Physiologic Changes in Pregnancy: Surgical Implications

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Pregnancy has measurable effects on essentially every organ system in a woman's body. An understanding of these changes is vital for determining what is normal or abnormal in a pregnant woman. These changes frequently alter symptoms and signs of surgical diseases during pregnancy. In addition, many surgical diseases, as well as their therapies, have multisystemic effects. It therefore is mandatory to appreciate the physiologic changes that occur in a normal pregnancy to avoid incorrect diagnoses and treatments.

The mechanisms behind these physiologic changes are complex and not always well understood. However, many are mediated via progressive increases in pregnancy-associated hormones, such as progesterone, estrogens, and human placental lactogen, or by progressive increases in maternal cardiac output and blood volume.

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This article will review these physiologic changes, concentrating on an organ–system format, with particular emphasis on manifestations that might be confused with surgical diseases or that have implications for treatment.

Optimum Weight Gain

Optimum weight gain during pregnancy is dependent upon the patient's preconceptual nutritional status. In thin women, optimum pregnancy outcome occurs with weight gains of 25–35 pounds. The enlarging uterus and its contents contribute to the woman's weight 11–14 pounds at term, but the majority of the remaining weight gain is caused by progressive expansion of maternal blood volume (3–4 pounds) and involuntary caloric retention in the forms of fat and protein (4–6 pounds). The latter occur principally in the second trimester. Maternal caloric retention is caused by the body's anticipation of the progressive late pregnancy caloric requirements of the fetus as

TABLE 1. Recommended Daily Allowances for Pregnancy and Lactation

Nutrient	For Nonpregnant Women	Additional Requirements for Pregnant Women	Additional Requirements for Lactating Women
Calories (kcal)	2,100	300	500
Protein (gm)	44	30	20
Vitamin A (RE)	800	200	400
Vitamin D (μg)	7.5	0–5	0–5
Vitamin E (mg)	10	2	3
Ascorbic acid (mg)	60	20	40
Folic acid (mg)	0.4	0.3	0.1
Niacin (mg)	14	2	5
Riboflavin (mg)	1.3	0.3	0.5
Thiamin (mg)	1.1	0.4	0.5
Vitamin B6 (mg)	2	0.6	0.5
Vitamin B12 (μg)	3	1	1
Calcium (mg)	800	400	400
Phosphorus (mg)	800	400	400
Iodine (μg)	150	25	50
Iron (mg)	18	Supplement	0
Magnesium (mg)	300	50	150
Zinc (mg)	15	5	10

well as the increased caloric requirements of lactation. Other contributions to maternal weight gain include extracellular fluid (2–3 pounds) and breast enlargement (1–2 pounds). Obese women have optimum pregnancy outcomes with weight gains of 15–20 pounds and characteristically have less weight gain in the second trimester than do thin women. Obese women already have a substantially expanded vascular volume as well as an adequate caloric reserve.

In surgical patients, nutrition may be compromised by prolonged periods without oral intake. Although 5%-dextrose solution supplies minimal energy substrate, it is usually sufficient to maintain the patient and fetus for several days.[1] However, those patients who require longer periods of parenteral nutrition without enteral nutrition may require nutritional supplementation with total parenteral nutrition (TPN). The indications for starting TPN in a pregnant patient include situations in which the bowel is not functional, such as biliary disease, pancreatitis, or complex bowel surgery, and diseases requiring prolonged bowel rest. If prolonged bowel rest is anticipated, TPN should be started before the patient's own nutritional stores are depleted. Whenever the bowel is functional, but the patient is unable to eat, for example with hyperemesis gravidarum or oral surgery, enteral nutrition via feeding tube is appropriate.

Firm guidelines for the pregnant patient do not exist for TPN or enteral nutrition. Therefore, a team approach between the obstetrician and nutritionist is desirable. This should include routine laboratory studies as well as periodic ultrasonography to verify fetal growth. Persistent ketonuria should be avoided, and indicates insufficient nutritional supplementation. Most importantly, malnutrition is best avoided rather than corrected, especially in the pregnant woman.

Over the years, a substantial effort has gone into the definition of recommended dietary allowances during pregnancy and lactation. These recommendations are listed in Table 1.[2]

Female Reproductive Tract

The increase in uterine size during pregnancy is due primarily to cellular hypertro-

phy but is also the result of modest hyperplasia. There is a 20-fold increase in cellular mass and a thousandfold increase in intrauterine volume.

Uterine blood flow also increases enormously. Uterine artery blood flow increases from approximately 50 ml/min in the nonpregnant woman to 600 ml/min at the end of pregnancy. These increases are primarily estrogen-mediated and are critical for adequate delivery of oxygen and nutrients to the developing fetus. Uterine blood flow also may be affected by many drugs and maternal conditions (Table 2).

There is also a 60-fold increase in pelvic venous capacity by the end of pregnancy. These dilated pelvic veins are a frequent site of thromboembolisms. Although pregnancy is associated with a modest increased incidence in thromboembolic disease, there is a substantial additional increase in such complications in the first few weeks postpartum. Women with reproductive tract infections and/or operative deliveries are at a particularly increased risk. Pregnant women requiring surgery are also at an increased risk over the general population for thromboembolic disease. This necessitates appropriate prophylactic measures during surgery, usually with pneumatic compression devices.

Increases in blood volume within the uterus and pelvic vasculature represent approximately 1,000 ml at any moment late in pregnancy. This increased volume is not the result of shunting from elsewhere in the maternal circulation but rather represents an increase of maternal blood volume and cardiac output during pregnancy.

The breasts increase in size from early in pregnancy in anticipation of lactation. The enlargement of the ductal system is due primarily to estrogen, and the enlargement of the alveolar system is due to progesterone. A complex interaction of estrogen, progesterone, prolactin, human placental lactogen, insulin, and cortisol is required for lactation.

TABLE 2. Drugs and/or Maternal Conditions That May Affect Uterine Blood Flow

Increased uterine blood flow
Correction of acute factors (vide infra) responsible for decreased uterine blood flow
Estrogens (specifically estradiol)
Prostaglandins (especially PGI_2, PGE_2)
Decreased uterine blood flow
Uterine contractions
Labor
Oxytocin administration
Hypertonus (e.g., abruption)
Hypertension
Toxemia
Essential
Hypotension
Sympathetic blockade
Hypovolemia
Vasoconstrictors
Alpha-adrenergic drugs
Excess sympathetic discharge

PGI_2 = prostacyclin; PGE_2 = prostaglandin E_2.

Cardiovascular System

Cardiac output increases by 30–50% during pregnancy, from a level of 4.0–4.5 l/min in nonpregnant women to a maximum during pregnancy of approximately 6.0 l/min.[3] The increase in output is directed primarily to the maternal uterus, kidneys, and skin, and does not represent shunting from other organs. Cardiac output is the product of heart rate and stroke volume, which both increase during normal pregnancy. Stroke volume increases early in pregnancy, then decreases somewhat near term, and the maternal pulse gradually increases through the course of pregnancy to 15–20 beats/min over rates in nonpregnant women.

As previously stated, maternal blood volume also is increased by 30–50% during pregnancy. However, maternal red blood cell volume is only increased by 20–30%. This results in a decrease in hematocrit throughout the course of pregnancy, even though total maternal oxygen-carrying capacity is increased. In fact, failure of the maternal hematocrit to decrease during pregnancy (i.e., the failure of the maternal blood volume to expand) is associated with

a distinct increased risk of suboptimum pregnancy outcome. This mechanism is probably in a large part under genetic control.[4] Certainly, it is not necessary to impose large quantities of iron and vitamin supplements on pregnant women to overcome this physiologic hemodilution; however, the maternal hematocrit should be maintained above 30% to facilitate optimum oxygen supply to the fetus. This may require a lower threshold for transfusion in the pregnant woman after acute surgical blood loss.

Circulatory volume expansion may interfere with the diagnosis of surgical disease during pregnancy. This is seen mainly in situations of hypovolemia, because tachycardia and hypotension may not develop in pregnant patients until they lose 30–35% of their expanded circulating blood volume.[1] This maternal blood volume expansion is also partly responsible for the altered medication requirements frequently seen during pregnancy.

There is a progressive increase in lower extremity venous pressure during pregnancy. This is the result of several factors, including the expanded blood volume and compressive effects of the enlarged uterus. The ovarian artery and venous plexus compress the right common iliac vein. This latter effect explains why many of the signs and symptoms of increased lower extremity venous pressure, such as varicosities, are more frequent and more severe on the maternal right side. Upper extremity venous pressure and central venous pressure remain unchanged during pregnancy.

There is a decrease in systemic vascular resistance during pregnancy. When combined with the increase in cardiac output and blood volume, several characteristic changes can be expected on physical examination. Because the uteroplacental bed functions as a low-pressure, left-to-right shunt, the maternal blood pressure characteristically drops during the midportion of normal pregnancy. In the second trimester, this usually represents a systolic decrease of 5–10 mmHg and a diastolic decrease of 10–20 mmHg. These changes gradually return toward, or perhaps slightly above, the prepregnant levels by the end of pregnancy. Thus, what is normal pressure in the nonpregnant state may be considered abnormal in the middle portion of pregnancy. For example, a blood pressure of 140/90 mmHg would be a considered borderline level in the nonpregnant state. However, it should be considered distinctly abnormal at 20 weeks' gestation, reflecting either a prepregnant pressure of approximately 145–150/100–110 mmHg or a failure of the maternal vascular volume to expand. In either case, such a pregnancy is at increased risk for superimposed preeclampsia, abruption, stillbirth, a small-for-gestational age fetus, and various neonatal complications.

Many of the normal cardiovascular changes in pregnancy could be misconstrued as representing primary cardiovascular disease. Cruikshank and Hays[5] note that a number of physiologic changes of normal pregnancy might be misdiagnosed as heart disease (Table 3).

TABLE 3. Signs and Symptoms of Normal Pregnancy That May Mimic Heart Disease

Symptoms
Reduced exercise tolerance
Dyspnea
Signs
Peripheral edema
Distended neck veins
Point of maximal impulse displaced laterally
Auscultation
Increased splitting of first and second heart sounds
Third heart sound (S3 gallop)
Systolic ejection murmur along left sternal border
Chest radiography
Straightening of left heart border
Heart position more horizontal
Increased cardiothoracic ratio
Increased pulmonary vascular markings
Electrocardiogram
Left axis deviation (without hypertrophy)
Nonspecific ST-T wave changes

From Cruikshank DP, Hays PM.[5] By permission.

Labor and delivery, as well as the immediate puerperium, are periods of increased cardiovascular stress. During labor, cardiac output may increase further by as much as 40%. Although some of this is undoubtedly the result of response to pain,[6] some is also due to the cardiovascular effects of labor contractions. Each contraction squeezes 300–500 ml of blood out of the uterus and into the maternal vasculature. This leads to increased venous return and subsequent increased cardiac output. The immediate puerperium also is associated with changes in cardiac output as a result of immediate "autotransfusion" of 500–800 ml of volume previously contained within the vasculature of the term uterus. There is also a substantial mobilization of intracellular fluid in the first 48 hours postpartum. Both result in a 10–20% increase in cardiac output, reflex bradycardia, and increased stroke volume.

Histologic changes in the peripheral vasculature also occur during pregnancy. These include hyperplasia of the arterial and venous intima and changes in the organization and content of the arterial media. These conditions may predispose the pregnant woman to the formation or rupture of arterial aneurysms.

Because of the multiple changes in the cardiovascular system during pregnancy, the hemodynamic status of the pregnant woman is often confusing. Therefore, acutely ill, pregnant surgical patients may benefit more often from invasive hemodynamic monitoring to facilitate appropriate fluid resuscitation and care.

Respiratory System

Maternal respiratory adaptations during pregnancy can be understood best if one considers that the pregnant woman must get oxygen in and carbon dioxide out for two individuals. Fetal oxygen requirements increase exponentially during pregnancy. This is reflected clinically as a progressive increase in minute volume during pregnancy. Although the diaphragm is elevated during pregnancy, actual diaphragmatic excursion is not impeded. This physiologic "hyperventilation" requires greater use of the accessory breathing muscles. The progressive circumferential expansion of the chest cage during pregnancy, averaging 5–7 cm, frequently results in disruption of chest wall proprioceptors. The combined reduction in maternal P_{CO_2} and increase in tidal volume accounts for the sensation of dyspnea and breathlessness reported by two thirds of pregnant women.

Changes in pulmonary-function testing associated with pregnancy also reflect the need for increased maternal gas exchange. The progressive increase in tidal volume and minute respiration reach 30–40% by term. Because vital capacity and respiratory rate remain unchanged, the increase in tidal volume occurs in association with a decrease in expiratory reserve volume.

Neither forced vital capacity nor forced expiratory volume are altered by pregnancy, consistent with the observation that large airway function is unaltered by pregnancy.[7] Likewise, there is no evidence of impaired small airway function in pregnancy.[8]

Analysis of arterial blood gases during pregnancy reflects this physiologic hyperventilation. Maternal P_{CO_2} is decreased, and maternal pH is increased. Because oxygen consumption increases less (15–20%) during pregnancy than does minute ventilation, a modest increase in maternal arterial P_{O_2} levels occurs. These changes in maternal P_{CO_2} and P_{O_2} are important because they enhance the exchange gradients between other and fetus for carbon dioxide and oxygen. The partially compensated respiratory alkalosis is apparent within the first few months of pregnancy. Women with significant pulmonary disease, especially of an obstructive nature, are affected adversely by the physiologic changes of pregnancy. By far, the most common respiratory disease seen in association with pregnancy is

asthma. Because of its intermittent nature, the predictability of its course during pregnancy is often difficult.

Ophthalmic Changes

Many of the ophthalmic changes in normal pregnancy are the result of the modest increase in extracellular fluid. Other physiologic changes that have ophthalmic implications include progressive increases in melanocyte-stimulating hormone and enlargement of the pituitary gland.

Progressive hyperpigmentation of the eyelids is the result of increased melanocyte-stimulating hormone. Pregnancy does not affect extraocular eye movements but is associated with a modest increase in corneal edema. As a result, contact lenses may not fit as well during pregnancy. In addition, there appears to be a decrease in corneal sensitivity during the third trimester. There is also a modest increase in extracellular fluid in the lens during pregnancy, resulting in a tendency toward myopia.

Intraocular pressure tends to decrease during the second half of pregnancy, suggesting that glaucoma and its sequelae might be less common in pregnant women. Because there are no normal pregnancy-associated changes in the retina, any observed retinal changes must be explored further. The pituitary gland increases in size during pregnancy, and a modest bitemporal hemianopsia can occur in some women.

There are no other normal pregnancy-associated changes in the optic nerve, chiasm, or retrochiasmatic structures. Specifically, normal pregnancy is not associated with increased intracranial pressure or papilledema.

Otorhinolaryngologic Changes

Most otorhinolaryngologic changes associated with pregnancy are the result of progesterone-mediated mucosal hyperemia. This hyperemia is most apparent in the oropharynx. Hyperemia of the nasal mucosa increases the frequency and severity of epistaxies and may cause symptomatic nasal congestion. In pronounced cases, this occurrence may be misinterpreted as a chronic upper respiratory infection, and only modest improvement is achieved with medications. However, these symptoms dramatically resolve 2–3 days postpartum, in conjunction with the postpartum decrease in mucosal hyperemia.

In addition, pregnant women with preexisting periodontal disease can anticipate exacerbation. There are changes in the oral cavity microbial flora that approximate those seen in the reproductive tract.

Mucosal edema in the oropharynx has significant anesthetic implications. As mucosal edema increases, especially in the third trimester or with preeclampsia, intubation and general anesthesia become more difficult. The visibility necessary for intubation may be compromised, requiring fiberoptic procedures, awake intubations, or, possibly, a significant delay of surgical procedures. In extreme emergencies, the surgeon must be prepared always to perform a tracheostomy to restore the maternal airway.

Mucosal hyperemia may predispose a woman to functional occlusion of the eustachian canal. This occlusion frequently becomes symptomatic when pregnant women experience sudden changes in altitude (e.g., during travel by airplane). The modest increase in extracellular fluid in the semicircular canals also may explain in part why pregnant women are likely to experience transient dizziness with sudden changes in position. Pregnant women are also relatively more likely to experience symptomatic accumulation of cerumen in the external auditory canal.

Endocrine System

The endocrine system undergoes profound alterations during pregnancy. Many of these

changes reflect progressive estrogen-mediated increases in hormone binding proteins.

Although hypothalamic function appears unaltered during pregnancy, there is a progressive increase in pituitary size and blood flow during pregnancy. This increase in pituitary blood flow is responsible partly for the increased susceptibility of the gland to ischemic necrosis during pregnancy and the immediate puerperium (Sheehan's syndrome).

Prolactin levels progressively increase from early in pregnancy. This change has obvious clinical importance, because it negates the usefulness of this blood test for diagnosing or following prolactinomas.

Pregnancy is associated with a progressive increase in thyroid-binding globulin. This increase results in a characteristic alteration in thyroid-function tests with an increase in total T_4, a decrease in T_3-resin uptake, and an unchanged thyroid function index (reported by most laboratories as a T_7 or free-thyroid index) (Table 4). Although recent laboratory analysis suggests that there may be a modest increase in free T_4 during pregnancy, this increase in free T_4 is controversial and is not of major clinical significance.

Pregnancy is also associated with a progressive increase in corticosteroid-binding globulin, resulting in an elevated plasma cortisol concentration. By the end of pregnancy, this increase in total cortisol may be as much as a threefold. Because the proportion of bound and free cortisol does not change during pregnancy, there is a relative increase in free cortisol during pregnancy. Although these increased levels may overlap with levels seen in Cushing's syndrome, diurnal variability is preserved and serves as a potentially valuable clinical discriminator.

There is no consistent increase in total weight of the normal adrenal gland, although there is a relative increase in the zona fasciculata. The zona fasciculata is responsible for glucocorticoid production. Its increase is compatible with laboratory observations that the increase in circulating glucocorticoids is the result not only of increased corticosteroid-binding globulin and decreased clearance, but of increased production as well. Those changes return to, or below, prepregnant values within the first 2 weeks postpartum and may explain in part the pregnancy-associated improvement of some autoimmune diseases (notably rheumatoid arthritis) as well as the puerperal exacerbation of others (e.g., systemic lupus erythematosus).

TABLE 4. Pregnancy-Associated Changes in Thyroid Function Tests

	Nonpregnant	Pregnant
TBG (ng/dl)	19–30	40–60
T_4 (ng/dl)	5–10	8–16
T_3 (ng/dl)	65–14	140–180
RT_3U (%)	30–40	<30
FTI ("T7)	1.5–4.0	1.5–4.0

Other alterations occur in maternal corticosteroid concentrations that are not the exclusive result of altered maternal physiology. Pregnancy is associated with progressive increases in deoxycorticosterone, but this reflects increased production by the fetoplacental unit. Maternal levels are not affected either by adrenocorticotrophic hormone administration or by dexamethasone suppression.

The adrenal medulla also is affected by pregnancy. Normal pregnancy is associated with a substantial and progressive increase in aldosterone levels. This increase promotes sodium reabsorption in the renal tubules. Although estrogens and deoxycorticosterone also function in this way, the major increase in circulating aldosterone levels is the predominant mechanism by which the net sodium requirements of pregnancy (900–1,000 mEq Na^+ in the fetus, placenta, and maternal intra- and extra-vascular space) are met. These changes are necessary because there otherwise exists during preg-

nancy the possibility of a significant natriuresis as a result of the increased glomerular filtration rate and increasing progesterone concentrations.

Normal pregnancy is characterized by accelerated starvation in the fasting state. Fasting blood sugars are normally 10–15 mg% below those seen in the nonpregnant state. This is the result primarily of the continuous transplacental metabolic drain of glucose to the fetus and is not due to a persistent hyperinsulinemia. In fact, the unfed state generally is thought to be associated with hypoinsulinemia. During pregnancy, starvation predisposes the woman to ketosis because of rapid transplacental shunting of glucose and a decrease in serum buffering capacity. On the other hand, the fed state during pregnancy is characterized by hyperglycemia and hyperinsulinemia. This apparently paradoxical situation is explained by the progressive increase of hormones that are functional insulin antagonists. These include estrogens, progestins, adrenal corticosteroids, and human placental lactogen. These result in a 60–80% increase in insulin resistance during pregnancy.

While most pregnant women respond to these changes by producing sufficient extra insulin, 44–6% of pregnant women will be unable to increase their insulin production adequately and will develop gestational diabetes. Women particularly prone to this complication include those who have a family history of type II diabetes or are obese, and those who have a past obstetric history of delivering large or anomalous babies or having unexplained stillbirths.

Together, the fetus and placenta produce the majority of biologically active hormones in the maternal compartment. Human chorionic gonadotropin, synthesized by the syncytiotrophoblast in the placenta, is a luteotrophic agent that maintains the corpus luteum during early pregnancy. It also enhances steroidogenesis in the placenta and the fetal adrenal gland and also is of value as a tumor marker for various trophoblastic and nontrophoblastic malignancies. Certain systemic diseases (e.g., urinary tract infection, proteinuria, hematuria, and systemic lupus erythematosus) can cause false-positive human chorionic gonadotropin assays, as can certain drugs (i.e., phenothiazines, barbiturates, methadone, and penicillin).

As previously mentioned, progesterone causes numerous physiologic effects in pregnancy. In the first few weeks after conception, it is produced primarily by the corpus luteum. After the first 8–10 weeks, the majority of progesterone is produced by the fetoplacental unit.

Human placental lactogen production by the syncytiotrophoblast is directly proportional to the functional placental size. It is secreted primarily into the maternal compartment, where it facilitates adequate nutrient delivery to the fetus (lipolysis, maternal insulin antagonism).[9]

Orthopedic Changes

Pregnancy is characterized by progressive ligamentous laxity, especially of the weight-bearing joints. This is caused by the effects of progesterone and relaxin. Mobility of the pelvic synchondroses and the pubic symphysis can be demonstrated radiographically and undoubtedly facilitates normal vaginal delivery. Unfortunately, these changes also may lead to pelvic discomfort late in pregnancy. In an attempt to maintain the center of balance over the legs, the pregnant woman experiences progressive outward rotation of the femurs as well as lumbar lordosis with thoracic kyphosis and cervical lordosis. Consequently, there is a greatly increased incidence of low back discomfort and exacerbation of preexisting lumbosacral disc disease. These changes predispose the pregnant woman to an unsteady gait, and pregnancy is a period of increased risk for falls and other trauma. However, pregnancy also is associated with increased rates of domestic violence, and

this possibility always should be considered in the differential diagnosis of orthopedic and soft tissue injury.

The increase in extracellular fluid accumulation during pregnancy predisposes the pregnant woman to entrapment syndromes, particularly carpal tunnel syndrome. Total maternal serum calcium concentrations gradually decrease during pregnancy, primarily because of the progressive decrease in serum albumin that occurs during pregnancy.[10] The ionized calcium concentration remains unchanged during gestation, in spite of several changes that might be expected to cause a decrease. These changes include transplacental calcium transfer, increased extracellular fluid volume, and the increased glomerular filtration rate. The ionized calcium concentration is maintained at a normal nonpregnant level as a result of a progressive increase in the parathyroid hormone concentration, which reaches over 100% above nonpregnant values by term. In spite of this increase in parathyroid hormone concentration, no significant calcium is lost from bone, perhaps because of a secondary increase in calcitonin concentration during pregnancy.

Neurologic Changes

There is no evidence that central nervous system blood flow is altered by pregnancy, although pregnancy does seem to increase the frequency of cerebrovascular disease. The majority of physiologic changes in the nervous system reflect peripheral nerve entrapment syndromes due to increased extracellular fluid retention or hormonally mediated ligamentous relaxation.

Muscle cramps are distinctly more common during pregnancy. It is estimated that as many as 30% of pregnant women experience painful muscle cramps,[11,12] almost always involving the leg muscles and frequently occurring at night. The cause of leg cramps during pregnancy remains unknown. It clearly is not related to preconceptual conditioning, although vigorous exercise may aggravate the tendency. Likewise, women who experience leg cramps before conception may find them to occur more frequently and be more severe during pregnancy, particularly if other predisposing factors, such as salt depletion, dehydration, uremia, or hypothyroidism also are present. Likewise, certain rare medical complications may be associated with muscle cramps plus generalized weakness including extrapyramidal or pyramidal dis orders, amyotrophic lateral sclerosis, tetanus, or myophosphorylase deficiency (McArdle's Disease).

Renal System

The major renal adaptations to pregnancy result from pregnant woman's efforts to clear not only her own fixed metabolic wastes but those of the fetus as well. This is accomplished via increased renal blood flow and glomerular filtration. Increased renal blood flow is associated with an increase in renal vascular and interstitial volume, resulting in increased renal size during pregnancy. Whether measured by renal plasma flow or glomerular filtration rate, renal blood flow increases within a few weeks after conception. This increase is associated with many alterations in normal laboratory values. There is an increase in creatinine clearance during pregnancy to an average of 110–160 ml/min, as well as a decrease in serum creatinine concentration (normal value in pregnancy, < 0.9 mg%), serum blood urea nitrogen concentration (normal value in pregnancy, < 15 mg%), and serum uric acid concentration (normal value in pregnancy, < 6 mg%). These changes are prominent by the end of the first trimester and are outlined in Table 5.

It is important to remember these changes, because a patient with moderate renal disease may have falsely normal-appearing laboratory parameters beyond the end of the first trimester. There is no sig-

TABLE 5. Changes during Pregnancy of Renal Function Parameters

Parameter	Relative Change	Nonpregnant	Late Pregnancy
Renal plasma flow (ml/min)	↑	428	695
Glomerular filtration rate (ml/min)	↑	100 ± 18	150 ± 30
Creatinine clearance	↑	80–120	120–180
Blood urea (BUN) (mg%)	↓	10–20	≤ 15
Creatinine (mg%)	↓	0.7–1.4	≤ 0.9
Uric acid (mg%)	↓	3.0–5.4	2.0–4.7
Plasma osmolality (mOsm/kg H_2O)	↓	285 ± 5	275 ± 5
Aldosterone (ng/l)	↑	100–200	200–700
Plasma renin activity	↑	0.45–1.28	3.33–4.09
Proteinuria (mg/24 hr)	–	100–300	100–300

nificant increase in urinary protein excretion during pregnancy, although specimen contamination with vaginal secretions normally may increase total urinary protein concentration to as much as 300 mg per 24 hours.

Pregnancy is associated with progressive ureteral and renal pelvic dilation, resulting in a doubling of collecting-system volume due to the effects of progesterone on ureteral smooth muscle as well as compression by the enlarging uterus and infundibulopelvic ligaments. These changes, more prominent on the maternal right side than on the left, result in characteristic changes on intravenous pyelography, including ureteral dilation (greater on the right than the left), blunting of the renal calyces, and an increase in renal size. As a result of these changes, pregnant women with bacteriuria are at an increased risk for developing symptomatic upper urinary tract infection. Pregnancy per se does not increase the risk of asymptomatic bacteriuria.

Plasma osmolality begins to decrease within the first month after conception, and by the end of the first trimester decreases by 10 mOsm/kg. This decrease is due primarily to a decrease in the serum sodium concentration. In spite of this change, sodium metabolism is altered during pregnancy to allow the accumulation of approximately 1,000 mEq of sodium. Although the increases in glomerular filtration rate and serum progesterone might be expected to cause an increase in urinary sodium excretion, these changes are more than offset by increased renal tubular reabsorption. Renal tubular absorption is mediated by increased concentrations of aldosterone, desoxycorticosterone, and estrogen during pregnancy.

There are also significant changes in the renin–angiotensin system during pregnancy, and these, in turn, are responsible for the observed increase in aldosterone. Plasma renin activity is increased by approximately five times, as are concentrations of angiotensin and angiotensinogen. The normal pregnant woman has a substantially reduced sensitivity to these vasopressors, but their increase leads to the aforementioned increase in aldosterone production. Women who subsequently develop preeclampsia show evidence of increased sensitivity to these vasopressors many weeks before their disease becomes clinically evident. Recent evidence suggests that this altered sensitivity has a strong genetic component.

Urinary glucose excretion is increased in most pregnant women, primarily because of the increased glomerular filtration rate. As a result, as much as 25% of all pregnant women have glycosuria during pregnancy. Clinicians appropriately manage diabetes via blood glucose determinations, because these physiologic alterations make urine

TABLE 6. Changes during Pregnancy in Serum Chemistries Reflecting Hepatic Function

Parameter	Change	Normal Nonpregnant Value	Late Pregnancy Value
Total protein (g/dl)	↓	6.5–7.5	5.7–6.5
Albumin (g/dl)	↓	3.2–3.8	2.4–3.1
Alkaline phosphatase (IU/l)	↑	30–115	100–210
Aspartate transaminase (IU/l)	–	0–31	Unchanged
Lactate dehydrogenase (IU/l)	–	100–210	Unchanged
Total bilirubin (mg/dl)	–	0.26–1.00	Unchanged
Prothrombin time (seconds)	–	10–13	Unchanged
Partial thromboplastin time (seconds)	–	22–33	Unchanged
Bleeding time	–	≤8	Unchanged
Cholesterol (mg/dl)	↑	120–190	190–330
Triglycerides (mg/dl)	↑	76–92	205–247

glucose values unreliable. Likewise, there is a progressive urinary excretion of many, but not all, amino acids.[13]

Gastrointestinal System

Most physiologic alterations of the gastrointestinal tract during pregnancy are the result of progesterone-mediated smooth muscle relaxation or mechanical displacement of the abdominal viscera by the enlarging uterus. This displacement occurs in superior, lateral, and posterior directions.

Progesterone causes a decrease in the tone of the functional gastroesophageal sphincter, resulting clinically in increased heartburn. Likewise, there is an increase in small bowel transit time, allowing more complete absorption of nutrients. The increased transit time in the colon promotes more complete water absorption and constipation.

Although appendicitis is no more common in pregnant women than it is in nonpregnant women, it is more serious in pregnancy for the following reasons: the appendix is displaced upward and outward from McBurney's point (and therefore often misdiagnosed as cholecystitis) late in pregnancy; there is a general reticence among physicians to perform exploratory laparotomies on pregnant women; and, if the appendix ruptures, the omentum is less capable of preventing a generalized peritonitis.[14]

Cholecystitis may be another source of acute abdominal pain in a pregnant woman. While 95% of nonpregnant women have gallstone cholecystitis, gallstones are found in only 50–90% of pregnant woman with symptomatic cholecystitis. Murphy's sign is positive in only about 5% of pregnant women with cholecystitis, and laboratory tests of liver function are less likely to be abnormal during pregnancy. Although conservative management is the initial treatment of choice, delaying appropriate surgical therapy is not warranted. Both open and laparoscopic techniques have been described during pregnancy with low complication rates.[15–17]

There is no change in hepatic blood flow during pregnancy, but several serum chemistries reflective of liver dysfunction may be altered by normal pregnancy (Table 6). There is a decrease in total protein and albumin concentrations. Serum alkaline phosphatase concentrations progressively increase during pregnancy and reflect placental production (heat-stable) rather than obstructive liver disease or bone disease. Serum cholesterol levels increase throughout pregnancy and are approximately double the nonpregnant levels by term.

There are no changes normally associated with pregnancy in the serum levels of transaminases, lactate dehydrogenase, and bilirubin. Alternative explanations for abnormalities in these values always must be sought.

Although concentrations of fibrinogen and factors VII–X increase during pregnancy, concentrations of factors V and XII, as well as factor II (prothrombin), remain unchanged, and concentrations of factors XI and XIII decrease. There are no changes in the standard coagulation function tests, and the bleeding time is normal during pregnancy. Nonetheless, pregnancy generally is considered a hypercoagulable state. Although pregnancy is associated with a 1.5–2.0-fold increase in thromboembolic disorders, the first few weeks of the puerperium is actually the period of greatest risk, with relative risks generally noted to be between four- and sixfold greater than in the nonpregnant state. This certainly demonstrates the importance of small vessel injury and stasis for the development of thromboembolic disorders.

Acute abdominal pain, regardless of cause, is a great source of confusion for the physician and surgeon. Almost 50% of preoperative diagnoses in pregnant women with acute abdominal pain are incorrect[19]; therefore, a firm preoperative diagnosis is not always essential. Although perinatal outcome depends on the severity of the underlying disease process, delay in the diagnosis and therapy is the major cause of excessive maternal and fetal morbidity and mortality.[1,18,19] By far, the most common complication reported from surgical diseases and procedures is preterm labor.

In addition to appendicitis and cholecystitis, other potential surgical diseases in pregnancy include gallstone pancreatitis, adnexal masses or torsion, and acute trauma.[20–22]

Hematologic Changes

Not only does maternal blood volume expand by 30–50% during normal pregnancy, but circulating red blood cell mass also increases by 20–30%. The net result is that pregnant women have an apparent decrease in their hematocrit, even though their total oxygen carrying capacity is increased. This makes teleologic sense: If a pregnant woman must pump 30–50% more blood through her vascular system 30–50% faster than she does in the nonpregnant state, it would be easier to do if that blood were less viscous. Certainly, the once-held opinion that pregnancy represented a "physiologic anemia" should be discarded. Normal pregnancy is associated with a 10–20% relative decrease in hematocrit, which is maximal at about 34 weeks' gestation. In fact, hematocrit levels that do not decrease are associated with failure of maternal volume expansion. This, in turn, places the pregnancy at risk for complications, including small-for-gestational age fetus, premature labor, and stillbirth. The increase in maternal blood volume also protects the mother from hemorrhage at the time of delivery, dissipates fetal metabolic heat, and provides adequate renal and placental perfusion.

Although iron and folate supplementation is appropriate to optimize maternal hematopoiesis, it need not be prescribed in quantities sufficient to maintain maternal hematocrits at nonpregnant levels. The purpose of iron supplementation during pregnancy is to prevent iron deficiency in the mother, not to maintain the maternal hematocrit or supplement the fetus. Iron is transported actively across the placenta, even with clinical and laboratory evidence of iron deficiency in the mother. In this regard, red blood cell indices do not change during a normal pregnancy.

Peripheral white blood cell counts progressively increase during pregnancy. By the end of the first trimester, the average white blood cell count is between 9,000 cells/mm and 10,000 cells/mm,^{3} with a modest further increase through the second and third trimesters. Labor and the immediate puerperium may be associated with a substantial leukocytosis, to as high as 20,000–30,000 cells/mm^3 and do not necessarily reflect other underlying pathology. These increases are primarily in leukocytes. Although the

number of lymphocytes remains unchanged, the number of helper T3-cells decreases through the course of pregnancy. This suggests that the acquired immune deficiency syndrome may be unmasked or exacerbated by pregnancy, although there is no clinical evidence for this hypothesis.

Platelet counts decrease modestly during pregnancy, although the platelet count in a normal pregnancy should remain within the normal range for a nonpregnant woman. There is evidence to suggest that the average platelet lifespan is somewhat shorter during pregnancy. This is manifested by a modest increase in platelet size during pregnancy, reflecting the presence of younger, and therefore larger, platelets in the peripheral circulation. Platelets also are likely to aggregate in late pregnancy and the puerperium. This may explain in part the increased incidence of cerebrovascular disease during this time.

The relative increase in circulating coagulation factors during pregnancy is associated with an increased incidence of cerebrovascular disease. This increase is particularly prominent in the first few weeks postpartum, especially if the pregnancy has been complicated by preeclampsia, chronic hypertension, or a significant hypotensive episode.

Dermatologic Changes

Pregnancy is associated with progressive, increased pigmentation in areas of high melanocyte concentration, particularly the eyelids, areola, linea nigra, and external genitalia. This is the combined effect of progressive increases of melanocyte-stimulating hormone, estrogen, and progesterone. Estrogen and progesterone also seem to be responsible for the occasional development of chloasma in pregnant women. This frequently is referred to as the "mask of pregnancy" and represents a photosensitive hyperpigmentation. It also may be seen in women taking oral contraceptives. Although this condition may fade after delivery, little can be done to treat it, and it is best prevented with sunscreen preparations.

Palmar erythema and/or spider nevi are seen commonly in pregnant women, with two thirds of women having one or both. The spider nevi are most common over the area of superior vena cava distribution. These changes reflect the progressive increase in circulating estrogen levels during pregnancy and do not represent hepatocellular dysfunction.

Pregnant women frequently report that their hair is coarser and/or straighter than normal. Alopecia is seen occasionally in association with pregnancy but is very common at 2–4 months postpartum. This is a transient phenomenon and should be expected to be resolved by 6–12 months postpartum.

Pregnancy also may be associated with a more masculine hair distribution pattern. This reflects a modest but progressive increase in circulating androgen levels during pregnancy, and patients can be reassured that these changes will be resolved postpartum. Significant masculinization is not normal and requires further investigation.

Women are more diaphoretic during pregnancy. In a large part, this represents their need to dissipate not only their own metabolic heat but that of the fetus as well.

Stretch marks, or striae, are common in pregnancy, being somewhat more common in women who are tall, obese, or blonde. They are seen most commonly on the breasts, lower abdomen, buttocks, and anterior thigh. Their cause remains unclear but is probably a combination of collagen-fibril weakening and mechanical disruption by expanding underlying tissue in genetically predisposed individuals. There as yet is no effective prophylaxis.

Psychiatric/Psychologic Changes

Most pregnant women have some degree of anxiety or apprehension about their preg-

nancy. This often is evident as the fear of delivering an abnormal infant, concern about injury or pain during labor and delivery, or ambivalence toward the pregnancy or parenthood. Appreciation that these apprehensions are common allows the health care provider to resolve them with explanations and/or counselling.

Pregnancy, labor and delivery, and parenthood are stressful events. Therefore, they might be expected to unmask latent psychiatric disease or psychologic dysfunction. This issue is confused further by the profound hormonal changes that occur during pregnancy and the puerperium, which may have psychologic implications.

Postpartum depression is a very common occurrence, with over half of all puerperal women having some degree of transient depression. This occurs most commonly around 3–7 days postpartum. As long as it is short lived (a few days) and is not associated with suicidal thoughts or attempts or delusional ideation, patients may be reassured. If any of the above psychiatric signs are seen, however, prompt psychiatric consultation is mandatory.

Conclusion

Almost every system is affected in some manner by pregnancy and the postpartum period. This may have profound effects on the course of surgical diseases in these women, the choice of diagnosis, and the treatment protocols used to treat them. It therefore is important for physicians dealing with women in the reproductive age group, especially during pregnancy, to obtain a working knowledge of the physiologic state of pregnancy and the puerperium. It also is important to remember that the most severe complications from surgical diseases in pregnant women result from delayed diagnosis and subsequently delayed treatment. Some of these complications can be avoided, given adequate understanding of the changes occurring during pregnancy and the puerperium along with the knowledge of the surgical disease processes.

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