnancy.

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