HISTOLOGY OF THE
MALE REPRODUCTIVE SYSTEM

Learning Objectives:
1. Describe the histology of and identify, in order, the passageways through which sperm pass as they exit from the body.
2. Describe the process of spermatogenesis and the cytology of the cells involved in that process.
3. Describe the blood-testis barrier and the cell that forms it.
4. Describe the cytology of the endocrine cells in the testis.
5. Identify the genital glands and describe their histology.
6. Describe the histology of the penis and the process of erection.

I. General concepts

A. Components

1. Testis - paired organs
   a. Seminiferous tubules
   b. Rete testis

2. Genital ducts
   a. Epididymis – paired organs
   b. Ductus deferens – paired ducts
   c. Ejaculatory duct – paired ducts
   d. Urethra

3. Major genital glands
   a. Seminal vesicles - paired glands
   b. Prostate - single gland
   c. Bulbourethral glands - paired glands

4. Penis

B. Functions of the male reproductive system components

1. Produce sperm
2. Produce male sex hormones
3. Produce seminal fluid
4. Propel sperm and seminal fluid (semen) to exterior
5. Copulation
THE TESTIS

I. General organization

A. Paired, ovoid organ - serves both exocrine (sperm production) and endocrine (testosterone production) functions

B. Coverings and CT framework (from external to internal):
   1. Scrotum: skin, muscle, connective tissue sheaths
   2. Tunica vaginalis
      a. Peritoneum that accompanied the testis in its embryological, retroperitoneal descent.
      b. Lines the interior surface of the scrotum (parietal layer)
      c. Covers anterior surface and sides of testis but not its posterior surface (visceral layer)
   3. Tunica albuginea - a layer of dense connective tissue beneath the tunica vaginalis
4. Mediastinum testis
   
a. Thickening of tunica albuginea, projecting into the testis from its posterior surface.

b. Contains the rete testis, a network of ducts that connect with the seminiferous tubules

5. Septa - CT partitions extending from the mediastinum to the tunica albuginea; separate each testis into about 250 lobules

C. Internal structure of testis
   
1. Consists of lobules that are pyramidal in shape with their apices directed toward the mediastinum and their bases adjacent to the tunica albuginea.

2. Composition of lobules
   
a. Stroma: loose CT, many blood vessels and lymphatics
b. Parenchyma

i. Seminiferous tubules - convoluted portion

1. 1-4 loop-shaped, tortuous tubules per lobule with both ends opening at the mediastinum; connect with the rete testis

2. Lined by the seminiferous epithelium where spermatozoa production occurs

3. Surrounded by a tunica propria, a connective tissue layer located beneath the basal lamina of the seminiferous epithelium with myoid (contractile) cells.

ii. Seminiferous tubules - straight portion (tubuli recti)

1. Non-coiled, terminal ends of each seminiferous tubule; connect with the rete testis in the mediastinum.

2. Lined by Sertoli cells only

iii. Interstitial cells of Leydig - clusters of endocrine cells lie within the CT stroma outside the seminiferous tubules; produce testosterone

II. Microscopic appearance and functions of the testis parenchyma

A. Interstitial cells of Leydig (endocrine portion)

1. Arranged as isolated clusters of cells in stroma between seminiferous tubules

2. Cytology

   a. Euchromatic nucleus

   b. Eosinophilic cytoplasm contains organelles indicative of steroid-hormone production: abundant SER, mitochondria with tubular cristae and lipid droplets

3. Secrete testosterone under the influence of luteinizing hormone (LH), from the gonadotrope cells in the adenohypophysis

B. Seminiferous tubules (exocrine portion) – lined by the seminiferous, or germinal, epithelium composed of Sertoli cells and spermatogenic (germ) cells
1. Sertoli cells (supporting cells)
   a. Tall, columnar cells that rest on the basement membrane and extend to the lumen.
   b. Nucleus - euchromatic, ovoid and infolded; its long axis usually lies perpendicular to, but not immediately adjacent to, the basement membrane.
   c. Numerous lateral processes surround and invest maturing germ cells. The most basal of these processes forms a series of occluding (tight) junctions with similar processes of adjacent Sertoli cells.
   d. Blood-testis barrier
      i. Formed by occluding junctions between lateral processes of adjacent Sertoli cells; dividing the seminiferous epithelium into basal and luminal compartments
      ii.) Basal compartment – fluid access to blood-borne materials and contains spermatogonia and earliest primary spermatocytes
      iii.) Luminal compartment
         1. Provides a unique microenvironment for developing germ cells that protects these cells from immunologic attack and concentrates hormones needed for sperm production.
         2. Contains later primary spermatocytes, secondary spermatocytes, and spermatids.
   e. Function regulated by follicle stimulating hormone (FSH) from the gonadotrope cells in the adenohypophysis
   f. Functions
      i. Mediate exchange of nutrients to germ cells
      ii. Form blood-testis barrier to protect developing germ cells from immunologic attack
      iii. Breakdown excess spermatid cytoplasm
      iv. Produce testicular fluid
v. Secrete androgen-binding protein that binds to and concentrates testosterone in the seminiferous epithelium

vi. Produce inhibin which inhibits the secretion of follicle stimulating hormone (FSH) from the adenohypophysis

vii. Orchestrate movement of germ cells through germinal epithelium and facilitate cytodifferentiation and subsequent release of spermatozoa into the lumen of the seminiferous tubule

2. Spermatogenic (germ) cells

a. Form a stratified, germinal (seminiferous) epithelium

b. Spermatogonia

i. Diploid cells resting on the basement membrane.

ii. Present as two varieties

1. Type A - divide mitotically to perpetuate self and to form Type B spermatogonia

2. Type B - divide mitotically to form primary spermatocytes

iii. Undergo incomplete cytokinesis so cells remain attached to each other during spermatogenesis
c. Primary spermatocytes
   i. Largest germ cell; nucleus is 1.5x larger than that of a spermatogonium nucleus
   ii. Form in the basal compartment, then probably migrate through the tight junctions between Sertoli cell processes to the luminal compartment.
   iii. Remain in prophase about one-third of the spermatogenic cycle, so many are seen. Nuclei contain highly condensed chromosomes.
   iv. Diploid cells that complete meiosis I (reductional division) to form secondary spermatocytes.

d. Secondary spermatocytes
   i. Haploid cells, nuclei are similar in size to those of the spermatogonia
   ii. Present for only eight hours of the entire 74-day spermatogenic cycle, therefore, very few are seen.
   iii. Divide by meiosis II (equational division) to form spermatids.

e. Spermatids
   i. Haploid cells whose nuclei are initially about two-thirds the size of spermatogonia nuclei.
   ii. Located near the lumen of the seminiferous tubules
   iii. Do not divide but undergo cyto-differentiation to form spermatozoa by a process called spermiogenesis.
      A. Intercellular bridges break down.
      B. Nucleus condenses and elongates
      C. Acrosome forms. An acrosome is a large vesicle that contains hydrolytic enzymes and is abundant carbohydrates. The enzymes aid the sperm in penetrating the zona pellucida surrounding the secondary oocyte.
D. Flagellum forms.
E. Excess cytoplasm is shed.

f. Spermatozoa
   i. Are haploid cells.
   ii. Are anatomically mature, but incapable of fertilization at this time.
   iii. Are released from Sertoli cells into the lumen of the seminiferous tubules by a process called spermiation

III. Spermatogenesis is the process by which diploid germ cells (spermatogonia) in the basal compartment become haploid spermatozoa lying free in the lumen of the seminiferous tubules.

A. Stages:
   1. Spermatocytogenesis - mitotic divisions of spermatogonia (diploid) to form primary spermatocytes (diploid); cytokinesis is incomplete.
   2. Meiosis - two cell divisions convert diploid cells to haploid, i.e., reduction of chromosomes and DNA by half; cytokinesis is incomplete.
      a. Meiosis I: Primary spermatocytes (diploid) form secondary spermatocytes (haploid)
      b. Meiosis II: Secondary spermatocytes form spermatids (haploid)
   3. Spermiogenesis - cytodifferentiation of spermatids (haploid) into spermatozoa (haploid)
   4. Spermiation - Release of mature sperm into lumen of seminiferous tubule

B. Under control of follicle stimulating hormone (FSH) from the adenohypophysis
C. Spermatogenesis lasts about 74 days with a new cycle beginning in any given location about every 16 days.

### STAGES OF SPERMATOGÉNESE

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<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tr>
<td>SPERMATOCYTOGENESIS (Mitosis)</td>
<td>Diploid - Spermatogonia (44+XY)</td>
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<tr>
<td>MEIOSIS I</td>
<td>Diploid - Primary spermatocytes (44+XY)</td>
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<td>MEIOSIS II</td>
<td>Haploid - Secondary spermatocytes (22+X or Y)</td>
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<td>SPERMIOGENESIS (Cytodifferentiation)</td>
<td>Haploid - Spermatids (22+X or Y)</td>
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<td>SPERMATION</td>
<td>Haploid - Spermatozoa (22+X or Y)</td>
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IV. Course of sperm within testis

A. Seminiferous tubules, convoluted portion: germinal epithelium where sperm production occurs; sperm released into lumen of this tubule from Sertoli cells

B. Seminiferous tubules, straight portion (tubuli recti)
   1. Lined by lined by simple columnar epithelium whose cells resemble Sertoli cells
   2. Connects convoluted portion of seminiferous tubules with rete testis

C. Rete testis
   1. Meshwork of channels within mediastinum of testis
   2. Lined by simple cuboidal cells, many of which possess a single flagellum.
   3. Connects straight portion of seminiferous tubules with efferent ducts leading to the head of the epididymis
GENITAL DUCTS
EXTERNAL TO THE TESTIS

I. Epididymis

A. A comma-shaped organ lying posterior to the testis that is divided into head, body and tail subdivisions.

B. Head region composition:

1. Efferent ducts

   a. Connect rete testis with duct of epididymis

   b. Consist of about 20 ducts, each of which is coiled into a cone shape. Each duct connects with the rete testis at the apex of the cone adjacent to the testis. All ducts anastomose to form the single duct of the epididymis at the bases of the cones.

   c. Form about 12 coni vasculosi (sing. conus vasculosus) that are composed of one coiled efferent duct plus its surrounding connective tissue that contains abundant blood vessels.
d. Histology

1. Lined with a simple epithelium composed of alternating taller, ciliated cells and shorter cuboidal cells with lysosomes. Therefore, efferent ducts present a characteristic, scalloped border adjacent to the lumen.

2. A thin muscularis layer surrounds the epithelium.

e. Function

1. Ciliated cells propel spermatozoa to duct of epididymis

2. Cuboidal cells absorb testicular fluid

2. Duct of epididymis - a single duct formed by fusion of efferent ducts

C. Body and tail regions of the epididymis

1. Contains the remainder of the duct of the epididymis

   a. Highly coiled, single tube (5 m long) formed by union of efferent ducts in the head region

   b. Lined by tall pseudostratified columnar epithelium with stereocilia, that decreases in height from head to tail regions. Creates a smooth lumen when compared with efferent ducts.

   c. Smooth muscle layer surrounds epithelium and increases in thickness and number of layers from head to tail.
2. Function
   a. Storage and maturation site for sperm
   b. Absorption of excess testicular fluid
   c. Movement of sperm toward ductus deferens

II. Ductus (vas) deferens
   A. A thick muscular tube conveying and propelling sperm from duct of epididymis to the ejaculatory duct.

   B. Composition
      1. Mucosa: longitudinal folds produce an irregular lumen
         a. Pseudostratified columnar epithelium with stereocilia surrounds a narrow lumen
         b. Thin lamina propria
         c. Muscularis mucosae is not present.

      2. Thick muscularis - inner and outer longitudinal, middle circular layers of smooth muscle

   C. Course
      1. Located in spermatic cord in the inguinal canal along with the spermatic artery, pampiniform venous plexus, and a nerve plexus
      2. Enters abdominal cavity through the inguinal canal, crosses above entrance of ureter into bladder, and enlarges to form the ampulla, that lies posterior to urinary bladder
      3. Joined by the duct of the seminal vesicle just before it enters the prostate

   D. Transports and propels sperm from the duct of the epididymis to ejaculatory duct in prostate

III. Ejaculatory duct
   A. The ejaculatory duct is formed by the union of the ductus deferens with the duct of the seminal vesicle.
B. No muscle layer is retained from the ductus deferens.
C. The ejaculatory duct traverses the prostate gland to join the prostatic urethra.

IV. Urethra

A. Prostatic urethra - within prostate; lined with transitional epithelium
B. Membranous urethra - pierces urogenital diaphragm (skeletal muscle); lined with stratified or pseudostratified columnar epithelium
C. Penile urethra - (discussed with penis)

GENITAL GLANDS

I. Seminal vesicles

A. Paired glands lying posterior to urinary bladder
B. Each is composed of a single, highly tortuous tube
C. Function - provides the bulk of the seminal fluid containing fructose, citrate, proteins and prostaglandins

D. Microscopic anatomy

1. Mucosa
   a. Pseudostratified columnar epithelium rests on a thin lamina propria.
   b. Mucosa is thrown into an intricate system of primary, secondary and tertiary folds to increase surface area. All of the irregular chambers thus formed, however, all communicate with the lumen.

2. Muscularis: thin layer surrounded by a fibrous coat. Muscularis contracts during ejaculation to discharge the secretion

II. Prostate

A. Single, midline gland; largest of the genital glands; surrounds the prostatic urethra

B. 30-50 tubulo-acinar glands open into the prostatic urethra; divided into three groups, central, transitional and peripheral. The peripheral glands constitute 70% of the prostate.

D. Capsule: dense connective tissue with abundant smooth muscle; septa from the capsule also possesses smooth muscle fibers and partition the gland into indistinct lobes.

E. Epithelium: usually pseudostratified columnar epithelium whose height varies with its
activity

F. Prostatic concretions - lamellated, spherical bodies that are the condensation of secretory products. The number of concretions increases with age.

G. Function - contributes a thin, milky fluid to semen, that is rich in citric acid and acid phosphatase. Contains hydrolytic enzymes including Prostate Specific Antigen (PSA) a serine protease and fibinolysin

H. Pathology

1. Benign prostatic hypertrophy (BPH)
   a. Present in 95% of men over 70, BPH is caused by hyperplasia of glands in the central and transitional zone.
   b. Leads to obstruction of urethra leading to urination problems

2. Prostate cancer - second most common cancer in males; originates in glands of the peripheral zone.

PENIS

I. Composition

A. Three cylindrical masses of erectile tissue

1. Corpora cavernosa - paired dorsal cylinders

2. Corpus spongiosum (corpus cavernosum urethrae)

   a. Single, ventral cylinder that houses the penile urethra
b. Expands to terminate in glans penis that caps the two corpora cavernosae

B. Microscopic anatomy

1. Outer covering of skin (epidermis and dermis)

2. Tunica albuginea
   a. Outer capsule of dense, non-elastic CT surrounding the three cylinders
   b. Thicker around corpora cavernosa than around corpus spongiosum
   c. Forms an incomplete septum between the corpora cavernosa

3. Structure of erectile tissue
   a. Sponge-like cavernous spaces (venous spaces) separated by CT trabecula with smooth muscle fibers
   b. Deep artery in each corpus cavernosum supplies blood to:
      i. Nutritive arteries that supply trabecula
      ii. Helicine arteries that supply cavernous spaces during erection

II. Process of erection

A. Flaccid state is effected by a minimal blood flow to the penis. This blood flow is regulated by the continuous input of the sympathetic division of the autonomic nervous system on the tone of the smooth muscle in the penile vasculature.
B. Erection
   a. Parasympathetic division of autonomic nervous system effects relaxation of smooth muscle (vasodilation) of the deep and helicine arteries.
   b. The subsequent filling of the cavernous spaces expands these vessels against the tunica albuginea, causing the penis to become erect and turgid.
   c. Corpus spongiosum does not become as erect as the other cavernous bodies because the tunica albuginea is thinner here. Therefore, sperm can be transported during ejaculation.

C. Return to flaccid state occurs with decline of parasympathetic activity.

III. Penile urethra
   A. Located within corpus spongiosum (corpus cavernosum urethrae)
   B. Microscopic anatomy
      1. Epithelium: pseudostratified columnar epithelium becomes stratified squamous moist in fossa navicularis, the terminal enlargement in glans penis
      2. Glands of Littre
         a. Mucous-secreting glands
         b. Originate in mucous-secreting recesses of urethra and extend obliquely toward base of penis
         c. Secrete a mucous fluid that is the initial ejaculate; provides lubrication

Virtual slides: Testis

You are responsible for identifying the following structures in the CD-ROM images.

**Immature Testis**
- Visceral and parietal layers of tunica vaginalis
- Processes vaginalis
- Tunica albuginea
- Mediastinum
Rete testis
Seminiferous tubules—convoluted portions
Seminiferous tubules—straight portions (tubuli recti)

Testis
Tunica albuginea
Mediastinum
Interstitial cells of Leydig
Sertoli cells
Spermatogonia
Primary spermatocytes
Spermatids
Spermatozoa

Genital ducts
Tubuli recti
Rete testis
Efferent ducts
Coni vasculosi
Duct of the epididymis
Head of epididymis
Body and tail of epididymis
Ductus deferens

Spermatic cord
Ductus deferens
Testicular artery
Pampinoform plexus of veins
Peripheral nerves

Genital glands
Seminal vesicle
Prostate
Prostatic concretions

Penis
Corpora cavernosa
Corpus spongiosum
Tunica albuginea
Deep arteries
Cavernous sinuses
Urethra
Glands of Littre