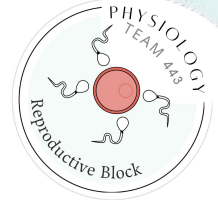







L5-Physiology of Androgens & Control of Male sexual Function

Reproductive physiology



Objectives



-  Understand the functions of the male reproductive organs and glands.
-  Describe the synthesis, secretion, metabolism and effects of testosterone.
-  Explain how the hypothalamus and anterior pituitary gland regulate male reproductive function.
-  Describe the major testicular abnormalities.
-  Discuss the normal mechanism of the male sexual act.



[Click here](#) for the team channel!



This Lecture was presented by:
PROF. MOHAMMED ALOTAIBI & Dr. Laila Al Dokhi.



[Editing File](#)

﴿ فَلْيَنْظُرِ الْإِنْسَانُ مِمَّ خُلِقَ (5) خُلِقَ مِنْ مَّاءٍ دَافِقٍ (6) يَخْرُجُ مِنْ بَيْنِ
الصُّلْبِ وَالتَّرَائِبِ (7) ﴾ سورة الطارق

Male Reproductive Anatomy



- Testes
- Epididymis
- Bulbourethral
- Seminal vesicle
- Vas deferens
- Prostate
- Urethra & Penis
- Ejaculatory duct

Testes

The testes reside outside the abdominal cavity in the scrotum.

- This location maintains testicular temperature at about **2°C lower** than body temperature.
- Each testis is composed of 300 lobules
- The seminiferous tubule is lined by a complex seminiferous epithelium

contains **two cell types**:

1. sperm cells in various stages of spermatogenesis
2. the Sertoli cell, which is a "nurse cell" in intimate contact with *all* sperm cells

الخلية "الحاضنة" تغذي الخلايا المنوية أثناء تطورها لتصبح حيوانات منوية لذلك هي لها علاقة بكل الخلايا المنوية.

Check pic 5,6

Sertoli and Leydig cells

Sertoli cell

الخلية الحاضنة
خلية داعمة

Dr. focused on functions.

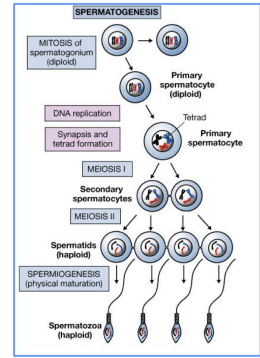
- Large with overflowing cytoplasmic envelopes.
- Surround the developing spermatogonia around the central lumen of the seminiferous tubules. Substance produced causes nourishment of the sperm
- **Form blood-testis barrier:**
 - 1- Prevents autoimmune destruction of sperm.
 - 2- Produce FAS ligand which binds to the FAS receptor on surface to T lymphocytes, triggering apoptosis of T lymphocytes.
 - 3- Prevents immune attack.
- **Secrete inhibin** (it will decrease FSH)
- **Phagocytize residual bodies:** (cytoplasm of sperms)
 - May transmit information molecules from germ cells to Sertoli cells.
- **Secrete androgen-binding protein (ABP):**
 - Binds to testosterone and concentrates testosterone in the tubules.

Leydig cell

تفرز التستوستيرون!
Interstitial cells is another name for Leydig cells

- Lie within the interstices between the seminiferous tubules.
- They are almost non-existent in the testis during childhood when the testes 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.**
- Interesting fact: These cells are also found in a woman's ovaries, and in very rare cases lead to cancer.

Spermatogenesis



Also Check pic 7

- ◆ Spermatogenesis: formation of sperm.
- ◆ Occurs in: the **seminiferous tubules** during active sexual life due to stimulation of AP-GnHs.
- ◆ Begin at the age of 13 years.
- ◆ Continue through life & decrease in old age.
- ◆ Seminiferous tubules **contain**:
 - Spermatogonia**: Stem cells involved in spermatogenesis.
 - Sertoli** (Sustentacular) cells: Sustain and promote development of sperm
 - ◆ **Spermiogenesis**: the final step of Spermatogenesis.
 - Maturation of spermatozoa.
 - Phagocytosis of cytoplasm by the Sertoli cells [Check pic 8](#)

Hormonal factors that stimulate Spermatogenesis

2-Luteinizing hormone (LH)

Secreted by the anterior pituitary gland, stimulates the **Leydig** cells to secrete testosterone.

4-Estrogen

Formed from testosterone by the sertoli cells under FSH stimulation, also essential for spermatogenesis. (Sperm has receptors for estrogen, mutation in estrogen receptors reduces fertility)

6-Inhibin feedback

FSH, testosterone – short & long loops

1-Testosterone

Secreted by the leydig cells which are located in the interstitium of the testis, is essential for the growth and division of the testicular germinal cells.

3-Follicle stimulating hormone (FSH)

Secreted by the anterior pituitary gland, stimulates the **Sertoli** cells, stimulate the conversion of spermatids to sperm (also important for spermatogenesis).

5-Growth hormone (GH) (also other body hormones)

is necessary for controlling metabolic functions of the testis. GH promotes early division of Spermatogonia; in its absence (as in pituitary dwarfs), the spermatogenesis is severely deficient or absent → infertility

Spermatogenesis

Maturation of Sperm in the Epididymis	<ul style="list-style-type: none"> After formation in the seminiferous tubules, the sperm require several days to pass through the epididymis (still non-motile). Sperm in the early portion of epididymis are non-motile. After the sperm have been in the epididymis for 18 to 24 hours, they develop the <u>capability of motility</u>, BUT some inhibitory proteins and cholesterol in the epididymal fluid prevent final motility until after ejaculation. (When they are in the epididymis they are capable of motility, but their motility is being inhibited) After ejaculation they become motile. Physiology of mature sperm: <ul style="list-style-type: none"> Mature sperm are <u>motile</u> & capable of fertilizing the ovum. Their activity is greatly enhanced in a neutral and slightly <u>alkaline</u> medium, but it is greatly depressed in a mildly acidic medium. The life expectancy of ejaculated sperm in the female genital tract is only <u>1 to 2 days</u>.
Storage of Sperm	<ul style="list-style-type: none"> The two testes of the adult human form up to 120 million sperm each day. Most of sperms stored in the epididymis, although a small quantity is stored in the vas deferens, maintaining their fertility, for at least a month. The sperms are kept inactive state by multiple inhibitory substances in the secretion of the ducts.
After Ejaculation	<ul style="list-style-type: none"> The sperm become motile and capable of fertilizing the ovum, a process called "<u>maturation</u>". The sertoli cells and the epithelium of the epididymis secrete nutrient fluid (that is ejaculated along with the sperm) which <u>contains</u>: hormones (<u>testosterone & estrogens</u>), <u>enzymes</u>, and special <u>nutrients</u> essential for sperm maturation.

Function of:	Seminal Vesicle	<ul style="list-style-type: none"> Secretes a mucoid material containing <u>fructose</u>, <u>citric acid</u>, and other nutrient substances & large quantities of prostaglandins & fibrinogen. The prostaglandins are important help in fertilization by: <ol style="list-style-type: none"> Reacting with the female cervical mucus making it more receptive to sperm movement. Causing backward reverse peristaltic contractions of the uterus & fallopian tubes to move the ejaculated sperm toward the ovaries. Helps to dissolve the mucus in the female tract
	Prostate Gland	<ul style="list-style-type: none"> The prostate gland secretes a <u>slightly alkaline</u> thin milky fluid that contains Ca^{2+} ion, citrate ion, phosphate ion, a clotting <u>proteins</u> /enzymes, and a <u>profibrinolysin</u>. The alkaline prostatic fluid (help in neutralizing other seminal fluids as well as the vaginal fluid) is important for successful fertilization of the ovum.
	Alkaline Prostatic fluid	<ol style="list-style-type: none"> Important for Successful fertilization of the ovum. Help to neutralize the slightly acidic fluid of the vas deferens (due to the presence of citric acid and metabolic products of the sperm that inhibit sperm fertility). Helps to neutralize the acidity of other seminal fluid during ejaculation and enhances the motility & fertility of the sperm.



IMPORTANT

Semen

- Milky white, sticky **mixture of sperm and accessory gland secretions**,  (65% of semen is from seminal vesicle, 25% prostate)

*Fluid from the seminal vesicles (~60%).
لحم وبنه شوفوا الناتج

*Fluid from the prostate gland (~30%).

*Fluid from the vas deferens (~10%+).

*Small amounts from the mucous glands, especially the bulbourethral glands.

- Ejaculated semen during sexual act is composed of the fluid & sperm.
- Provides a transport medium and nutrients (fructose), protects and activates sperm, and facilitates their movement.
- 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 and mucous glands give the semen a mucoid consistency.
- Prostaglandins in semen:
 - Decrease the viscosity of mucus in the cervix
 - Stimulate reverse peristalsis in the uterus
 - Facilitate the movement of sperm through the female reproductive tract
- Clotting factors coagulate semen immediately after ejaculation, then fibrinolysin liquefies the sticky mass during the next 15-30 minutes.
- After ejaculation, sperms can live 24-48 h.

Fertility

Factors Affecting Fertility

Sperm Count

- The quantity of ejaculated semen during each coitus is about 3.5 ml (2-5 ml only) but it contains 35-200 million sperm/ml (<20 million infertile)
- Normal male count vary between 35 million to 200 million sperm. (Each milliliter contains about 120 million sperm).
- Sperm count below 20 million leads to infertility.

Sperm Morphology & Motility

usually the sperms that reach uterus are normal.
When the majority of the sperm are morphologically abnormal or nonmotile then person is likely to be infertile. [Check pic 8](#)

Abnormal Shape

Sometimes sperm count is normal but still infertile when about one half (50%) of the sperm have abnormal shape.

Abnormal Motility

Sometimes the shape of the sperm is normal but they're either relatively non-motile or entirely non-motile which causes infertility.

Capacitation of spermatozoa

Capacitation; Making it possible for spermatozoa to penetrate the ovum:

- ▶ Sperm in the epididymis is kept inactive by multiple inhibitory factors secreted by the genital duct epithelia.
- ▶ And They will be activated in the **female genital tract**, for the processes of fertilization. These activation changes are called **capacitation** of the spermatozoa (it requires from 1 to 10 hrs).

1

Uterine and fallopian tube fluids wash away the inhibitory factors which suppress the sperm activity in the male genital ducts.

2

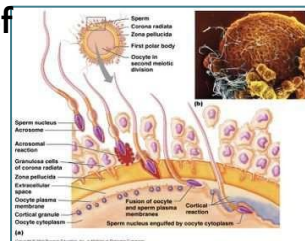
Cellular membrane covering the acrosome is covered with cholesterol which prevent the release of its enzymes. After ejaculation, the sperm is removed -swims away- from the cholesterol vesicles & this makes the membrane of the sperm head (the acrosome) becomes weaker.

3

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

Acrosome enzymes, the "Acrosome Reaction" & Penetration of the ovum:

- The **acrosome** of the sperm store large quantities of **hyaluronidase and proteolytic enzymes**.
- Hyaluronidase depolymerizes hyaluronic acid polymers in the intercellular cement that hold the ovarian granulosa cells together.
- Also the proteolytic enzymes digest the proteins.



Female slides

Male slides

Dr.explained it orally without slide and he mentioned the name of the enzyme.

Stages of Male Sexual Act

I- Penile erection

Erection → Parasympathetic

► Enlargement and stiffening of the penis from engorgement of erectile tissue with blood.

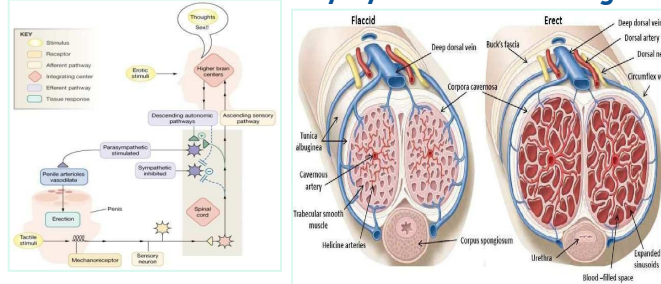
► Erection is caused by parasympathetic impulses that pass from the sacral portion of the spinal cord through the pelvic nerves to the penis.

► Erection is initiated by sexual stimuli including:

-Touch and mechanical stimulation of the glans penis and other parts.

Erotic sights, sounds, and smells.

Erection can be induced or inhibited solely by emotional or higher mental activity



Mechanism:

► During sexual arousal, a parasympathetic reflex promotes the release of nitric oxide, VIP, and Acetylcholine. Nitric oxide relaxes the penis arteries and causes erectile tissue to fill with blood

► Expansion of the corpora cavernosa:

-Compresses their drainage vein

-Retards blood outflow and maintains engorgement

2-Lubrication

Parasympathetic impulses cause the urethral glands & the bulbourethral glands to secrete mucous.

3-Emission and ejaculation

Ejaculation → Sympathetic

Emission

► When the sexual stimulus becomes extremely intense, spinal cord begins to send sympathetic impulses to initiate **emission**.

► Function of the sympathetic nerves.

► Emission begins with contraction of the vas deferens and the ampulla to cause expulsion of the sperm into the internal urethra.

► Contraction of the prostate & seminal vesicles to expel their fluid into the urethra .

► All these fluids mix in the internal urethra with the mucus already secreted by the bulbourethral glands to form the semen.

This process at this point is called emission.

ejaculation

► Filling of the internal urethra with semen **elicits** / **causes** sensory **signals** / **impulses**, through pudendal nerves to the sacral region of the cord, **that promotes ejaculation**.

► Fullness of the internal urethra causes rhythmical contractions of the internal genital organs which increases their pressure to ejaculate the semen to the outside. This process is called ejaculation.

4. Resolution

After orgasm, the excitement disappears within 1-2 minutes (resolution)

Testosterone

Male slides

Secretion & Chemistry of androgens in the body:

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

Secretion & Chemistry of androgens in the body:

- From the testes and adrenal glands. It is synthesized either from cholesterol or directly from acetyl acetylcoenzyme A.

Metabolism of testosterone

- Testosterone binds to a beta globulin and circulates in the blood for 30 minutes to several hours.
- Converted to estrogen in the liver. Excreted either into the gut through liver bile or into the urine through the kidneys.

Hormonal Regulation of Testicular Fun

[Check pic 10](#)

- The hypothalamus releases gonadotropin-releasing hormone (GnRH).
- GnRH stimulates the anterior pituitary to secrete FSH and LH.
- FSH causes Sertoli cells to release androgen-binding protein (ABP).
- LH stimulates interstitial (Leydig) cells to release **testosterone**.
- ABP binding of testosterone enhances spermatogenesis.
- **Feedback inhibition on the hypothalamus and pituitary results from:** [Check pic 11](#)
 - Rising levels of testosterone.
 - Increased inhibin.

Mechanism and Effects of Testosterone Activity / The basic intracellular mechanism of action of testosterone:

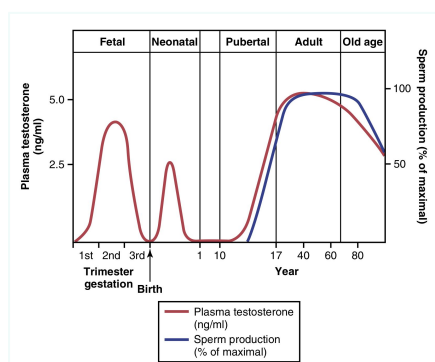
- Once it diffuses to cells it either binds to androgen receptor or converted to DHT (by **5-alpha reductase**) which then binds to the androgen receptor.
- It increases the rate of protein synthesis in target cells
- This combination moves to the cell nucleus, where it binds a nuclear protein and induces protein formation.
- It binds to testosterone-binding globulin (TeBG), ABP, serum albumin, or to corticosterone-binding globulin (CBG)

[Check pic 13](#)

Testosterone functions

- 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.
- During childhood there is no more testosterone production
- At puberty under the anterior pituitary gonadotropic hormones stimulation and throughout life
- Beyond 80 years it decline to 50%.

Female slides



Testosterone functions

It targets all male reproductive organs and accessory glands, its deficiency causes these organs to atrophy

It causes testes descent during the last 2-3 months of gestation

Causes the appearance of pubic, axillary, and facial hair, It also causes hair growth (pubic, axillary) and libido in females

Enhances growth of the chest and deepening of the voice

Skin thickens and becomes oily **acne & baldness**.

Bones grow and increase in density and calcium retention. It is also responsible for the male pelvis shape (narrow, long, funnel-like shape).

It increases basal metabolic rate

Increases red blood cells

Spermatogenesis and erection.

1. Function of testosterone during fetal development- fetal life-

- Testosterone secreted by the genital ridges.
- Later by the fetal testis
- It is responsible for development of the male body characteristics including 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 testis descend into the scrotum during the last 2 to 3 months of gestation when the testis begin secreting reasonable quantities of testosterone

2. After puberty

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

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

Effect on distribution of body hair	-Testosterone causes growth of hair: Over the pubis (upward along the linea alba of the abdomen to the umbilicus) On the face, chest -Less often on other regions such as the back.
Baldness	Testosterone decreases the growth of hair on the top of the head. two factors causes baldness: 1) Genetic background 2) Large quantities of androgenic hormones.
Effect on voice	It causes hypertrophy of the laryngeal mucosa, enlargement of the larynx (typical adult masculine voice)
skin and acne	Testosterone increases the thickness of skin over the body & subcutaneous tissues. It also increases the secretion of the sebaceous tissues & sebaceous glands of the face causing acne
Protein & muscle	Testosterone have anabolic effect by: Increasing muscular development after puberty by 50% in muscle mass over that in female Increasing protein content in non-muscle parts of the body
Increase bone matrix & Ca ²⁺ retention	Bones grow thicker & deposit additional Ca ²⁺ thus it the total quantity of bone matrix. causes Ca ²⁺ 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.
Increase basal metabolic rate	It increases the basal metabolic rate by about 15% (indirectly as a result of the anabolic effect).
RBC	It increases red blood cells/ml (due to increase metabolic rate).
Effect on electrolyte and water balance	It increase the reabsorption of Na ⁺ in the distal tubules of the kidneys.

Abnormality of Male sexual Function

Prostate gland and its abnormalities

Benign prostatic fibroadenoma, develops in older men, due to overgrowth of prostate tissue (not caused by testosterone).
Cancer of the prostate gland caused by stimulation of cancerous cells by testosterone.

Cryptorchidism

Failure of the testes to descend in the scrotum which normally occur 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 hypogonadism in male

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

Hypogonadism in male

During fetal life when the testis 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 have 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, 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.

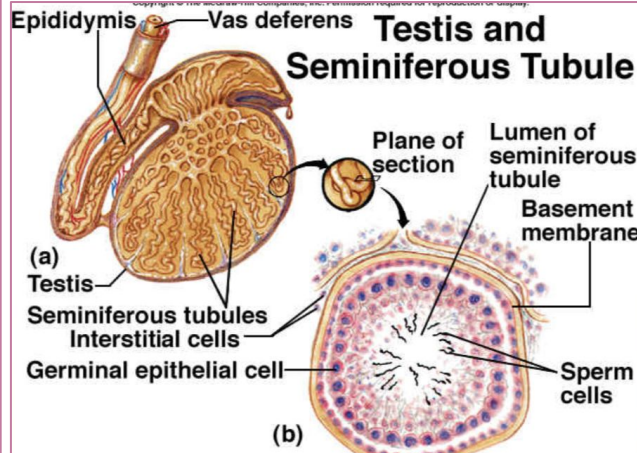
Female Dr: Testicular feminization syndrome, complete androgen insensitivity syndrome.

للقراءة أكثر عن هذه الحالة، اضغط هنا

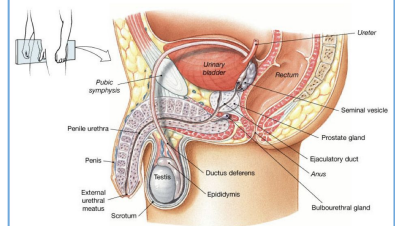
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Pictures

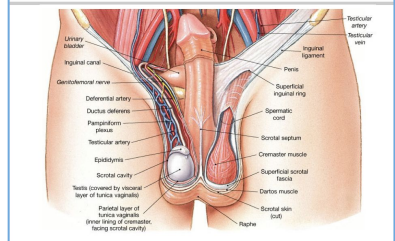
Cross section of seminiferous tubule



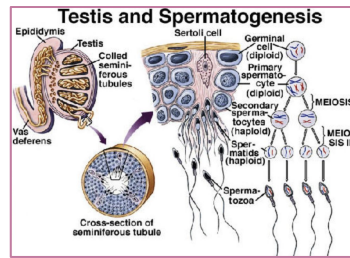
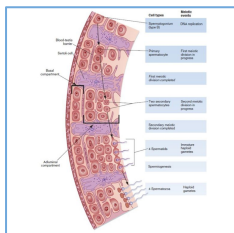
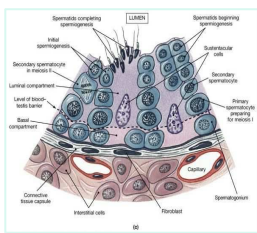
Male Reproductive Anatomy



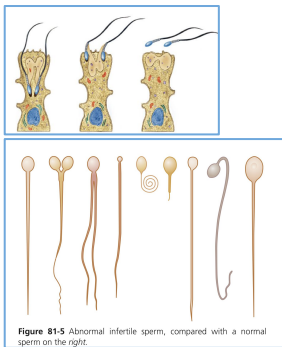
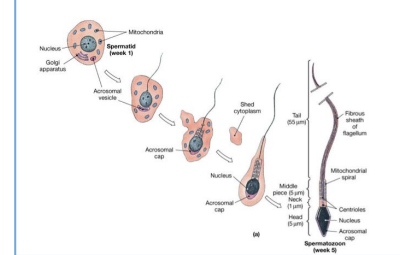
The Male Reproductive System in Anterior View



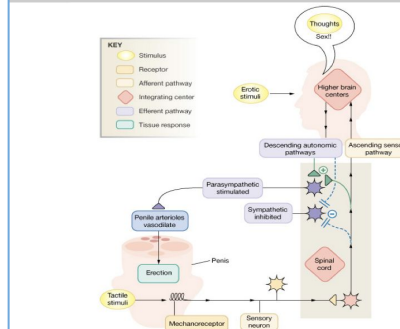
The seminiferous tubules



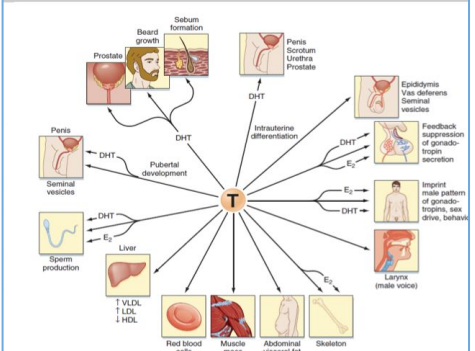
Spermiogenesis and Spermatozoon Structure



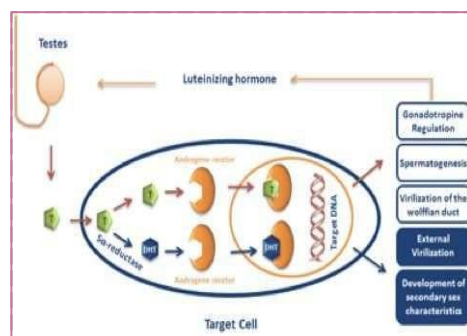
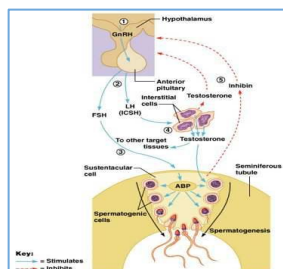
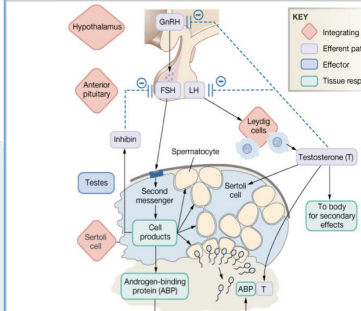
The Erection Reflex



Testosterone Functions:



HPG Axis



MCQs

Spermatogenesis is regulated by a negative feedback control system in which follicle-stimulating hormone (FSH) stimulates the steps in sperm cell formation. What is the negative feedback signal associated with sperm cell production that inhibits pituitary formation of FSH?

Testosterone

Inhibin

Estrogen

LH

Estrogen is required for normal reproductive function in the male. Where is the principal site of estrogen synthesis in the male?

Leydig cell

Osteoplast

Prostate cell

Liver cell

ترا يمكن صح!

A man is taking a number of medications, one of which appears to be interfering with the emission phase of the sexual act. Which of the following medications could cause this problem?

سؤال جيد للإختبار

A medication that prolongs the duration of action of nitric oxide

A medication that blocks the smooth muscle receptors for nitric oxide

A medication that increases the release of nitric oxide

An inhibitor of beta-adrenergic nervous system receptors

Want Explanation 🤔? [Your Finger HERE!](#)

Leaders

Rafan Alhazzani

Fahad Almughaiseeb



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(Very special Thanks for your words!)