THE MALE REPRODUCTIVE SYSTEM

I. Overview of the Reproductive System

1. The reproductive system consists of primary and secondary sex organs. The primary sex organs (gonads) are those that produce gametes.
2. The secondary sex organs are those that are essential to reproduction, such as ducts, glands, and a penis in males.
3. Secondary sex characteristics are features that are not essential for reproduction but that attract the sexes to each other.

II. Puberty and Climacteric

A. Endocrine control of puberty

The earliest hormonal (invisible) change heralding the onset of puberty is increased secretion of androgens / (dehydroepiandrosterone, dehydroepiandosterone sulfate) from the adrenal cortex. The level of these hormones increases progressively from the age of 6 to 8 years.

1. As the hypothalamus matures, it begins producing gonadotropin-releasing hormone (GnRH) at puberty. This hormone travels to the anterior pituitary and stimulates the production of follicle-stimulating hormone (FSH) and luteinizing hormone (LH).
   a. LH stimulates the interstitial cells of the testis to secrete androgens (mainly testosterone).
   b. FSH is needed in order for testosterone to have an effect on the testis because it stimulates the Sertoli cells to secrete androgen-binding protein (ABP).

<table>
<thead>
<tr>
<th>Function of Sertoli Cells</th>
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<tbody>
<tr>
<td>• maintenance of blood-testes barrier which prevents many substances from entering or leaving the seminiferous tubules</td>
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<tr>
<td>• removal of any damaged germ cells</td>
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<tr>
<td>• keep the sperm in the tubules from diffusing into the blood</td>
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<tr>
<td>• production of seminiferous tubular fluid</td>
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<tr>
<td>• nourishment of developing germ cells</td>
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<tr>
<td>• synthesize of ABP (androgen binding protein)</td>
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<tr>
<td>• synthesize of Inhibin</td>
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</tbody>
</table>

2. The androgens stimulate spermatogenesis (in the presence of ABP), suppress the secretion of GnRH, stimulate the development of secondary sex characteristics and other somatic changes of puberty.
   a. Inhibin, a hormone from the Sertoli cells, selectively suppresses FSH output from the pituitary that effectively slows sperm production without inhibiting testosterone production.
Testosterone-Dependent Changes at Puberty:
- penis and testes enlarge and become pigmented
- growth of facial, pubic and axillary hair. Hair appears also on chest and extremities.
- stimulates the secretion of growth hormone, resulting in an increase of rate of long bone growth (3 inches per year).
- deepening of voice because of vocal cords and larynx enlargement.
- increase of muscle mass and thickness of skin.
- stimulates the brain and awakens the libido

B. Aging and Sexual Function

1. Testosterone production peaks at about age 20 then declines steadily to as little as one-fifth of this level by age 80.
2. As testosterone and inhibin levels decline, they stop to inhibit the pituitary. Consequently FSH and LH levels rise significantly in the late 40s to early 50s, producing changes called male climacteric (andropause).

III. Spermatogenesis, Spermatozoa, and Semen

A. Spermatogenesis

1. The first cells destined to become sperm cells are the primordial germ cells. These differentiate into spermatogonia, which lie along the periphery of the seminiferous tubule outside the blood-testis barrier (BTB).
2. Spermatogonia differentiate into cells called primary spermatocytes. Sertoli cells transfer these cells through the BTB toward the inside of the tubule.
3. After the BTB closes behind it, the primary spermatocyte undergoes meiosis I, giving rise to two haploid secondary spermatocytes. Each of these undergoes meiosis II, dividing into two spermatids. Each stage is a little closer to the lumen of the tubule.
4. The rest of spermatogenesis is called spermiogenesis and involves no further cell division but maturation of the sperm cells.

B. The Sperm

The sperm has a pear-shaped head and a long tail.
1. The head contains the haploid nucleus, an acrosome bearing enzymes used to dissolve a path to penetrate the egg.
2. The tail contains large mitochondria that produce ATP for sperm motility.

C. Semen

1. The fluid expelled during orgasm is called semen or seminal fluid.
   a. The average volume of semen ejaculated is 3 to 5 ml.
   b. The normal concentration of sperm in the ejaculate is 40-120 million/ml
   b. The lifespan of sperm-72 hours
THE FEMALE REPRODUCTIVE SYSTEM

I. Sex Differentiation

1. The female reproductive tract develops NOT because of estrogens action but in the absence of testosterone and mullerian-inhibiting factor influence.
2. In the absence of these influences the penis becomes a clitoris, the urogenital folds develop into labia minora, and the labioscrotal folds develop into labia majora. The paramesonephric duct becomes the uterus, oviducts, and vagina.

II. Puberty and Menopause

A. Puberty.

The earliest hormonal (unviable) change heralding the onset of puberty, like in boys, in girls is increased secretion of androgens / (dehydroepiandrosterone, dehydroepiandrosterone sulfate) from the adrenal cortex. The level of these hormones increases progressively from the age of 6 to 8 years.

1. Rising levels of GnRH stimulate the anterior pituitary to produce FSH and LH. FSH stimulates the development of the ovarian follicles, which in turn secrete:
   - estrogens
   - progesterone
   - inhibin
   - small amount of androgen.
   a. Estrogens levels rise gradually from ages 8 to 12. These are feminizing hormones with widespread effects on the body. They include estradiol (the most abundant), estriol, and estrone.
   b. The earliest notable change is thelarche, the development of the breasts. Soon after this comes pubarche, development of the pubic and axillary hair. Next comes menarche, the first menstrual period. Menarche does not occur until a girl has reached 17% body fat, so it can be delayed in girls who are very athletic. Most girls begin ovulating about a year after they begin menstruating.

<table>
<thead>
<tr>
<th>Succession of Appearance of Secondary Sexual Characteristics in Girls:</th>
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<tbody>
<tr>
<td>• adrenarche - increased production of adrenal androgens</td>
</tr>
<tr>
<td>• fluor pubertalis - beginning of appearance of vaginal secretion</td>
</tr>
<tr>
<td>• telarche - development of the breast buds</td>
</tr>
<tr>
<td>• pubarche - development of pubic and axillary hair</td>
</tr>
<tr>
<td>• peak of growth rate - / about 12 years age /</td>
</tr>
<tr>
<td>• menarche - the first menstrual flow</td>
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</tbody>
</table>

2. Estradiol stimulates growth of the ovaries and secondary sex organs. It stimulates osteoblasts, causing a growth spurt and widening of the pelvis. Estradiol is largely responsible for the feminine physique.
3. Progesterone acts primarily on the uterus, preparing it for possible pregnancy. Estrogens and progesterone also suppress FSH and LH through negative feedback.
B. Climacteric and Menopause

The menopause usually occurring between the ages of 45 and 55 and is defined as the final episode of menstrual bleeding in women. However, the term is used commonly to refer to the period of several years before and after the menopause.

1. With age, the ovaries are less responsive to gonadotropins. Consequently, they secrete less estrogen and progesterone. Without these steroids, the uterus, vagina, and breasts atrophy.

<table>
<thead>
<tr>
<th>Symptoms of Menopause:</th>
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<tbody>
<tr>
<td>• depression</td>
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<tr>
<td>• osteoporosis</td>
</tr>
<tr>
<td>• hot flushes / due to vascular instability /</td>
</tr>
<tr>
<td>• psychic sensations of dyspnea</td>
</tr>
<tr>
<td>• irritability</td>
</tr>
<tr>
<td>• fatigue</td>
</tr>
<tr>
<td>• anxiety</td>
</tr>
<tr>
<td>• atrophy of the urogenital epithelium and skin</td>
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<tr>
<td>• decreased size of the breasts</td>
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</table>

III. Oogenesis

1. Egg production, called oogenesis, is a cyclic event.
2. The female germ cells colonize the gonads and then differentiate into oogonia. Oogonia multiply until the sixth month of fetal development, reach 6–7 million in number. At the time of birth some of them transform into primary oocytes.
3. Most primary oocytes undergo a process of degeneration called atresia. Only 2 million remain at the time of birth, and by puberty, only 400,000 remain.
4. In the beginning of puberty FSH stimulates the primary oocytes to complete first meiosis division, which yields two haploid cells. One becomes the egg, the other a polar body.

IV. The Sexual Cycle

1. The female sexual cycle is a monthly sequence of changes caused by cyclic patterns of hormone secretion. During the menstrual cycle of woman we can list ovarian cycle and endometrial cycle.
2. The ovarian cycle can be divided into 3 phases:
   a. follicular phase
   b. ovulation
   c. luteal phase (14 +/- 2 days)
3. The endometrial cycle also can be divided into 3 phases:
   a. proliferative phase
   b. secretory phase
   c. menstruation
4. An oocyte has only 24 hours to be fertilized. The chance of fertilization is enhanced because the cervical mucus changes at the time of ovulation, becoming thinner and more viscous.
5. During the luteal phase, the ovulated follicle becomes a structure called the corpus luteum. If pregnancy occurs, the corpus luteum remains active for about 3 months. In the absence of pregnancy, it begins to degenerate and undergo involution and become corpus albicans.

6. During the menstrual phase, necrotic tissue falls away from the uterine wall, mixes with blood in the lumen, and forms the menstrual fluid.

7. The first day of vaginal discharge is considered **day 1-st of the new cycle**.

8. Involution of the corpus luteum ends the negative feedback effect of progesterone on the hypothalamus. Thus, GnRH secretion rises, followed by FSH and a new hormonal cycle is started.

V. Pregnancy and Childbirth

A. Prenatal Development

1. Physiologically fertilization occurs in the distal half of the uterine tube (ampulla of oviduct)- unfertilized egg does not live long enough to reach the uterus alive.
2. Soon after it reaches the uterus, the zygote becomes a blastocyst, which consists of an inner cell mass destined to develop into the embryo and an outer trophoblast that plays various supporting roles.
The trophoblast is responsible for implantation in the uterine lining and later gives rise to the placenta. Implantation occurs approximately 6 days after fertilization.

B. Hormones of Pregnancy

1. Human chorionic gonadotropin (HCG) is secreted by the trophoblast cells. Its presence is the basis of pregnancy tests. HCG secretion peaks around 10–12 weeks and then falls. It stimulates growth of the corpus luteum, which doubles in size and secretes increasing amounts of progesterone and estrogen.

<table>
<thead>
<tr>
<th>Function of Human Chorionic Gonadotropin</th>
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<tbody>
<tr>
<td>• prevent degeneration of the corpus luteum</td>
</tr>
<tr>
<td>• stimulates the corpus luteum to secrete estrogen and progesterone</td>
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<tr>
<td>• stimulates steroid synthesis in the developing fetal adrenals</td>
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<tr>
<td>• stimulates fetal gonads, especially testosterone production by the fetal testes.</td>
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<tr>
<td>• suppresses maternal lymphocytes and reduces the possibility of immunoreactions against the fetus.</td>
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</tbody>
</table>

2. **Estrogen** secretion increases and stimulates tissue growth in the fetus and mother. They cause the mother's uterus and external genitalia to enlarge, the mammary ducts to grow, and the breasts to increase. They make the pubic symphysis more elastic.

3. The placenta secretes a great amount of **progesterone**. This, coupled with estrogen secretion, suppresses the secretion of FSH and LH, preventing follicles from developing during pregnancy. Progesterone also suppresses uterine contractions and prevents menstruation.

4. The amount of human chorionic somatotropin (HCS) secreted in pregnancy is several times that of all other hormones combined. The placenta begins secreting HCS around the fifth week, and HCS output increases steadily from then until term. It promotes the release of free fatty acids from the mother's adipose tissue among other unknown functions.
C. Adjustments to Pregnancy

1. Many women experience morning sickness and nausea during the early stages of pregnancy, and constipation and heartburn later in the pregnancy. The basal metabolic rate increases by 15% during the second half of gestation. During the last trimester, the fetus needs more nutrients than the mother's digestive tract can absorb. In preparation for this, the placenta stores nutrients early in gestation and releases them in the final trimester. The demand is especially high for protein, iron, calcium, and phosphates.

2. The mother's blood volume rises about 30% during pregnancy due to fluid retention and hemopoiesis; she eventually has 1 to 2 L of extra blood.

3. The uterus weighs about 50 g when a woman is not pregnant and 1,100 g at the end of pregnancy.

D. Childbirth

1. The process of giving birth is called parturition.

2. Uterine Contractility
   a. Over the course of gestation, the uterus exhibits relatively weak Braxton Hicks contractions.
   b. During the first 6–7 months, progesterone inhibits uterine contractions, but by the seventh month, progesterone secretion levels off or declines slightly. The secretion of estrogen, which stimulates uterine contractions, continues to rise.
   c. As the pregnancy reaches full term, the posterior pituitary releases more oxytocin and promotes labor by stimulating the muscle of the myometrium and by stimulating fetal tissue to secrete prostaglandins, which are synergists of oxytocin.

3. Labor Contractions
   Labor contractions begin about 30 minutes apart. As labor progresses, they become more intense and eventually occur every 1 to 3 minutes. Each contraction sharply reduces maternal blood flow to the placenta, so the uterus must periodically relax to restore blood flow and oxygen delivery to the fetus.

4. Labor occurs in three stages.
   a. The first stage of labor, dilation, is the longest, and involves effacement and dilation of the cervix to 10 cm.
   b. The second stage of labor is the expulsion of the fetus and may last from 1 minute to 30 minutes in first-time mothers. Delivery of the head is the most difficult part, with the rest of the body following much more easily.
   c. During the placental stage, the uterus continues to contract after expulsion of the baby.

E. Puerperium

1. The first six weeks postpartum are called the puerperium, a period in which the mother's anatomy and physiology stabilize and the reproductive organs shrink to their condition prior to pregnancy.

2. Shrinking of the uterus, called involution, is achieved through autolysis of uterine cells by their own lysosomal enzymes.
VI. Lactation

A. Development of the Mammary Glands in Pregnancy

1. Lactation, the synthesis and ejection of milk from the mammary glands.

B. Colostrum and Milk Synthesis

1. In late pregnancy, the mammary acini and ducts become distended with a secretion called colostrum. This is similar to breast milk in protein and lactose content but contains about one-third less fat. It is the infant's only natural source of nutrition for the first 2 to 3 days postpartum. Colostrum has a thin, watery consistency and a cloudy, yellowish color.
2. A major benefit of colostrum is that it contains immunoglobulins, especially IgA, which may protect the infant against gastroenteritis.
3. Milk synthesis is promoted by prolactin, a hormone of the anterior pituitary gland.

C. Milk Ejection

1. Milk ejection is mediated by a neuroendocrine reflex. The infant's suckling stimulates nerve endings of the nipple and areola, which in turn signal the hypothalamus and posterior pituitary to release oxytocin. Oxytocin stimulates myoepithelial cells, which form a basketlike mesh around each gland acinus.

D. Breast Milk

Colostrum and milk have a laxative effect that helps clear the neonate intestine of meconium, a sticky, greenish-black fecal matter composed of bile, epithelial cells, and other wastes. By clearing bile and bilirubin from the system, breast-feeding also reduces the incidence and degree of jaundice in neonates.

VII. Human Development - Fertilization and Preembryonic Development

A. Sperm Migration

An egg must be fertilized within 24 hours after ovulation. Because the egg takes about 72 hours to reach the uterus, sperm must migrate up the female reproductive tract and meet it in the distal one-third of the uterine tube.

B. Capacitation

1. During their migration, sperm undergo a process of capacitation that makes it possible to penetrate an egg.
   a. Prior to ejaculation, the membrane of the sperm head contains quite big amount of strengthening cholesterol.
   b. After ejaculation, however, fluids of the female reproductive tract wash away the cholesterol and other inhibitory factors in the semen. The membrane of the sperm head becomes more fragile.
C. Fertilization

1. When a sperm and egg meet, the sperm undergoes an acrosomal reaction that releases the enzymes necessary for penetration of the egg.

2. Fertilization combines the haploid (n) set of chromosomes from each gamete, producing a diploid (2n) zygote.

3. Implantation
   a. About 7 days after ovulation, the blastocyst attaches to the endometrium.
   b. The trophoblast cells secrete enzymes that stimulate thickening of the adjacent endometrium.
   c. Implantation takes about a week and is completed about the time the next menstrual period would have occurred if the woman had not become pregnant.

4. Prenatal Nutrition
   The placenta begins to develop about 11 days after conception. It starts with development of chorionic villi from the former trophoblast.

<table>
<thead>
<tr>
<th>Function of the Placenta</th>
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<tbody>
<tr>
<td>• exchange of gases between fetus and mother</td>
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<tr>
<td>• delivery of nutrients from mother to fetus</td>
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<tr>
<td>• delivery of antibodies from mother to fetus</td>
</tr>
<tr>
<td>• removal of fetal waste</td>
</tr>
<tr>
<td>• secretion of hormones including: human chorionic gonadotropin, progesterone, estrogen and human chorionic somatotropin</td>
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