

Respiratory Physiology in Pregnancy

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Introduction

Pregnancy is a normal but altered physiologic state that results in significant hormonal, mechanical, and circulatory changes. The increases in progesterone and estrogen associated with pregnancy contribute to vascular and central nervous system effects, changes in the balance of bronchoconstrictor and bronchodilator prostanoids, and increases in peptide hormones that alter connective tissue characteristics. The course of pregnancy is accompanied by structural changes to the ribcage and abdominal compartments as a consequence of the hormonal changes and the enlarged uterus. Cardiac output, pulmonary blood flow, and circulating blood volume are all increased due to increased metabolic demands. This increase in blood volume without an increase in red cell mass results in a decreased hemoglobin concentration. There is a reduction in plasma oncotic pressure due to both increased blood volume and a decrease in albumin concentration. The combination of increased pulmonary blood flow, increased pulmonary capillary blood volume, and decreased oncotic pressure all promote the formation of edema in the periphery and in the lung. Given the dramatic physical and hormonal alterations of pregnancy, perhaps the most remarkable aspect of respiratory physiology is the relatively minor impact that pregnancy has on the function of the lung. To be able to accurately identify and diagnose respiratory abnormalities in pregnant patients, the clinician must first understand normal physiologic changes of pregnancy. Over the years, there have been several excellent reviews of the effects of pregnancy on the respiratory system in health and disease (1–6). This chapter provides an updated overview of respiratory physiology in healthy pregnant women (6).

Chest Wall and Lung Mechanics in Pregnancy

During pregnancy, the ribcage undergoes structural changes in response to hormonal changes (7). Progressive relaxation of the ligamentous attachments of the ribs cause the subcostal angle of the rib-cage to increase from 68° to 103° early in

pregnancy before the uterus is substantially enlarged. This change persists for months after the end of pregnancy when the uterus returns to normal size. The increased elasticity of the rib-cage is probably the result of the same factors that induce changes in the elastic properties of the pelvis. One of the important mediators is thought to be the polypeptide hormone relaxin which is increased during pregnancy. This substance is responsible for the softening of the cervix and the relaxation of the pelvic ligaments (8, 9).

Pregnancy causes the diaphragm to elevate about 4 cm and the circumference of the lower rib-cage to increase about 5 cm (10). The lower end-expiratory lung volume leads to an increased area of apposition of the diaphragm to the chest wall, which improves the coupling of the diaphragm and chest wall (11). Thus, the increased tidal volume in pregnancy is achieved without an increase in the respiratory excursion of the diaphragm. The enlarging uterus results in increasing abdominal pressure which decreases chest wall compliance, which falls about 35–40% (12).

The decrease in chest wall compliance causes a reduction in functional residual capacity (FRC). Reductions in the FRC and the expiratory reserve volume are the most consistent changes in static lung volumes with pregnancy. As the uterus enlarges, FRC falls by 10–25% of the previous value, starting about the 12th week of pregnancy (13). The normal reduction in FRC in the supine position is further accentuated in pregnancy (14, 15). By contrast, the total lung capacity is usually preserved or minimally decreased as a result of the mild increase in the inspiratory capacity. The residual volume tends to fall slightly, leading to a small increase or stability of the vital capacity (16, 17, 10, 13, 18–21). The lung compliance remains normal during pregnancy but chest wall compliance is slightly reduced because of the effect of the enlarging uterus leading to a distention of the abdominal cavity. Expiratory muscle strength is in the low-normal range (19).

Airflow Mechanics

Pregnancy has no significant effect on FEV_1 or the FEV_1/FVC ratio (22, 23, 24). Peak expiratory flow rates remain close to the normal range and do not change during pregnancy (25). The shape of the flow-volume curve and absolute flow rates at low lung volumes are normal in pregnant women (17, 26). Thus, it is possible to use non-pregnant reference values to evaluate lung function in pregnant women. A reduction in FEV_1 or FVC should not be attributed to pregnancy alone. This is important for clinicians to understand, particularly as they are following patients with underlying lung diseases, such as asthma (27, 28). Measurement of airway conductance by several methods demonstrates normal or increased large airway conductance (19, 23). A relatively recent epidemiologic study has raised the possibility that pregnancy may induce changes in the lung that improve airway function and persist throughout life (29). Small airway function as measured by closing volume is normal (30–32). However, because the FRC is low, airways may close during tidal breathing and increase the alveolar-arterial oxygen gradient in the supine position.

Ventilation and Gas Exchange

Resting minute ventilation increases during pregnancy (33–35). This is primarily due to an increase in tidal volume with a relatively constant breathing rate and pattern. Because the dead space-tidal volume ratio remains normal during

pregnancy, the increased tidal volume leads to increased alveolar ventilation (36). Dead space may be decreased in pregnancy because of increased cardiac output and better perfusion to the apices, so ratio of VD/VT is even more advantageous.

Most studies find that this hyperventilation (increase in tidal volume) is a progesterone effect that occurs early in pregnancy during the first trimester, and stays constant or increases slightly as pregnancy progresses (37). Typically, resting minute ventilation is increased about 30% during pregnancy compared to the postpartum value. This primary increase in minute ventilation is enhanced secondarily, by an increase in metabolic rate and carbon dioxide production. During pregnancy, carbon dioxide production at rest increases by about 30–300 ml/min. Despite this increase in production, overcompensation results in a low to normal CO_2 during pregnancy.

The increase in minute ventilation exceeds that which is required to maintain a normal arterial carbon dioxide level. As a result, the arterial PaCO_2 falls from 40 mmHg in the non-pregnant state to 32–34 mmHg in pregnancy (38). The kidney excretes excess bicarbonate to compensate for the respiratory alkalosis and maintains a serum bicarbonate level of about 15–20 meq/L to preserve a normal arterial pH. Likely contributes to a rightward shift in the oxyhemoglobin dissociation curve the chronic alkalosis stimulates 2,3-diphosphoglycerate synthesis and this, in conjunction with anemia, that favors the unloading of oxygen in the periphery, presumably aiding oxygen transfer across the placenta (39). There is general agreement that the main cause of the increased respiratory drive that causes the hyperpnea of pregnancy is the elevation of serum progesterone, a direct respiratory stimulant. The progesterone-induced increase in chemosensitivity results in an increase in the slope and a leftward shift of the CO_2 ventilatory response curve. The increase in chemosensitivity occurs early in pregnancy and remains constant up until delivery. The respiratory center output, which integrates both chemical and mechanical stimuli, is measured by the mouth pressure 100 ms following airway occlusion ($P_{0.1}$). This measure increases progressively throughout pregnancy, compatible with the idea that the hyperpnea of pregnancy is the result of both increased chemosensitivity and the metabolic and mechanical loads imposed by the gravid state. Shortly after delivery, the respiratory drive returns to normal with the fall in progesterone levels and the reduction in metabolic and mechanical loads induced by pregnancy.

The evidence that progesterone is a respiratory stimulant is strong (40). When administered to non-pregnant individuals, progesterone increases minute ventilation, CO_2 chemosensitivity, and airway occlusion pressure (41–43). It has been debated whether progesterone acts through a direct stimulatory effect on the respiratory center or through an increase in the gain of the chemoreceptors (44). The most recent evidence shows that both the threshold for hypercapnic ventilation as well as the gain in ventilation is increased in pregnancy, suggesting that both intrinsic and chemically-driven responses are more sensitive in the pregnant hormonal milieu (45).

The hypoxic ventilatory response is increased in pregnancy to about twice the normal level (46). This occurs despite the blood and cerebrospinal fluid alkalosis that tends to suppress hypoxic drive. In contrast to the response to carbon dioxide, the hypoxic ventilatory response in pregnancy is not well correlated with progesterone levels. It is thought that the increased sensitivity to hypoxia is due to the increases in both estrogen and progesterone (47, 48).

Arterial oxygen tensions are slightly increased in pregnancy as a result of the pregnancy-induced hyperpnea, with a normal pregnant level of 100–105 mmHg

(36). This high level of oxygen tension may facilitate oxygen transfer across the placenta by diffusion. However, the increased metabolic rate and the low oxygen reservoir in the lung at end-expiration make the pregnant woman particularly susceptible to develop hypoxemia in the presence of respiratory depression or apnea (49, 50). In some women, the low end-expiratory lung volume may predispose them to decreasing oxygen tensions in the supine position in the late stages of pregnancy (51).

The overall effect of pregnancy on diffusing capacity for carbon monoxide (Dco) is determined by the relative contributions of opposing physiologic changes. Pulmonary blood volume and cardiac output are increased in pregnancy, which should recruit capillary surface area and thereby increase Dco. This is offset by the dilutional reduction in hemoglobin concentration that occurs, leading to a constant or slightly diminished Dco in the majority of pregnant patients (22). The normal increase in Dco that occurs in the supine position is absent in pregnancy, which might indicate that the gravid uterus prevents the normal increase in systemic venous return, or that the pulmonary capillary bed is already fully recruited (26). The latter explanation is less plausible because exercise causes a normal increase in Dco in pregnant people (52). One study suggests that there are different effects of pregnancy on Dco in high-altitude dwellers. Pregnant women dwelling at high altitude have a higher Dco than those at sea-level, but during the third-trimester they have a lower Dco than non-pregnant altitude dwellers. At sea-level, the Dco is similar throughout pregnancy compared to non-pregnant controls (53). High altitude also acts additively with progesterone and ventilation is increased to a greater extent in high altitude residents compared to low altitude residents. The increase in ventilation, along with increased hemoglobin concentrations, appears to raise arterial oxygen saturation to levels similar to those of low altitude dwellers (54).

Physiologic Dyspnea of Pregnancy

The increase in minute ventilation that accompanies pregnancy is often perceived as shortness of breath. About 75% of pregnant women have exertional dyspnea by 30 weeks of gestation (55–58). Shortness of breath at rest or with mild exertion is so common that it is often referred to as “physiologic dyspnea.” The proposed causes of dyspnea are the increased drive to breathe and the increased respiratory load. The increase in minute ventilation and the load imposed by the enlarging uterus cause an increase in the work of breathing. Other factors that are thought to contribute to the sensation of dyspnea include increased pulmonary blood volume, anemia, and nasal congestion. Studies of the psycho-physiology of dyspnea in pregnancy indicate that the dyspnea can be accounted for by the increased effort of breathing rather than an increased sensitivity to mechanical loads (59).

The cardiovascular response to endurance exercise in late pregnancy is relatively unchanged compared to the post-partum state (60). Similarly, exercise efficiency (change in oxygen consumption per change in work load) is unchanged (61, 62). However, ventilation at any level of oxygen consumption or carbon dioxide production is increased in pregnancy which leads to increased perception of respiratory effort. This excess exercise ventilation and sensation of breathlessness can be somewhat reduced by aerobic training (63). In general, fetal responses to short duration of exercises are usually

moderate and return to baseline in the post-exercise state and moderate prenatal physical conditioning does not significantly affect fetal growth (6).

It can be challenging for a physician to differentiate the normal dyspnea of pregnancy from that due to disease pathology. Findings that raise the question of pathologic dyspnea include: increased respiratory rate greater than 20 breaths per minute, arterial PCO_2 less than 30 or greater than 35, hypoxemia or abnormal measures on forced expiratory spirometry, or cardiac echocardiography. The time course of symptoms is also helpful in differentiating pathologic conditions. Abrupt or paroxysmal episodes of dyspnea suggest an abnormal condition.

Summary and Conclusions

In summary, an understanding of the normal changes that occur in respiratory physiology during pregnancy (Table 2.1) is fundamental to recognizing how the presentation of lung diseases is altered by pregnancy. Although these changes in cardiovascular and respiratory physiology are remarkably well tolerated, there is diminished reserve capacity to deal with intercurrent respiratory insults. Thus, prompt recognition and treatment of altered respiratory function is needed to protect the health of the mother and fetus.

Table 2.1 Normal respiratory physiologic changes in pregnancy.

Chest Wall/Lung Mechanics	
Chest wall compliance	Decreased
Thoracic diameter	Increased
Diaphragm	Elevated
Lung compliance	Unchanged
Lung Volumes	
Total Lung Capacity	Unchanged or slightly decreased
Vital capacity	Unchanged or slightly increased
Inspiratory capacity	Slightly increased
Functional residual capacity	Decreased
Residual volume	Slightly decreased
Expiratory reserve volume	Decreased
Spirometry	
FEV_1	Unchanged
FVC	Unchanged
FEV_1/FVC	Unchanged
Gas Exchange	
D_{CO}	Unchanged or slightly decreased
Ventilation	
Minute ventilation	Increased
Tidal volume	Increased
Respiratory rate	Unchanged
Blood gas	
pH	Normal (7.39–7.42)
PaO_2	Slightly elevated (100–105 mmHg)
PaCO_2	Slightly decreased (32–34 mmHg)
Bicarbonate	Slightly decreased (15–20 meq/L)

Abbreviations

cm	Centimeters
Dco	Diffusing capacity for carbon monoxide
FEV ₁	Forced expiratory volume in one second
FRC	Functional residual capacity
FVC	Forced vital capacity
PaCO ₂	Partial pressure of carbon dioxide in arterial blood
PaO ₂	Partial pressure of oxygen in arterial blood
RV	Residual volume
TLC	Total lung capacity

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