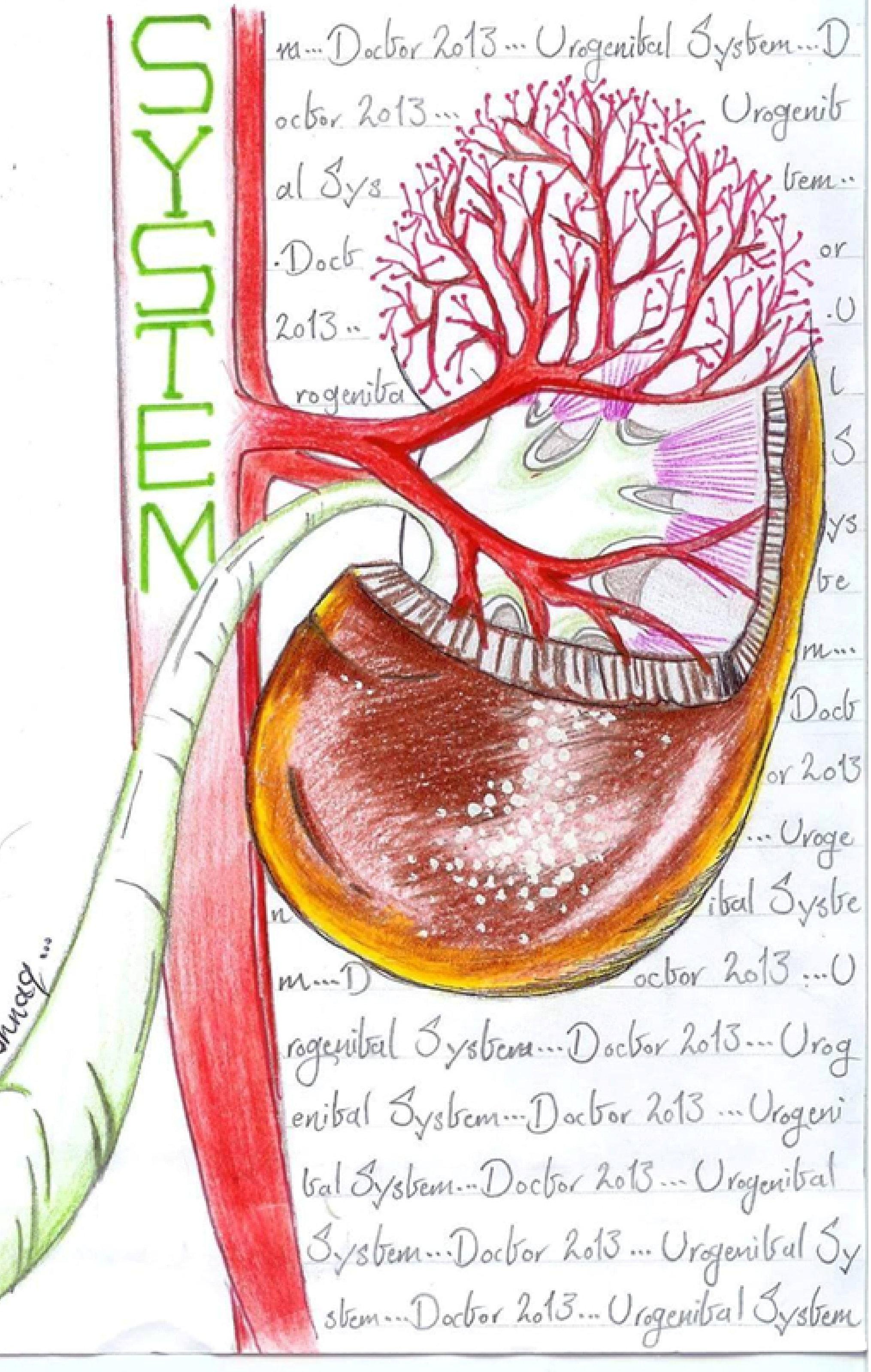
URO-GENITAL SYSTEM

- ○ Handout
- ● Sheet
- ○ Slide

- ○ Anatomy
- ● Physiology
- ○ Pathology
- ○ Biochemistry
- ○ Microbiology
- ○ Pharmacology
- ○ PBL



Done By: **Hiba Mihyar**

Dr. Name: **Dr. Saleem**

Lec. #: **1**

Urogenital Physiology "1"

The anterior pituitary secretes the Follicle stimulating hormone (FSH) and the Luteinizing hormone (LH) that act on the primary sex organs: testes and ovaries. Their secretion is controlled by the Gonadotropin releasing hormone (GnRH) secreted by the hypothalamus.

Usually there is one cell type for each hormone formed in the pituitary gland. FSH and LH are secreted by the Gonadotropes. Some gonadotropes secrete LH, others secrete FSH and some secrete FSH and LH (both). Each of these three types has receptors for GnRH on its surface. Gonadotropes account for only 5% of the total cells in the anterior pituitary.

Spermatogenesis:

Leydig and Sertoli cells:

These cells represent the physiologic function of the testes. They function as one unit, they can't function separately. If we remove leydig cells, sertoli cells can't function and vice versa.

Leydig cells are stimulated by LH to produce testosterone that passes to sertoli cells.

Sertoli cells have many functions:

1- Produce Androgen Binding Protein (ABP); without it the testosterone will be lost from the body.

2- Produce estradiol by the aromatase enzyme that is essential for spermatogenesis.

3- Produce growth factors and other products that are essential for the sperms normal survival and production.

-LH and FSH produce factors such as: Steroidogenic factor 1 (SF1) and cAMP response element binding protein (CREB). These factors activate enzymes that control the production of testosterone by Leydig cells.

- LH also stimulates the synthesis of sterol carrier proteins (SCP) and sterol activating proteins (SAP) that are important for the production of testosterone and normal spermatogenesis.

Leydig cells produce 95% of the testosterone produced in the body. Although testosterone is the main secretory product, testes also secrete **pregnenolone, progesterone, 17-hydroxyprogesterone, androsterone, dihydrotestosterone and androstenedione. Androstenedione serves as precursor for extraglandular estrogen formation.**

Relation between prolactin and LH in males:

Physiologic levels of prolactin in males enhance luteinizing hormone-receptors in Leydig cells, resulting in testosterone secretion, which leads to spermatogenesis (synergistic effect). But in abnormal conditions, prolactin occupies LH receptors on Leydig cells and decreases the production of testosterone (antagonistic effect).

LOOK AT FIGURE 37.1 IN THE HANDOUT:

Regulation of reproduction in male:

Brain centres are affected by: hormonal state, age, stress levels, environment, various disease states, drugs, and genetic factors.

Brain centres then affect the hypothalamus to produce GnRH that acts on the anterior pituitary to produce LH and FSH which act on the testes.

Testes produce testosterone; the main male hormone beside other hormones like activin, inhibin and follistatin that regulate the release of gonadotropins FSH and LH. Generally, testosterone, estradiol and inhibin reduce the secretion of LH and FSH in male (-ve feedback). Activin stimulates the secretion of FSH, whereas follistatin inhibits FSH secretion. Inhibin acts directly on the anterior pituitary and inhibits the secretion of FSH but not LH.

The difference between females and males depends on a single Y chromosome in males and a single pair of endocrine organs (testes and ovaries).

Few notes:

- The differentiation of primitive gonads into testes (or ovaries) is genetically determined but the formation of normal male genital organs depends on functional testes to produce testosterone.
- In both sexes, testes or ovaries have primarily two functions: production of sex hormones and production of gametes (sperms and oocytes) and the functional state of these organs depend on the functional state of pituitary gland and hypothalamus.
- In males, testosterone is responsible for the development of secondary sex organs (epididymis, vas deferens, seminal vesicles, prostate and penis) and the appearance and maintenance of secondary sex characteristics at the age of puberty (laryngeal changes, pubic, axillary and facial hair and body shape etc).
- According to the doctor, ampulla of vas transfers and stores sperms. -.-

Spermatogenesis: (Figure 36.8 in the handout)

It occurs in all seminiferous tubules and has three phases:

1- Mitosis: production of cells having the same number of chromosomes (46).

2- Meiosis: production of cells having half the number of chromosomes (23).

3- Spermiogenesis: maturation of sperms from spermatids to spermatozoa (mature sperms).

These phases are regular, ordered (affected by some chemicals or factors) and sequential.

The duration of spermatogenesis ranges from 70 to 75 days. Although hormones are essential for normal spermatogenesis, they can't alter its duration but they can alter the number of spermatozoa and can cause chromosomal abnormalities.

Because sperm cells are rapidly dividing and undergoing meiosis, they are sensitive to external agents that alter cell division. Chemical carcinogens, chemotherapeutic agents, certain drugs, environmental toxins, irradiation and extreme temperatures are factors that can reduce the number of replicating germ cells or cause chromosomal abnormalities in individual cells.

New cycles are initiated at regular intervals; every 16 days at puberty and approximately 200M spermatozoa are produced daily in adulthood by both testes; one testis is sufficient.

If testes were exposed to infection or injuries, antibodies might be produced against sperms and may cause infertility if they were high in number. Sometimes, although rare, antibodies against sperms may also be found in both the female and the male and this surely leads to infertility.

Look at figure 36.4: (cross sectional view of the testis)

More functions of Sertoli cells:

Sertoli cells are critical to germ cell development as indicated by their close contact.

1- Sertoli cells can phagocytose residual bodies (excess cytoplasm resulting from the transformation of spermatids to spermatozoa) and damaged germ cells.

2- They provide structural support and nutrition for germ cells, secrete fluids and assist in **spermeation which is the final detachement of spermatozoa from sertoli cells into the lumen of seminiferous tubules.**

- Spermeation may involve plasminogen activator which converts plasminogen to plasmin; a proteolytic enzyme that assists in the release of mature sperms into the lumen

3- Sertoli cells also synthesise large amounts of transferrin; an iron transport protein important for sperm development.

4- Sertoli cells also produce glycoprotein hormones; inhibin, activin and follistatin that regulate the secretion of FSH.

Maturation:

Maturation of sperms occurs in the epididymis and they remain there from one day to some days until they become active, motile and fertile and their metabolism increases. If we remove sperms from the head of epididymis, they will be totally infertile/inactive and can't fertilize the ovum. But if we remove sperms from the body of epididymis, the majority will be fertile and motile (some are not) compared to the tail where all of the sperms will be active and fertile and completely mature; being able to fertilize the ovum.

- The ability to gain this motility in the epididymis involves the activation of a unique protein called **CatSper** (**cat**ion channels of **sper**ms). It is a calcium ion channel that permits cAMP generalized calcium influx and this permits the sperms to become motile and move forward.
- Again the doctor mentions that sperms maturation will be halted in the epididymis and continued in the ampulla of vas and they are stored there for several days or even weeks if they aren't utilised.

Capacitation:

After ejaculation to the female reproductive tract, sperms move upward the uterus to the isthmus of uterine tube where they slow down and undergo capacitation which is essential to fertilize the ovum. It lasts from one hour to a day or more.

It consists of two things: increasing the motility of sperms and facilitating the penetration of acrosomal cap into the ovum. However, the role of capacitation appears to be facilitatory rather than obligatory because fertilization is readily produced in vitro.

Chemotaxis theory:

Some researchers say that sperms are guided to the ovum by chemoattractants; sperms express olfactory receptors and eggs produce odorant-like molecules and chemotaxis occurs; however, other scientists do not believe in this theory.

Sperms can survive for many weeks in the male reproductive tract but only for 1-2 days in the female reproductive tract and this also applies on the ova.

Summary of hormones that affect spermatogenesis:

1- Testosterone: No spermatogenesis occurs without testosterone since it's necessary for the conversion of primary spermatocytes to secondary spermatocytes.

2- Luteinizing hormone: No testosterone is produced without LH.

3- Follicle stimulating hormone: acts on sertoli cells.

4- Estrogen: produced by sertoli cells and passes to leydig cells.

5- Growth hormone and almost all the other hormones especially thyroid hormones are essential for spermatogenesis. (Doctor says that infertility occurs in thyroid cancer.)

- Spermatogenesis is also affected by diet, radiation, diseases specially those that raise body temperature like mumps or typhus.

Descent of testes:

In the last three months of pregnancy, testosterone and insulin-like hormones from leydig cells promote the descend of testes from the abdominal cavity into the scrotum. If these hormones are deficient , testes could remain in the abdominal cavity and this condition is called cryptorchidism. This condition occurs in about 1%-3% of full term and 30% of premature infant boys.

Factors essential for sperms viability:

1- Testes in scrotum keep temperature of sperm 2°C below normal body temperature. Necessary for fertility.

2- Pampiniform plexus: it serves as counter current heat exchanger between warm arterial blood reaching the testes and cool venous blood leaving the testes.

3- Cremastric muscle: it responds to temperature changes by moving the testes closer or further away from the body.

Look at figure 44-5: (plasma testosterone profile during the life span of a normal male)

- Testosterone never reaches zero level at any stage in the normal life of a male from foetal life until death. It is high in foetal life for the development of male genital organs and descent of testes. Then it becomes low during childhood. (During childhood there is no difference between females and males in every aspect; testosterone levels, muscles, adipose tissue, etc). It rises during adulthood and starts a steady decrease after the ages 60-70 and this is called climacteric (the reduction of testosterone level after a certain age usually between 70-80 years or earlier, similar to menopause in females).

  Age doesn't affect fertility in males; (Even a man at 90 can have children).

In the human foetus, the period between week 8 to week 18 is marked by active steroidogenesis which is obligatory for the differentiation of the male genital organs. Leydig cells are prominent and active reaching their maximal activity at about 14 weeks when they constitute more than 50% of testicular volume. Because the foetal hypothalamic pituitary axis is still underdeveloped, human chorionic gonadotropin (HCG) from placenta rather than LH from foetal pituitary controls the steroidogenesis. Also, small amounts of HCG are secreted in the testes and pituitary and other non-placental tissues. (Important)

Before puberty there is almost no difference between boys and girls because testosterone level is very low, they both have same mean body mass, skeletal mass and body fat. However, after puberty men have 150% of the average woman's lean and skeletal body mass, and women have 200% of the body fat of men. Men have twice number of muscle cells that women have and 1.5 times muscle mass.

Look at figure 36.11: conversion of testosterone to different products in extratesticular sites:

Testosterone is a prohormone that is found in the testes, pituitary and muscles. It is found in fat, hair, liver, skin and CNS as estradiol. It is found as dihydrotestosterone in prostate, penis, scrotum and bone and also as conjugates or 17-ketosteroids in the liver and kidney.

- Drugs that inhibit 5α-reductase are currently used to reduce prostatic hypertrophy because DHT induces hyperplasia of prostatic epithelial cells.
- The biologic activity of DHT is 30-50 times higher than that of testosterone.
- Several tissues beside the testes including adipose tissue, brain, muscle, skin and adrenal cortex produce testosterone and other androgens. These substances may be synthesised de novo or produced by peripheral conversion of precursors. So testosterone isn't only produced by Leydig cells.

Read figure 44-6 about the spectrum of androgen effects.

Remember the effect of testosterone on erythropoietin; it increases erythropoietin and induces erythrocytosis.

Notes:

- Conversion of testosterone to DHT is essential for life since it protects against osteoporosis in males.
- Castration of an adult causes regression of the reproductive tract; involution of accessory reproductive glands and secondary sex organs and characteristics will be affected as well.
- Unlike most species which mate only to produce offspring, human sexual activity and procreation are not tightly linked.
- Superimposed on the base of reproductive mechanisms dictated by hormones are numerous psychological and social factors.
- No correlation has been found between circulating testosterone levels and sexual drive, frequency of intercourse or sexual fantasies.
- Similarly there is no correlation between testosterone levels and impotence or homosexuality. Impotent and homosexual patients may have normal testosterone levels.
- Castration of an adult also results in a slow decline but not a complete elimination in sexual interest (psychological only) and activity. (the Dr read this then said he believes that sexual interest is not affected that much but sexual activity is eventually affected.)

Written by: Hiba Mihyar

Pardon me for any unintended mistakes.

May God guide you all to his best ☺