**physiology of lactation and details on the physiology of pregnancy in a normal woman**

**LACTATION;**

Lactation is the process by which milk is synthesized and secreted from the mammary glands of the postpartum female breast in response to an infant sucking at the nipple. Breast milk provides ideal nutrition and passive immunity for the infant, encourages mild uterine contractions to return the uterus to its pre-pregnancy size (i.e., involution), and induces a substantial metabolic increase in the mother, consuming the fat reserves stored during pregnancy.

**Structure of the Lactating Breast**

Mammary glands are modified sweat glands. The non-pregnant and non-lactating female breast is composed primarily of adipose and collagenous tissue, with mammary glands making up a very minor proportion of breast volume. The mammary gland is composed of milk-transporting lactiferous ducts, which expand and branch extensively during pregnancy in response to estrogen, growth hormone, cortisol, and prolactin. Moreover, in response to progesterone, clusters of breast alveoli bud from the ducts and expand outward toward the chest wall. Breast alveoli are balloon-like structures lined with milk-secreting cuboidal cells, or lactocytes, that are surrounded by a net of contractile myoepithelial cells. Milk is secreted from the lactocytes, fills the alveoli, and is squeezed into the ducts. Clusters of alveoli that drain to a common duct are called lobules; the lactating female has 12–20 lobules organized radially around the nipple. Milk drains from lactiferous ducts into lactiferous sinuses that meet at 4 to 18 perforations in the nipple, called nipple pores. The small bumps of the areola (the darkened skin around the nipple) are called Montgomery glands. They secrete oil to cleanse the nipple opening and prevent chapping and cracking of the nipple during breastfeeding.

**The Process of Lactation**

The pituitary hormone prolactin is instrumental in the establishment and maintenance of breast milk supply. It also is important for the mobilization of maternal micronutrients for breast milk.

Near the fifth week of pregnancy, the level of circulating prolactin begins to increase, eventually rising to approximately 10–20 times the pre-pregnancy concentration. We noted earlier that, during pregnancy, prolactin and other hormones prepare the breasts anatomically for the secretion of milk. The level of prolactin plateaus in late pregnancy, at a level high enough to initiate milk production. However, estrogen, progesterone, and other placental hormones inhibit prolactin-mediated milk synthesis during pregnancy. It is not until the placenta is expelled that this inhibition is lifted and milk production commences.After childbirth, the baseline prolactin level drops sharply, but it is restored for a 1-hour spike during each feeding to stimulate the production of milk for the next feeding. With each prolactin spike, estrogen and progesterone also increase slightly.

When the infant suckles, sensory nerve fibers in the areola trigger a neuroendocrine reflex that results in milk secretion from lactocytes into the alveoli. The posterior pituitary releases oxytocin, which stimulates myoepithelial cells to squeeze milk from the alveoli so it can drain into the lactiferous ducts, collect in the lactiferous sinuses, and discharge through the nipple pores. It takes less than 1 minute from the time when an infant begins suckling (the latent period) until milk is secreted (the let-down).

**Changes in the Composition of Breast Milk**

In the final weeks of pregnancy, the alveoli swell with colostrum, a thick, yellowish substance that is high in protein but contains less fat and glucose than mature breast milk. Before childbirth, some women experience leakage of colostrum from the nipples. In contrast, mature breast milk does not leak during pregnancy and is not secreted until several days after childbirth.

mature breast milk does not leak during pregnancy and is not secreted until several days after childbirth.

| **Table 1. Compositions of Human Colostrum, Mature Breast Milk, and Cow’s Milk (g/L)** |
| --- |
|  | **Human colostrum** | **Human breast milk** | **Cow’s milk\*** |
| **Total protein** | 23 | 11 | 31 |
| **Immunoglobulins** | 19 | 0.1 | 1 |
| **Fat** | 30 | 45 | 38 |
| **Lactose** | 57 | 71 | 47 |
| **Calcium** | 0.5 | 0.3 | 1.4 |
| **Phosphorus** | 0.16 | 0.14 | 0.90 |
| **Sodium** | 0.50 | 0.15 | 0.41 |
| \*Cow’s milk should never be given to an infant. Its composition is not suitable and its proteins are difficult for the infant to digest. |

Colostrum is secreted during the first 48–72 hours postpartum. Only a small volume of colostrum is produced—approximately 3 ounces in a 24-hour period—but it is sufficient for the newborn in the first few days of life. Colostrum is rich with immunoglobulins, which confer gastrointestinal, and also likely systemic, immunity as the newborn adjusts to a nonsterile environment.

After about the third postpartum day, the mother secretes transitional milk that represents an intermediate between mature milk and colostrum. This is followed by mature milk from approximately postpartum day 10. As you can see in the accompanying table, cow’s milk is not a substitute for breast milk. It contains less lactose, less fat, and more protein and minerals. Moreover, the proteins in cow’s milk are difficult for an infant’s immature digestive system to metabolize and absorb.

The first few weeks of breastfeeding may involve leakage, soreness, and periods of milk engorgement as the relationship between milk supply and infant demand becomes established. Once this period is complete, the mother will produce approximately 1.5 liters of milk per day for a single infant, and more if she has twins or triplets. As the infant goes through growth spurts, the milk supply constantly adjusts to accommodate changes in demand. A woman can continue to lactate for years, but once breastfeeding is stopped for approximately 1 week, any remaining milk will be reabsorbed; in most cases, no more will be produced, even if suckling or pumping is resumed.

Mature milk changes from the beginning to the end of a feeding. The early milk, called **foremilk**, is watery, translucent, and rich in lactose and protein. Its purpose is to quench the infant’s thirst. **Hindmilk** is delivered toward the end of a feeding. It is opaque, creamy, and rich in fat, and serves to satisfy the infant’s appetite.

During the first days of a newborn’s life, it is important for meconium to be cleared from the intestines and for bilirubin to be kept low in the circulation. Recall that bilirubin, a product of erythrocyte breakdown, is processed by the liver and secreted in bile. It enters the gastrointestinal tract and exits the body in the stool. Breast milk has laxative properties that help expel meconium from the intestines and clear bilirubin through the excretion of bile. A high concentration of bilirubin in the blood causes jaundice. Some degree of jaundice is normal in newborns, but a high level of bilirubin—which is neurotoxic—can cause brain damage. Newborns, who do not yet have a fully functional blood–brain barrier, are highly vulnerable to the bilirubin circulating in the blood. Indeed, hyperbilirubinemia, a high level of circulating bilirubin, is the most common condition requiring medical attention in newborns. Newborns with hyperbilirubinemia are treated with phototherapy because UV light helps to break down the bilirubin quickly.

**physiology of pregnancy in a normal woman**

Pregnancy causes physiologic changes in all maternal organ systems; most return to normal after delivery. In general, the changes are more dramatic in multifetal than in single pregnancies.

**Cardiovascular**

Cardiac output (CO) increases 30 to 50%, beginning by 6 weeks gestation and peaking between 16 and 28 weeks (usually at about 24 weeks). It remains near peak levels until after 30 weeks. Then, CO becomes sensitive to body position. Positions that cause the enlarging uterus to obstruct the vena cava the most (eg, the recumbent position) cause CO to decrease the most. On average, CO usually decreases slightly from 30 weeks until labor begins. During labor, CO increases another 30%. After delivery, the uterus contracts, and CO drops rapidly to about 15 to 25% above normal, then gradually decreases (mostly over the next 3 to 4 weeks) until it reaches the prepregnancy level at about 6 weeks postpartum.

The increase in CO during pregnancy is due mainly to demands of the uteroplacental circulation; volume of the uteroplacental circulation increases markedly, and circulation within the intervillous space acts partly as an arteriovenous shunt. As the placenta and fetus develop, blood flow to the uterus must increase to about 1 L/min (20% of normal CO) at term. Increased needs of the skin (to regulate temperature) and kidneys (to excrete fetal wastes) account for some of the increased CO.

To increase CO, heart rate increases from the normal 70 to as high as 90 beats/min, and stroke volume increases. During the 2nd trimester, blood pressure (BP) usually drops (and pulse pressure widens), even though CO and renin and angiotensin levels increase, because uteroplacental circulation expands (the placental intervillous space develops) and systemic vascular resistance decreases. Resistance decreases because blood viscosity and sensitivity to angiotensin decrease. During the 3rd trimester, BP may return to normal. With twins, CO increases more and diastolic BP is lower at 20 weeks than with a single fetus.

 Exercise increases CO, heart rate, oxygen consumption, and respiratory volume/min more during pregnancy than at other times.

 The hyperdynamic circulation of pregnancy increases frequency of functional murmurs and accentuates heart sounds. X-ray or ECG may show the heart displaced into a horizontal position, rotating to the left, with increased transverse diameter. Premature atrial and ventricular beats are common during pregnancy. All these changes are normal and should not be erroneously diagnosed as a heart disorder; they can usually be managed with reassurance alone. However, paroxysms of atrial tachycardia occur more frequently in pregnant women and may require prophylactic digitalization or other antiarrhythmic drugs. Pregnancy does not affect the indications for or safety of cardioversion.

**Hematologic**

Total blood volume increases proportionally with cardiac output, but the increase in plasma volume is greater (close to 50%, usually by about 1600 mL for a total of 5200 mL) than that in red blood cell (RBC) mass (about 25%); thus, hemoglobin (Hb) is lowered by dilution, from about 13.3 to 12.1 g/dL. This dilutional anemia decreases blood viscosity. With twins, total maternal blood volume increases more (closer to 60%).

WBC count increases slightly to 9,000 to 12,000/mcL. Marked leukocytosis (≥ 20,000/mcL) occurs during labor and the first few days postpartum.

Iron requirements increase by a total of about 1 g during the entire pregnancy and are higher during the 2nd half of pregnancy—6 to 7 mg/day. The fetus and placenta use about 300 mg of iron, and the increased maternal RBC mass requires an additional 500 mg. Excretion accounts for 200 mg. Iron supplements are needed to prevent a further decrease in Hb levels because the amount absorbed from the diet and recruited from iron stores (average total of 300 to 500 mg) is usually insufficient to meet the demands of pregnancy.

**Urinary**

Changes in renal function roughly parallel those in cardiac function. Glomerular filtration rate (GFR) increases 30 to 50%, peaks between 16 and 24 weeks gestation, and remains at that level until nearly term, when it may decrease slightly because uterine pressure on the vena cava often causes venous stasis in the lower extremities. Renal plasma flow increases in proportion to GFR. As a result, blood urea nitrogen (BUN) decreases, usually to < 10 mg/dL (< 3.6 mmol urea/L), and creatinine levels decrease proportionally to 0.5 to 0.7 mg/dL (44 to 62 micromole/L). Marked dilation of the ureters (hydroureter) is caused by hormonal influences (predominantly progesterone) and by backup due to pressure from the enlarged uterus on the ureters, which can also cause hydronephrosis. Postpartum, the urinary collecting system may take as long as 12 weeks to return to normal.

 Postural changes affect renal function more during pregnancy than at other times; ie, the supine position increases renal function more, and upright positions decrease renal function more. Renal function also markedly increases in the lateral position, particularly when lying on the left side; this position relieves the pressure that the enlarged uterus puts on the great vessels when pregnant women are supine. This positional increase in renal function is one reason pregnant women need to urinate frequently when trying to sleep.

**Respiratory**

Lung function changes partly because progesterone increases and partly because the enlarging uterus interferes with lung expansion. Progesterone signals the brain to lower carbon dioxide (CO2) levels. To lower CO2 levels, tidal and minute volume and respiratory rate increase, thus increasing plasma pH. oxygen consumption increases by about 20% to meet the increased metabolic needs of the fetus, placenta, and several maternal organs. Inspiratory and expiratory reserve, residual volume and capacity, and plasma PCO2 decrease. Vital capacity and plasma PCO2 do not change. Thoracic circumference increases by about 10 cm.

Considerable hyperemia and edema of the respiratory tract occur. Occasionally, symptomatic nasopharyngeal obstruction and nasal stuffiness occur, eustachian tubes are transiently blocked, and tone and quality of voice change.

Mild dyspnea during exertion is common, and deep respirations are more frequent.

**Gastrointestinal (GI) and hepatobiliary**

As pregnancy progresses, pressure from the enlarging uterus on the rectum and lower portion of the colon may cause constipation. GI motility decreases because elevated progesterone levels relax smooth muscle. Heartburn and belching are common, possibly resulting from delayed gastric emptying and gastroesophageal reflux due to relaxation of the lower esophageal sphincter and diaphragmatic hiatus. Hydrochloric acid production decreases; thus, peptic ulcer disease is uncommon during pregnancy, and preexisting ulcers often become less severe.

Incidence of gallbladder disorders increases somewhat. Pregnancy subtly affects hepatic function, especially bile transport. Routine liver function test values are normal, except for alkaline phosphatase levels, which increase progressively during the 3rd trimester and may be 2 to 3 times normal at term; the increase is due to placental production of this enzyme rather than hepatic dysfunction.

**Endocrine**

Pregnancy alters the function of most endocrine glands, partly because the placenta produces hormones and partly because most hormones circulate in protein-bound forms and protein binding increases during pregnancy.

The placenta produces the beta subunit of human chorionic gonadotropin (beta-hCG), a trophic hormone that, like follicle-stimulating and luteinizing hormones, maintains the corpus luteum and thereby prevents ovulation. Levels of estrogen and progesterone increase early during pregnancy because beta-hCG stimulates the ovaries to continuously produce them. After 9 to 10 weeks of pregnancy, the placenta itself produces large amounts of estrogen and progesterone to help maintain the pregnancy.

 The placenta produces a hormone (similar to thyroid-stimulating hormone) that stimulates the thyroid, causing hyperplasia, increased vascularity, and moderate enlargement. Estrogen stimulates hepatocytes, causing increased thyroid-binding globulin levels; thus, although total thyroxine levels may increase, levels of free thyroid hormones remain normal. Effects of thyroid hormone tend to increase and may resemble hyperthyroidism, with tachycardia, palpitations, excessive perspiration, and emotional instability. However, true hyperthyroidism occurs in only 0.08% of pregnancies.

 The placenta produces corticotropin-releasing hormone (CRH), which stimulates maternal adrenocorticotropic hormone (ACTH) production. Increased ACTH levels increase levels of adrenal hormones, especially aldosterone and cortisol, and thus contribute to edema.

Increased production of corticosteroids and increased placental production of progesterone lead to insulin resistance and an increased need for insulin, as does the stress of pregnancy and possibly the increased level of human placental lactogen. Insulinase, produced by the placenta, may also increase insulin requirements, so that many women with gestational diabetes develop more overt forms of diabetes.

The placenta produces melanocyte-stimulating hormone (MSH), which increases skin pigmentation late in pregnancy.

 The pituitary gland enlarges by about 135% during pregnancy. The maternal plasma prolactin level increases by 10-fold. Increased prolactin is related to an increase in thyrotropin-releasing hormone production, stimulated by estrogen. The primary function of increased prolactin is to ensure lactation. The level returns to normal postpartum, even in women who breastfeed.

**Dermatologic**

Increased levels of estrogens, progesterone, and MSH contribute to pigmentary changes, although exact pathogenesis is unknown. These changes include

• Melasma (mask of pregnancy), which is a blotchy, brownish pigment over the forehead and malar eminences

 • Darkening of the mammary areolae, axilla, and genitals

 • Linea nigra, a dark line that appears down the midabdomen

**Symptoms and Signs**

Pregnancy may cause breasts to be engorged because of increased levels of estrogen (primarily) and progesterone—an extension of premenstrual breast engorgement. Nausea, occasionally with vomiting, may occur because of increased secretion of estrogen and the beta subunit of human chorionic gonadotropin (beta-hCG) by syncytial cells of the placenta, beginning 10 days after fertilization (see Conception and Prenatal Development). The corpus luteum in the ovary, stimulated by beta-hCG, continues secreting large amounts of estrogen and progesterone to maintain the pregnancy. Many women become fatigued at this time, and a few women notice abdominal bloating very early.

Women usually begin to feel fetal movement between 16 and 20 weeks.

During late pregnancy, lower-extremity edema and varicose veins are common; the main cause is compression of the inferior vena cava by the enlarged uterus.Pelvic examination findings include a softer cervix and an irregularly softened, enlarged uterus. The cervix usually becomes bluish to purple, probably because blood supply to the uterus is increased. Around 12 weeks gestation, the uterus extends above the true pelvis into the abdomen; at 20 weeks, it reaches the umbilicus; and by 36 weeks, the upper pole almost reaches the xiphoid process

**Diagnosis**

• Urine beta-hCG test

Usually urine and occasionally blood tests are used to confirm or exclude pregnancy; results are usually accurate several days before a missed menstrual period and often as early as several days after conception.

Levels of beta-hCG, which correlate with gestational age in normal pregnancies, can be used to determine whether a fetus is growing normally. The best approach is to compare 2 serum beta-hCG values, obtained 48 to 72 hours apart and measured by the same laboratory. In a normal single pregnancy, beta-hCG levels double about every 1.4 to 2.1 days during the first 60 days (7.5 weeks), then begin to decrease between 10 and 18 weeks. Regular doubling of the beta-hCG level during the 1st trimester strongly suggests normal growth.

 Other accepted signs of pregnancy include the following:

• Presence of a gestational sac in the uterus, seen with ultrasonography typically at about 4 to 5 weeks and typically corresponding to a serum beta-hCG level of about 1500 mIU/mL (a yolk sac can usually be seen in the gestational sac by 5 weeks)

 • Fetal heart motion, seen with real-time ultrasonography as early as 5 to 6 weeks

 • Fetal heart sounds, heard with Doppler ultrasonography as early as 8 to 10 weeks if the uterus is accessible abdominally

 • Fetal movements felt by the examining physician after 20 weeks