Hormones Affecting Female Breast

Physiological Structure and the Development of Breasts

- The breasts begin to develop at puberty **(Figure 83-10)**. This development is stimulated mainly by the **estrogens** of the monthly female sexual cycle.
- Estrogens stimulate growth of the **breasts' *mammary glands*** plus the deposition of fat.

Estrogens Stimulate Growth of the Ductal System of the Breasts

All through pregnancy, the large quantities of **estrogens** secreted by the placenta cause the ductal system of the breasts to grow and branch. Simultaneously, the stroma of the breasts increases in quantity, and large quantities of fat are laid down in the stroma.

Also important for the growth of the ductal system are at least four other hormones: *growth hormone, prolactin,* the *adrenal glucocorticoids,* and *insulin.* Each of these hormones is known to play at least some role in protein metabolism

Progesterone Is Required for Full Development of the Lobule-Alveolar System

Final development of the breasts into milk-secreting organs also requires **progesterone**. Once the ductal system has developed, progesterone—acting synergistically with estrogen, as well as with the other hormones mentioned above —causes additional growth of the breast lobules, with budding of alveoli and development of secretory characteristics

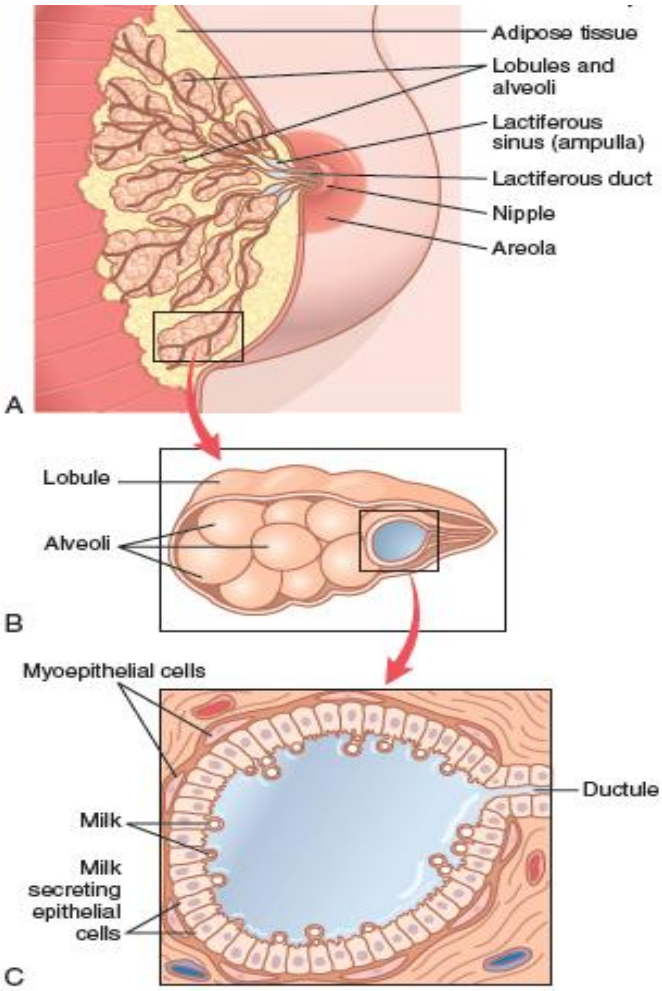


Figure 83-10. The breast and its secretory lobules, alveoli, and lactiferous ducts (milk ducts) that constitute its mammary gland (**A**). The enlargements show a lobule (**B**) and milk-secreting cells of an alveolus (**C**).

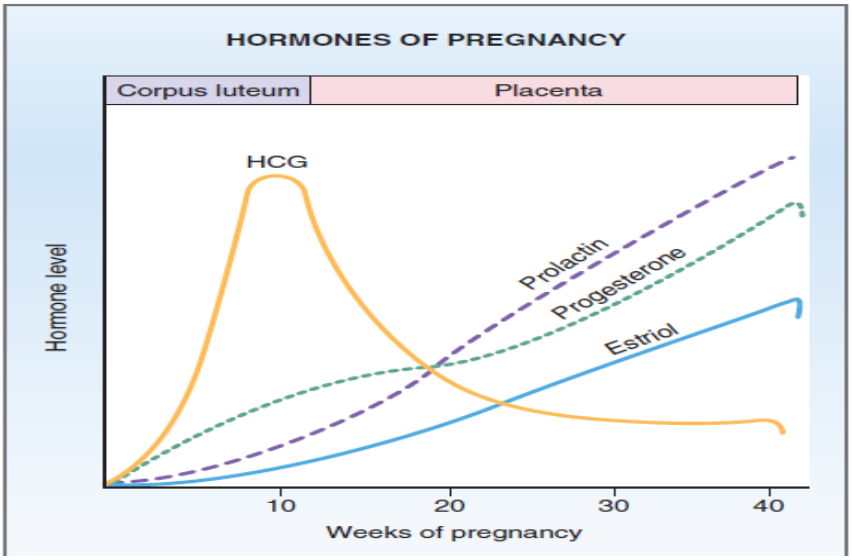
Hormonal Control of Lactation

❖ Estrogens and Progesterone

- Throughout pregnancy, estrogens and progesterone stimulate the growth and development of the breasts, preparing them for lactation.

❖ Prolactin

- Estrogens stimulate prolactin secretion by the mother's anterior pituitary gland, and prolactin levels steadily increase from the 5th week of pregnancy until the birth of the baby, where it rises to 10 to 20 times the normal nonpregnant level (See graph below).



- However, although prolactin levels are high during pregnancy, lactation *does not* occur because estrogen and progesterone block the action of prolactin on the breast.
- After parturition, when estrogen and progesterone levels fall suddenly, their inhibitory effects on the breast are removed and lactation can be initiated.
- The *basal level* of prolactin secretion returns to the nonpregnant level during the next few weeks after parturition, as shown in **Figure 83-11**. However, each time the mother nurses her baby, nervous signals from the nipples to the hypothalamus cause a 10- to 20-fold surge in prolactin secretion that lasts for about 1 hour.
- This prolactin acts on the mother's breasts to keep the mammary glands secreting milk into the alveoli for the subsequent nursing periods.
- If this prolactin surge is absent or blocked as a result of hypothalamic or pituitary damage or if nursing does not continue, the breasts lose their ability to produce milk within 1 week or so.

- However, milk production can continue for several years if the child continues to suckle, although the rate of milk formation normally decreases considerably after 7 to 9 months.
- The fluid secreted during the first few days after parturition is called ***colostrum;*** it contains essentially the same concentrations of proteins and lactose as milk, but it has almost no fat.
- 1 to 7 days after parturition, the breasts begin to secrete copious quantities of milk instead of colostrum. This secretion of milk requires an adequate background secretion of most of the mother's other hormones as well, but most important are *growth hormone, cortisol, parathyroid hormone,* and *insulin*. These hormones are necessary to provide the amino acids, fatty acids, glucose, and calcium required for the formation of milk.

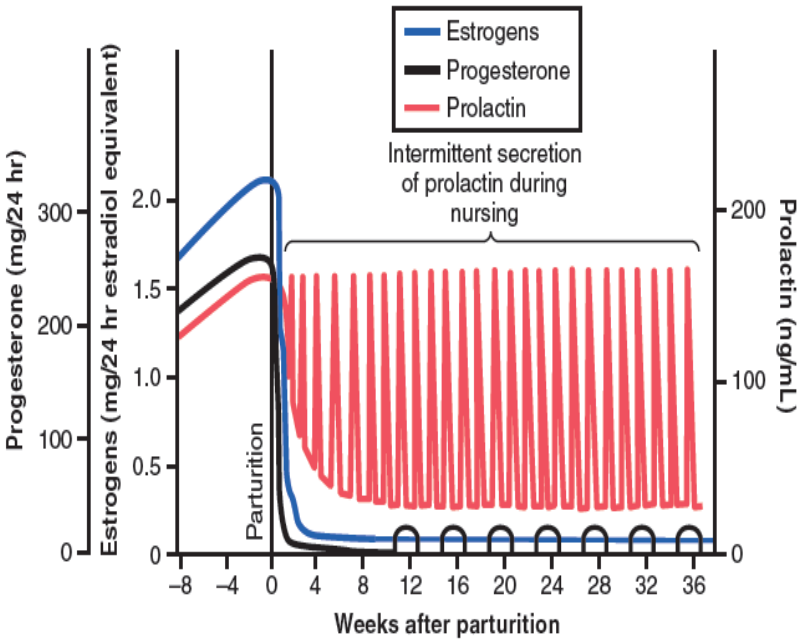


Figure 83-11. Changes in rates of secretion of estrogens, progesterone, and prolactin for 8 weeks before parturition and 36 weeks thereafter. Note especially the decrease of prolactin secretion back to basal levels within a few weeks after parturition, but also the intermittent periods of marked prolactin secretion (for about 1 hour at a time) during and after periods of nursing.

Function of Prolactin

- ✓ Prolactin, in a supportive role with estrogen and progesterone, stimulates development of the breasts during pregnancy by stimulating the proliferation and branching of the mammary ducts.
- ✓ Prolactin stimulates milk production by inducing the synthesis of the components of milk including **lactose** (the carbohydrate of milk), **casein** (the protein of milk), and **lipids** (major action).
- ✓ Prolactin suppresses ovulation and menstruation by inhibiting the hypothalamic GnRH.

❖ Human Chorionic Somatomammotropin (Human Placental Lactogen; hPL)

- Secreted in large quantities by the placenta.
- Causes at least partial development of the breasts and in some instances causes lactation.
- Has lactogenic properties, thus supporting the prolactin from the mother's pituitary during pregnancy.

❖ Prolactin Inhibitory Hormone *(PIH)*

- The hypothalamus inhibits the production of prolactin hormone from the anterior pituitary gland by *prolactin inhibitory hormone (PIH),* or the *dopamine.*

❖ Glucocorticoids

- Cortisol induces differentiation of rough endoplasmic reticulum and the Golgi apparatus of the mammary epithelial cells. This differentiation is essential to permit prolactin to induce synthesis of milk proteins. This indicates the essential synergism between prolactin and the glucocorticoids to induce lactogenesis.

❖ Insulin and Growth Hormones

- Both insulin and insulin-like growth factor (IGF) may be involved in glucose uptake which is critical for lactose biosynthesis. Insulin may also be involved in expression of milk protein genes. Growth hormone may have an indirect effect of lactogenesis by increasing the secretion of IGFs

Milk Production and Secretion:

- It is the synthesis of milk by alveolar epithelial cells and the secretion through the ductal system.
- **Two Phases:**
  1. **Lactogenesis:** Cellular changes by which *mammary epithelial cells* are converted from a nonsecretory to a secretory state. It involves **2 stages**:
     - ✓ **Lactogenesis 1:** (Cytologic and enzymatic differentiation of alveolar epithelial cells). Starts mid pregnancy until parturition and is controlled by *prolactin, hPL, progesterone, growth hormone and cortisol.*
     - ✓ **Lactogenesis 2:** (Copious secretion of all milk components). Starts after the removal of placenta until few days after parturition and it is usually shorter than stage 1. It is controlled by *prolactin and oxytocin.*
  2. **Galactopoiesis:** Maintenance of the milk secretion once lactation has been established and is controlled by *prolactin, growth hormone, cortisol, insulin, parathyroid and thyroid hormones.*

EJECTION (OR "LET-DOWN") PROCESS IN MILK SECRETION—FUNCTION OF OXYTOCIN

- Milk is secreted continuously into the alveoli of the breasts, but it does not flow easily from the alveoli into the ductal system and, therefore, does not continually leak from the nipples.
- The milk must be *ejected* from the alveoli into the ducts before the baby can obtain it. This ejection is caused by a combined neurogenic and hormonal reflex that involves the posterior pituitary hormone ***oxytocin***.
- When the baby suckles, sensory impulses is transmitted through somatic nerves from the nipples to the mother's spinal cord and then to her hypothalamus, where they cause nerve signals that promote *oxytocin* secretion at the same time that they cause prolactin secretion.
- The oxytocin is carried in the blood to the breasts, where it causes contraction of the *myoepithelial cells* (which surround the outer walls of the alveoli), thereby expressing the milk from the alveoli into the ducts.
- Then the baby's suckling becomes effective in removing the milk. This process is called *milk ejection* or *milk let-down.*

Feedback inhibitor of lactation

- Milk production is also controlled in the breast by a substance called the *feedback inhibitor of lactation*, or FIL (a polypeptide), which is present in breast milk.
- Sometimes one breast stops making milk while the other breast continues, for example if a baby suckles only on one side. This is because of the local control of milk production independently within each breast.
- If milk is not removed, the inhibitor collects and stops the cells from secreting any more, helping to protect the breast from the harmful effects of being too full. If breast milk is removed the inhibitor is also removed, and secretion resumes.
- If the baby cannot suckle, then milk must be removed by expression. FIL enables the amount of milk produced to be determined by how much the baby takes, and therefore by how much the baby needs. This mechanism is particularly important for ongoing close regulation after lactation is established. At this stage, prolactin is needed to enable milk secretion to take place, but it does not control the amount of milk produced.

Inhibition of Milk Ejection: Oxytocin secretion can be inhibited by *psychogenic factors* or even *generalized sympathetic nervous system stimulation* and consequently depress milk ejection.