

# #4 Physiology of androgens and control of male sexual functions

## **Objectives:**

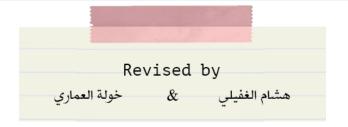
- Understand the functions of the male reproductive organs and glands
- Describe the synthesis, secretion, metabolism and effects of testosterone
- Explain how the hypothalamus and anterior pituitary gland regulate male reproductive function
- Describe the major testicular abnormalities
- Discuss the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

You are recommended to study the anatomy of male genital system first

Important
Males notes
Females notes
Extra

Resources: 435 female's & male's slides

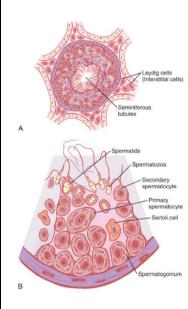
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## Spermatogenesis

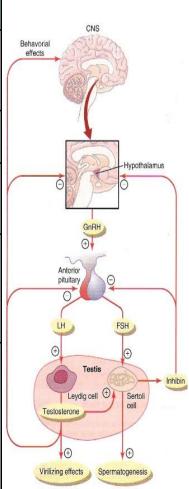
## **Definitions:**

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Spermatogenesis	<ul> <li>It's the formation of sperms from spermatogonia</li> <li>occurs in the seminiferous tubule during active sexual life (due to stimulation by Anterior pituitary Gonadotropin hormones).</li> <li>Begins at age 13, continues throughout life and decrease in old age. There no menopause for male. Spermatigonia are cells dividing all the time.</li> </ul>
Sertoli cells	<ul> <li>large cells with overflowing cytoplasmic envelope</li> <li>surround the developing spermatogonia around central lumen of the seminiferous tubules.</li> </ul>
Leydig cells	<ul> <li>Lie within the interstitium between the seminiferous tubules.</li> <li>Numerous in the newborn male in the first few months &amp; then disappear until puberty when it appears again and become active</li> <li>They don't exist in the testis during childhood (when the testis secretes almost no testosterone)</li> <li>Active at puberty and throughout adult life and secrete testosterone.</li> </ul>



## **Hormonal factors that stimulate spermatogenesis:**

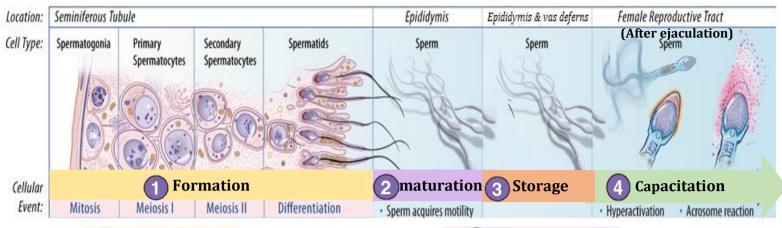
HORMONE	SECRETED BY	FUNCTION	
Testosterone	Leydig cells, (located in the interstitium of the testis)	Essential for the growth and division of the testicular germinal cells.	
LH	Anterior pituitary	Stimulates the leydig cells to secrete testosterone.	
FSH	Anterior pituitary	Stimulates the sertoli cells, 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.  *Adipocytes can release enzyme aromatase that convert testosteron to estrogen The estrogen has a receptors in the primary spermatocytes and secondary spermatocytes.	
Growth hormone	Anterior pituitary	<ul> <li>(And also other body hormones) is necessary for controlling metabolic functions of the testis.</li> <li>Gh promotes early division of spermatogonias in its absence (pituitary dwarfs), the spermatogenesis is severely deficient or absent infertility.</li> </ul>	



## **Developmental Events of sperm(sperm journey):**

MITOTIC DIVISION

Spermati (haploid)



## **Formation**

- The 2 testis of adult human formed up to 120 million sperm each day.
- Spermatogonia become progressively modified and enlarged to form large primary spermatocytes. Each of these, in turn, undergoes meiotic division to form two secondary spermatocytes.
- After another few days, these too divide to form spermatids that are eventually modified to become sperm (spermatozoa).
- The entire period ofspermatogenesis, from spermatogonia to sperm, takes about 74 days

Storage

- Small amount of stored in the epididymis but 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. They will stored up to month if the person is not sexually active the sperms undergo lysis

## maturation

#### Maturation of sperm in the epididymis steps:

- 1-sperms formation occurs in the seminiferous tubule
- 2- then sperms require several days to pass through the epididymis (not motile yet)
- 3- After the sperm have been in the epididymis for 18 to 24 hour, they develop the capability of motility. (Some inhibitory proteins in the epididymal fluid prevent final motility until after ejaculation)

موضوع الحركة بسيط لو بقى الحيوان المنوي لأكثر من يُوم في البريخ راح يصير قادر على الحركة وماتب مادام في جسم الذكر ما راح يتحرك إلا لو تم قذفه ويبدأ يتحرك في الرحم أو الجهاز التناسلي الإنثوي عموماً.

Physiology of mature sperms:

After ejaculation, Mature sperm are motile & Head capable of fertilizing the ovum.

The sertoli cells and epithelium of the epididymis secrete nutrient fluid which contains (testosterone & estrogens), enzymes & nutrients essential for sperm maturation.

Their activity is enhanced in a neutral & slightly alkaline medium & depressed in mildly acidic الستات زمان قبل مايطلع الاورال كونتراسبتف كانوا يشطفوا الفجاينا بالخل

The life expectancy of ejaculated sperm in the female genital tract is only 1 to 2 days.

## Capacitation of The Sperm

(making the sperm possible to penetrate the ovum)

#### What is the capacitation? without capacitation the sperm won't be able to penetrate the ovum thus fertilization won't occur.

Sperm in the epididymis is kept inactive by multiple inhibitory factors secreted by the genital duct epithelia, and they get activated in the female genital tract, for the processes of fertilization. These activation changes are called capacitation of the spermatozoa (requires 1 to 10 hrs).

#### Some changes that are believed to occur are the following:

- 1. Uterine and fallopian 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 enzyme. After ejaculation the sperm is removed from the cholesterol vesicles and this makes the membrane of the sperm head become weaker\*
- 3. The sperm membrane becomes more permeable to Ca2+ ion which increase their movements and help to release the proteolytic enzymes from acrosome which aid in penetrating the ovum\*.

# Flagellum Nucleus (2) Sperm binds zona pellucida

Nucleus containing

Middle piece

Mitochondria

#### \* Acrosome enzymes, "Acrosome Reaction" and penetration of the ovum:

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

The ovum after ovulation has an outer layer called zona pellucida the proteolytic enzymes that found in the acrosome help in penetrating the layers surrounding the ovum and the fertilization occurs

### **Glands:**

Seminal vesicles	Prostate gland
Secrete mucoid material containing fructose, citric acid & nutrient substances & large quantities of prostaglandins* & fibrinogen (clotting factor)  The semen after ejaculation become one plug " يتخثر " within few minutes, and after 10-15 minutes or more become more liquid and watery	Secrete thin milky (alkaline) fluid contains Ca2+ ion, citrate ion, phosphate ion, a clotting enzyme & profibrinolysin (lysis)
*prostaglandins help in fertilization in two ways:  1) Reacting with the female cervical mucus making it more receptive to sperm movement  2) Causing backward reverse peristaltic contractions of the uterus & fallopian tubes to move the ejaculated sperm toward the ovaries  Backward Reverse Peristaltic Contractions:  Backward Reverse Peristaltic Contractions:  Jie	Functions of alkaline prostate fluid:  1) Important for Successful fertilization of the ovum.  2) The alkaline fluid help to neutralize the slightly acidic fluid of the vas deferens (due to the presence of citric acid and metabolic product of the sperm that inhibit sperm fertility) and other seminal fluids during ejaculation  3) Enhances motility & fertility of sperm ,by neutralizing the acidic vaginal secretions <sup>1</sup> .

## Semen<sup>2</sup>:

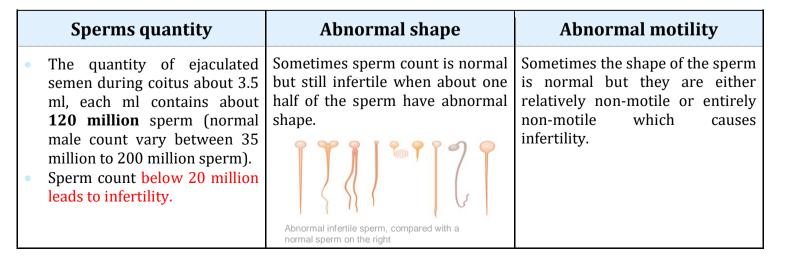
- It's average pH is about 7.5.
- Ejaculated semen during sexual act is composed of:
  - o Fluid & sperm from the vas deferens ( $\sim$ 10%).
  - o Fluid from the prostate gland ( $\sim 30\%$ )\*.
  - Fluid from the seminal vesicles ( $\sim 60\%$ )\*\*.

Small amounts from the mucous glands\*\* and the bulbourethral(cowper) glands.
 \*The alkaline prostatic fluid helps to neutralize the mild acidity of other portions of the semen and gives the semen a milky appearance. The texture of the semen is due to the prostatic secretion.
 \*\*The seminal vesicles and mucous glands fluid give the semen mucoid consistency.

COMPOSITION OF THE SEMEN

nrostate fluid

## Effect of sperm count, morphology and motility on fertility: Both the count and the the ability to function are important to avoid infertility; and infertility and infertility and infertility.



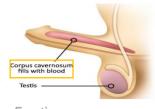
<sup>1</sup> the vaginal secretions of the female are acidic (pH of 3.5 to 4.0). Sperm do not become optimally motile until the pH of the surrounding fluids rises to about 6.0 to 6.5.

<sup>2</sup> the male reproductive fluid, containing spermatozoa in suspension.المنى

#### **Male Sexual Act**

## Stages of male sexual act:

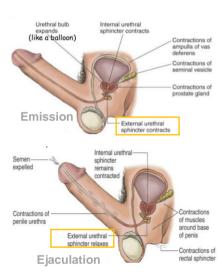
1. **Penile erection:** Penile erection is the first effect of male sexual stimulation, and the degree of erection is proportional to the degree of stimulation, whether psychic or physical Erection is the process of filling the erectile tissue of the penis with blood at a pressure level near that of the arterial pressure. The arteries leading to the erectile tissue dilate in response to parasympathetic impulses, which stimulate release of nitric oxide at the nerve endings on the arterial smooth muscle, erection is caused by



**Erection** 

**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 and bulbourethral glands to secrete mucous. Without satisfactory lubrication, the male sexual act is seldom successful because unlubricated intercourse causes grating, painful sensations that inhibit rather than excite sexual sensations.
- 3. **Emission and ejaculation:** function of the **sympathetic nerves**.
  - Emission begins by contraction of the vas deferens and ampulla to cause expulsion of the sperm in the internal urethra. Contraction of the prostate and seminal vesicles to expel their fluid in the urethra(both urethral sphincters close). 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**<sup>3</sup>.
  - 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. This is called ejaculation.



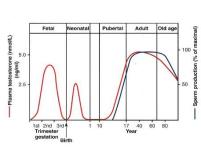
#### **Testosterone and Other Male Sex Hormones**

## Secretion and chemistry of the male sex hormone:

- Secretion of testosterone by the interstitial cell of leydig in the testis.
- The testis secretes several male sex hormones called androgens including testosterone, dihydrotestosterone and androstenedione. Testosterone is the most abundant form, while dihydrotestosterone is the most active, and testosterone converted into dihydrotestosterone in the target cells.
- Secretion of androgens in the body: from the adrenal glands and synthesized either from cholesterol or directly from acetyl coenzyme A.

## Stimulation of testosterone release:

- **During fetal life**: the testis are stimulated by **placenta chorionic gonodotropin** 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%.



 $<sup>^{3}</sup>$  Define as deposition of the seminal fluid into the posterior urethra الانبعاث

## Metabolism of the male sex hormone:

↑ basal metabolism

↑ Acne & skin thickness

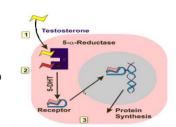
• Testosterone is bound to beta globulin, and circulates in the blood for 30 minutes to several hours, and it is converted to estrogen in the liver, and excreted either into the gut through liver bile or into the urine through the kidneys.

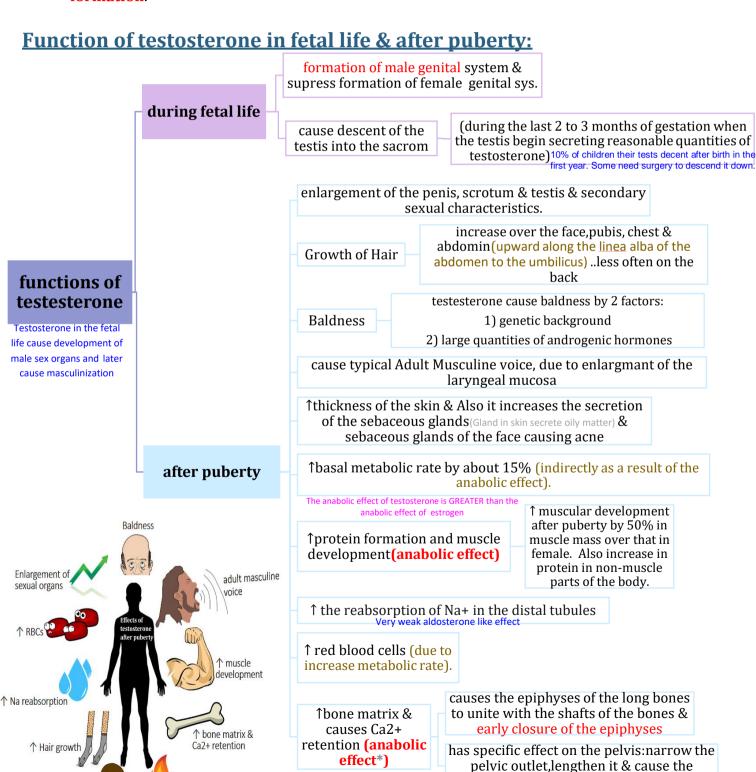
## The basic intracellular mechanism of action of testosterone:

Testosterone "androgen" are not stored they are secreted once they are released "cell membrane can't protect them, vesicles can't contain them 'they either go to the circulation or to the seminiferous tubules" once they bound to their receptors they cause gene expression.

It increases the rate of protein synthesis in target cells, by the following steps:

- (1)Testosterone converted by the intracellular enzyme  $5\alpha reductase$  to dihydrotestosterone,
- (2) then it binds with cytoplasmic "receptor protein".
- (3) This combination moves to the nucleus where it binds a nuclear protein and **induces protein formation**.





<sup>\*</sup>The increase in bone matrix is believed to result from the general protein anabolic function of testosterone plus deposition of calcium salts in response to

funnel-like shape

## Abnormalities of male sexual function maturation

#### Prostate gland **Benign prostatic fibroadenoma** in older age due to overgrowth of prostate tissue (not caused by testosterone). and its **Cancer of the prostate gland**caused by stimulation of cancerous cells by abnormalitis testosterone. During fetal life when the testis are **Adiposogenitial** hypogonadism due to non-functional: none of the male sexual syndrome. genetic inability of Hypogonadism Frohlich's the hypothalamus to characteristics develop in the fetus. in male: Instead female organs are formed. syndrome or secrete normal hypothalamic amount of GnRH & If the boy loses his testis before eunuchism: abnormality of the puberty: a state eunuchism<sup>4</sup> (he have feeding center of the infantile sex organs & infantile sexual hypothalamus result characteristics) & the height of an adult in obesity with eunuch is slightly greater than normal eunuchism. because of slow union of the epiphyses. If a man is castrated<sup>5</sup> after puberty: sexual organ regress in size and voice regress - loss of the thick musculine bones- loss of masculine hair production loss of musculature of the virile male. **Cryptorchidim:** It's 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 Interstitial leydig cell tumors (rare), over production of testosterone. In children,

## 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 union of the epiphyses and causes excessive development of male sexual organs.
- Tumor of the germinal epithelium (more common).

Other disorder(sertoli cell only syndrome): في ذي الحالة ماراح : يكون عند المريض خلايا غير اليسرتولي فأكيد ماراح يكون عنده حيوانات منوية وبيصير عقيم

#### **IMPORTANTE POINT**

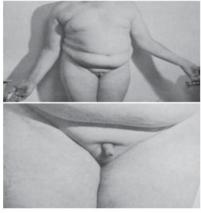
#### Effect of Temperature on Spermatogenesis.:

increasing the temperature of the testes can prevent spermatogenesis by causing degeneration of most cells of the seminiferous tubules besides the spermatogonia. It has often been stated that the reason the testes are located in the dangling scrotum is to maintain the temperature of these glands below the internal temperature of the body, although usually only about 2°C below the internal temperature.

ليه تنزل التيستيس لمكان خارج الحوض ...؟ لأن عملية تصنيع الحيوانات المنوية تحتاج لحرارة أقل من الحرارة الموجودة في الجسم ٣٧ درجة في الصيف لما يكون الجو حار راح تمتلئ التيستس بالغدد العرقية ووبيكون عندهم قدرة على الاستطالة علشان تساعد على تخفيف الحرارة في البرد راح تنقبض علشان تحافظ على الحرارة و ترتفع لمكان أقرب للجسم علشان تحافظ على مستوى معين من الحرارة واللي هو أقل من حرارة الجسم بدرجتين . لوظت التيستيس في الحوض راح يقل تصنيع الحيوانات المنوية بشكل كبير.



**Cryptorchidim:** undescended testes



**Adiposogenital syndrome** in an adolescent male. Note the obesity and childlike sexual organs.

<sup>&</sup>lt;sup>4</sup> The state of being a eunuch; absence of the testes or failure of the gonads to develop or function with consequent lack of reproductive and sexual function and of development of secondary sex

<sup>&</sup>lt;sup>5</sup> remove the testicles

## **SUMMARY**

Definitions			
Spermatogenesis	<ul> <li>It's the formation of sperms, occurs in the seminiferous tubule due to stimulation Gonadotropin hormones, Begins usually at age 13 &amp; ↓ by by aging</li> </ul>		
Sertoli cells large cells with overflowing cytoplasmic envelope			
Leydig cells	<ul> <li>Lie between the seminiferous tubules.</li> <li>Numerous in the newborn male then disappear until puberty</li> <li>Active at puberty and throughout adult life and secrete testosterone.</li> </ul>		

Spermatogenesis					
Hormonal Factors That Stimulate Spermatogenesis:					
Hormone	Secreted By	Secreted By Function			
LH	Anterior	summates the regular to see the testes of the			
FSH	pituitary				
Growth hormone					
Testosterone	Leydig cells	eydig cells  Essential for: growth division of the testicular germinal cells.			
Estrogen	sertoli cell	<ul> <li>Essential for spe</li> </ul>	ermatogenesis.		
	Developmental Events of sperm:				
Formation	ma	turation	Storage	Capacitation	
<ul> <li>occurs in the seminiferous tubule.</li> <li>Spermatogonia</li></ul>	<ul> <li>After 18 to 24 hour in the epididymis, sperm develop the capability of motility.</li> <li>Epididymis sertoli cells secrete nutrient fluid contain (testosterone&amp; estrogens) which is essential for sperm maturation.</li> <li>Sperm activity enhanced in a neutral &amp; slightly alkaline medium.</li> <li>life expectancy in the female genital tract is only 1 to 2 days.</li> </ul>		<ul> <li>The majority stored in the vas deferens, maintaining their fertility for at least a month.</li> <li>Small amount of stored in the epididymis</li> <li>sperm kept inactive by multiple inhibitory substances in the secretion of the ducts.</li> </ul>	1)sperm activated by female genital tract:Uterine and fallopian fluids wash away the inhibitory factors  2)Acrosomal reaction:The sperm membrane becomes more permeable to Ca2+ ion which increase help to release the hyaluronidase and proteolytic enzymes from sperm acrosome which aid in penetrating the ovum.	
Seminal vesicles		Prostate gland			
<ul> <li>Secrete mucoid material containing fructose, citric acid &amp; nutrient substances &amp; large quantities of prostaglandins* &amp; fibrinogen.</li> <li>*prostaglandins help in fertilization in two ways:         <ol> <li>Reacting female cervical mucus making it more receptive to sperm movement</li> <li>Causing backward reverse peristaltic contractions of the uterus &amp; fallopian tubes to move the ejaculated sperm toward the ovaries</li> </ol> </li> </ul>		<ul> <li>Secrete thin milky fluid contains Ca2+ ion, citrate ion, phosphate ion, a clotting enzyme &amp; profibrinolysin.</li> <li>Functions of alkaline prostate fluid:         <ol> <li>Important for Successful fertilization of the ovum.</li> <li>help to neutralize the slightly acidic fluid of the vas deferens and other seminal fluids during ejaculation</li> <li>Enhances motility &amp; fertility of sperm</li> </ol> </li> </ul>			

#### Semen

- average pH is about 7.5.
- Ejaculated semen during sexual act is composed of:
  - o Fluid & sperm from vas deferens ( $\sim 10\%$ ).
  - o Fluid from: prostate gland ( $\sim$ 30%)& the seminal vesicles\*\* ( $\sim$ 60%).
  - o Small amounts from the mucous glands\*\* and the bulbourethral glands.
- \*The **alkaline prostatic fluid** helps to neutralize the mild acidity of other portions of the semen and gives the semen a milky appearance.
- \*\*The seminal vesicles and mucous glands fluid give the semen mucoid consistency.

#### Effect of sperm count, morphology and motility on fertility:

Sperms quantity	Abnormal shape	Abnormal motility
35m - 200m sperm Sperm count below 20 m leads to infertility	count is normal but still infertile whenit comes to shape of half of sperms .	shape is normal but either they are relatively non-motile or entirely non-motile which causes infertility.

## **Stages of Male Sexual Act**

- 1. **Penile erection:** process of filling the erectile tissue of the penis with blood at a pressure level near that of the arterial pressure. caused by **parasympathetic impulses** that pass from the sacral portion of the spinal cord.
- 2. **Lubrication:** parasympathetic impulses cause the urethral glands and bulbourethral glands to secrete mucous.
- 3. Emission and ejaculation: by sympathetic nerves impulses.

#### **Testosterone and Other Male Sex Hormones** Secretion and chemistry of Stimulation of testosterone release: **TestosteronIntracellular** the male sex hormone: mechanism of action: The testis secretes several sex (1) Testosterone converted During fetal life: the testis are Timeline of Testosterone hormones called androgens stimulated by placenta by the intracellular enzyme 5 including testosterone, reductase to chorionic gonodotropin to dihydrotestosterone and produce testosterone throughout dihydrotestosterone. androstenedione. fetal life & up to 10 weeks after (2) then it binds with Testosterone is the most cytoplasmic "receptor birth. abundant form, while protein". At puberty: under the anterior dihydrotestosterone is the most (3) moves to the nucleus pituitary gonadotropic where it binds a nuclear active. **hormones** stimulation throughout life & then decline protein and induces protein beyond 80 years to 50%... formation. Function of testosterone in fetal life & after puberty after puberty: fetal life: formation male genital system formations formation of female genital sys T RBCs cause descent of the testis into the sacrom ↑ Na reabsorption

	Abnormalities of male sexual function maturation			
Prostate gland abnormalites		Adiposogenitial syndrome, Frohlich's syndrome or hypothalamic eunuchism:	Cryptorchidim:	Testicular tumors and hypergonadism in male:
	Benign prostatic fibroadenoma in older age due to overgrowth of prostate tissue (not caused by testosterone).	Inability of Hypothalamus to secrete normal amount of GnRH	It's Failure of the testes to descend	Interstitial leydig cell tumors Tumor of the germinal epithelium
	Cancer of the prostate gland caused by stimulation of cancerous cells by testosterone.			

## **MCQs**

#### 1-The cells that lies within interstitium between 7- the count of sperm that considered to be seminiferous tubules:

- a. sertoli cells
- b. leyding cells
- c. spermatogonia
- d. all of them

#### 2- in which stage in male reproductive system the sperm are motile:

- a. storage form in epididymis
- b. storage form in vas deference
- c. after ejaculation
- d. all of them

## 3- which of these are function of seminal vesicle:

- a. secret mucoid material
- b. secret nutrient substances
- c. secret prostaglandins
- d. all of them

#### 4- What is the function of prostate gland:

- a. secret milky material
- b. secret mucoid material
- c. secret mucinous material
- d. non of them

## 5-Which of these structure secret profibrinolysin:

- a. prostate gland
- b. vas deference
- c. epididymis
- d. all of them

## 6- what is the structure that secret the highest composition of semen:

- a. prostate gland
- b. seminal vesical
- c. vas deference
- d. cooper gland

## infertile:

- a. less that 20M
- b. more than 20M
- c. between 20-40M
- d. less than 10M

### 8- the count of sperm that considered to be sterile:

- a. less that 20M
- b. more than 20M
- c. between 20-40M
- d. less than 10M

## 9- penile erection caused mainly by:

- a. parasympathetic innervation
- b. sympathetic innervation
- c. estrogen
- d. progesterone

## 10- what of these condition is mainly associated with untreated or late treatment of cryptorchidism:

- a. benign tumour
- b. malignant tumour
- c. non of them

## Answer kev:

1 (b) | 2 (c) | 3 (d) | 4 (a) | 5 (a) | 6 (b) | 7 (a) | 8 (d) | 9 (a) | 10 (b)



## Thanks to this amazing team!

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