

MALE REPRODUCTIVE SYSTEM

The male reproductive system is composed of the testes, genital ducts, accessory glands, and penis.

The genital duct system includes the tubuli recti, tubules of rete testis, ductuli efferentes, ductus epididymidis, ductus deferens, ejaculatory duct and urethra.

The accessory glands include the seminal vesicles, prostate and bulbourethral glands.

Development of the male reproductive system

The gonads do not acquire male or female morphologic characteristics until week 7 of embryo development. The early genital system is similar in both sexes, and in the beginning all human embryos are bisexual. Therefore, the period of the early genital development is called the indifferent or primitive stage.

The human primordial germ cells appear at about day 21 of embryonic life in the wall of the yolk sac. Then the primordial germ cells migrate, by ameboid movement along of the hindgut задняя кишка during week 5 and reach the lumbar region of the developing embryo, where there is the mesonephros or Wolffian body. The coelomic epithelium, which covered the mesonephros from outside thickens to form the gonadal ridge. Therefore the gonadal primordium develops at the internal, anterior side of the mesonephros.

In week 6, the primordial germ cells invade and incorporated into the primary sex cords, which proliferate and grow from the coelomic epithelium of the mesonephros gonadal ridge into the underlying mesenchyme. Therefore the primary sex cords consist of coelomic epithelium and primordial germ cells

The gonad is called “indifferent” at this stage because it has the same morphologic appearance in both male and female embryos. The indifferent gonads at this stage consist of an outer cortex and an inner medulla. In embryos with an XY chromosome complex, the medulla differentiates into a testis, and the cortex regresses.

The male gonad develops into the testes toward week 7 of development. In testes the sex cords become the seminiferous or testicular cords which soon lose their connections with the coelomic epithelium because the thick fibrous capsule called

tunica albuginea is developed from the mesonephros mesenchyme. Then, the seminiferous cords develop into the seminiferous tubules, tubuli recti and rete testis. Mesenchyme lying between seminiferous tubules gives rise to the interstitial or Leydig cells which reach their maximum development between 3,5 and 4 months of the embryonic life.

The coelomic epithelium of the sex cords give rise to the supporting sustentacular or Sertoli cells of the seminiferous tubules. The primordial germ cells of the sex cords give rise to the spermatogonia.

Toward the end of month 2, the mesonephros begins to regress. But the part of mesonephric tubules remain in region linking the mesonephros to genital gonad. These mesonephric tubules give rise to the ductuli efferentes. The ductuli efferentes open into the mesonephric duct which becomes the ductus epididymidis and ductus deferens. From the lower end of the ductus deferens a diverticulum grows out to form the seminal vesicle. The seminal vesicle in side to join the ductus deferens to form the ejaculatory duct, that is portion between the seminal vesicle and the urethra. The ejaculatory ducts open on the posterior wall of the urogenital sinus. Glandular epithelium of the prostate is developed from the entodermal epithelium of the urogenital sinus. The pea-shaped bulbourethral or Cowper's glands develop from paired entodermal outgrowths from the urethra.

The paramesonephric or Mullerian ducts develop laterally from the mesonephric ducts on the lateral aspects of the mesonephroi. But it is quickly disappear almost completely in the male because the Sertoli cells of the fetal testis produced an anti-Mullerian hormone. However upper end of the paramesonephric duct persist as the appendix testis and while the fused lower ends persist as the prostatic utricle. Both paramesonephric ducts regress completely in the male by week 11.

The upper end of the mesonephric ducts persist as the appendix epididymis.

Remnants of mesonephric and paramesonephric ducts around the testis and epididymis are called hydatids that can sometimes give rise to cysts in period of the male postnatal life.

TESTIS

The testis performs 2 functions—reproductive and endocrine.

It is surrounded by a tunica vaginalis and a thick capsule, lying just beneath it, and called the tunica albuginea. The tunica vaginalis is a visceral layer of peritoneum presenting by mesothelium from outside. The tunica albuginea is dense connective tissue. The tunica albuginea forms the thickened mediastinum at the posterior part of testis and fibrous septa, dividing testis into about 250 conical shaped testicular lobules. Each lobule contains one to four highly convoluted seminiferous tubules, which produce the spermatozoa. Loose connective tissue containing small blood vessels and the interstitial or Leydig cells lie between the tubules. Leydig cells are endocrine cells that produce steroid male hormones, including testosterone.

Near mediastinum, the seminiferous tubules are continuous into short straight tubules called the tubuli recti, which form the first segment of the genital duct system. The tubuli recti are continuous with the tubules of rete testis lying in the mediastinum. Thus in testis there are three types of tubules: seminiferous tubules, tubuli recti and tubules of rete testis. Last two belong to the genital duct system.

Seminiferous Tubules

The main function of seminiferous tubules is the process of sperms production called spermatogenesis.

The wall of seminiferous tubules consists of the following components:

1) a tunica of fibrous connective tissue. This outer layer also contains muscle-like (myoid) cells. Contractions of these cells probably help to move spermatozoa along the tubule.

2) a well-developed basal lamina;

3) a seminiferous or germinal epithelium.

Seminiferous epithelium consists of two general types of cells: spermatogenic cells and Sertoli cells. Sertoli cells also called supporting or sustentacular cells.

The spermatogenic cells are stacked up in 4-8 layers that occupy the space between the basal lamina and the lumen of the tubule. They represent the various stages in the continuous process of spermatogenesis.

The Sertoli cells are less numerous and nonproliferating cells with period of puberty. The Sertoli cells are columnar or irregular pyramidal shape cells with the complex of apical and lateral processes that surround the adjacent spermatogenic cells and fill the spaces between them. The Sertoli cells extend from the basal membrane to the lumen. The nucleus of Sertoli cells lying in basal part of cell is ovoid or angular, large, lightly stained and often contains a large nice visible nucleolus.

Adjacent Sertoli cells are bound together at the level of the spermatogonia by tight junctions of their lateral processes. Junctional complexes divide the seminiferous epithelium into two compartments: a basal (abluminal) and a superficial (adluminal). Tight junctions may temporarily open to permit the passage of spermatogenic cells from the basal compartment into the adluminal compartment. The spermatogonia are present in the basal compartment of seminiferous epithelium. More mature forms such as primary and secondary spermatocytes and spermatids are present in the adluminal compartment.

This compartmentalization serves *служит* as the blood-testis barrier. The function of the blood-testis barrier is to prevent an autoimmune reaction. The blood-testis barrier serves an essential role in isolating of adluminal compartment spermatogenic cells from the immune system. Therefore, spermatozoa and spermatocytes are recognized as "foreign" cells by the immune system at causes of some trauma of testis and surgical operation called vasectomy.

Functions of the Sertoli cells include:

- 1) Providing mechanical support for the spermatogenic cells.
- 2) Mediating the movements across the seminiferous epithelium of steroids, metabolites, and nutrients for the spermatogenic cells.
- 3) Participation in the formation of the blood-testis barrier that protect spermatogenic cells from autoimmune destruction.
- 4) Phagocytosis of degenerating spermatogenic cells and residual bodies. Residual body is excess cytoplasm that is shed from the spermatids during their maturation into spermatozoa.
- 5) Secretory function:

- a) secretion of fructose-rich testicular fluid to help nourish and move sperm from the seminiferous tubules to the epididymis;
- b) secretion of androgen-binding protein (ABP), to maintain the concentration of testosterone in the seminiferous tubules, thereby promoting spermatogenesis;
- c) secretion of antagonistic hormones - inhibin and activin, regulating FSH secretion by pituitary gland.
- d) secretion of anti-Mullerian hormone to prevent oviduct development from the Mullerian duct in the early stage of the male embryo.

Spermatogenesis

Spermatogenesis is the process by which spermatogonia develop into spermatozoa.

There are three phases of spermatogenesis:

- 1) Spermatogonial phase (mitotic), in which spermatogonia divide by mitosis to replace themselves as well as provide a population of spermatogonia that will eventually differentiate into primary spermatocytes;
- 2) Spermatocyte phase (meiotic), in which primary spermatocytes undergo two meiotic divisions to reduce both the chromosome number and amount of DNA to produce haploid cells;
- 3) Spermatid phase (spermiogenesis), in which spermatids differentiate into mature sperm cells.

Spermatogonia are the first cells of spermatogenesis. There are two types of spermatogonia in the human seminiferous epithelium. Type A spermatogonia have a rounded nucleus with very fine chromatin granules and one or two nucleoli. They are stem cells, which divide to form new generations of both type A and type B spermatogonia.

Type B spermatogonia have rounded nuclei with chromatin granules of different sizes, which often attach to the nuclear membrane, and one nucleolus. Although type B spermatogonia may divide repeatedly, they do not function as stem cells and their final mitosis always results in the formation of primary spermatocytes.

For mitotic phase the type B spermatogonia begin to differentiate into primary

spermatocytes. The primary spermatocytes increase in size. They immediately enter the prophase of the first meiotic division, which is extremely prolonged and lasts about 22 days. They pass through the leptotene, zygotene, pachytene, and diplotene stages of the meiotic prophase. Therefore, primary spermatocytes are cells in prophase of the first meiotic division.

The first meiotic division results in the formation of haploid secondary spermatocytes, which are smaller than primary spermatocytes. There is no replication of DNA in a secondary spermatocyte. They rapidly enter and complete the second meiotic division to produce spermatids.

Spermatids are small spherical cells with interphase nuclei. They undergo a maturation into spermatozoa. The process by which a spermatid becomes a spermatozoon is called spermiogenesis. For spermiogenesis the nucleus of spermatid undergoes condensation and changes shape to form the head of sperm. The Golgi complex is transformed into the acrosomic cap, which lie over one side of the nucleus. The acrosome marks the future anterior pole of the spermatozoon. It contains hydrolytic enzymes for penetration into the egg. The centriole divides into two parts. They migrate to the pole of the cell that is away from the acrosome. The axial filament grows out of the distal centriole. The region occupied by the two centrioles later becomes the neck of the spermatozoon. The proximal centriole forms the basal body. The part of the axial filament surrounded by mitochondria, and together with them forms the middle piece. Most of the spermatids cytoplasm of is shed, and is phagocytosed by Sertoli cells.

Complete spermatogenesis lasts about 64 - 74 days.

Leydig cells

The spaces between the seminiferous tubule are filled by loose connective tissue containing numerous blood vessels and interstitial or Leydig cells. Leydig cells constitute the endocrine component of the testis. They are large polygonal cells. The nucleus is large, round and often located eccentric in the cell. The cytoplasm is strongly acidophilic, and contain smooth endoplasmic reticulum, mitochondria with tubular cristae and lipid droplets. These ultrastructural features are seen in steroid-secreting

cells. They synthesize and secrete the principal circulating male androgen called testosterone. High local levels of testosterone within the testis are necessary for normal maturation of the sperms.

Hormonal regulation of testis

Spermatogenesis depends on the follicle stimulating (FSH) and luteinizing (LH) hormones of the pituitary gland. LH acts on the interstitial cells, stimulating the production of testosterone that promotes spermatogenesis. FSH acts on the Sertoli cells, stimulating the synthesis of androgen-binding protein (ABP). ABP protein combines with testosterone and is secreted into the lumen of the seminiferous tubules to maintain the concentration of testosterone in the seminiferous tubules.

Genital ducts

The series of ducts, which transport spermatozoa from the seminiferous tubules to the outside of the male body are called genital ducts. They include intratesticular genital ducts and extratesticular genital ducts. The intratesticular genital ducts lying within the testis are tubuli recti and rete testis. The extratesticular genital ducts include ductuli efferentes, ductus epididymis, ductus deferens and ejaculatory duct.

The ductuli efferentes and the ductus epididymis produce an organ anatomically binding with testis called epididymis. Epididymis is a comma shaped structure on the posterior-lateral aspect of testis. Anatomically it consists of head, body and tail.

About 12 to 20 ductuli efferentes arise from the rete testis. As the efferent ductules exit the testis, they become highly coiled and form 6 to 10 the coni vasculosi, whose bases form a head of the epididymis. At the lower end of the epididymis head, these tubules join to form a single convoluted ductus epididymis producing the body and tail of epididymis. The ductus deferens is a muscular more straight tube extending from the lower end of epididymis to the prostatic urethra.

The walls of genital duct system's most parts consist of 3 layers. They are mucous membrane, muscular membrane, providing the movement of spermatozoa, and adventitia.

The mucous membrane of genital duct system consists of epithelium and lamina

propria. There are different types of epithelium lining tubules of genital duct system.

The tubuli recti and rete testis are lined by simple cuboidal epithelium. Epithelial cells of tubuli recti and rete testis contain a few microvilli on apical parts.

Epithelium of ductuli efferentes is pseudostratified with three types of epithelial cells lying by alternating groups:

a) nonciliated cuboidal cells with microvilli (absorptive cells) that absorb the excess testicular fluid secreted in the seminiferous tubules;

b) ciliated columnar cells that provide the movement of spermatozoa and testicular fluid toward the epididymis;

c) basal cells which are stem cells, providing regeneration.

The basal cells are interspersed among the ciliated columnar cells.

The ductus epididymis and ductus deferens are lined by pseudostratified columnar epithelium, containing two types of cells:

1) The most numerous cells in this epithelium are called principal cells. They have long stereocilia (modified microvilli) on apical parts. Functionally the principal cells are secretory and absorptive cells. They absorb large volumes of testicular fluid. The principal cells also play an important role in the secretion of glycerophosphocholine, which inhibits capacitation of the premature sperm in the male reproductive tract. Capacitation is final step of sperm maturation. Normally, capacitation happens only after the sperm enters the female reproductive tract.

2) Basal cells are small, round cells resting on the basal lamina. They are the stem cells, providing regeneration.

Also, the epithelial cells lying the epididymis have capacity to phagocytose any residual bodies not removed by the Sertoli cells as well as sperm that degenerate in the duct.

Thus the main functions of epididymis are:

1) Phagocytosis of defective spermatozoa;

2) Absorption of excess testicular fluid;

3) Secretion of substances (sialic acid, glycerylphosphorylcholine) that play a role in maturation of spermatozoa.

Maturation of spermatozoa is acquisition of some motility after their passage through the epididymis. But, spermatozoa become fully motile only after ejaculation.

Prostate gland

The prostate is the largest accessory gland of the male reproductive system. The prostate surrounds the upper part of urethra where the urethra exits the urinary bladder.

At the periphery the prostate is surrounded by connective tissue capsule. The capsule and septa, penetrating into parenchyma of the prostate gland from capsule are fibromuscular stroma, because represented by two tissues:

- 1) fibrous connective tissue and
- 2) smooth muscle tissue.

The thick septa surround and separate the groups of prostate's glands. Thus, the parenchyma of the prostate is represented by 30 to 50 compound branched tubuloalveolar glands. They are arranged in 3 concentric areas around urethra and subdivided into mucosal, submucosal and main. The ducts of these glands open into the prostatic urethra. The shape of prostate's glands secretory portions is sometimes irregular. These glands are covered by simple or pseudostratified columnar epithelium. Spherical bodies called prostatic concretions or amyloid bodies (corpora amylacea) normally occur in some of the alveoli especially in older men. They are present condensation of the secretory products of gland. They are often calcified.

The prostate gland secretes slightly acid colorless fluid that is rich in prostatic acid phosphatase (PAP), fibrinolysin, citric acid, and prostate-specific antigen (PSA).

Prostate-specific antigen (PSA) is one of the most clinically important tumor markers, because in prostate cancer, serum concentration of PSA increases.

The prostatic acid phosphatase (PAP) is enzyme that regulates cell growth and metabolism of prostate glandular epithelium.

Fibrinolysin, secreted from the prostate gland, liquefies semen.

The secretory process of the prostate depends on testosterone.

The prostate gland produces secretions that empty into the urethra to mix with spermatozoa and seminal vesicles fluid to form semen.

Seminal vesicles

The seminal vesicles are paired, elongate, and highly folded tubular glands (about 15 cm in length) located on the posterior wall of the urinary bladder, parallel to the ampulla of the ductus deferens. A short excretory duct from each seminal vesicle combines with the ampulla of the ductus deferens to form the ejaculatory duct. The wall of the seminal vesicle consists of 3 layer: mucousa, thin muscule coat and external adventitia.

A folded mucousa forming primary, secondary and tertiary folds consists of 2 sublayers – epithelium and lamina propria. Epithelium is pseudostratified columnar. It consists of nonciliated columnar cells and short, round cells. The short cells are the stem cells from which the columnar cells are derived. The columnar cells have the morphology of protein-secreting cells, with a well-developed rER and large secretory vacuoles in the apical cytoplasm.

The epithelium of seminal vesicles depends on hormonal support of testosterone.

The secretion of the seminal vesicles is a whitish yellow, viscous material, containing ascorbic acid, fructose and prostaglandins. Fructose is important for the nutrition of spermatozoa, and prostaglandins may assist fertilization by an influence on the female reproductive tract.

Bulbourethral glands

The bulbourethral glands are paired bodies, each the size of a pea lying in the connective tissue behind the membranous urethra. Each bulbourethral gland is compound tubule-alveolar gland whose duct enters the posterior portion of the cavernous segment of the urethra.

The bulbourethral gland is surrounded by connective tissue capsule. The connective tissue septa with skeletal muscle fibers pass into the gland to divide it into lobules.

The secretory end pieces which may be alveolar, saccular or tubular shape are covered simple cuboidal or columnar epithelium. The secretory ducts are lined with a pseudostratified epithelium with patches of mucous cells.

The secretion of bulbourethral glands is a clear mucous that acts as a lubricant of

the penile urethra.

Semen

Semen contains sperms and fluid from the testis and secretory products from the epididymis, ductus deferens, prostate, seminal vesicles, and bulbourethral glands.

The average ejaculate of semen has a volume of about 3 mL and normally contains up to 100 million sperm per milliliter. It is estimated that 20% of the sperm in any ejaculate are morphologically abnormal and nearly 25% are immotile.