Physiology of androgens and control of male sexual functions

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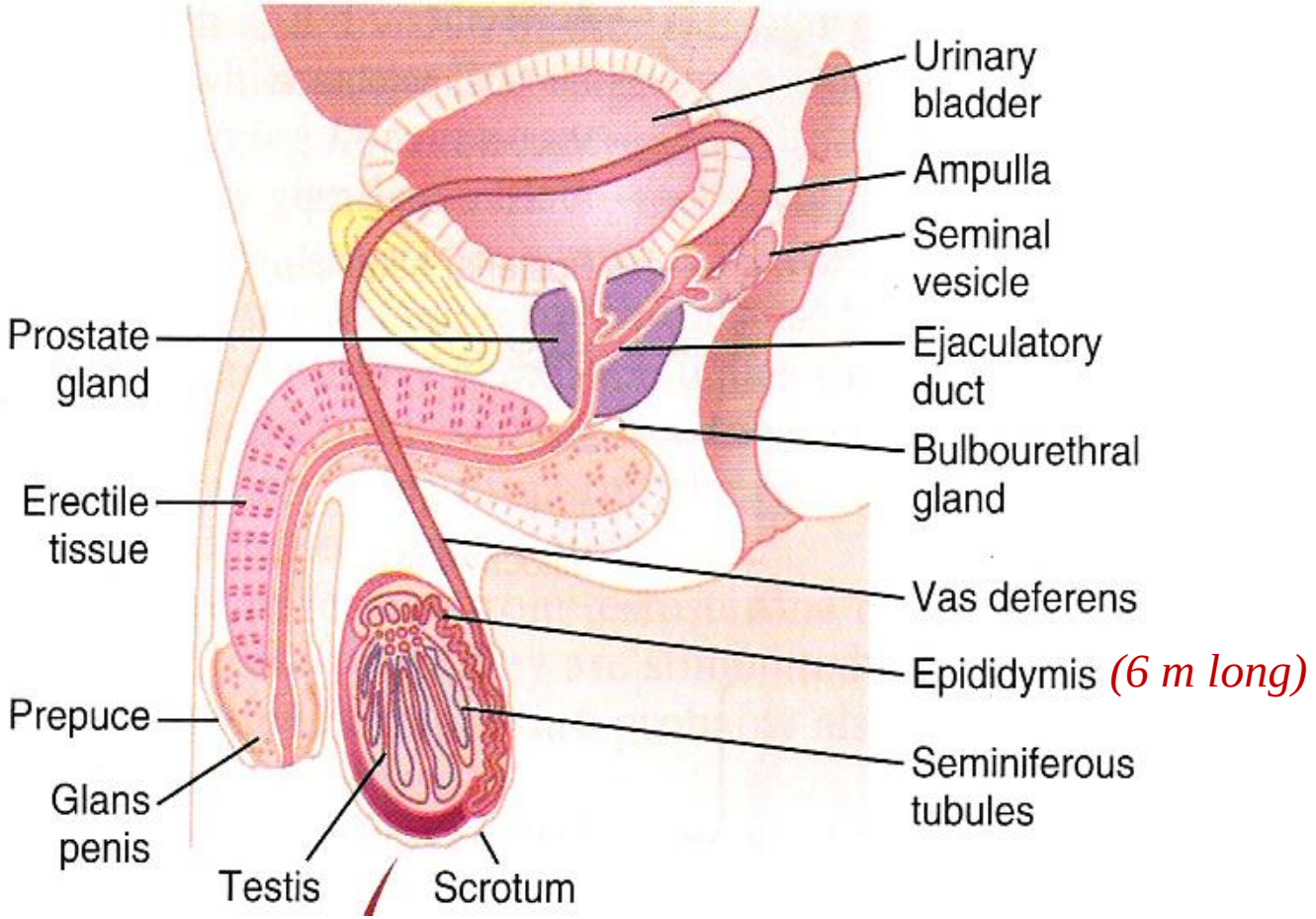
Objectives

By the end of this lecture, you should be able to:

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

Male Reproductive Organs



Spermatogenesis:

Formation of sperm from spermatogonia which occur in the ***seminiferous tubules*** during active sexual life due to stimulation of HPG axis.

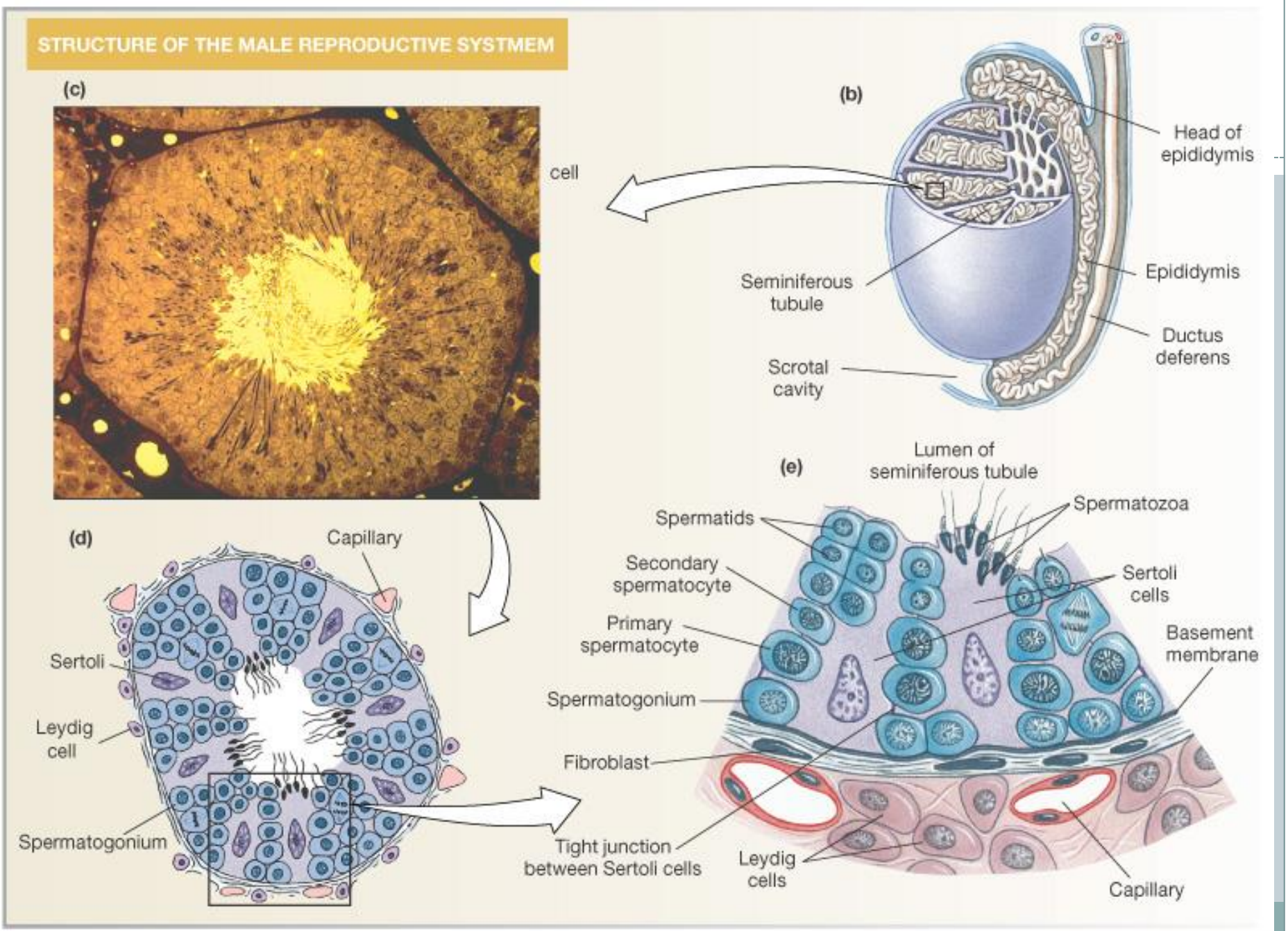
begin at an average age of 13 years ,continue throughout life & decrease in old age.

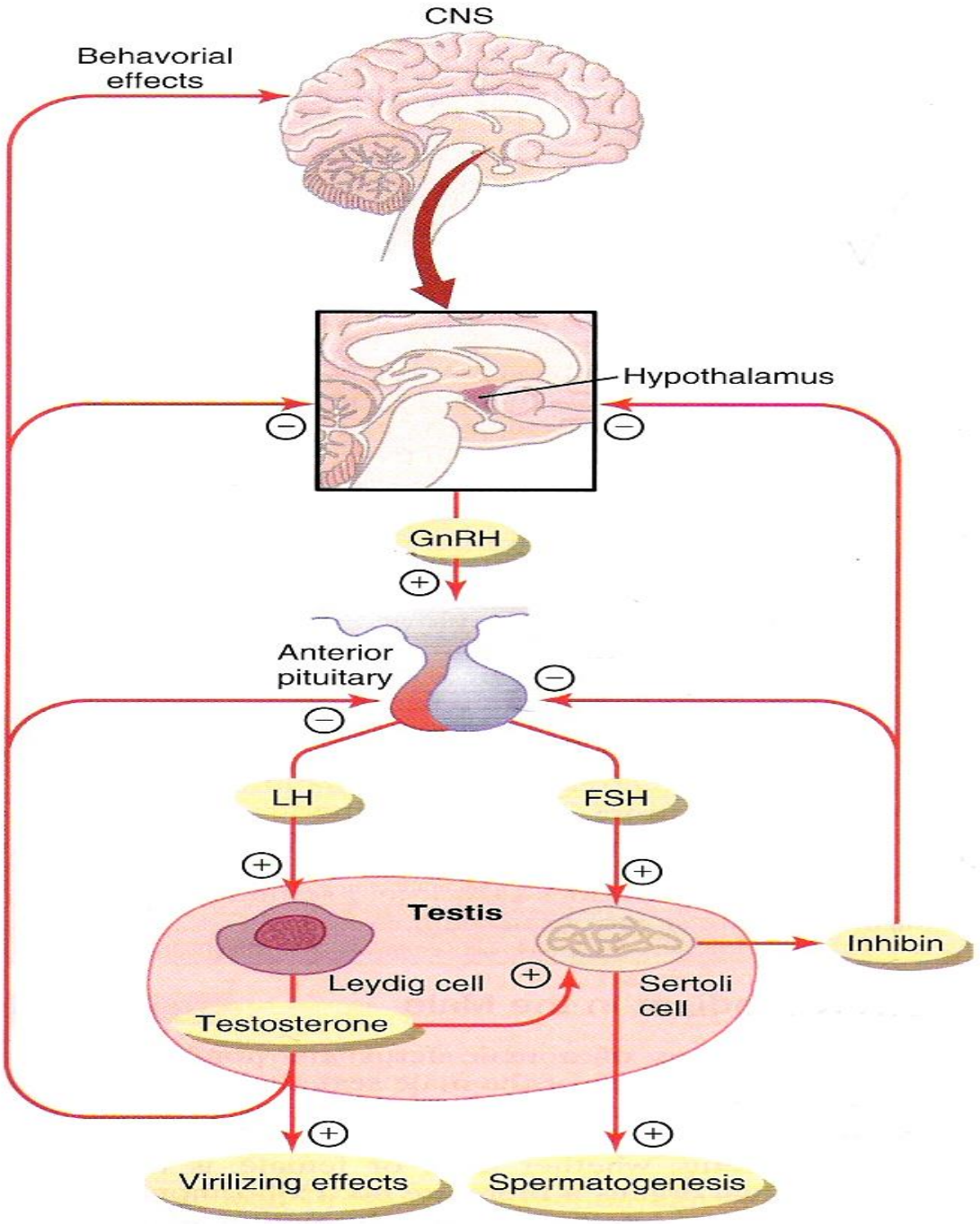
Sertoli cells: large with overflowing cytoplasmic envelopes that surround the developing spermatogonia around the central lumen of the seminiferous tubules.

Leydig cell: lie with interstitium between the seminiferous tubules. They are not active 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.

STRUCTURE OF THE MALE REPRODUCTIVE SYSTMEM




CNS
Behavorial effects
Hypothalamus
GnRH
Anterior pituitary
LH
FSH
Testis
Leydig cell
Testosterone
Sertoli cell
Inhibin
Virilizing effects
Spermatogenesis

Maturation of sperm in the epididymis

- After their formation in the seminiferous tubules, sperms require several days to pass through the epididymis (still non-motile).

- After the sperm have been in the epididymis for about 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 sperms

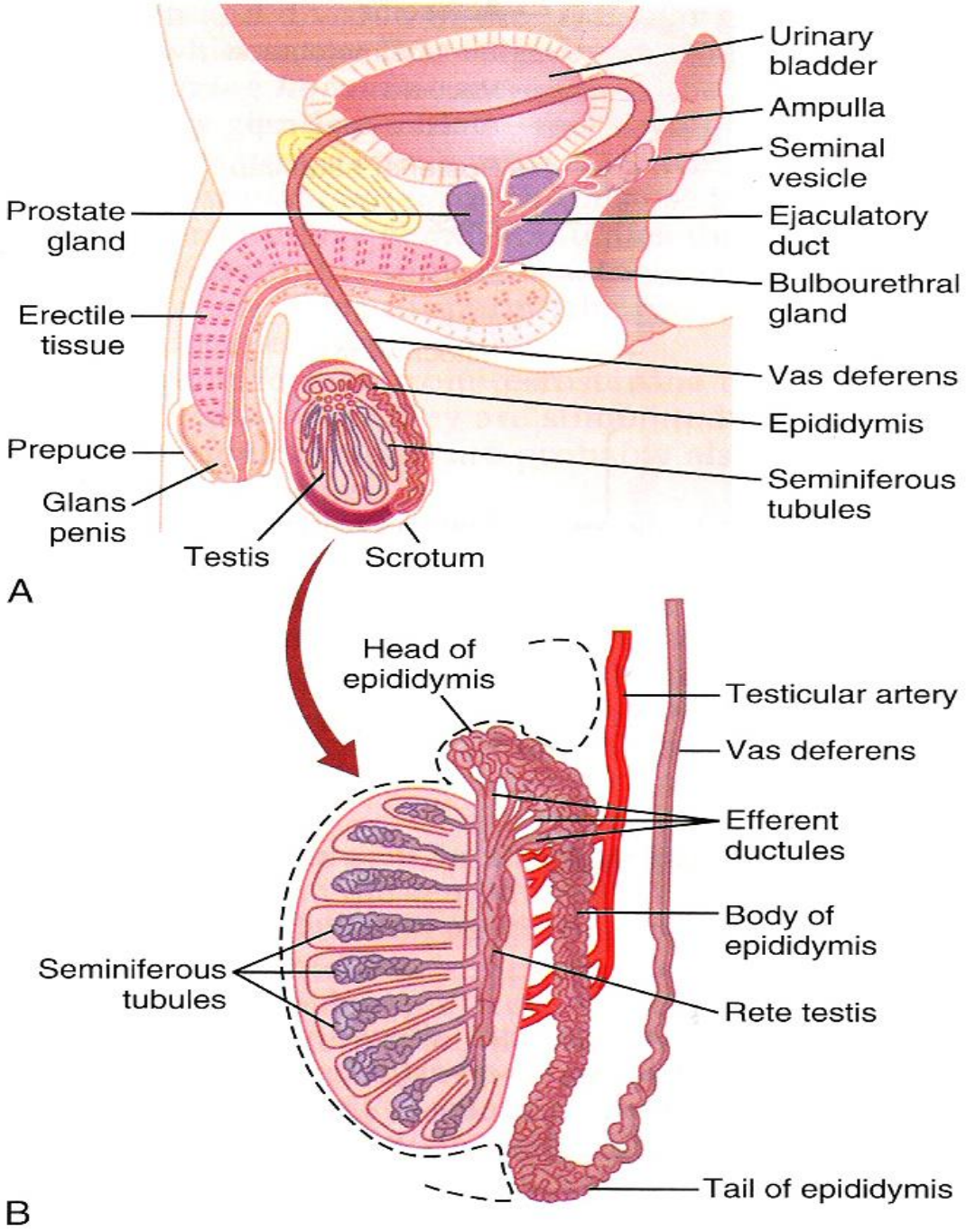
The 2 testes of adult human form up to 120 million sperm each day.

– 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.

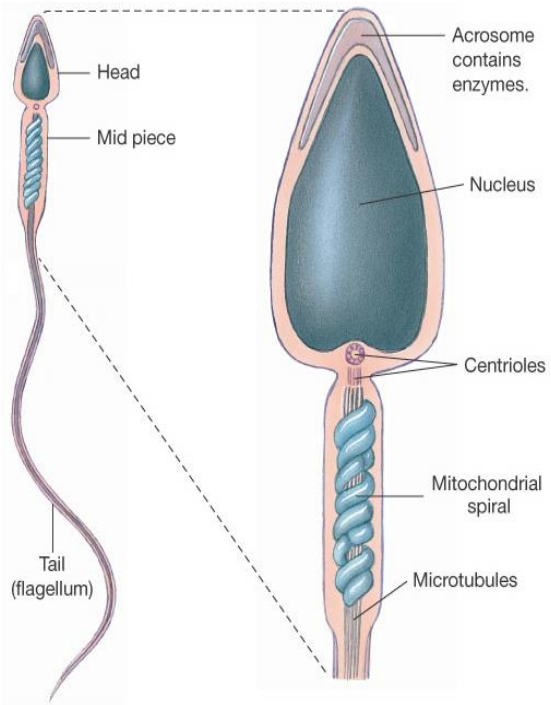
After ejaculation, the sperm becomes motile & capable of fertilizing the ovum "maturation"

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


Urinary bladder
Ampulla
Seminal vesicle
Prostate gland
Ejaculatory duct
Bulbourethral gland
Erectile tissue
Vas deferens
Epididymis
Prepuce
Seminiferous tubules
Glans penis
Testis
Scrotum
A
Head of epididymis
Testicular artery
Vas deferens
Efferent ductules
Body of epididymis
Seminiferous tubules
Rete testis
Tail of epididymis
B

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



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

Function of the **seminal vesicles**

– secrete mucoid material containing fructose, citric acid & nutrient substances & large quantities of prostaglandins & fibrinogen.

The prostaglandins help in fertilization in two ways:

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 Ca2+, citrate ion, phosphate ion, a clotting enzyme & profibrinolysin. The alkaline prostatic fluid is important for successful fertilization of the ovum.

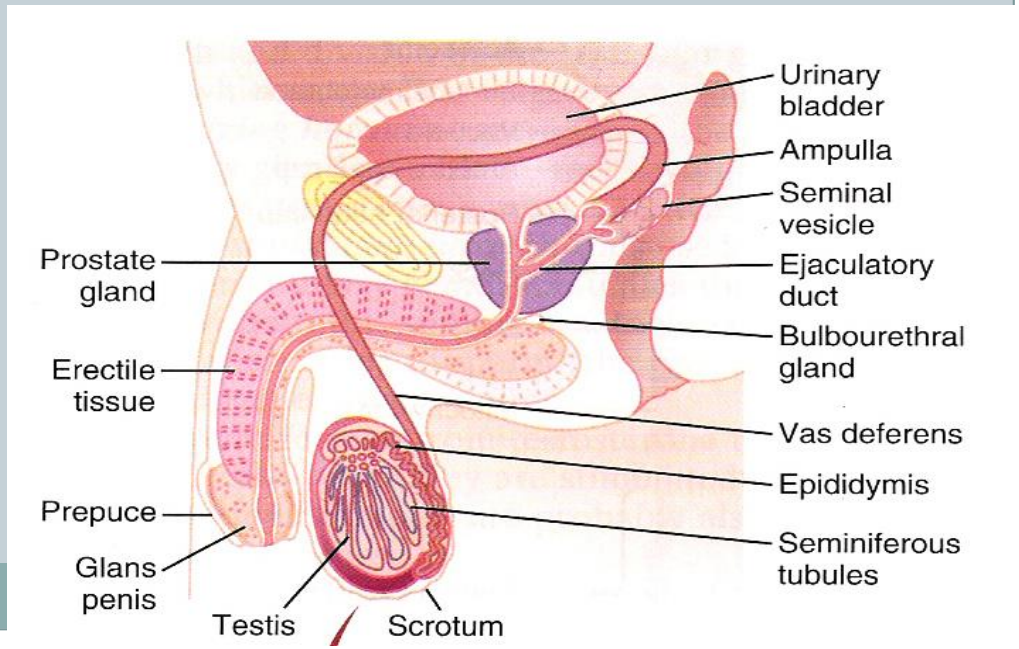
Alkaline prostate fluid function:

1- helps to neutralize the slightly acidic fluid of the vas deferens (due to the presence of citric acid and metabolic product of the sperm which inhibits its fertility).

2- helps to neutralize the acidic vaginal secretions (pH 3.5-4.0) to optimize it for better sperm motility (pH 6.0-6.5)

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.



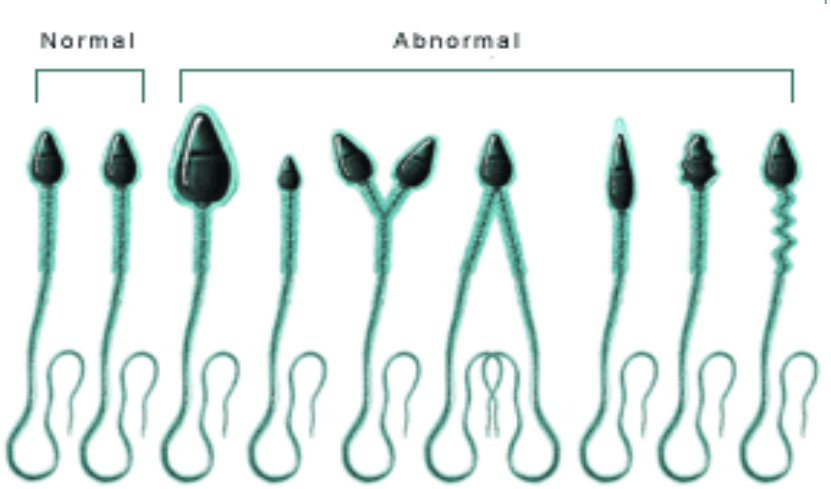
Effect of sperm count on fertility:

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

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:

- Sperms in the epididymis are kept inactive by multiple inhibitory factors secreted by the genital duct epithelia. They are activated in the female genital tract by a process called **CAPACITATION** which requires 1-10 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 are 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 swims away from the cholesterol vesicles & this makes the membrane of the sperm & head becomes weaker.

- The sperm membrane becomes more permeable to Ca2+ ion which increase their movements & help to release the proteolytic enzymes from acrosome which aid in penetrating the ovum.

Hormonal factors that stimulate spermatogenesis:

1-Testosterone: secreted by the leydig cells which located in the interstitium of the testis, is essential for the growth and division of the testicular germinal cells.

2-Luteinizing hormone (LH) secreted by the anterior pituitary gland, stimulates the leydig cells to secrete testosterone.

3-Follicle stimulating hormone: FSH also secreted by the anterior pituitary gland, stimulates the sertoli cells, stimulate the conversion of spermatids to sperm (also important for spermatogenesis).

4-Estrogen: formed from testosterone by the sertoli cell under FSH stimulation also essential for spermatogenesis.

5-Growth hormone (also other body hormones) is 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 called **ejaculation**.

Testosterone and other male sex chromosomes: secretion, metabolism and chemistry of the male sex hormone:

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 more abundant form while dihydrotestosterone is more active and testosterone converted into dihydrotestosterone in the target cells.

Secretion & chemistry of androgens in the body:

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

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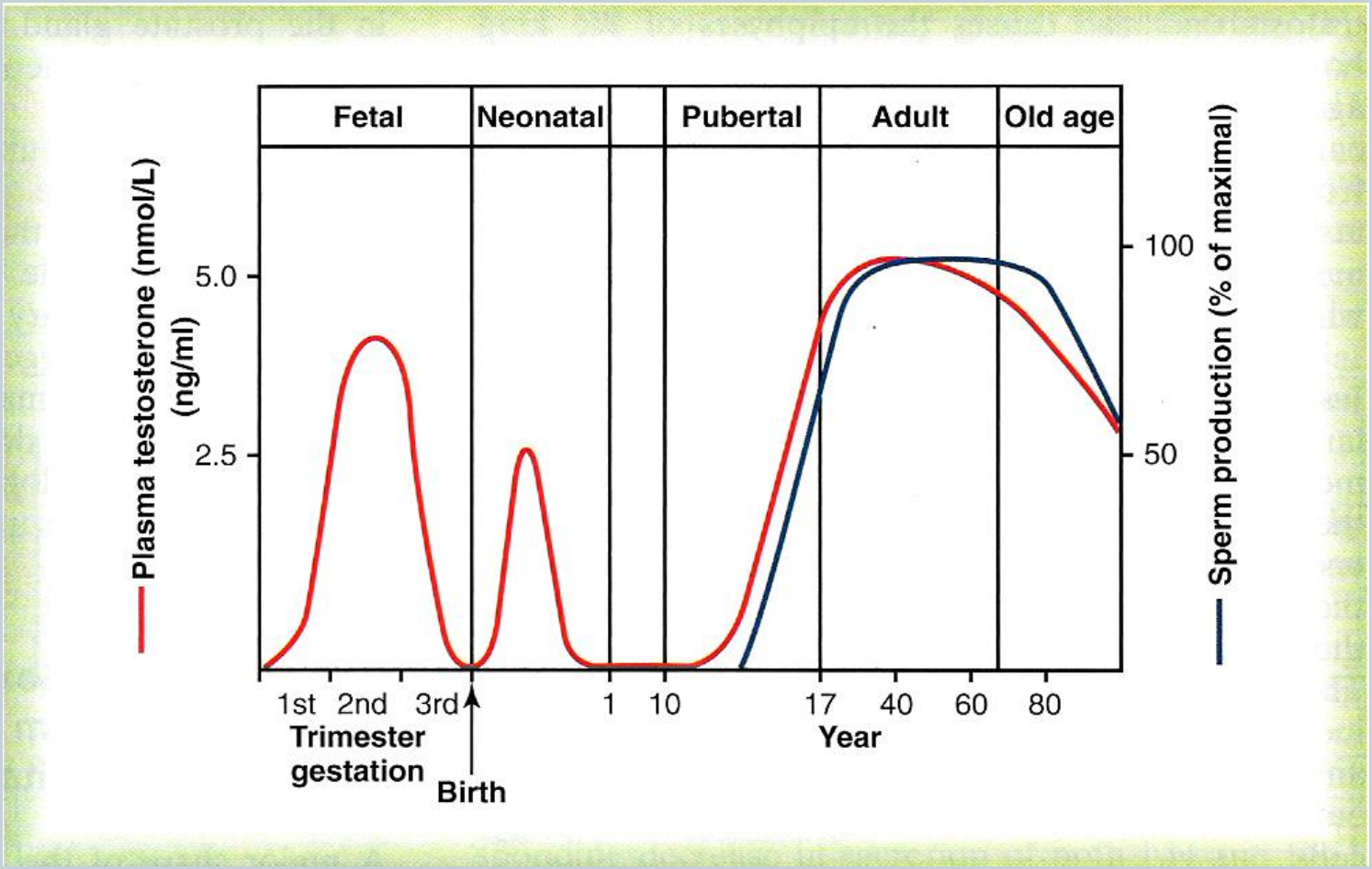
Functions of testosterone:

It is responsible for the characteristic masculine body. 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%.


Fetal
Neonatal
Pubertal
Adult
Old age
Plasma testosterone (nmol/L)
(ng/ml)
5.0
2.5
100
50
Sperm production (% of maximal)
1st
2nd
3rd
Trimester
gestation
Birth
1
10
17
40
60
80
Year

Functions of testosterone:

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 testis 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 linea 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 and 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 increase metabolic rate).

10- Effect on electrolyte and water balance:

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

The basic intracellular mechanism of action of testosterone:

It increases the rate of protein synthesis 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 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:

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 musculine bones- loss of masculine hair production -loss of musculature of the virile male.

Adiposogenitial 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.

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 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).

The End

Thank You