



Female Reproductive System

Congratulations on making it to the LAST sheet EVER written... Try not to be overwhelmed with emotions while reading it =P It's a relatively easy lecture =)

- Fertilization

- As we can recall, the sperm and ova are capable of fertilizing each other for 2 days, a mother is considered pregnant at the moment of fertilization, the duration of pregnancy is approximately 38 weeks from time of ovulation or 40 weeks from first day of last menstrual period.

In the female reproductive, we can see the uterus, the fallopian tubes and the ovaries, the fallopian tubes transport the sperms from the uterus towards the fertilization site, and they also transport the fertilized ovum from the fertilization site to the uterus (so movement occurs in both directions), this requires coordination between smooth muscle contractions, ciliary movement, peristaltic movement (for the ovum) and fluid secretion, all of which are under hormonal and neural control.

What about sperm movement?

The female sex response facilitates sperm transport through the female reproductive tract, using 5 mechanisms

1. Uterine and cervical activity is increased by the spinal reflexes during orgasm.
2. The cervix dilates during orgasm.
3. Oxytocin release at the time of orgasm increases uterine contractility.
4. The mucus of the cervical canal increases the movement of the sperm under estrogen dominance and orgasm.
5. Peristaltic activity and fluid flow in the oviduct assists transport.

Now we know how the sperm moves to the fertilization site and how the fertilized ovum moves from the fertilization site towards the uterus.



*Note from writer: I think the doctor forgot to mention this point and it is written in last year's sheet; " The peristaltic activity in the uterine tube: another important point about the movement of the zygote towards the uterus; is that it is unidirectional, behind the zygote are contractions and in front of it relaxations".

-After 1 week of fertilization, implantation occurs.

During pregnancy the cycles are suspended, within the first two weeks after implantation, the placenta is formed and produces **human chorionic gonadotropin hormone (hCG)**. This hormone rescues the corpus luteum, the corpus luteum continues to grow until it occupies 30-50% of the volume of the ovary. It produces progesterone and estrogen, reaches the maximum level of secreting hormones at week 6 then falls back to a reduced function at the end of second month, then stops functioning at end of 4th month. By that time the placenta takes over, if this taking over period doesn't occur properly >abortion.

There are receptors in the ovum in order to accept specific sperm, because sometimes -especially in animals - different species mate, so the sperm usually cannot penetrate the ova due to absence of specific glycoprotein receptors.

Very rarely, a sperm penetrates the ovum, especially in very close species such as a wolf and a dog, if they do produce an animal, it would be from a non-specific species and that animal would be sterile (can't reproduce).

The **blastocyst** produces many enzymes and factors such as

1- Immunosuppressive agents 2- Metalloproteases.

From these the most important one is **hCG**, it acts as:

I- immunosuppressant agent

II- growth promoting activity

III- autocrine growth factor that promotes trophoblast growth and placental development.

IV- may also play a role in the adhesion of trophoblast to epithelial cells of uterus

V- has enzymatic activity



If you can recall the function of this hormone on the testis: similar to LH (since LH is not produced properly in fetal life), it also has an effect on beta-adrenal glands.

Here are the hormones produced by the **placenta**:

1-Peptide hormones and neuropeptides.

2-Steroid hormones; progesterone and estrogen

Even with those substances, still the most important hormone being produced here is hCG.

Along with other hormones are **human chorionic somatomammotropins (hCS) 1 and 2 (hCS is also known as human placental lactogen, hPL)**. Those hormones (1 and 2) are polypeptides that are structurally related to growth hormone, placental-variant growth hormone and prolactin. They play a role in the conversion of glucose to fatty acids and ketones, thus coordinating the fuel economy of the fetoplacental unit. The fetus and placenta use fatty acids and ketones as energy sources and store them as fuels in preparation for the early neonatal period; when a considerable reservoir of energy is necessary for the transition from intrauterine life to life outside uterus. They also promote the development of maternal mammary glands during pregnancy.

Although hCG and human placental lactogens (1, 2) are produced by the same cells, it seems that the pattern of secretion is different indicating the possibility of different regulatory mechanisms.

Morning sickness is most probably caused by the high concentrations of thyroxin and hCG. (doesn't occur in all women, but when it does it happens in the first **2-3 months**, since during this period these two hormones are relatively high).

From the second week hCG increases drastically and it reaches the highest concentration between week 10 and 15.

The fetoplacental unit and steroidogenesis

The placenta produces steroid hormones, progesterone, estrone- estradiol but mainly estrone.



When testing the levels of estriol in plasma, amniotic fluid and urine are used as an index for fetal well-being. Low levels of estriol would indicate potential fetal distress, although rare inherited sulfatase deficiencies can also lead to low estriol.

"There is cooperation between these three compartments (Maternal, Placenta, Fetus) to produce androgens and estrogens; to produce the androgens and estrogens the placenta needs the substrates from both maternal and fetal compartments." *not mentioned in this year's recording*

Fetal nervous system and immune system develop slowly, however the fetal endocrine system develops quicker as it plays a vital role in fetal growth, development and homeostasis.

Fetal hormones perform the same functions in the adults, but also have unique processes such as sexual differentiation and initiation of labor.

Adrenal glands are unique in size, structure and function. At about the fourth month of gestation the size of the adrenal glands in the fetus is larger than the size of its kidneys. The fetal adrenal gland (adrenal cortex) produces androgens, aldosterone and cortisol (which has multiple functions); cortisol is essential for the growth and maturation of the lungs, pancreas, hepatic enzymes and GIT cytodifferentiation.

The adrenal medulla functions properly and begins to produce catecholamines after week 10. (not as important as the adrenal cortex)

The fetus grows and increases in weight, however the role of the growth hormone of the mother and GH of fetus on it, is very little.

The **most important factor** in the fetus as far as the **growth** is concerned is insulin. Fetal insulin is the most important hormone in regulating fetal growth. Glucose is the main metabolic fuel for the fetus. Fetal insulin is produced by the pancreas by **week 12 of gestation**. It regulates tissue glucose use, controls liver glycogen storage, and facilitates fat deposition. It doesn't control the supply of glucose; this is determined by the **maternal gluconeogenesis** and **placental glucose transport**. The release of insulin in the fetus is relatively **constant**.



Parturition/Delivery:

During pregnancy (all first 8 months) the uterus is **inactive** (no contractions) under the effect of **progesterone (pregnancy hormone) and relaxin**. (Remember: No progesterone, no pregnancy)

During the last month of pregnancy, weak and irregular uterine contractions occur, these contractions end in strong/forceful rhythmic contractions that last for hours-one day or even more, and end in delivery.

Not all the pathways leading to delivery are known but endocrine, paracrine and mechanical stretching of the uterus all play a role. Once labor is initiated it is sustained by a series of positive feedback mechanisms.

The last theory of initiation of labor is that labor is initiated by hormones released from the fetus. **Fetal pituitary ACTH is the initiator of labor**, it affects fetal adrenals, and DHEA-S (dehydroepiandrosterone sulfate) is produced, this affects the placenta which leads to an **increase in local estrogen and progesterone ratio** which in turn increases local prostaglandins. Fetal adrenals also produce cortisol. Oxytocin (from the maternal pituitary), the high local estrogen progesterone ratio, local prostaglandins (both of these from the fetus) and catecholamines (both maternal and fetal) contribute in the contractions of the uterus for labor to occur.

After delivery, the mother needs prolactin in order to feed the baby; estradiol modulates the release of prolactin by two ways

1. Increases the sensitivity of Lactotrophs for stimulation by PRH.
2. Decreases the sensitivity of the Lactotrophs for inhibition by Dopamine.

If the mother doesn't nurse her baby within 2 weeks, prolactin concentration decreases and returns to the levels of a non-pregnant woman. If the mother nurses her baby, prolactin secretion will be maintained as long as there is suckling.

Lactation inhibits the ovarian cycles; suckling reduces the release of GnRH from the hypothalamus. However if the mother continues to nurse her infant for a long period, the cycle eventually resumes.



A study that was conducted about “Breast feeding in Bangladesh women” shows that the average period of un-ovulation is 18-24 months. (in this country the women breastfeed for a very long amount of time)

If the mother doesn't nurse the infant the cycle will resume after delivery up to 18 weeks. (averagely 8-10 weeks)

Oxytocin and suckling cause the ejection of milk.

Menopause

In males, low testosterone levels occur between 65-70, while in females, menopause takes place at about 55-60 years, and sometimes women can even reach the age of 80 before reaching menopause. The doctor then showed two articles about Spanish women that had babies at the age of 70 and 66; he claimed that menopause nowadays can be a bit postponed due to different lifestyles.

Gonadotropins (FSH & LH)

In females - high at menopause. In Males - low, due to the presence of Androgens.

Infertility is more common with women, 1 out of 5 women in the US are infertile, and in order understand this major problem we need to investigate endocrine, anatomy and physiology. Several factors may cause infertility:

1. Environmental.
2. Disorders of the central nervous system.
3. Hypothalamic diseases.
4. Pituitary disorders.
5. Ovarian abnormalities.

These can interfere with hormonal production and/or ovulation. **However the most common cause of female sterility is failure to ovulate.**

Contraceptive use and efficacy rate in the US



TABLE 39.A Contraceptive Use and Efficacy Rates in the United States

Method	Estimated Use (%)	Accidental Pregnancy in Year 1 (%)
Pill	32	3
Female sterilization	19	0.4
Condom	17	12
Male sterilization	14	0.15
Diaphragm	4–6	2–23
Spermicides	5	20
Rhythm	4	20
Intrauterine device	3	6

From *Developing New Contraceptives: Obstacles and Opportunities*. Washington, DC: National Academy Press, 1990.

Female sterilization: a reversible technique where we ligate the uterine tubes

Male sterilization: ligation of vas deferens

Pills (hormones) have the most side effects, and IUD has almost no side effects, however the estimated use rate for pills is 32% while for IUD 3% ... why?

Pills are easier to use, IUD may rarely cause bleeding then needs to be removed.

Please refer to slide 20 from the second sets of slides, you will find a table explaining the following:

Pills could be a mixture of estrogen and progesterone, effectiveness is more than 99%.

Taking progesterone only pills is also very effective (99%). Both those previous methods prevent ovulation

Emergency pills which are taken within 72hours of intercourse, they contain high concentration of progesterone and estrogen, they prevent implantation,



Depot lasts 8-12 weeks and prevents ovulation, it is also very effective

Lastly we have synthetic progesterone; it lasts for 5 years, prevents ovulation and is very effective.

All these have **lots** of side effects.

Nowadays the rhythm contraceptive method is used in order **to have** children, not avoid being pregnant.

Let's recall some points about the menstrual cycle:

The duration of the cycle is about 28 days; this is the average in almost 85% of women. Menstrual phase 4-5 days roughly. Ovulation occurs at day 14.

Sometimes the duration shortens or prolongs. So we could say the average duration is 28 days (+ or - 7) that is equal to (21-35) days. Shorter than 21 never recorded but longer than 35 was recorded up to 42.

Recall: The second half of the cycle (after ovulation) is **constant**, always two weeks.

The cycle regularity is not changed in normal females (i.e. the duration of the period is almost constant all the time in a normal female -for ex. Every 28 days, there's menstruation-, except upon stress, having an illness; like flu, or upon the use of certain medications).

Life span of the ovum and sperm: Most sperms will die within 1-2 days after ejaculation, even inside the uterus. On the other hand, the ovum has a life-span of only about 12-24 hours at most from the time it ovulates.

If a couple wants to reduce the chances of pregnancy, they should avoid the sexual intercourse within three days before the onset of ovulation (day 14 minus 3 days) and 3 days after (day 14 plus 3). So from day 11 to 17 (in a typical menstrual cycle: 28 days), this is called the **unsafe period (U.S.P)**.

From day 17 to the end of the cycle (day 28) this is the **safe period (S.P)**.

From the end of menses to the 11th day, this period is **probably safe period (P.S.P)** However, this method of contraception doesn't work as expected all the time, there might be pregnancy in some cases.



What if the cycle was 21 days? Then $21 - 14 = 7$, Ovulation occurs at day 7. (-3 and + 3) so unsafe period is from day 4 till day 10, women use those calculations in order to get pregnant.

Women are advised to take estrogen 2-3 years before menopause when during this period some signs of menopause could be seen. Estrogen:

- 1- prevents osteoporosis
- 2- maintains the beauty of a woman as well as prevents wrinkles
- 3- treats extreme facial and body hair
- 4- increases sexual desire
- 5- maintains size of breasts
- 6- prevents urine incontinence (recall anatomy of female genital organs)
- 7- contributes to treatment of Alzheimer's and amnesia

This sheet is dedicated to my two favourite Virgos; Sophia & Duha <3 , the beautiful Zain Sawwaf, the gorgeous Tasneem Melhem, the amazing Rashid, and my second family; batch of 2013 <3

وتهدينا الحياة اضوائا في اخر النفق

تدعونا كي ننسا الما عشناه

نستسلم لكن لا ما دمنا احياء نرزق

ما دام الامل طريقا فسنحيا