بسم الله الرحمن الرحيم

Male Reproductive Physiology (Pt.2)

FINAL | Lecture 5

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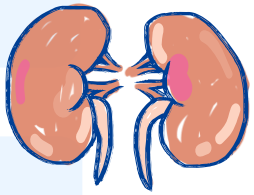
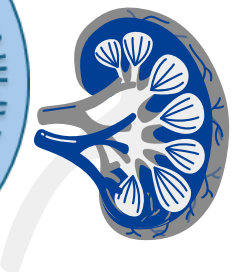


﴿ قُلْ بِفَضْلِ ٱللَّهِ وَبِرَحْمَتِهِۦ فَبِذَٰلِكَ فَلْيَفْرَحُوا۟ هُوَ خَيْرٌ مِّمَّا يَجْمَعُونَ ﴾



MALE REPRODUCTIVE PHYSIOLOGY PART II

GUYTON & HALL, CHAPTER 81

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OBJECTIVES

- Describe the synthesis, secretion, metabolism, signaling and the effects of testosterone
- Describe peaks of Testosterone during different stages and role of Testosterone in fetal life
- Puberty onset in male and GnRH influence
- Define *male climacteric*
- Touch base on some abnormalities of male reproductive function

TESTOSTERONE AND OTHER MALE SEX HORMONES

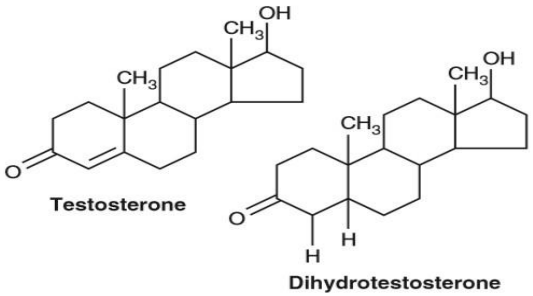


Figure 81-8. Testosterone and dihydrotestosterone.

- The testis secretes several male sex hormones called **androgens;** including testosterone, dihydrotestosterone and androstenedione.
- Testosterone is the most abundant form (primary testicular hormone) while dihydrotestosterone (DHT) is the most active form (most Test. is converted to DHT in target tissues such as the prostate gland, making it responsible for some Test. effects).
- The term "androgen" means any steroid hormone with masculinizing effects. Formed in the testes and adrenal glands. Synthesized either from cholesterol or directly from acetylcoenzyme A.

TESTOSTERONE AND OTHER MALE SEX HORMONES

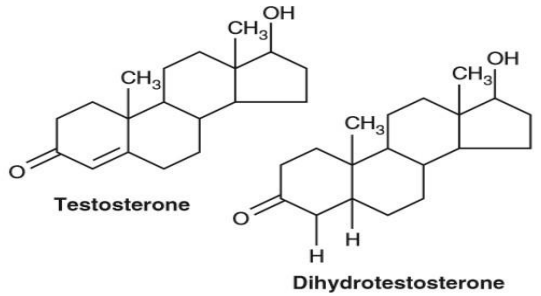


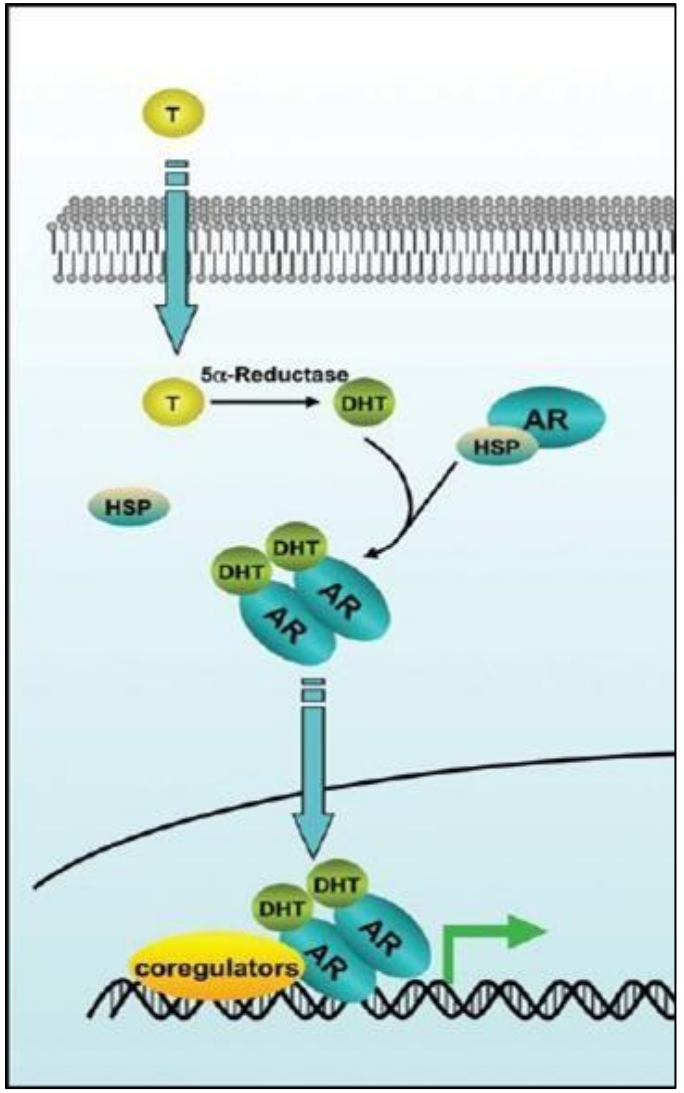
Figure 81-8. Testosterone and dihydrotestosterone.

- 97 percent of the testosterone becomes either loosely bound with plasma albumin or more tightly bound with a beta globulin called *sex hormone-binding globulin*.
- These globulins are synthesized by Sertoli cells under the influence of FSH and play an important role in maintaining adequate levels of testosterone.
- Testosterone is either transferred to the tissues or degraded into inactive products that are subsequently excreted.
- Metabolized by the liver, into *androsterone* and *dehydroepiandrosterone* and simultaneously conjugated as either glucuronides or sulfates (glucuronides, particularly).
- Excretion: both biliary (Gut) and Urinary excretion

THE INTRACELLULAR MECHANISM OF ACTION OF TESTOSTERONE

- Testosterone is a steroid which is lipid soluble which allows it to enter the prostatic cells as an example within a few minutes after secretion.
- Most often converted, by the intracellular enzyme 5α-reductase, to *dihydrotestosterone*, which binds with a cytoplasmic "receptor protein" (a cytosolic androgen receptor).
- Translocates to the cell nucleus, where it binds with a nuclear protein which is mostly a transcription factor that alters transcription and induces DNA-RNA transcription.
- Within 30 minutes, RNA polymerase has become activated, and the concentration of RNA begins to increase in the prostatic cells, which is followed by a progressive increase in cellular protein (translation).
- After several days, the quantity of DNA in the prostate gland has also increased, and a simultaneous increase in the number of prostatic cells has occurred.

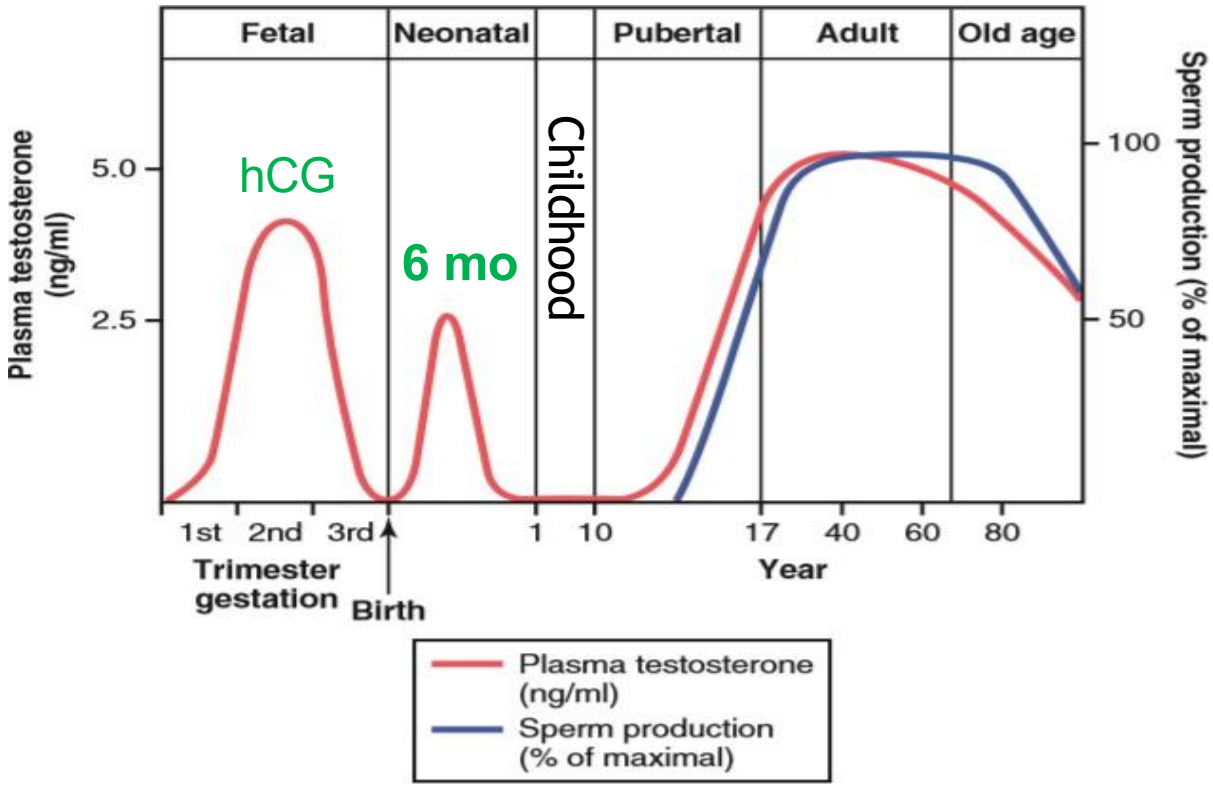
In summary, testosterone increases the rate of protein synthesis in target cells.



LEVELS & FUNCTIONS OF TESTOSTERONE

Testosterone levels during different stages of male life:

- Starting with fetal development, we can see that there's high peak of testosterone in the fetus during the middle trimester. This increase is mediated by hCG which functions as a luteinizing hormone in inducing testosterone production. It is important in this period for the development of male sex organs.
- In the neonatal life after birth there's another peak during the first 6 months of age, this increase is related to fine completion and tuning of maturation of the reproductive system of the male.
- We can see that in childhood there's no significant increase in levels until about the age of 13, where there is an increase in testosterone along with a triggered increase in spermatogenesis in early puberty and adulthood. However, in older age both might decline slightly.



HUMAN CHORIONIC GONADOTROPIN SECRETED BY THE PLACENTA DURING PREGNANCY STIMULATES TESTOSTERONE SECRETION BY THE FETAL TESTES

- During pregnancy the hormone *human chorionic gonadotropin* (hCG) is secreted by the placenta and circulates both in the mother and in the fetus.
- This hormone has almost the same effects on the sexual organs as LH.
- During pregnancy, if the fetus is a male, hCG from the placenta causes the testes of the fetus to secrete testosterone.
- It is critical for promoting formation of the male reproductive organs

FUNCTIONS OF TESTOSTERONE DURING FETAL DEVELOPMENT

- Testosterone begins to be elaborated by the male fetal testes at about the seventh week of embryonic life.
- One of the major functional differences between the female and the male sex chromosome is that the male chromosome has the *sex-determining region Y (SRY)* gene that encodes a protein called the *testis determining factor* (also called the *SRY protein*).
- The SRY protein initiates a cascade of gene activations that cause the genital ridge cells to differentiate into cells that secrete testosterone and eventually become the testes, whereas the female chromosome causes this ridge to differentiate into cells that secrete estrogens.
- Injection of large quantities of male sex hormone into pregnant animals causes development of male sexual organs, even though the fetus is female, which highlights its importance in the development of male sexual organs regardless of the genetic background.
- Also, early removal of the testes in the male fetus causes development of female sexual organs.

FUNCTIONS OF TESTOSTERONE DURING FETAL DEVELOPMENT (cont.)

- Testosterone secreted by the genital ridges in the first 7 weeks of gestation & later by the fetal testes in the last trimester is responsible for development of the male body characteristics including the formation of penis & scrotum & suppression of the formation of female genital organs.
- Its absence causes development of female organs rather than male organs.

Effect of testosterone on descending the testis:

The testes usually descend into the scrotum during the last 2 to 3 months of gestation when the testes begin secreting reasonable quantities of testosterone. Failure of this function might be treated by a non-surgical intervention through testosterone injection (do your own search).

EFFECT OF TESTOSTERONE ON SPERMATOGENESIS WITH FSH

- FSH binds with specific FSH receptors attached to the Sertoli cells in the seminiferous tubules, which causes the Sertoli cells to grow and secrete various spermatogenic substances.
- Simultaneously, testosterone (and dihydrotestosterone) diffusing into the seminiferous tubules from the Leydig cells into the interstitial spaces also has a strong tropic effect on spermatogenesis.
- Thus, both FSH and testosterone are necessary to initiate spermatogenesis.

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 over the pubis and on the face and abdomen.

3 **Baldness:**

Testosterone decreases the growth of hair on the top of the head; under the presence of 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 which initially causes voice cracking and then development of typical adult masculine voice.

5 **Testosterone increases thickness of the skin and can contribute to development of acne through increase in sebaceous gland secretions.**

6 **Testosterone increases protein formation and muscle development** It is responsible for the characteristic masculine body of a male. (Anabolic action of testosterone)

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

Bones grown thicker and stronger & deposit additional Ca2+.Thus, it increases the total quantity of bone matrix & causes Ca2+ retention (anabolic effect).

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 up to 15-20% (due to increased metabolic rate). Independent of erythropoietin levels.

10 **Effect on electrolyte and water balance:**

It slightly increases the reabsorption and retention of electrolytes and water, particularly of Na+ in the distal tubules of the kidneys, similar to but to a lesser extent than mineralocorticoids. ECFV of the male after puberty increase as much as 5-10%.

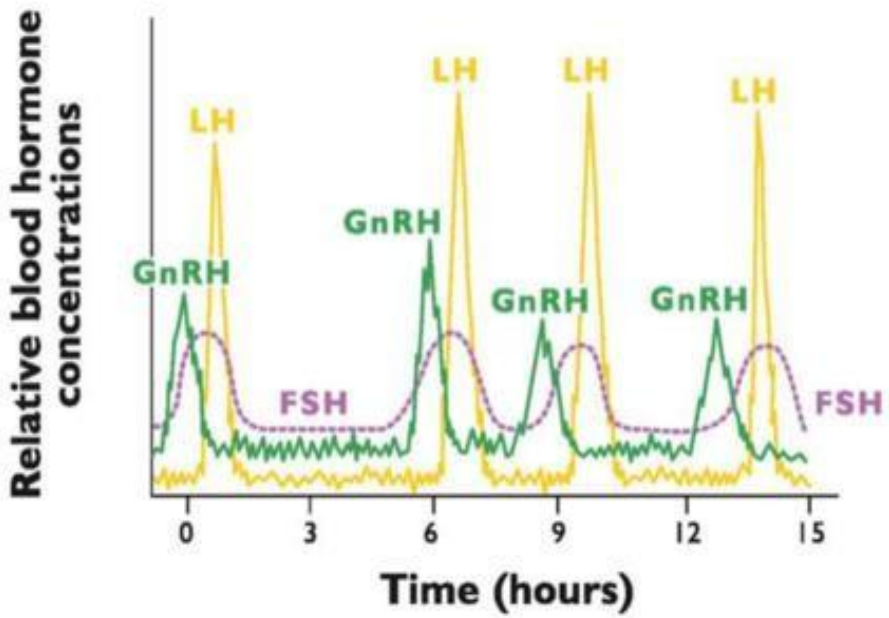
ECFV: Extracellular fluid volume

PUBERTY AND REGULATION OF ITS ONSET

- *During childhood no significant amounts of GnRH and testosterone released*.
- Probably, during childhood, the slightest secretion of any sex steroid hormones exerts a strong inhibitory effect on hypothalamic secretion of GnRH. (Very sensitive to negative feedback)
- At the time of puberty, the secretion of hypothalamic GnRH breaks through the inhibition and adult reproductive system function starts.

- In the absence of GnRH, almost no LH or FSH (no gonadotropins from anterior pituitary), so GnRH has a primary role in inducing their secretion.

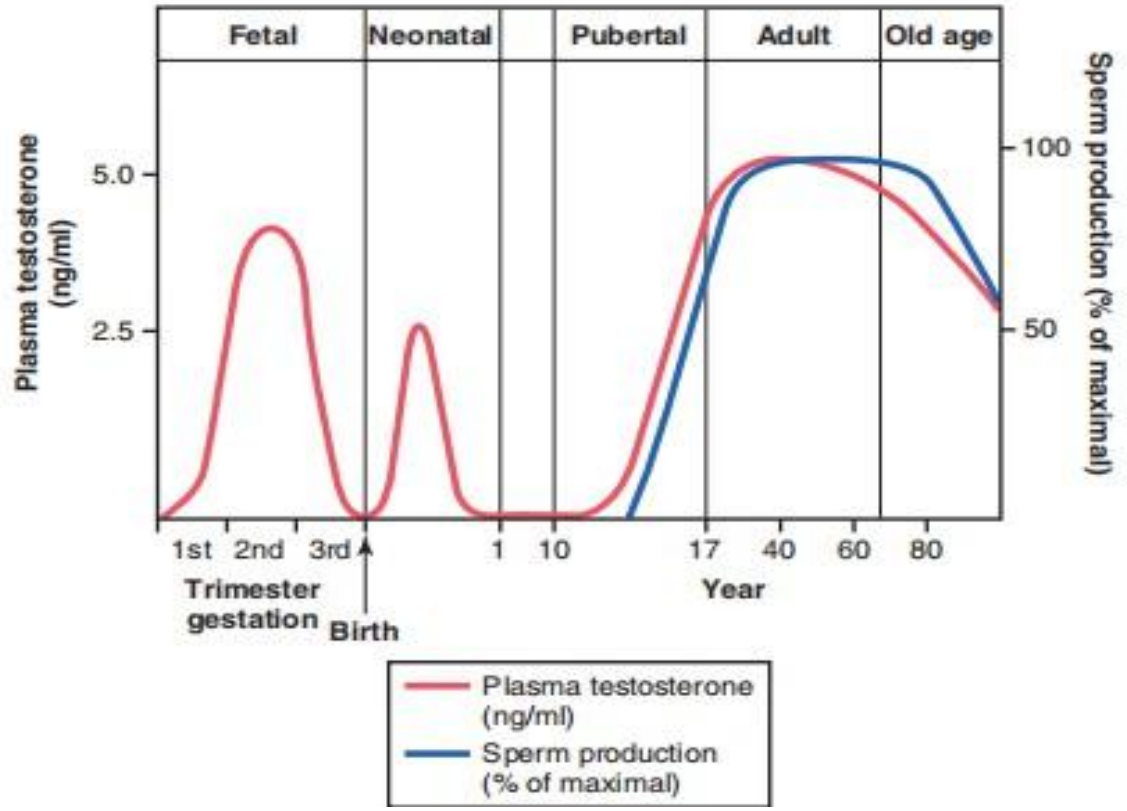
- GnRH is secreted intermittently in a pulsatile manner for a few minutes at a time once every 1 to 3 hours. The intensity of this hormone's stimulus is determined in two ways:
  (1) by the frequency of these cycles of secretion
  (2) by the quantity of GnRH released with each cycle.



- The secretion of LH by the anterior pituitary gland is also cyclical, with LH following fairly faithfully the pulsatile release of GnRH.
- Conversely, FSH secretion increases and decreases only slightly with each fluctuation of GnRH secretion, it changes more slowly over a period of many hours in response to longer-term changes in GnRH.
- GnRH is also widely known as *LH-releasing hormone* due to their very strong relationship of secretion patterns.

MALE CLIMACTERIC

- The decrease in male sexual function is called the *Male climacteric*.
- After puberty, gonadotropic hormones are produced by the male pituitary gland for the remainder of life, and at least some spermatogenesis usually continues until death.
- Most men, however, begin to exhibit slowly decreasing sexual functions in their late 50s or 60s.
- Variable decline, with some men continuing to be virile (fertile) until their 80s and 90s.
- The gradual decline in sexual function is related, in part, to a decrease in testosterone secretion.

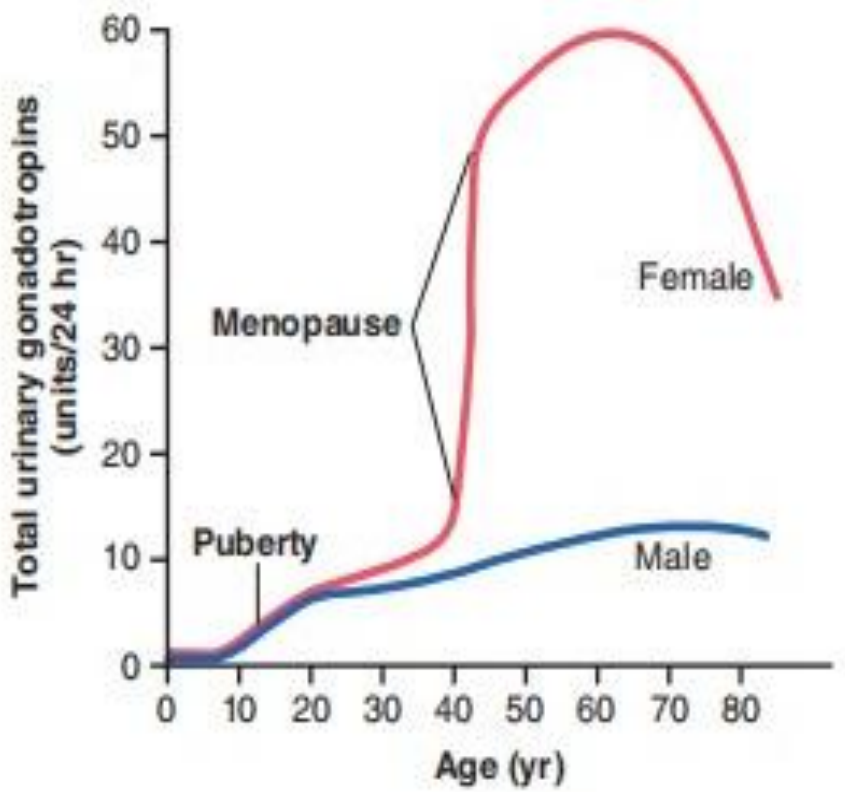


MALE VS FEMALE CLIMACTERIC

- This figure shows how levels of gonadotropins increase after menopause/climacteric in male vs female. This increase is related to an attempt to restore the reduced sex hormones. So, the sharper the decline in hormones, the higher levels of gonadotropins.

- In female menopause, the levels of hormones are reduced significantly, which is reflected by a great increase in secretion of gonadotropins.

- Conversely, in males, gonadotropins are only elevated mildly, reflecting a milder decrease in testosterone than the drop of hormones that occurs in females.



ABNORMALITIES OF SPERMATOGENESIS AND MALE SEXUAL FUNCTION (1)

Effect of sperm count on fertility:

- The quantity of ejaculated semen during coitus is about 3-5 ml
- 1ml >>>120 million sperm (normal sperm count 35 - 200 million sperm/ml).

Effect of sperm morphology and motility on fertility:

- Sperm count is normal but infertile? abnormal shape.
- Even if shape of the sperm is normal but relatively non-motile or entirely non-motile, this can cause infertility.

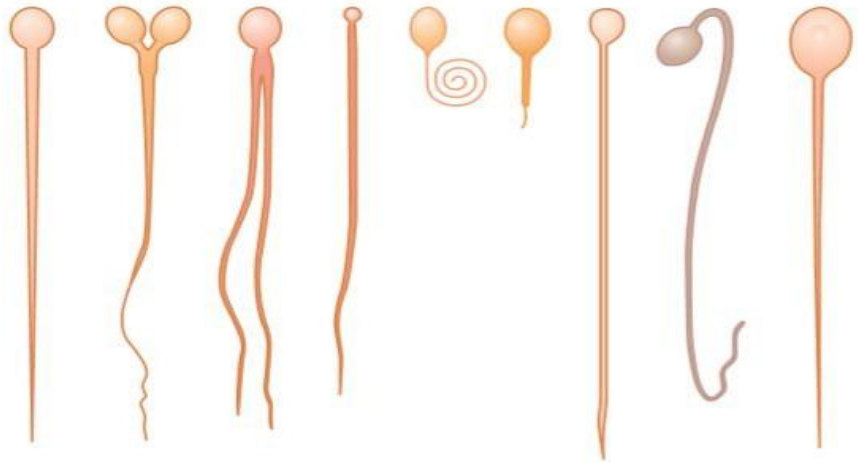


Figure 81-5. Abnormal infertile sperm, compared with a normal sperm on the right.

ABNORMALITIES OF SPERMATOGENESIS AND MALE SEXUAL FUNCTION (2)

Prostate gland and its abnormalities

- Benign prostatic fibroadenoma 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 can take place in different stages of male development:

- During fetal life when the testes are nonfunctional, **none of the male sexual characteristics develop in the fetus**. Instead, female organs are formed.
- If the boy loses his testes before puberty ⟶ eunuchism (infantile sex organs & infantile sexual characteristics) is developed
- If a man is castrated after puberty, sexual organ regress in size and voice regress but main male secondary characteristics will remain.

Adiposogenital syndrome, Fröhlich syndrome, or hypothalamic eunuchism:

- Hypogonadism due to genetic inability of the hypothalamus to secrete normal amount of GnRH & accompanied with abnormality of the feeding center of the hypothalamus resulting in obesity with eunuchism.

ABNORMALITIES OF SPERMATOGENESIS AND MALE SEXUAL FUNCTION (3)

Cryptorchidism:

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

Testicular tumors and hypergonadism in male:

Interstitial leydig cell tumors (very rare), **overproduction 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. However, in adults, it might be harder to recognize the effect of high testosterone secretion.

SELF STUDY

MALE SEXUAL ACT

STAGES OF MALE SEXUAL ACT

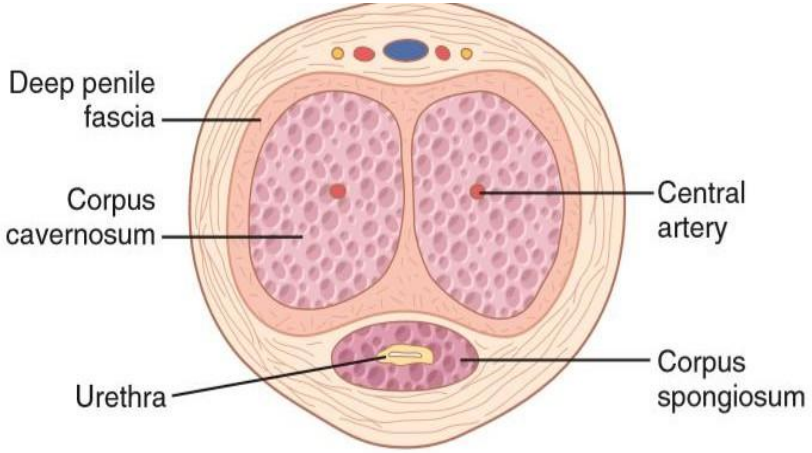


Figure 81-6. Erectile tissue of the penis.

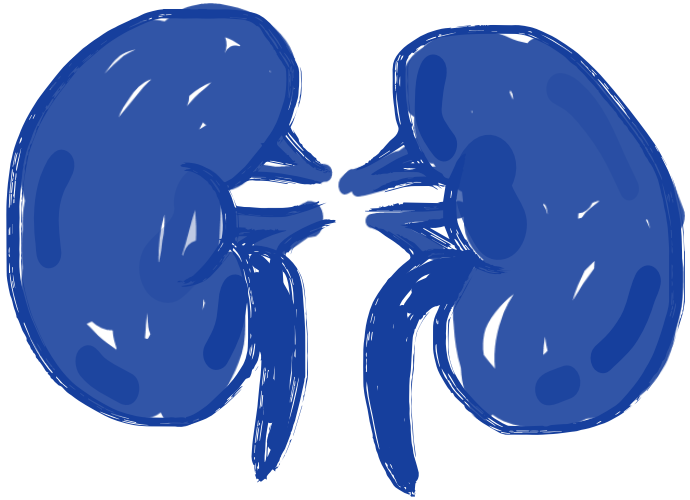
1 **Penile erection.** by parasympathetic impulses.

2 **Lubrication**, Parasympathetic impulses cause the urethral glands & bulbourethral glands to secrete mucous.

3 **Emission and ejaculation.** Function of the sympathetic nerves. 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 called **ejaculation**

- The male sexual act results from inherent reflex mechanisms integrated in the sacral and lumbar spinal cord, and these mechanisms can be initiated by either psychic stimulation from the brain or actual stimulation from the sex organs, but usually it is a combination of both. Can be intact even after spinal cut above lumbar.



PHYSIOLOGY QUIZ LECTURE 5

رسالة من الفريق العلمي

اللهم إن عمر عطية في ذمتك وحبل جوارك، فقِه من فتنة القبر وعذاب النار،
أنت أهل الوفاء والحق، فاغفر له وارحمه إنك أنت الغفور الرحيم.

بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

قُلْ يَا عِبَادِيَ الَّذِينَ أَسْرَفُوا عَلَىٰ
أَنفُسِهِمْ لَا تَقْنَطُوا مِن رَّحْمَةِ اللَّهِ ۚ
إِنَّ اللَّهَ يَغْفِرُ الذُّنُوبَ جَمِيعًا ۚ إِنَّهُ
هُوَ الْغَفُورُ الرَّحِيمُ

الزمر : ٥٣

Scan the QR code or click it for FEEDBACK

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	4 (the original slides contained the mistake)	Most Test. is converted to DHEA	Most Test. is converted to DHT
V1 → V2			