

Physiology Team 431

Reproductive Block



Lecture 2

*Physiology of androgens and control of male
sexual functions*

Done by : Hayfa Al-abdulkarim

Revised by : Mohammed Asiri

PHYSIOLOGY OF ANDROGENS AND CONTROL OF MALE SEXUAL FUNCTIONS

◆ Spermatogenesis:

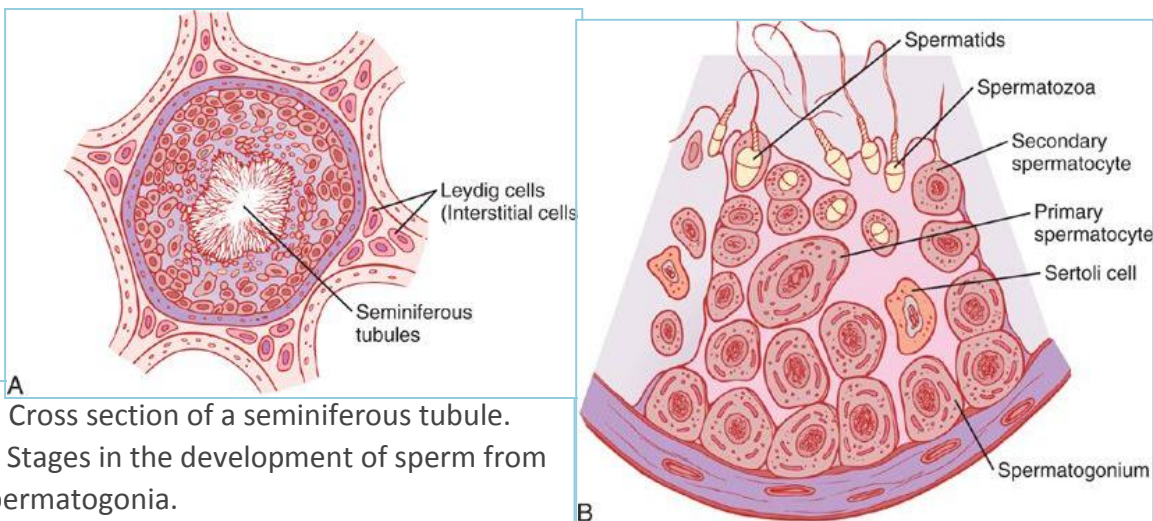
Formation of sperm & occur in the **seminiferous tubules** during active sexual life due to stimulation by AP-GnHs (**Anterior Pituitary-Gonadotropic Hormones**), begin at age of **13 years**, continue throughout life & decrease in old age.

◆ Sertoli cells:

Large with overflowing cytoplasmic envelopes that surround the developing spermatogonia around the central lumen of the seminiferous tubules.

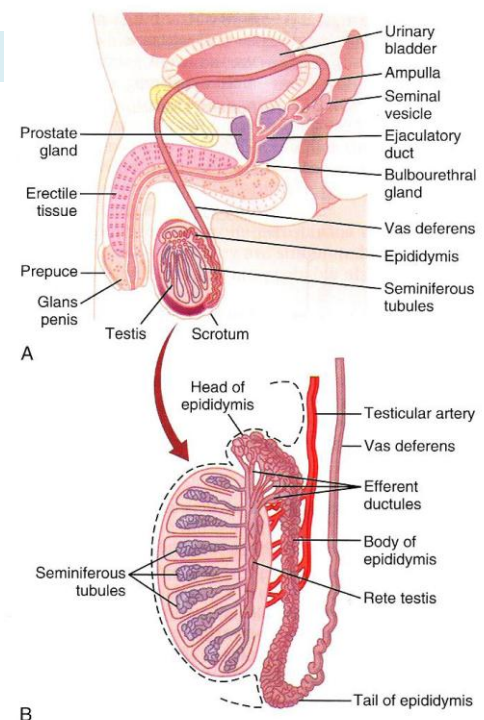
◆ Leydig cel:

Lie with **interstices** between the seminiferous tubules. They are **non-existent** in the testis during childhood when the testis secrete almost no testosterone,
-Numerous in the newborn male infants for **the first few months of life**.
-Active at **puberty & throughout adult life & secrete testosterone**.



Maturation of sperm in the epididymis

- **After** formation in the **seminiferous tubules**, the sperm require several days to pass through the **epididymis** (still non-motile).
- **After** the sperm have been in the epididymis for some **18 to 24 hour**, they develop the capability of motility (some inhibitory proteins in the epididymal fluid **prevent final motility until after ejaculation**).



◆ Storage of sperm:

The 2 testis of adult human formed up to 120 million sperm each day.

- **Small** amount stored in the epididymis.
- The **majority stored in the vas deferens**, maintaining their fertility for at least a month. The sperm are kept inactive state by **multiple inhibitory substances** in the secretion of the ducts.

◆ After ejaculation, the sperm **become motile** & capable of fertilizing the ovum, a process called **maturation**.

- The sertoli cells and epithelium of the epididymis secrete **nutrient fluid** “**ejaculated along with the sperm**” which contains (**testosterone & estrogens**), enzymes & **nutrients essential** for sperm maturation.

Guyton:

After formation in the seminiferous tubules, the sperm require several days to pass through the 6-meter-long tubule of the epididymis. Sperm removed from the seminiferous tubules and from the early portions of the epididymis are nonmotile, and they cannot fertilize an ovum. However, after the sperm have been in the epididymis for 18 to 24 hours, they develop the capability of motility, even though several inhibitory proteins in the epididymal fluid still prevent final motility until after ejaculation.

Physiology of mature sperm

◆ Mature sperm are:

- **motile** & **capable of fertilizing the ovum**
- Their activity is enhanced in a **neutral** & slightly **alkaline** medium & depressed in **mildly acidic medium**. So, **A strong acidic medium can cause rapid death of sperm**.
- The life expectancy of ejaculated sperm in the female genital tract is only 1 to 2 days.

Function of the Seminal Vesicles:

- Secrete mucoid material containing **fructose, citric acid & nutrient substances** & large quantities of **prostaglandins & fibrinogen**.
 - The prostaglandins are important help in fertilization:
 - 1- By reacting with the female cervical mucus making it more receptive to sperm movement.
 - 2- By causing **backward reverse peristaltic contractions** of the uterus & fallopian tubes **to move** the ejaculated sperm toward the ovaries.

Function of the Prostate Gland:

The prostate gland secretes **thin milky fluid** contains Ca^{2+} ion, citrate ion, phosphate ion, a clotting enzyme & profibrinolysin. The alkaline prostatic fluid is important for successful fertilization of the ovum.

• Alkaline prostate fluid function:

- 1- Successful fertilization of the ovum
- 2- Help to **neutralize the slightly acidic fluid of the vas deferens** (due to the presence of citric acid and metabolic & product of the sperm inhibit sperm fertility).
- 3- Helps to neutralize the acidity of other seminal fluids during ejaculation & enhances motility & fertility of sperm

Semen:

- Ejaculated semen during sexual act is composed of the **fluid & sperm** from the vas deferens (~10%)+fluid from the prostate gland (~30%), +fluid from the seminal vesicles (~60%) + small amounts from the mucous glands the bulbourethral glands.
- The average pH is **about 7.5**, the alkaline prostatic fluid help to neutralize the mild acidity of other portions of the semen & gives the semen a **milky appearance**
- Fluid from the seminal vesicles & mucous glands give the semen **mucoïd consistency**.

◆ Effect of sperm count on fertility:

The quantity of ejaculated semen during coitus about 3-5 ml, each milliter contains about 120 million sperm (normal male count vary between 35 million to 200 million sperm).

Sperm count below 20 million leads to infertility.

◆ Effect of sperm morphology and motility on fertility:

- Sometimes sperm count is normal but still infertile when about one half of the sperm having **abnormal shape**.
- Sometimes the shape of the sperm is normal but they either relatively **non-motile** or entirely **non-motile**, which causes infertility.

Capacitation of the spermatozoa

◆ Making it possible for them to penetrate the ovum:

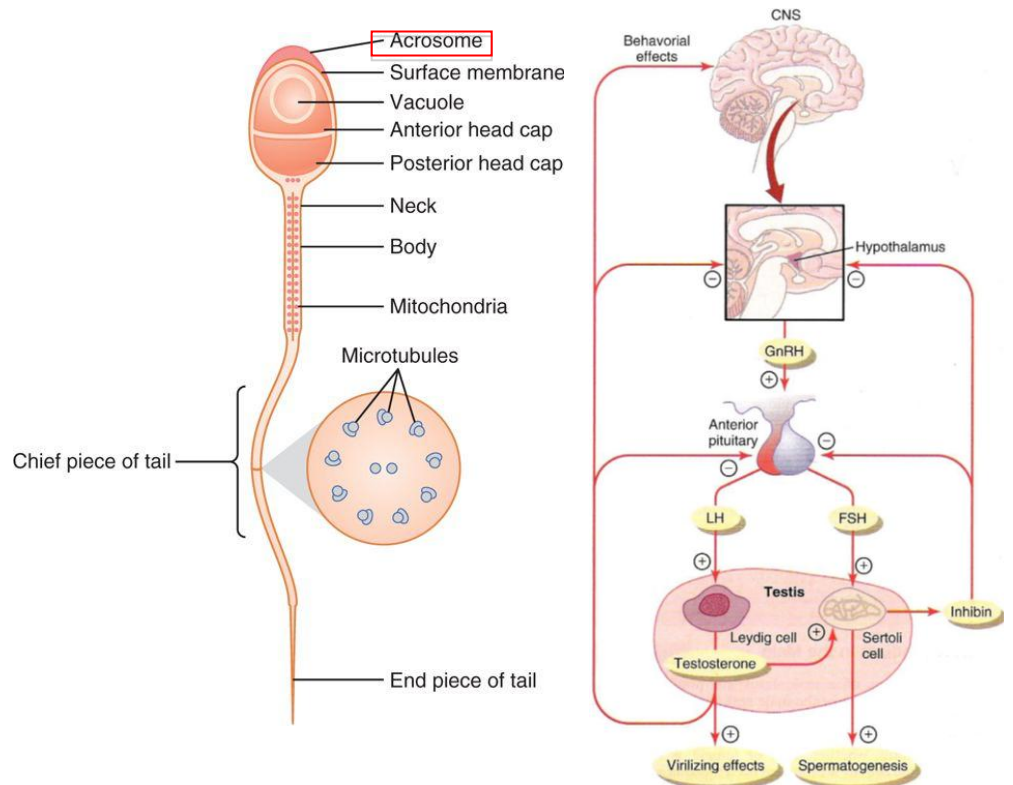
- Sperm in the epididymis is kept **inactive** by multiple inhibitory factors secreted by the genital duct epithelia & they activated in female genital tract, for the processes of fertilization. These activation changes are called **capacitation** of the spermatozoa (require 1 to 10 hrs).
- **Uterine & fallopian fluids wash away the inhibitory factors**, which suppress the sperm activity in the male genital ducts.
- While the spermatozoa remain in the fluid of the **male** genital ducts, they exposed to many floating vesicles from the seminiferous tubules containing **large amount of cholesterol**. This cholesterol is added to the **cellular membrane covering the acrosome** making it **more rough & prevent the release of its enzyme**.
- **After ejaculation** the sperm removed from the cholesterol vesicles & this makes the membrane of the sperm & head becomes **weaker**.

- The sperm membrane becomes more permeable to Ca^{2+} ion, which increase their movements & help to release the proteolytic enzymes from acrosome, which aid in penetrating the ovum.

◆ **Acrosome enzymes, the “Acrosome Reaction” and penetration of the ovum:**

The acrosome of the sperm stored large quantities of hyaluronidase and proteolytic enzymes.

- **Hyaluronidase**
depolarizes hyaluronic acid polymers in the intracellular cement that hold the ovarian granulosa cells together.
- **Proteolytic** enzymes digest the proteins in the structural elements of tissue cells that still adhere to the ovum.



Hormonal Factors That Stimulate Spermatogenesis:

Hormon	Secreted By	Function
Testosterone	Leydig cells which located in the interstitium of the testis	Essential for the growth and division of the testicular germinal cells
Luteinizing Hormone (LH)	Anterior pituitary gland	Stimulates the leydig cells to secrete testosterone.
Follicle Stimulating Hormone (FSH)	Anterior pituitary gland	Stimulates the sertoli cells, stimulate the conversion of spermatids to sperm (also important for spermatogenesis).
Estrogen	Formed from testosterone by the sertoli cell under FSH stimulation	Essential for spermatogenesis.
Growth Hormone & Other Body Hormones	-	Necessary for controlling metabolic functions of the testis. - GH promotes early division of spermatogonias, in its absence (pituitary dwarfs) , the spermatogenesis is severely deficient or absent → infertility.

Male sexual act - Stages of male sexual act:

- 1- Penile erection:** Erection is caused by **parasympathetic** impulses that pass from the sacral portion of the spinal cord through the pelvic nerves to the penis.
- 2- Lubrication:** **Parasympathetic** impulses cause the **urethral glands & bulbourethral** glands to secrete mucous.
- 3- Emission and ejaculation:** Function of the **sympathetic** nerves. Emission begins by **contraction of the vas deferens & ampulla to cause expulsion of the sperm in the internal urethra. Contraction of the prostate & seminal vesicles to expel their fluid in the urethra.** All these fluid mix in the internal urethra with the mucous secreted by the bulbourethral glands to form the semen. This process at this point is called **emission**.
 - **Filling of the internal urethra** with semen causes sensory impulses through **Pudendal nerves** to the sacral region of the cord. Fullness of the internal urethra **causes rhythmical contractions of the internal genital organs**, which increases their pressure to ejaculate the semen to the outside, a process called **ejaculation**.

Testosterone and other male sex chromosomes

Secretion of testosterone by the interstitial cell of Leydig in the testis. The testis secrete several male sex hormone called androgens including testosterone, dihydrotestosterone and androstenedione. Testosterone is the more **abundant** form while dihydrotestosterone is **more active** and testosterone converted into dihydrotestosterone in the target cells.

◆ Secretion & chemistry of androgens elsewhere in the body:

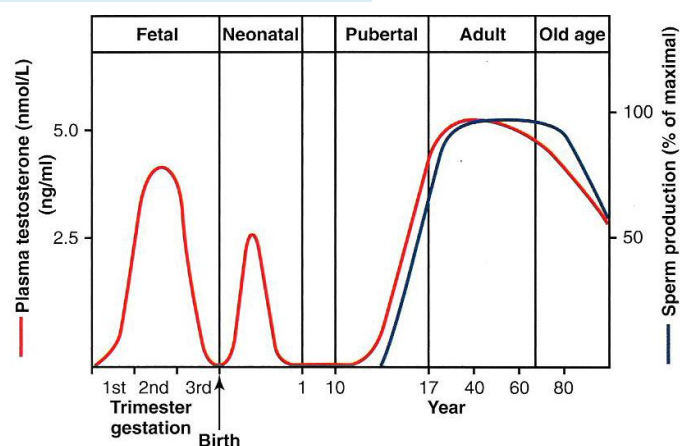
- From the **adrenal glands** & synthesized either from cholesterol or directly from acetylcoenzyme A.

◆ Metabolism of testosterone:

Testosterones bound with beta globulin and circulate in the blood for 30 minutes to several hours and converted to estrogen in the liver and excreted either into the gut through liver bile or into the urine through the kidneys.

Functions of testosterone:

It is responsible for the characteristic masculine body. During fetal life the testis are stimulated by placenta chorionic gonadotropin to produce testosterone throughout fetal life & the 10 weeks after birth then no more testosterone production during childhood & at puberty under the anterior pituitary gonadotropic hormones stimulation throughout life & then decline beyond 80 years to 50%.



Function of testosterone during fetal development:

Testosterone secreted by the **genital widges** & later by the fetal testis is responsible for development of the male body characteristics including the formation of penis & scrotum. & prostate gland, seminal vesicles & male genital ducts & suppressing the formation of female genital organs.

Effect of testosterone to cause descent of the testis:

The testes descend into the scrotum during the last 2 to 3 months of gestation when the testis begin secreting reasonable quantities of testosterone.

Effect of testosterone on development of adult primary and secondary sexual characteristics:

1- After puberty:

The increasing amounts of testosterone cause enlargement of the penis, scrotum & testis & secondary sexual characteristics.

2- Effect on the distribution of body hair:

Testosterone causes growth of hair: 1) over the pubis, 2) upward along the line alba of the abdomen to the umbilicus; 3) on the face; 4) on the chest; 5) less often on other regions such as the back.

3- Baldness:

Testosterone decreases the growth of hair on the top of the head (two factors 1) genetic background; 2) large quantities of androgenic hormones.

4- Effect on voice:

It causes hypertrophy of the laryngeal mucosa, enlargement of the larynx (typical adult masculine voice)

5- Testosterone increases thickness of the skin & can contribute to development of acne:

Testosterone increases the thickness of skin over the body & subcutaneous tissues. Also it increases the secretion of the sebaceous glands & sebaceous glands of the face causing **acne**.

6- Testosterone increased protein formation and muscle development:

Increase muscular development after puberty by 50% in muscle mass over that in female. Also increase in protein in non-muscle parts of the body. These effect due to the anabolic effect of testosterone.

7- Testosterone increases bone matrix and causes Ca²⁺ retention:

Bones grown thicker & deposit additional Ca²⁺. Thus it increases the total quantity of bone matrix & causes Ca²⁺ retention (anabolic effect). Testosterone has specific effect on the pelvis 1) narrow the pelvic outlet; 2) lengthen it; 3) cause the funnel-like shape instead of the broad ovoid shape of the female pelvis. It causes the epiphyses of the long bones to unite with the shafts of the bones & early closure of the epiphyses.

8- Testosterone increases basal metabolism:

It increases the basal metabolic rate by about 15% (indirectly as a result of the anabolic effect).

9- Effect on red blood cells:

It increases red blood cells/ml (due to ↑ metabolic rate).

10- Effect on electrolyte and water balance:

It increase the reabsorption of Na⁺ in the distal tubules of the kidneys.

◆ **The basic intracellular mechanism of action of testosterone:**

It increases the rate of protein synthesis “anabolic” in target cells. Testosterone converted by the intracellular enzyme 5 α reductase to dihydrotestosterone, then it binds with cytoplasmic “receptor protein”. This combination moves to the nucleus where it binds a nuclear protein and induces protein formation.

Abnormalities of male sexual function:

◆ **Prostate gland and its abnormalities:**

- **Benign prostatic fibro adenoma(also called hyperplasia)** in older age due to overgrowth of prostate tissue (not caused by testosterone).
- **Cancer of the prostate gland** caused by **stimulation of cancerous cells by testosterone**.

◆ **Hypogonadism in male:**

- During fetal life when the testes are non-functional, none of the male sexual characteristics develop in the fetus. **Instead female organs are formed**.
- If the boy loses his testis before puberty, a state eunuchism (he has infantile sex organs & infantile sexual characteristics) & the height of an adult eunuch is slightly greater than normal because of slow union of the epiphyses.
- If a man is castrated after puberty, sexual organ regress in size and voice regress, loss of the thick masculine bones, loss of masculine hair production, loss of musculature of the virile male.
- **Adiposogenital syndrome (also called: Frohlich’s syndrome or hypothalamic eunuchism):** hypogonadism due to genetic inability of the hypothalamus to secrete normal amount of GnRH & abnormality of the feeding center of the hypothalamus result in obesity with eunuchism.

◆ **Cryptorchidism**

Failure of the testes to descend in the scrotum, which normally occurs during fetal life.

- 10% of newborn males and it falls to 2% at age 1 year
- 0.3% after puberty
- They should be treated before puberty because of higher incidence of malignant tumors.

◆ **Testicular tumors and hypergonadism in male:**

- Interstitial leydig cell tumors (rare): over production of testosterone. In children, causes rapid growth of the musculature and bones and early uniting of the epiphyses and causes excessive development of male sexual organs.
- Tumor of the germinal epithelium (more common).

Summary

- Spermatogenesis is formation of sperm which occur in the **seminiferous tubules**
- Leydig cell is active at puberty & throughout adult life & secrete testosterone.
- **Maturation** of sperm in the **epididymis**
- Small amount of sperm stored in the epididymis and the **majority stored in the vas deferens**
- **After ejaculation**, the sperm becomes motile & capable of fertilizing the ovum "maturation".
- **Seminal vesicles** secrete **mucoïd** material containing fructose, citric acid & nutrient substances & large quantities of prostaglandins & fibrinogen
- **The prostate** gland secretes thin **milky fluid** contains Ca^{2+} , citrate ion, phosphate ion, a clotting enzyme & profibrinolysin.
- The alkaline prostatic fluid is important for successful fertilization of the ovum.
- **Semen** is composed of the fluid & sperm from the vas deferens (~10%)+fluid from the prostate gland (~30%),+fluid from the **seminal vesicles** (~60%)
- Infertility occur due to low sperm count , abnormality of sperm shape or non-motile sperm
- **Capacitation** of the spermatozoa is Making it possible for them **to penetrate the ovum:**
- Testosterone, LH, FSH, Estrogen and Growth hormone stimulate **spermatogenesis**
- Male sexual act → 1-Penile erection 2-Lubrication 3-Emission and ejaculation
- **Testosterone actions**
 - ❖ After puberty → enlargement of the penis, scrotum & testis & **secondary sexual characteristics**
 - ❖ Effect on the distribution of body hair
 - ❖ Baldness
 - ❖ Effect on voice → typical adult masculine voice
 - ❖ Testosterone increases thickness of the skin and can contribute to development of acne
 - ❖ Testosterone increased protein formation and muscle development
 - ❖ Testosterone increases bone matrix and causes Ca^{2+} retention
 - ❖ Testosterone increases basal metabolism
 - ❖ increases red blood cells
 - ❖ It increase the reabsorption of Na
- **Hypogonadism** in male → testis are **non-functional**
- **Adiposogenital syndrome** → **genetic inability** of the hypothalamus to secrete normal amount of **GnRH** & abnormality of the feeding center of the hypothalamus
- Cryptorchidism → Failure of the testes to descend in the scrotum
- Testicular tumors and hypergonadism in male → over production of testosterone

Question

- 1- The process in which sperm cells, secretions of the prostate and secretions of the seminal vesicles accumulate in the prostatic urethra is called
 - A. Erection
 - B. Ejaculation
 - C. Emission
 - D. Orgasm

- 2- Testosterone has negative feedback effect on
 - A. GnRH secretion
 - B. FSH secretion
 - C. LH secretion
 - D. All of the above

- 3- the following hormones are involved in the spermatogenesis except
 - A. Testosterone
 - B. Progesterone
 - C. Estrogen
 - D. Growth hormones

- 4- which one of the following is the function of the testosterone hormones ?
 - A. Growth of the external genital during childhood .
 - B. Decrease basal metabolic rate
 - C. Increase protein synthesis
 - D. Increase glucose synthesis

Answers:

- 1- C
- 2- D
- 3- B
- 4- C