Urogenital System

Sheet 5

Subject | Physiology

Done by | Rawan Almujaibel

Correction | Maryam Ali

Doctor | Ebaa

Physiology of pregnancy

By the end of this sheet you should be able to:

1- Recognize the placenta as an endocrine organ.
2- Discribe the physiological functions of placental hormones.
3- Explain's the mother's physiological response to pregnancy.

Placenta

-The placenta is not an organ that is only providing the essential substances for the embryo such as oxygen, glucose, and eliminating wasting products such as CO2. It is also an endocrine organ that's secret important hormones for pregnancy and development of the fetus such as Human Chorionic Gonadotropin (hCG), Estrogen, progesterone and somatomamotropine.

-Normally menstration starts 2 weeks after ovulation, in case the fertilization didn't accurre the sloughing is happened. However, if fertilization happened the menstrual sloughing is prevented by secretion of hCG by newly developed embryonic tissues.

-The hCG is first measured in the blood about 8-9 days after ovulation (blastocyst implant), this period of time when the women can use pregnancy test at home.

-HCG reaches its maximum level at the 10^{th} week of pregnancy. Then it declines back to low level by 16 -20 weeks till the reminder of the pregnancy.

Hormones are secreted by placenta:

1-HCG is secreted by placenta specifically by the syncytial trophoblast cells and the ,the most important functions of the hormone:

- Is to maintain corpus luteum and prevent its involution to continue secreting Estrogen and progesterone (at the begaining of the pregnancy)till 13 -17 weeks of gestation. So the

Estrogen and Progesterone are maintaining the secretory function of the decidual cells (they will be greatly swollen and nutritious to the implanted ovum).

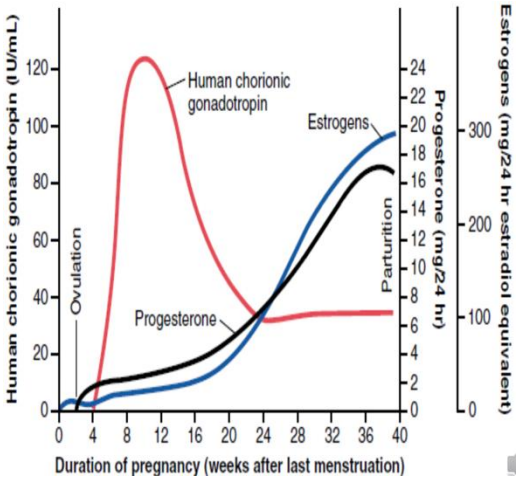
- For a male fetus, it has LH like stimulating effect on the interstitial leyding cells in the testes by stimulating these cell to produce testosterone in the fetus until birth (growth of the male sex organs).
- The corpus luteum will involute slowly after the 13^{th} – 17^{th} week of gestation, so that placenta will take over and starts to secret Estrogen and Progesterone.

Q: what if the corpus luteum was removed before the 7^{th} week of pregnancy?

Ans: spontaneous abortion will occurred due to losing lots of important hormones for maintaining pregnancy.(no estrogen , no progesterone , no HCG)

In the figure below; it shows different level of hormones in different period of time during pregnancy.

1- HCG; after ovulation starts to increase gradually from the 4^{th} week and continue increasing until it reaches its maximum level around 10^{th}-12^{th} week. Then, it's decrease again until 20^{th} -24^{th} week to remain the same till the reminder of pregnancy.
2- Estrogen & progesterone; are slowly increase after ovulation until 20^{th} – 24^{th} week of pregnancy where they will be at the same level as HCG. Then they continue to raise until the reminder of the pregnancy.



2-Estrogen is also secreted by placenta (syncytial trophoblast cells). It reached maximum level 30X towards the end of pregnancy. It is derived from weak androgen (DHEA) -it is not synthesized de novo from cholesterol due to the lack of the required enzyme of placenta- which is released by maternal And fetal adrenal cortex. It's functions in the mother:

- Is the enlargement and growth of the uterus, breast (ductal), and genitalia.
- Helps in relaxation of pelvic ligaments in preparation for labor (sacroiliac join & symphysis pubis).
- Activation of the uterus (gap junctions).

3-Progesterone is also secreted by placenta and it's essential for a successful pregnancy. It is secreted within moderated amount by corpus luteumat the beginning of pregnancy. Then, later in pregnancy it will be secreted in large quantities by placenta 10X times by syncytial trophoblast cells from cholesterol.

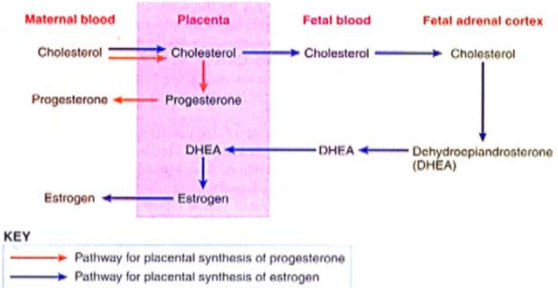


FIGURE 20-31 Secretion of estrogen and progesterone by the placenta. The placenta secretes increasing quantities of progesterone and estrogen into the maternal blood after the first trimester. The placenta itself can convert cholesterol into progesterone *(orange pathway)* but lacks some of the enzymes necessary to convert cholesterol into estrogen. However, the placenta can convert DHEA derived from cholesterol in the fetal adrenal cortex into estrogen when DHEA reaches the placenta by means of the fetal blood *(blue pathway)*.

The effect of progesteron in pregnancy or its functions:

- Induces the development of the decidual cells in the uterine endometrium (for nutrition of the early embryo).
- Decreases the contractility of the pregnant uterus, thus preventing spontaneous abortion.
- Contributes to the development of the embryo and the conceptus before implantation by the secretion of the Fallopian tubes and uterus that provides nutrition for the developing morula and blastocyst.
- Effects cell cleavage in the early developing embryo. → also the estrogene can do that.
- Prepares the mother breast for lactation after delivery.

4-Human Chorionic somatomamotropin or Human Placental Lactogen (HPL) is a protein hormone that is secreted by placenta as well around 5^{th} week of gestation. It is secreted with extremely larg quantities and greater than all of the other pregnancy hormones combined. Its functions in the mother (not all functions well known):

- Breast development and lactation in animal (can't induce milk in human).
- It has weak growth hormone's action about 100X less in potency than growth hormone.
- It inhibits insulin sensitivity; thus decreases glucose utilization by mother. So that might help in utilization of glucose in fetus instead.
- It is believed that this hormone has mainly metabolic actions to provides fetus with important resources of energy. Also, it promotes the release of the fatty acids from the female which can be used an ulternative source of energy for the fetus.

5-Relaxin is a polypeptide hormone that is secreted by both placenta and corpus luteum. The functions of the hormone in the mother:

- ✓ Helps in relaxation of the symphasis pubic ligaments (weak effect).
- ✓ It softens the cervix at delivery.
- ✓ Has vasodilator effect which may have a role in increasing blood flow, venous return and cardiac output in pregnant women.

Changes in Maternal Endocrine system

The changes that happened in the maternal endocrine system either due to maternal load or due to the response to placenta hormones. Some examples:

1- Anterior pituitary gland enlargement (50% in size), as a result of this is increasing of the release of the ACTH, TSH, PL, however FSH and LH almost totally suppressed due to high levels of Estrogen and Progesteron that will have a negative feedback on anterior pituitary gland.
2- Adrenal gland will increase the secretion of glucocorticoids (mobilization of amino acids in maternal circulation into fetal circulation with are required for growth of the fetus). Also, it increase in aldosterone secreation 2X times (retaining the fluids in pregnant women due to increase Na & Cl reabsorption inducing hypertension called pregnancy-induced hypertension).

3- Thyroid gland enlargement (50% in size), will increase the production of thyroxine and increase the metabolic rate in pregnant women.
4- There are some thyrotropic effect of HCG, TSH, and placenta human chorionic thyrotropin (increases the stimulation of thyroid gland)
5- Parathyroid gland enlargement specially when there is deficiency of the Ca in pregnant women(due to use it by the fetus inorder to develop his/her bones) , as a result it will increases PTH secretion to maintain normal Ca2+ level.

Some changes in different organs:

1- Increases in the size uterus (50 mg to 1100 gm).
2- The size of the breast will double.
3- Vagina enlargement.
4- Some Developments of acne and edema on the skin
5- It will appear some musculine and acromegaly features due to overall growth that takes place during pregnancy.
6- Gaining weight around 10 – 12 kg specially in the last 2 trimesters (nearly 4 kg is fetus weight and the rest of the gained weight is the retained fluids(from the retention fluid ,amionitic fluid) and fat deposition)
7- Increases the appetite due to highly removal of nutrients by fetus for the growth and developments & hormonal effects.

The metabolism of pregnant women:

During pregnancy the metabolic rate will increase by 15% due to the thyroxine, ACTH, and sex hormones. There will an increase in the daily requirements for iron, calcium, phosphate and Vit D (for Ca+ absorption from GI tract to develop the bone).

Kidney function during pregnancy:

The kidney function will be effected as well. Renal tubules' reabsorption capacity for sodium, chloride and water is increased 50% from normal days by:

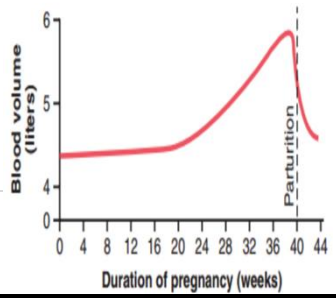
- Cortical and placenta steroid hormone will induce the reabsorption rate as well as The renal blood flow and GFR increase the reabsorption up to 50% (the renal blood flow will increase by the releasing of NO and relaxin hormone). Increasing in blood flow will have feedback on the tubuloglomerular.

Normal pregnant women will accumulates only about 2.5 kg of extra water and salt which will be excreted after delivery.

Changes in circulatory system:

The most important physiological changes of the pregnant women that take place is circulatory system:

- Increase in blood flow through placenta (625 ml/min).
- Increase in maternal blood volume (about 30% more), due to
  1- Increase of aldosterone and estrogen, which helps to increase the extra cellular fluid volume (fluid retention).



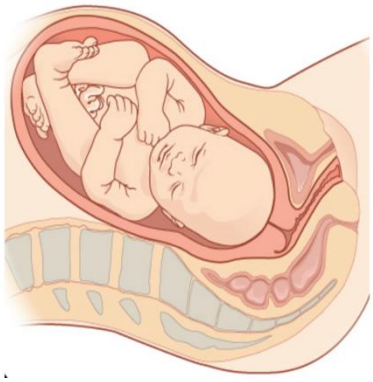
2- Increase the activity of the bone marrow producing more RBCs which in turn involve in increasing the extra cellular fluid.
3- Increase extra 1 to 2 liters in the end of pregnancy (for safety factor), because it's protect the mother from losing much blood during delivery.
4- Blood flow and cardiac output are increased during pregnancy about 30%-40% during the 27th week, due to increase the demand of metabolism and increase blood flow. In the last 8 weeks of pregnancy the cardiac output is declined due to the blood flow in some other tissues may reduced.

Changes in respiration:

- Increase in the O2 assumption about 20% due to increase in basal metabolic rate (hormones secreation) and increase in body size of pregnant women so the demand will increase.
- Increase in respiratory rate; due to influence of the Progesterone in increasing the sensitivity of respiratory center to CO2 level. Also, because of growing the uterus presses upward against the abdomin, which presses upward against the diaphragm, so the total excursion of the diaphragm is decreased. Thus, respiratory rate is increased to maintain the extra ventilation.
- As a result→Increase in minute ventilation by 50% and a decrease in arterial PCO2 to several ml.

Amniotic fluid

-Amniotic fluid is the fluid that surround the fetus inside the membranes of the fetus. Normally, the volume of amniotic fluid 500ml to 1L (sometimes it could be more than liter). The water in the amniotic fluid is replaced every 3 hours and the electrolytes (Na+ & K+) are replaced once every 15 hours. Large portion of the fluid is derived renal excretion by the fetus. There will be some absorption of amniotic fluid occurs by its way of the gastrointestinal tracts and lungs of the fetus. Furthermore, there is a contribution from the amniotic membranes in either forming or absorbing of amniotic fluid. Recently was proven that even the fetus is died there is some turn over of the amniotic fluid from the membran.



Some abnormalities in pregnancy

1- Pre-eclampsia:

About 5% of pregnant women experience pregnancy-induced hypertension (a rapid rise in arterial blood pressure to hypertensive levels during the last few months of pregnancy). Increased in blood pressure usually a combined with Proteinuria (preseance of protein in urin).

It is characterized by:

- ✓ excess salt and water retention by the mother's kidney.
- ✓ Some weight gain

- ✓ Edema
- ✓ Hypertension
- ✓ Vascular endothelial disfunction
- ✓ Arterial spasm occurs in many parts of the mother's body such as kidneys, brain, and liver.
- ✓ Renal blood flow & glumerular filtration rate are decreased.

There is a theory suggested that the cause behind pre-eclampsia is that excessive secretion of placenta or adrenal hormones and some other studies suggested that some type of autoimmunity or allergy in the mother caused by the fetus (immune reaction of the mother against fetus).

There is an evidence about the reason behind pre-eclampsia is initiated by insufficient blood supply to the placenta that starts early in pregnancy, resulting in placenta's release of substances that cause widespread vascular dysfunction ,(maternal arterioles fail to undergo adaptive changes). Pre-eclampsia has a role for increased levels of inflammatory cytokines such as TNF-a and IL-6. Also, it has been suggested that placental factors that imped angiogenesis (blood vessel growth) as well.

2- <u>Eclampsia:</u>

Eclampsia is an extreme degree of pre-eclampsia, vascular spasms occur throughout body. It is characterized by:

- o Clinic seizures in the mother, sometimes followed by coma.
- o Decreased kidney output (greatly).
- o Liver malfunction.
- o Extremehypertension.
- o A generalized toxic condition of the body.
- o Usually occurs shortly before the birth of the baby.

Without treatment a high percentage of mothers with eclampsia die. However, with optimal and immediate use of rapidly acting vasodilating drugs, followed by immediate termination of pregnancy the mortality is reduced to 1% or less.