PHYSIOLOGICAL CHANGES DURING PREGNANCY
A REVIEW

GERTIE F. MARX, M.D., AND LOUIS R. ORKIN, M.D.

A variety of physiological changes occur in women during normal pregnancy. Many of these alterations, noted in organ systems other than the generative tract, are important to the management of a carefully chosen and well-conducted anesthesia. Of particular interest are changes related to blood volume, relative and absolute alterations in blood constituents, circulatory and respiratory homeostasis, and metabolism. These manifestations are the subject of this report.

THE BLOOD

Except for the primary fetal and uterine development, an increase in total blood volume is the greatest single physiological change during gravidity (1). There is an absolute increase in plasma as well as in cell volume, and in both red cell and white cell masses. These augmentations are all progressive, reaching their peaks in the ninth month, and then decline slowly (2, 3). The plasma volume increases steadily beginning in the first month, whereas red cell and total blood volumes exhibit an initial drop during the first two months. The plasma volume decreases prior to delivery and continues to decline slowly during the puerperium, but is still slightly elevated at six weeks postpartum. The red cell volume is reduced to subnormal values at and immediately after delivery, and is still moderately decreased at six weeks postpartum. Total blood volume, however, returns to normal between shortly after delivery (3) to one week postpartum (4, 5). The individual variations in blood volume are considerably more pronounced during pregnancy than in nonpregnant and postpartum women (4). The augmentation of the blood volume serves a twofold purpose. It facilitates the interchange of oxygen and carbon dioxide between the maternal and fetal circulation by making more blood available for transport through the placental lake. It also enables the parturient woman to withstand hemorrhage better by holding blood in reserve in the dilated vascular system (2). On the other hand, it imposes on the heart the burden of circulating a proportionally larger quantity of blood per minute (1). This factor is of frequent importance in patients with rheumatic heart disease.

The increases in cell and plasma volume have been measured by many investigators, by different methods, with varying results. At
Physiological Changes during Pregnancy

Present, the common methods described are a modified Evans blue dilution test (4, 5, 6) and labeling of the red cells with a radioactive tracer, P\textsuperscript{32} (3). The values are listed in table 1. This table indicates that, although there is an actual increase in red cell volume and hemoglobin mass, the rise in solid constituents fails to keep pace with the augmentation in plasma volume. The result is a hemodilution, previously called the "pseudo-anemia" or "physiological anemia" of pregnancy. A reduction in blood viscosity of 12 per cent occurs con-

**TABLE 1**

<table>
<thead>
<tr>
<th>Blood Volume Changes (Per Cent) During Pregnancy and Puerperium</th>
</tr>
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<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Total blood volume</td>
</tr>
<tr>
<td>-2.5</td>
</tr>
<tr>
<td>+38.0</td>
</tr>
<tr>
<td>+32.0*</td>
</tr>
<tr>
<td>+29.5</td>
</tr>
<tr>
<td>0.0</td>
</tr>
<tr>
<td>0.0</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Plasma volume</td>
</tr>
<tr>
<td>+5.0</td>
</tr>
<tr>
<td>+48.0†</td>
</tr>
<tr>
<td>+41.0*</td>
</tr>
<tr>
<td>+45.0</td>
</tr>
<tr>
<td>+9.0</td>
</tr>
<tr>
<td>+5.0</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Red cell volume</td>
</tr>
<tr>
<td>-13.5</td>
</tr>
<tr>
<td>+17.5</td>
</tr>
<tr>
<td>+6.0</td>
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<tr>
<td>-13.0</td>
</tr>
<tr>
<td>-9.0</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Hemoglobin mass</td>
</tr>
<tr>
<td>No data</td>
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<tr>
<td>No data</td>
</tr>
<tr>
<td>No data</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>


comitant with the hemodilution (1, 7). A diagnosis of secondary anemia in pregnancy should not be made, unless the red cell count falls below 3.75 million, the hemoglobin level below 11 to 12 Gm. per cent, and the hematocrit below 32 per cent (5, 6, 8, 9). There is no alteration in red cell morphology or dimensions (9), but the hemoglobin content of the individual cell is increased during the last month of gestation, since the hemoglobin mass continues to increase until term (6). However, there is a distinct tendency toward true anemia during pregnancy due to a discrepancy in iron demand and supply (10). The reticulocytes show a moderate increase during the period of enlargement of the total circulating red cell volume (9). The platelets remain within normal range (230,000 to 250,000). During the last week of pregnancy and in early labor they are somewhat decreased (210,000 to 220,000), and then an abrupt rise occurs in late labor and the puerperium (270,000); there seems to be a definite stimulus for platelet production during labor (11).

The white cell count is in the upper limits of normal, that is between 9,000 and 11,000 until the end of pregnancy (5, 9, 12). Only leucocytosis in excess of 12,000 should be regarded as indicative of infection. The polymorphonuclears are progressively increased, from 68 per cent in the second month to 75 per cent in the ninth month, and
82 per cent in labor. The lymphocytes are decreased, from 28 per cent in the second month to 18 per cent in the ninth month, and 14 per cent during labor. The monocytes are maintained at a normal relationship. There is a steady decline in the number of circulating eosinophiles, from 167 per cubic millimeter in the second month to 126, in the ninth month and 27, in labor. These changes are consistent with a rise in the 17-oxy steroids (9). During and immediately after parturition, there is a further and often marked elevation in the total white cell count, the greatest increases (20,000 to 30,000) occurring in patients with prolonged labor (2, 9). At this time and during the first three postpartum days, leucocyte counts are of little diagnostic significance. The maximum leucocytosis is reached on the second or third day postpartum. Thereafter, the white cells gradually decrease to normal by the thirtieth day (5). These changes are summarized in table 2.

| TABLE 2 |
| Changes in the Formed Elements of the Blood During Pregnancy |

<table>
<thead>
<tr>
<th></th>
<th>Total Number</th>
<th>Number per 100 cc. Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocytes</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Reticulocytes</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Leucocytes</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Polymorphonuclears</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Circulating eosinophils</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

The plasma proteins undergo changes in concentration similar to those observed in the cell volume of the blood. The concentration is decreased; the greatest decline, 7 per cent below normal, occurring early in the ninth month (13, 14). Thereafter, a gradual increase takes place, and normal values are reached at about six to eight weeks postpartum. The diminution in concentration of plasma proteins is only relative, and is a reflection of the extent to which the plasma augmentation exceeds the protein increase. There is an actual gain in total circulating plasma proteins amounting to 18 per cent near term (15). The albumin fraction is always decreased progressively, the globulin fraction remains fairly constant, and the fibrinogen fraction is markedly augmented (13, 14, 15). Fibrinogen is both actually and relatively increased, the total amount at term being 40 per cent greater than normal (15). This is of clinical importance as an essential factor in the prevention of hemorrhage.

Nonprotein nitrogen is slightly diminished during pregnancy to about 10 per cent below normal in the last trimester. Blood urea is reduced to levels of approximately one-third less than normal at term. Uric acid and creatinine values are unchanged (16, 17, 18). These changes are summarized in table 3.
TABLE 3

CHANGES IN PLASMA PROTEINS DURING PREGNANCY

<table>
<thead>
<tr>
<th></th>
<th>Increase (per cent)</th>
<th>Decrease (per cent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total proteins</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Proteins per 100 cc. blood</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Albumin per 100 cc. blood</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Globulin per 100 cc. blood</td>
<td></td>
<td>Unchanged</td>
</tr>
<tr>
<td>Total fibrinogen</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Fibrinogen per 100 cc. blood</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Nonprotein nitrogen</td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Urea</td>
<td></td>
<td>33</td>
</tr>
</tbody>
</table>


The sedimentation rate (corrected and uncorrected for the effects of hydremia) is progressively accelerated during gestation closely paralleling the rise in fibrinogen (5, 19). The rate (uncorrected) increases up to five times as term approaches (1). After a peak during the first or second postpartum day, it declines to within normal range on the thirty-first day (5). Therefore, a rapid sedimentation rate is of little or no diagnostic help during the major part of pregnancy and the first week of the puerperium.

The specific gravity of whole blood and plasma is normal in the early months, declines progressively late in pregnancy, but rises again with approach of term. It reaches normal values shortly after delivery. These findings are consistent with the changes in cell volume and plasma protein, and indicate dilution as a common mechanism (20).

Both oxygen and carbon dioxide dissociation curves in the mother's blood are shifted slightly to the right. Accordingly, maternal blood releases oxygen at lower tensions than fetal blood or normal adult blood, and also carries carbon dioxide more readily (21).

The acid-base relationship is one of compensated alkali deficit (22-26). The consistent diminution in serum protein concentration represents a reduction in electrolyte activity which becomes evident after the sixteenth week (2), increases with the progress of pregnancy and gradually returns to normal following delivery (22). However, total base is likewise progressively decreased (22, 23). Carbon dioxide content of serum is diminished 6 to 10 volumes per cent below normal (22). Carbon dioxide combining power declines to about 45 volumes per cent at term as compared to a norm of approximately 52 volumes per cent in nonpregnant women (1, 17). This reduction in alkali reserve does not represent a true acidosis. There is no clinical evidence of acidosis nor is there an increase in organic acids or any indication of abnormal acids (1). Normal gestation is characterized not only by a decrease in the buffer anions, sodium proteinate and sodium bicarbonate, but also by a corresponding reduction in total base, with both factors returning to normal early in the puerperium (24).
hydrogen ion concentration, on the other hand, shows no change and remains constant at pH 7.4 (22, 23). Serum chloride likewise is normal or only slightly decreased, 1 per cent (22). Accordingly, we are dealing with a compensated carbon dioxide deficit rather than with a true acidosis. The mechanism for this is not quite understood. It has been suggested that the increased pulmonary ventilation which is present during gestation, reduces the carbon dioxide, and that total base undergoes a compensatory reduction (25, 26). The long duration of pregnancy allows for the establishment of an equilibrium in which the potentially increased pH, due to physiologic hyperventilation, is returned to normal by a lowered plasma bicarbonate and a proportionally decreased carbonic acid (25).

**Water Balance**

Increased water retention is a regular occurrence in normal pregnancy (20, 27-31). This increase is compensated for by negative fluid balance with diuresis (27) and diaphoresis (28) during the second to fifth postpartum days (29) and a resultant weight loss of approximately 5 pounds (1, 30). Retention of water is noted in all compartments, but the amounts retained in vascular and extravascular spaces vary in each trimester. The water concentrations of whole blood, plasma and cells follow the same general trend, namely, a rise to the last month and a significant prelabor fall. This curve is the reciprocal of that previously described for specific gravities, cell volume, plasma proteins and hemoglobin content. The gain in extravascular fluid, on the other hand, is especially marked and accelerated in the last trimester, continuing steadily to the end of pregnancy without a decline prior to labor. During the first and second trimesters, the percentage increase of plasma volume exceeds the percentage augmentation of extravascular fluid volume. In the last trimester, the percentage increase in extravascular fluid volume is greater than the percentage rise in plasma volume. These changes suggest a selective retention of fluid in the extravascular compartment rather than simple hydration (31).

Exaggeration of water retention with excessive accumulation of extravascular fluids is seen in preeclampsia and eclampsia (32). The diagnosis of generalized edema during pregnancy can be made earliest by the gain in weight and by evidence of swelling of fingers and hands. Pitting edema of ankles and legs alone is not an indication of abnormal water retention, for it is the result of hydrostatic factors (increased venous pressure and retarded venous blood flow) (1). The protein concentration is not sufficiently lowered to affect the water balance in normal pregnancy. However, slightly abnormal conditions may accentuate the deficiency sufficiently to initiate edema (2).

The generalized water retention in pregnancy is closely related to salt retention (27, 28, 33). It was found on direct analysis of various tissues that the sodium content is always increased in normal gestation.
and significantly so in eclampsia (34). The total loss of sodium during the first ten postpartum days is about 5 Gm. (28). Most observers state that the main cause of water and salt retention lies in the steroid sex hormones (27, 28, 33, 35). The sodium retaining effect of the estrogens has been shown clinically to explain premenstrual edema (36). Since these hormones are present in much greater concentration and over a much longer period of time during gestation, a more pronounced retention of sodium and fluids can be expected. Balance studies revealed that in pregnancy and puerperium, sodium was retained during periods of high estrogen concentration and lost during periods of diminishing levels (28). Progesterone was also capable of causing salt retention (28). The large excretion of salt and water after delivery of the fetus and placenta is independent of the mechanical evacuation of the uterus and is due to the sudden suppression of one or several sex hormones (33).

**Circulatory System**

Physiological alterations during pregnancy are encountered in the heart and in the peripheral vascular bed. In the heart, both anatomical and functional changes are of importance.

The growing uterus pushes the diaphragm upward, resulting in changes in the chest wall and in the position of the heart (37, 38, 39). The thorax decreases in height and increases in circumference. The heart, which resists the displacement of the diaphragm more than the lungs, is lifted upward in toto, shifted to the left and anteriorly, and rotated towards a transverse position (37–40). The degree of all these positional alterations is related to the size and position of the fetus, resistance of abdominal musculature, volume of the thorax and the woman’s physical habitus.

An increase in the outline of the heart is observed on percussion (41). Roentgenograms reveal lengthening of longitudinal and transverse diameters in most patients (10, 38). The question arises as to whether this enlargement is caused by cardiac hypertrophy, cardiac dilatation or both (10, 41). Primary factors to be considered are the augmentation in blood volume, the increase in interstitial and pericardial fluids, and the change in position. On autopsy, the heart is slightly heavier in pregnancy than in the nonpregnant state (2). This increase in weight, however, seems to be in proportion to the general weight gain, that is, the relation of the weight of the heart to the body weight remains within normal limits in uncomplicated cases (38).

Functional changes include a higher basal heart rate, a more forceful apical beat, louder heart sounds with accentuated pulmonary second sound, and faint systolic murmurs over pulmonary and tricuspid areas (40, 41, 42). There is increased susceptibility to premature contractions, sinus tachycardia and paroxysmal supraventricular tachycardia. All disorders of the cardiac rhythm except ventricular fibril-
lation have been observed in pregnant women with otherwise normal hearts (42). The most important finding, however, is a significant increment in cardiac output (10, 43-49). Hemodynamics in gestation have recently been studied by cardiac catheterization (44-48). It was observed that the augmentation in cardiac output begins early, before the fourteenth week, has its peak at the end of the second trimester, and then falls slowly to reach normal values just prior to term (46, 47). A recent and very thorough investigation, done on 46 normal pregnant women, showed the figures in Table 4 for resting cardiac outputs.

**Table 4**

<table>
<thead>
<tr>
<th>Weeks of Gestation</th>
<th>Liters per Minute</th>
<th>Per Cent Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>14 to 20</td>
<td>6.53</td>
<td>31.9</td>
</tr>
<tr>
<td>25 to 27</td>
<td>6.96</td>
<td>37.4</td>
</tr>
<tr>
<td>28 to 30</td>
<td>6.53</td>
<td>26.7</td>
</tr>
<tr>
<td>31 to 35</td>
<td>5.75</td>
<td>16.1</td>
</tr>
<tr>
<td>36 to 40</td>
<td>5.53</td>
<td>10.9</td>
</tr>
</tbody>
</table>


These represent a maximum rise of nearly 40 per cent during the twenty-fifth to twenty-seventh week. Another study, done on 47 patients in active labor, used a modified pulse pressure method, recording from an intrabrachial catheter with an electromanometer. Here it was observed that cardiac output increases during the first stage of labor, and that during effective uterine contractions it rises an average of 30.9 per cent over the output in the resting stage (48). The work done by the heart is a function mainly of the cardiac output and the resistance to flow. Some lessening of the cardiac load, therefore, is accomplished by a reduction in total peripheral resistance and by the diminution in the viscosity of the blood which results from hemodilution. Yet, one can readily state that the heart is obliged to perform considerably more work as the result of pregnancy, and that labor produces a more acute strain (43, 48). In spite of this burden, no impairment in the myocardial reserve is demonstrable in pregnant women without heart disease. Tests of increased cardiac output in response to exercise proved normal (47). Thus, while both cardiac output and plasma volume rise early in pregnancy, and tend to fall to normal towards the end, the changes in cardiac output are much more abrupt. It reaches its peak earlier and has returned to normal prior to term, while plasma volume is still elevated. The following explanation is offered. Both increase in cardiac output and in plasma volume occur in response to the higher oxygen and metabolic requirements of the fetus for which the mother must augment the blood flow to uterus and placenta. The cardiac output, being controlled by reflexes, rises rapidly with the need for greater blood flow. The aug-
mentation in plasma volume, depending on the movement of fluid from the extravascular space and the formation of plasma proteins and other formed elements, requires several weeks. Once plasma volume is sufficiently increased, the high cardiac output is no longer necessary and declines (49).

Oxygen consumption is consistently increased, reaching a value at term approximately 10 per cent greater than the normal for non-pregnant women (47). The arteriovenous oxygen difference varies inversely with the cardiac output; it falls to minimum values at the twenty-fifth to twenty-seventh week and returns gradually to normal levels at term (40, 45–47). Apparently, the fall in cardiac output in the last trimester is compensated for by a changing efficiency of the tissues to extract oxygen from the blood.

The occurrence of electrocardiographic changes in pregnancy is questionable. While some observers found no noticeable alteration, most investigators report a progressive tendency toward left axis deviation from the second to the sixth month with no change in the seventh to eighth month and definite shifting back to the right in the ninth month. These findings are solely due to the positional changes of the heart and are thus mechanical in nature. An inverted lead 3, the result of the transverse position, is of no significance (10, 50).

The pulse rate during normal gestation is increased from 12 to 20 beats per minute (10, 40, 51).

The arterial blood pressure never rises above nonpregnant levels in uncomplicated pregnancy. The systolic component is either unchanged (52) or slightly lowered (51); the diastolic is always diminished (51, 52). It follows that the pulse pressure becomes larger (average of 10 mm. of mercury during the major part of gestation) (1). However, all values return to normal during the last month.

The calculated peripheral resistance is reduced and reflects the decrease in mean blood pressure (46, 47, 49). This change, together with the augmentation in cardiac output and total blood volume, leads to a progressive increase in blood flow to the extremities. Studies on the velocity of blood flow by the cyanide method (vein to carotid sinus) show that the rate starts to increase at about the seventeenth week and begins to decrease at the thirty-sixth week. This general trend is present in both peripheral and pulmonary circulation but is more marked in the former (10, 53). The higher peripheral blood flow helps to dissipate the excess heat generated by the elevated metabolism (1).

The capillaries exhibit intermittent increases in tonus. The arterial loops in particular, contract longer and more frequently. As a result of this increase in vasomotor activity, the duration of the contraction increases five-fold, and occurs five times as frequently in the capillaries of pregnant women as compared to nonpregnant women. Thus, the venous ends of the capillaries become dilated and the circulation within them is retarded (53). Evidence of increased capillary
vasoconstriction is best viewed in the eye (54). The active capillary bed of the bulbar conjunctivae shows a progressive reduction throughout pregnancy. Late in the third trimester and during labor this is seen as a definite tissue ischemia. There is also a noticeable tendency toward increased capillary fragility during labor which recedes rapidly after the confinement (55).

The venous pressure in the arm is not significantly changed during the course of pregnancy. In the lower extremities venous pressure begins to rise in the early part of the second trimester (40), increasing first rapidly, and then more slowly to reach an average peak value at term of approximately 24 cm. of water. This represents a rise of about 16 cm. above prepregnancy values (56). Measurements with radioactive sodium to compare foot-groin and hand-axilla blood flow times showed that the slowing of the venous flow is confined to the legs and is not part of a generalized increase in circulation time (57). The abnormal femoral venous pressure is probably the result of obstruction to venous return by the pregnant uterus. In cesarian sections, femoral venous pressure declines immediately after delivery of the fetus, but is not at all affected by opening of the peritoneal cavity, incising of the uterine wall or removal of the placenta (56). The high level of pressure in the veins of the lower extremities and pelvic organs promotes distention with increased tendency toward varicosities in legs, vulva and anus. It is also responsible for the pitting edema of the ankles and legs seen in many pregnant women near term. This localized edema should not be confused with generalized edema due to abnormal water retention.

Studies on uterine blood flow and comparison of uterine and cerebral circulations reveal several interesting facts (58). During the last months of pregnancy, the uterus receives about one-quarter of the amount of blood that the brain obtains in a normal woman at rest (15 cc. versus 54 cc. per 100 Gm. per minute). However, the oxygen consumption of the uterus approximates two-thirds of that of the brain (2 cc. compared to 3.3 cc. per 100 Gm. per minute). These figures indicate that the pregnant uterus extracts much more oxygen per unit of blood flow than does the brain. It is probable that the fetus is responsible for this large oxygen consumption.

The mechanism of the cardiac and circulatory changes is not entirely explained. While hemodynamic effects of hypervolemia may play a role, most of the alterations may be explained on the basis of a modified arteriovenous shunt at the placental site with obstruction to venous return by the enlarged uterus (40, 46, 51, 59). When arteriovenous fistulae in other parts of the body are sufficiently large, they cause circulatory adjustments similar to those observed during gestation. Changes common to circulatory shunts are (40, 51, 59): (1) augmentation of total blood volume, (2) acceleration in heart rate, (3) increase in cardiac output, (4) increase in oxygen consumption, (5) decrease in blood pressure with increase in pulse pressure, (6) eleva-
tion of venous pressure in pelvis and legs, and (7) souffle (continuous bruit with systolic accentuation).

Further evidence for the theory of the arteriovenous leak through the placenta is found in animal investigations on pregnant bitches which showed that the pressure in the uterine vein is even higher than the elevated femoral venous pressure and that the blood taken from the uterine vein has a higher oxygen content than the blood in the right ventricle (40, 51). The fall in cardiac output towards the end of gestation may be explained by a reduction in the shunt effect caused by obliteration of portions of the placental maternal vascular bed (46).

**Respiratory System**

Capillary engorgement takes place throughout the respiratory tract during pregnancy. The mucous membranes of the nasopharynx and tracheobronchial tree become hyperemic and edematous. The false cords and arytenoid region of the larynx swell and redden in 75 per cent of pregnant women (1, 2).

The capacity of the lungs might be expected to diminish owing to the previously described upward displacement of the diaphragm by the growing uterus. A physiological decrease, however, is counteracted by a compensatory broadening of the chest wall (1, 2, 39), an increase in the minute volume of respired air (1, 25), and a change from abdominal to thoracic breathing (2).

Broadening of the chest wall is accomplished by increases in the anteroposterior and transverse diameters which more than compensate for the 4 centimeter or less shortening of the vertical diameter (39). In other words, the effect of the diminished height of the pleural cavities is nullified by an increase in width (25). In addition, the ribs flare out, broadening the substernal angle from 63.5 degrees in the first trimester to 103.5 degrees at term. These alterations in toto lead to an enlargement of the circumference of the thoracic cage of from 5 to 7 cm. (39).

From the investigations on cardiac output, which are based on oxygen consumption per unit of time, and which as discussed reveal a 9 per cent to 10 per cent rise in oxygen uptake, it is evident that there must be a significant augmentation in the minute volume exchange. The ratio of air respired to the carbon dioxide expired per minute was found to be 13.4 per cent greater in pregnant than in non-pregnant women (25). Thus, more air passes through the lungs per unit of time. The increase in pulmonary ventilation which is already apparent in the first trimester and then disappears during the first two postpartum weeks is an expression of a rise in both tidal volume and respiratory rate. By the end of gestation, the augmentation in minute volume at rest amounts to an average of 43 per cent for multigravidae and 45 per cent for primigravidae (25), maximum observed 57 per cent (26).

The tidal volume rises progressively, paralleling the change in pul-
monary ventilation, and ranges from 334 ml. in early pregnancy to 396 ml. (multigravidas) or to 416 ml. (primigravidas) in later pregnancy (25). The respiratory rate is elevated from the fourth lunar month until term from an average of 14 per minute to 16.6 per minute (25) (table 5). Furthermore, pulmonary function tests showed greater air flows for given pressures during late pregnancy (26). This means that there is a lowered total pulmonary resistance, possibly owing to relaxation of the smooth muscles of the tracheobronchial tree.

**TABLE 5**

<table>
<thead>
<tr>
<th>Changes in Respiratory Values During Pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Percentage Above Normal</td>
</tr>
<tr>
<td>Minute volume</td>
</tr>
<tr>
<td>Tidal volume</td>
</tr>
<tr>
<td>Respiratory rate</td>
</tr>
<tr>
<td>44.0</td>
</tr>
<tr>
<td>21.5</td>
</tr>
<tr>
<td>18.5</td>
</tr>
</tbody>
</table>


Vital capacity has been reported as unchanged, increased or decreased, but variations mentioned were of no significant magnitude (60). The expiratory reserve is regularly decreased (26, 60); the inspiratory reserve is either unchanged or increased (60).

Roentgenograms show increased lung markings (39) and simulate a picture of mild congestive failure. An increase of the vascular bed in the lungs is the most probable explanation (10).

Dyspnea appears in about 60 per cent of normal pregnant women during the last trimester. It is probably related to the increased ventilatory requirement, but such respiratory distress is rarely sufficient to interfere with ordinary physical activity (26).

**Metabolism**

Metabolic changes during pregnancy include an increase in basal metabolic rate, the retention and storage of water (see "water balance"), protein, minerals and salts, and the acquisition of fat (61).

The average weight gain amounts to 20 to 25 pounds (62). It is attributable in part to the weight of the products of conception ("reproductive" weight gain 40 per cent) and in part to the metabolic alterations cited above ("net" maternal weight gain 60 per cent), (1, 2, 61).

The basal metabolic rate shows a definite elevation in the latter half of gestation (43, 61, 63, 64). After a small dip of 3 to 4 per cent in the early weeks, it rises near term to over +10 per cent (63). The mean increase in basal metabolic rate during pregnancy has been recorded as 14.27 (64). Women with the lowest nonpregnant basal rates tend to have the greatest gains (64). Recent studies found no correlation between basal metabolic rate changes and length of pregnancy, average weight gain of mother, or average weight and sex of offspring (63).
The protein metabolism is characterized by a substantial retention of nitrogen, provided an adequate diet is ingested (61, 65, 66). The retention is most marked in the middle of pregnancy, especially in the seventh month (65). During this same month, a peak of phosphorus and sulphur retention occurs which signifies protein formation and deposition (61). It is interesting that the highest rise in cardiac output also is manifest at this time.

Most minerals are retained in excess of the fetal needs in a large maternal store (61). Phosphorus storage is highest in the middle of pregnancy, and calcium retention at the end. It appears that phosphorus retention is related early to the nitrogen storage and later associated with the greater calcium deposition (65). Magnesium retention is irregular and inconsistent (65). Serum calcium and serum phosphorus levels decline gradually until the ninth month, when they begin to rise again. The depression of both is sufficiently small to make their clinical significance questionable (67–69).

Iron is retained by the maternal body during the first six months of pregnancy in excess of the low fetal needs then existing. However, during the last three months, the daily iron retention rarely reaches the necessary minimum without therapy (1). In addition to fetal demands, the mother has additional need for iron in connection with the greatly hypertrophied uterus and the augmented blood volume with its concomitant increase in red cells and hemoglobin. Only one-third of pregnant women not receiving supplemental iron maintain their hemoglobin above the lowest normal value for pregnancy (12 Gm. per cent) (7, 9). Radioactive iron was fed in single doses to women near term. It appeared in the fetal circulation in definitely measurable amounts within 40 minutes. This rapid rate suggests that plasma is the vehicle of transfer for the larger part, and that hemoglobin formation accounts for only a small portion (70).

The fat metabolism is marked by an increase in all lipid fractions in the maternal blood (61). The fats are more thoroughly absorbed from the intestines as shown by a diminution in the unabsorbed fats, fatty acids, and soaps in the feces (2). The hyperlipemia is due almost entirely to a rise in plasma fats; the red cells showing only slight changes. Neutral fat begins to increase in the first trimester and cholesterol and phospholipids in the second trimester. At term, neutral fat is elevated over 100 per cent, phospholipids and cholesterol are each raised about 25 per cent over their normal values (71). The ratios of phospholipid to cholesterol and cholesterol esters to total cholesterol are only slightly altered and there is no change in the composition of the fatty acids (71). The reasons for the alterations in fat during pregnancy are not known. However, they are similar to those found in the persistent lipemias of diabetes, experimental anemias and continued hemorrhage. A high fat intake during gestation causes a greater increase in the ketone bodies of the blood than is produced otherwise (2). An increase in plasma ketones, especially
in the beta-hydroxybutyric acid fraction, is common during the first trimester (18).

The carbohydrate metabolism per se is unaltered. Carbohydrates are not retained in excess, but there is an increased tendency to excrete sugars in the urine (61, 72). Glycosuria is found in 67 per cent of pregnant women at some time during the antepartum period and laetosuria in 94 per cent during the latter months (73). Blood sugar levels tend to fall slightly as pregnancy advances and average 85 to 80 mg. per cent throughout gestation. Sugar tolerance curves on normal pregnant women indicate that the glycosuria is the result of a lowered renal threshold, upon which is superimposed a diminished tolerance for sugar due to the decreased ability of the liver to store glycogen (2). The laetosuria is caused by a spillage of lactose formed by the mammary glands (73).

Ketosis is not normally present in pregnancy; the renal threshold to ketones is the same as in the nonpregnant state (74). The raised basal metabolism together with the drain by the fetus on the carbohydrates of the mother reduces the antiketogenic substances of the blood, and their replacement may be delayed because of the diminished storage of glycogen in the liver. At the same time, the lipids of the maternal blood are increased and the alkali reserve is lowered. These circumstances may readily lead to a disturbance of the ketogenic-antiketogenic balance and favor the production of ketosis (2).

Adrenal function is characterized by a marked increase in the secretion of the corticoids with very little change in the 17-ketosteroids (75). The high output of corticoids indicates an increase in the activity of the adrenal (75) and may account for the decrease in circulating eosinophiles (76) and the effect on the carbohydrate metabolism (2).

**Discussion**

The course of events outlined above progresses to a happy family, if recognition of normal variations permits the obstetrical team to temper action with judgment. The many alterations in the physiological mechanisms and laboratory findings may lead the uninured physician to active therapy with which the patient cannot cope. The changes during pregnancy are progressive and reach their peaks in different trimesters. Pregnant women coming to the hospital for intercurrent disease must be successfully guided through the surgical procedure to preserve not only their own welfare, but also the course of normal development. Attempts to treat normal variations from the non-pregnant state or return variations to normal values by anesthesiologists, surgeons, obstetricians or other members of the hospital team may be disastrous.

Evaluation of laboratory and clinical reports in recognition of the physiological changes are important to the competent anesthesiologist. In general, there is a retention of water and sodium, a large arterio-
venous shunt across the uterus, an intra-abdominal mass producing pressure and displacement, and respiratory and cardiac changes associated with these primary alterations. Metabolic changes are manifested by an increased metabolic rate and a compensated alkali deficit.

The retention of water and sodium is noted in the hemodilution and increased blood volume. This, together with the vascular shunt, causes an increased cardiac output and decreased peripheral resistance. Increased sympathetic tone partially compensates for the shunt (76, 77). Although the potential mother has slowly adapted to these stresses throughout pregnancy, the delicate balance may be easily disturbed. Stress of hemorrhage or high spinal anesthesia is poorly tolerated. The additional cardiac work and high blood volume may produce dyspnea by an incipient pulmonary edema. Overhydration or pulmonary obstruction may change this to a frank pulmonary edema. The rapid return of water and salt balance to normal after delivery and the decreased intra-abdominal pressure may play a role in the high incidence of headache following spinal anesthesia.

The effect of the large uterine mass is twofold. Actual obstruction, partial or complete, of venous return from the pelvic viscera and lower extremities slows venous flow in these areas, and thrombophlebitis is a frequent complication of pregnancy. Attempts to early ambulation has reduced the incidence somewhat, but patients must be vigorously encouraged to move their lower limbs following spinal anesthesia. The mass also reduces pulmonary reserve, and special attention to adequate ventilation under local, spinal or general anesthesia is essential.

The respiratory system is always a problem for the anesthesiologist. The engorgement of the larynx and mucous membranes does not usually result in obstruction, but endotracheal manipulations must be atraumatic. The decreased pulmonary reserve, the high basal metabolic rate, and the compensated alkali deficit serve as a basis for the production of acidosis and hypercarbia unless ventilation is regulated.

Reports through the years have indicated that all methods of anesthesia can be successfully employed during pregnancy, if sufficient attention is paid to detail by a skillful anesthesiologist. Each method and drug has specific advantages and disadvantages, but the anesthesiologist who knows the problems and is capable of managing an anesthetic technique is the prime advantage.

**Summary**

Those physiological changes in pregnancy which are of clinical importance to the anesthesiologist have been presented.

The most important findings in the blood are a hypervolemia combined with hemodilution and hypoproteinemia, a polymorphonuclear leucocytosis with reduction in lymphocytes and circulating eosinophiles, a significant increase in fibrinogen, an elevation in sedimentation rate, and a lowering of the carbon dioxide combining power.
The water balance is altered by a retention of water in all compartments.

The common changes in the circulatory system consist of an increase in cardiac output, a rise in basal heart rate, a higher susceptibility to functional murmurs and disorders of rhythm, a decrease in mean arterial blood pressure with an increase in pulse pressure, and an elevation of the venous pressure of the lower extremities.

The most striking alterations in the respiratory system are a rise in oxygen consumption, and an increase in the ventilation at rest.

The metabolism is characterized by an elevation in the basal metabolic rate, and by a tendency to iron deficiency, glycosuria and ketosis.

REFERENCES


