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Physiology of Lactation in Normal Women

Lactation is the secretion and yielding of milk by females after giving birth. The milk is produced by the mammary glands, which are contained within the breasts.The breasts, unlike most of the other organs, continue to increase in size after childbirth. Although mammary growth begins during pregnancy under the influence of ovarian and placental hormones, and some milk is formed, copious milk secretion sets in only after delivery. Since lactation ensues after a premature birth, it would appear that milk production is held back during pregnancy. The mechanism by which this inhibitory effect is brought about, or by which lactation is initiated at delivery, has long been the subject of an argument that revolves around the opposing actions of estrogen, progesterone, and prolactin, as studied in laboratory animals, goats, and cattle. During pregnancy the combination of estrogen and progesterone circulating in the blood appears to inhibit milk secretion by blocking the release of prolactin from the pituitary gland and by making the mammary gland cells unresponsive to this pituitary hormone. The blockade is removed at the end of pregnancy by the expulsion of the placenta and the loss of its supply of hormones, as well as by the decline in hormone production by the ovaries, while sufficient estrogen remains in circulation to promote the secretion of prolactin by the pituitary gland and so favour lactation.

For lactation to continue, necessary patterns of hormone secretion must be maintained; disturbances of the equilibrium by the experimental removal of the pituitary gland in animals or by comparable diseased conditions in humans quickly arrest milk production. Several pituitary hormones seem to be involved in the formation of milk, so that it is customary to speak of a

lactogenic (“milk-producing”) complex of hormones. To some degree, the role of the pituitary hormones adrenocorticotropin, thyrotropin, and growth hormone in supporting lactation in women is inferred from the results of studies done on animals and from clinical observations that are in agreement with the results of animal studies. Adrenal corticoids also appear to play an essential role in maintaining lactation.

The stimulus of nursing or suckling supports continued lactation. It acts in two ways: it promotes the secretion of prolactin (and possibly other pituitary hormones of value in milk formation), and it triggers the release of yet another hormone from the pituitary gland—oxytocin, which causes the contraction of special muscle cells around the alveoli in the breast and ensures the expulsion of milk. It is in this way that a baby’s sucking at one breast may cause an increase in milk flow from both, so that milk may drip from the unsuckled nipple. About 30 seconds elapse between the beginning of active suckling and the initiation of milk flow.The nerve supply to the mammary glands is not of great significance in lactation, for milk production is normal after the experimental severing of nerves to the normal mammary glands in animals or in an udder transplanted to the neck of a goat. Milk ejection, or “the draught,” in women is readily conditioned and can be precipitated by the preparations for nursing. Conversely, embarrassment or fright can inhibit milk ejection by interfering with the release of oxytocin; alcohol, also, is known to block milk ejection in women, again by an action on the brain. Beyond its action on the mammary glands, oxytocin affects uterine muscle, so that suckling can cause contractions of the uterus and may sometimes result in cramp. Since oxytocin release occurs during sexual intercourse, milk ejection in lactating women has been observed on such occasions. Disturbance of oxytocin secretion, or of the milk-ejection reflex, stops lactation just as readily as a lack of the hormones necessary for milk production, for the milk in the breast is then not extractable by the infant. Many instances of nursing failure are due to a lack of milk ejection in stressful circumstances; fortunately, treatment with oxytocin, coupled with the reassurance gained from a successful nursing, is ordinarily successful in overcoming the difficulty.

Suckling can initiate lactation in nonpregnant women. This has been seen most often in women of childbearing age but also has been observed in older persons. A baby who had lost his mother

was suckled by his 60-year-old grandmother, who had borne her last child 18 years before. The grandmother produced milk after a few days and continued to nurse the baby until he was a year old and could walk. Rarely, lactation has been reported to set in after operations on the chest; in such instances it is attributed to injury or irritation of the nerves in this region. Such observations argue against the possibility that lactation continues simply as a consequence of emptying the breasts.

Composition and properties of milk

Milk can be regarded as an emulsion of fat globules in a colloidal solution of protein together with other substances in true solution. Two constituents of milk—the protein casein and milk sugar, or lactose—are not found elsewhere in the body.

Breastfeeding is particularly advantageous because of the nutritional, immunologic, and psychological benefits. Human breast milk is superior to modified cow's milk formulas, which may lack essential and beneficial components and are not absorbed as easily or as quickly by the infant. Maternal breast milk provides vitamins, minerals, protein, and anti-infectious factors; antibodies that protect the infant's gastrointestinal tract are supplied, resulting in a lower rate of enteric infection in breast-fed than in bottle-fed babies. The bonding that is established through breast-feeding is advantageous to building the parent-child relationship.

The nutritional status of the mother is important throughout this period. The mother's daily caloric intake must increase significantly in order to replenish the mother's nutrient and energy stores. The use of drugs or smoking by the mother can adversely affect the infant; many drugs are secreted in breast milk, and smoking reduces breast milk volume and decreases infant growth rates.

The milk released from the breast when lactation starts differs in composition from the mature milk produced when lactation is well established. The early milk, or colostrum, is rich in essential amino acids, the protein building blocks essential for growth; it also contains the proteins that convey immunity to some infections from mother to young, although not in such

quantity as among domestic animals. The human infant gains this type of immunity largely within the uterus by the transfer of these antibody proteins through the placenta; the young baby seldom falls victim to mumps, measles, diphtheria, or scarlet fever. For a short time after birth, proteins can be absorbed from the intestine without digestion, so that the acquisition of further immunity is facilitated. The growth of harmful viruses and bacteria in the intestines is probably inhibited by immune factors in human milk. After childbirth the composition of milk gradually changes; within four or five days the colostrum has become transitional milk, and mature milk is secreted some 14 days after delivery.

Some variations between human colostrum, transitional milk, and mature milk and cow's milk are shown in Table 2. The greater amount of protein in unmodified cow's milk is largely responsible for its dense, hard curd, which the infant cannot digest; the difficulty can be avoided by heat treatment or dilution of the milk. Ordinarily, when cow's milk is fed to young infants, it is modified so as to match its composition as far as possible to breast milk.

Physiology of Pregnancy in Normal Women.

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 (CO_2) levels. To lower CO_2 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 PCO_2 decrease. Vital capacity and plasma PCO_2 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

Melasma due to pregnancy usually regresses within a year.
Incidence of spider angiomas, usually only above the waist, and of thin-walled, dilated capillaries, especially in the lower legs, increases.

Symptoms and signs.

Pregnancy may cause breasts to be enlarged 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. 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.