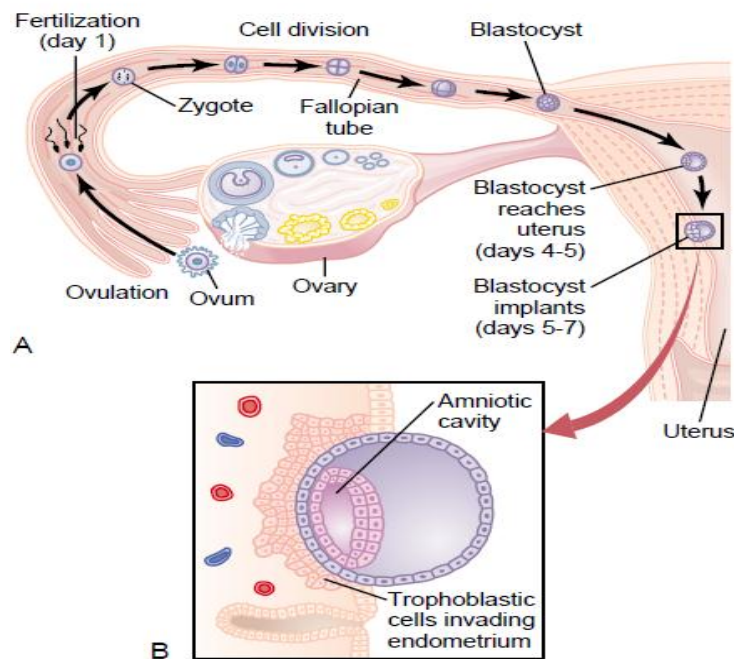


Lecture No.10



Hormonal Factors in Pregnancy

In pregnancy, the placenta forms especially large quantities of *human chorionic gonadotropin*, *estrogens*, *progesterone*, and *human chorionic somatomammotropin*, the first three of which, and probably the fourth as well, are all essential to a normal pregnancy.

Function of Human Chorionic Gonadotropin.

Human chorionic gonadotropin is a glycoprotein having a molecular weight of about 39,000 and much the same molecular structure and function as luteinizing hormone secreted by the pituitary gland. By far, its most important function is to prevent involution of the corpus luteum at the end of the monthly female sexual cycle. Instead, it causes the corpus luteum to secrete even larger quantities of its sex hormones—progesterone and estrogens—for the next few months. These sex hormones prevent menstruation and cause the endometrium to continue to grow and store large amounts of nutrients rather than being shed in the menstruum.

Under the influence of human chorionic gonadotropin, the corpus luteum in the mother's ovary grows to about twice its initial size by a month or so after pregnancy begins, and its continued secretion of estrogens and progesterone maintains the decidual nature of the uterine endometrium, which is necessary for the early development of the fetus. If the corpus luteum is removed before approximately the 7th week of pregnancy, spontaneous abortion almost always occurs, sometimes even up to the

12th week. After that time, the placenta secretes sufficient quantities of progesterone and estrogens to maintain pregnancy for the remainder of the gestation period. The corpus luteum involutes slowly after the 13th to 17th week of gestation.

Effect of Human Chorionic Gonadotropin on the Fetal Testes

Human chorionic gonadotropin also exerts an *interstitial cell*–stimulating effect on the testes of the male fetus, resulting in the production of testosterone in male fetuses until the time of birth. This small secretion of testosterone during gestation is what causes the fetus to grow male sex organs instead of female organs. Near the end of pregnancy, the testosterone secreted by the fetal testes also causes the testes to descend into the scrotum.

Function of Estrogen in Pregnancy

In the discussions of estrogens in Chapter 81, we pointed out that these hormones exert mainly a proliferative function on most reproductive and associated organs of the mother. During pregnancy, the extreme quantities of estrogens cause (1) enlargement of the mother's uterus, (2) enlargement of the mother's breasts and growth of the breast ductal structure, and (3) enlargement of the mother's female external genitalia. The estrogens also relax the pelvic ligaments of the mother, so that the sacroiliac joints become relatively limber and the symphysis pubis becomes elastic. These changes allow easier passage of the fetus through the birth canal. There is much reason to believe that estrogens also affect many general aspects of fetal development during pregnancy, for example, by affecting the rate of cell reproduction in the early embryo.

Secretion of Progesterone by the Placenta

Progesterone is also essential for a successful pregnancy—in fact, it is just as important as estrogen. In addition to being secreted in moderate quantities by the corpus luteum at the beginning of pregnancy, it is secreted later in tremendous quantities by the placenta, averaging about a 10-fold increase during the course of pregnancy. The special effects of progesterone that are essential for the normal progression of pregnancy are as follows:

1. Progesterone causes decidual cells to develop in the uterine endometrium, and these cells play an important role in the nutrition of the early embryo.
2. Progesterone decreases the contractility of the pregnant uterus, thus preventing uterine contractions from causing spontaneous abortion.
3. Progesterone contributes to the development of the conceptus even before implantation, because it specifically increases the secretions of the mother's fallopian tubes and uterus to provide appropriate nutritive matter for the developing *morula* and *blastocyst*. There is also reason to

believe that progesterone affects cell cleavage in the early developing embryo.

4. The progesterone secreted during pregnancy helps the estrogen prepare the mother's breasts for lactation .

Human Chorionic Somatomammotropin

A more recently discovered placental hormone is called *human chorionic somatomammotropin*. It is a protein with a molecular weight of about 38,000, and it begins to be secreted by the placenta at about the fifth week of pregnancy. Secretion of this hormone increases progressively throughout the remainder of pregnancy in direct proportion to the weight of the placenta. Although the functions of chorionic somatomammotropin are uncertain, it is secreted in quantities several times greater than all the other pregnancy hormones combined. It has several possible important effects. human chorionic somatomammotropin causes decreased insulin sensitivity and decreased utilization of glucose in the mother, thereby making larger quantities of glucose available to the fetus. Because glucose is the major substrate used by the fetus to energize its growth, the possible importance of such a hormonal effect is obvious. Further, the hormone promotes the release of free fatty acids from the fat stores of the mother, thus providing this alternative source of energy for the mother's metabolism during pregnancy. Therefore, it appears that human chorionic somatomammotropin is a general metabolic hormone that has specific nutritional implications for both the mother and the fetus.

Secretion of "Relaxin" by the Ovaries and Placenta

Another substance besides the estrogens and progesterone, a hormone called relaxin, is secreted by the corpus luteum of the ovary and by placental tissues. Its secretion is increased by a stimulating effect of human chorionic gonadotropin at the same time that the corpus luteum and the placenta secrete large quantities of estrogens and progesterone.

Relaxin is a polypeptide having a molecular weight of about 9000. This hormone, when injected, causes relaxation of the ligaments of the symphysis pubis in the estrous rat and guinea pig. This effect is weak or possibly even absent in pregnant women. Instead, this role is probably played mainly by the estrogens, which also cause relaxation of the pelvic ligaments. It has also been claimed that relaxin softens the cervix of the pregnant woman at the time of delivery.

Effect of Fetal Hormones on the Uterus.

The fetus's pituitary gland secretes increasing quantities of oxytocin, which might play a role in exciting the uterus. Also, the fetus's adrenal glands secrete large quantities of cortisol, another possible uterine stimulant. In addition, the fetal membranes release prostaglandins in high

concentration at the time of labor. These, too, can increase the intensity of uterine contractions.

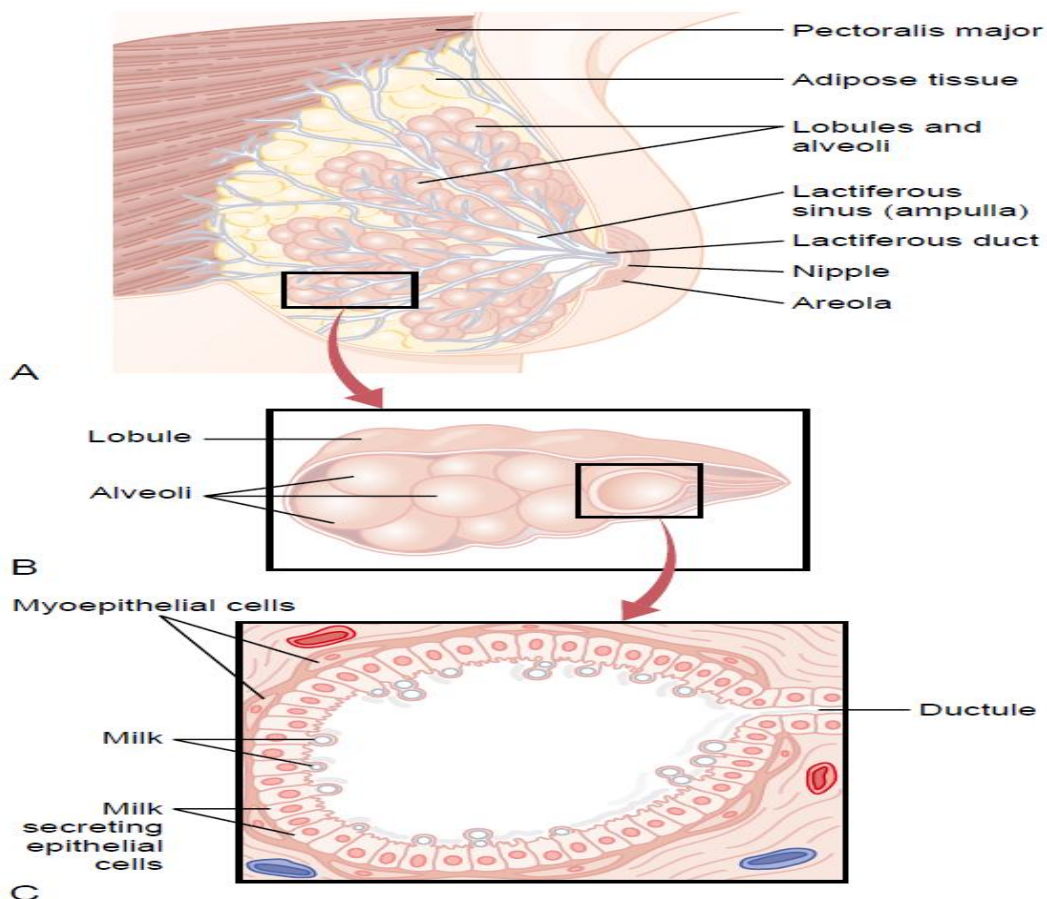
Lactation

Development of the Breasts

The breasts, shown in figure below, begin to develop at puberty. This development is stimulated by the estrogens of the monthly female sexual cycle; estrogens stimulate growth of the breasts' *mammary glands* plus the deposition of fat to give the breasts mass. In addition, far greater growth occurs during the highestrogen state of pregnancy, and only then does the glandular tissue become completely developed for the production of milk.

Growth of the Ductal System—Role of the Estrogens

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 at least four other hormones: *growth hormone*, *prolactin*, the *adrenal glucocorticoids*, and *insulin*. Each of these is known to play at least some role in protein metabolism, which presumably explains their function in the development of the breasts.



Development of the Lobule-Alveolar System—Role of Progesterone

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 just mentioned—causes additional growth of the breast lobules, with budding of alveoli and development of secretory characteristics in the cells of the alveoli. These changes are analogous to the secretory effects of progesterone on the endometrium of the uterus during the latter half of the female menstrual cycle.

Initiation of Lactation—Function of Prolactin

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*. Conversely, the hormone *prolactin* has exactly the opposite effect on milk secretion—promoting it. This hormone is secreted by the mother's anterior pituitary gland, and its concentration in her blood rises steadily from the fifth week of pregnancy until birth of the baby, at which time it has risen to 10 to 20 times the normal nonpregnant level. This high level of prolactin at the end of pregnancy.

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 over 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 milk formation.