Physiology Sheets

Number	16
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"In the name of God, the Most gracious, the most merciful'

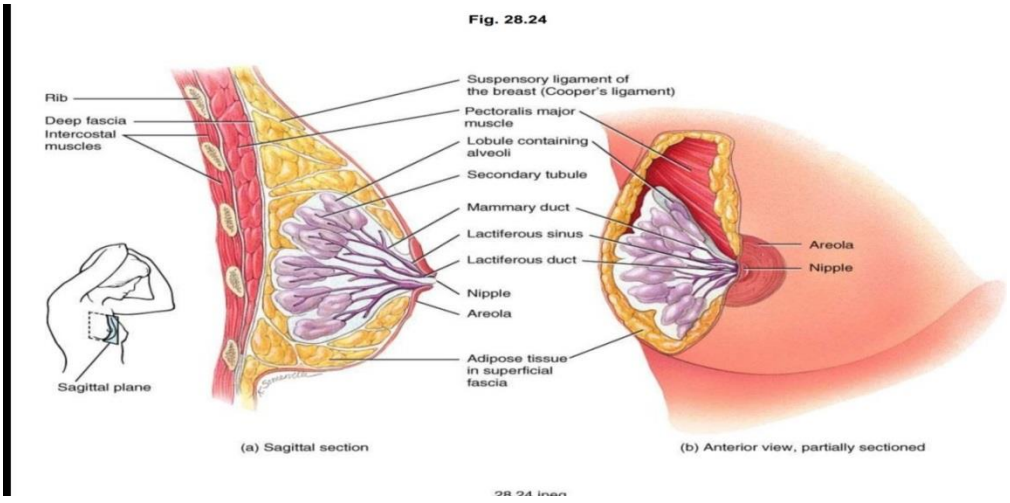
Lactation

Mammary glands or milk producing glands are an accessory glands that give a specialized type of nutrients (milk) for the newly delivered baby, through a process called **lactation** that occurs in the breast.

Structure of the breast:

The structure of the breast in terms of function:

1. Alveolar system responsible for milk synthesis and secretion.
2. Ductal system allows milk to go outside, around this ductal system we have myoepithelium cells which are contractile elements that participate in milk ejection.
   -So we have three elements secretory or alveolar, ductal elements allowing the milk to go outside and surrounded by contractile elements that eject milk.
3. Outside the breast in the nipple area we have a sensory area, which is a receptive area connected with sensory neurons that go to the spinal cord all the way to the hypothalamus(paraventricular nuclei and supraoptic nuclei), by second order neurons.



Development of the breasts:

Development of breasts in female is divided into TWO stages prepubertal and pubertal.

1. **In Prepubertal stage:**

   There will be development of the nipple and small amount of ducts, but there are no alveoli or lobules.

2. **In pubertal stage: "In non pregnant female "**

   The breasts begin to develop at puberty by deposition of fat to give the shape of the breasts and certain rudimentary elements start to appear in terms of alveoli but not all the alveoli.

now what determines that?

We have the cyclic patterns of estrogens, prolactin and progesterone; estrogens stimulate growth of the breasts' mammary glands plus the deposition of fat to give the breast's mass.

So all in all during puberty stage we have:

- Fat mainly, ducts and rudimentary elements.
- No alveoli nor lobules.

this pattern is more developed in females than males whom breast is composed by skin layer, nipple, ducts, and minimal amount of fat, but there are no alveoli. So in female due to the cyclic patterns of estrogen, progesterone, prolactin and presence of glucocorticoids, insulin and thyroxin females develop a little bit more fat and rudimentary element but no alveoli at all.

Remember: By the time of maturity there are no alveoli.

Prolactin hormone and ways of regulations:

Prolactin (**PRL**), also known as **luteotropic hormone** or **luteotropin**, is a protein that is best known for its role in enabling mammals, usually females, to produce milk.
It is a single chain protein made of 200 amino acids and it is not a glycoprotein.

What regulates prolactin secretion?

It is believed that anterior pituitary secretion of prolactin is controlled either entirely or almost entirely by an inhibitory factor formed in the hypothalamus and transported through the hypothalamichypophysial portal system to the anterior pituitary gland. This factor is sometimes called prolactin inhibitory hormone, but it is almost certainly the same as the catecholamine dopamine, which is known to be secreted by the dopaminergic neurons in the paraventricular and supraoptic nuclei of the hypothalamus, and it can decrease prolactin secretion as much as 10-fold.So lactotropic cells under continues suppression by Dopamine. If we block the release of dopamine, prolactin secretion will increase.
So dopamine is the main regulator and we have other regulators:

- **Thyrotropin releasing hormone TRH:**

  The main regulator of TSH and it is found to have an effect to stimulate the prolactin secretion.

- **GnRH associated peptide:**

  GnRH stimulates the release of LH and FSH and inhibits the release of prolactin. During pregnancy and post-pregnancy period there will be suppression of GnRH, so the release of prolactin inreases. In certain pathological conditions we will have another peptide called GnRH associated peptide (GAP) and it will inhibit prolactin secretion, so It's not a physiological regulator of prolactin.

- **Pregnancy:**

  During pregnancy estrogen causes mitosis of the lactotropic cells producing more prolactin.

- **Sleep:**

  Because hypothalamus is connected to everywhere in our brain and we have neural supply to suprachiasmatic nucleus from optic tract which makes it sensitive to dark light cycle, so at night we have certain type of circadian secretion of prolactin.

- **Somatostatin :**

  Is an inhibitor for most of pituitary hormones .

- **Prolactin:**

  We have certain concept that blood prolactin that goes to hypothalamus can suppress prolactin secretion or we have a vascular pathway back from medial eminence to the hypothalamus suppressing the level of prolactin secretion.

  So all in all males have minor regulators,sleep, stress and TRH (all three cause stimulation), but in female there is estrogen during menstrual cycle,
  prepubertal stage and during pregnancy.

What other stimulators for prolactin ?

Psychic behaviour, maternal behaviour, thinking of the baby and nursing the baby will lead to more inhibition of dopamine and more stimulation of prolactin.

Development of breast during pregnancy:

In terms of alveolar structure the breast of non-pregnant female is not well develop.

What happens during pregnancy?

Structural and functional development; 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 growth of the ductal system are atleast 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, which presumably explains their function in the development of the breasts. progesterone -acting synergistically with estrogen, as well as with the other hormones just mentioned- causes additional growth of the breast lobules, with budding of alveoli and development of secretory characteristics in the cells of the alveoli.

So pregnancy is a must for the complete development of the breast and it will stay forever and will not regress after the pregnancy.

Prolactin promotes lactation:

Although estrogen and progesterone are essential for the physical development of the breasts during pregnancy, a specific effect of both these hormones is to inhibit the actual secretion of milk.
The high level of progesterone and other hormones stimulate the anatomical and functional development but the functional is under suppression during pregnancy until there is relief of that suppression by the decrease in progesterone and estrogen level. Conversely, the hormone prolactin has exactly the opposite effect and promotes milk secretion. Immediately after the baby is born, the sudden loss of both estrogen and progesterone secretion from the placenta allows the lactogenic effect of prolactin from the mother's pituitary gland to assume its natural milk

promoting role, and during the next 1 to 7 days, 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. After the birth of the baby, the basal level of prolactin secretion returns to the nonpregnant level during the next few weeks, 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, which is also shown in Figure 83-11. 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.

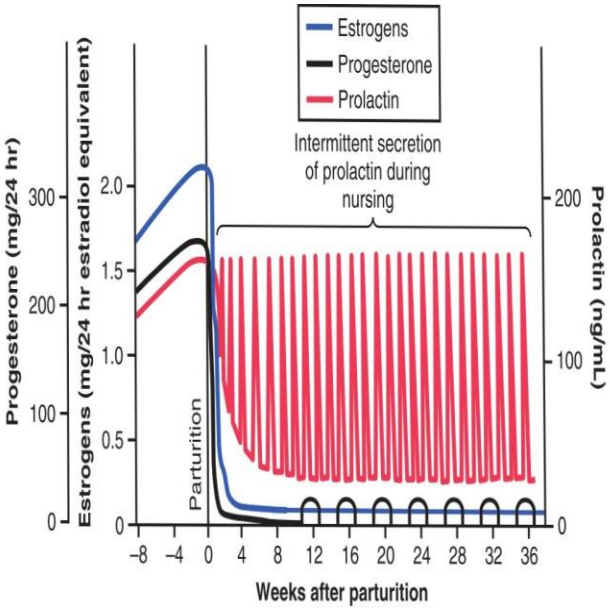


Figure 83-11. Changes in rates of secretion of estrogens, progesterone, and prolactin for 8 weeks before parturition and 36 weeks thereafter. Note especially the decrease of prolactin secretion back to basal levels within a few weeks after parturition, but also the intermittent periods of marked prolactin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

Milk Ejection :

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. Instead, 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.

Mechanism of oxytocin:

When the baby suckles (mechanorecepter stimulation), it receives virtually no milk for the first half minute or so. Sensory impulses must first be 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 from the non-neuronal end to the posterior pituitary gland at the same time that they cause prolactin secretion. The oxytocin is carried in the blood to the breasts, where it causes myoepithelial cells (which surround the outer walls of the alveoli) to contract, thereby expressing the milk from the alveoli into the ducts at a pressure of +10 to 20 mm Hg. Then the baby's suckling becomes effective in removing the milk. Thus, within 30 seconds to 1 minute after a baby begins to suckle, milk begins to flow. This process is called ***milk ejection or milk let-down.***

Suckling on one breast causes milk flow not only in that breast but also in the opposite breast. It is especially interesting that fondling of the baby by the mother or hearing the baby crying often gives enough of an emotional signal to the hypothalamus to cause milk ejection.Nipple stimulation will not leads to oxytocin secretion only, but also send signals to the dopaminergic neurons in the hypothalamus to inhibit the release of dopamine increasing the level of prolactin.

So the process in sequential way is > at the end of pregnancy high level of prolactin and other hormones leads to development of breast structurally and functionally and after that due to nipple stimulation will frequently stimulate prolactin secretion by inhibition of dopamine which will add to secretion of milk and the ejection by negative pressure, mother applied pressure and contraction of myoepithelium.

So what facilitates milk ejection?

1)Negative pressure due to suckling.
2)Pressure on breast performed by the mother.
3)Contraction of myoepithelium cells.

And what stimulates oxytocin secretion?

1) By stimulation of mechanoreceptors in the nipple area that are connected to sensory neurons that are going to suprachiasmatic nucleus mainly and partially to paraventricular nucleus.
2) by stretching or manipulation of the opening of the cervix .
So oxytocin can be release due to nipple or cervix stimulation.

Why we need oxytocin ?

1- To stimulate the myoepithelial cells in the breast and stimulate contractile myometrium. Decrease in hormonal balance at the end of pregnancy will remove the suppression on the contractile muscle. Contraction of myoepithelium will help in increase the pressure inside and push the contents of the uterus through the cervix and this will dilate the cervix , dilatation of the cervix will give us a form of positive feedback mechanism that is going through **cervix > uterine contraction> more pressure on the cervix due to dilatation until the baby get delivered > then it will be repeated again to deliver the placenta .**
2- Oxytocin has effect on the uterus after delivery, it leads to continuous contraction of the uterine muscle that will lead to occlude blood vessels and reduce bleeding and due to daily contraction the uterus will shrink and go back to prepregnancy size.

If there is stimulation for male nipples there will be oxytocin and prolactin secretion but not like the concentration in the pregnant women and there will be no development of the breast size, they will have small alveoli.Those alveoli can secret some material similar to milk if they have continuous hyperprolactinemia. But hyperprolactinemia without estrogen, progesterone and pregnancy hormones, male will not develop breast.Same thing happens for women who never get pregnant.