MALE REPRODUCTIVE SYSTEM

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READINGS

Educational Goals

- Review gross structural and functional relationships of the male reproductive organs
- Investigate the microscopic structure of the testis and seminiferous epithelium
- Investigate the microscopic structure of the male genital ductal system
- Investigate the microscopic structure of the male accessory sex glands
- Investigate the microscopic structure of the penis and male urethra

Key Words

- Blood-testis barrier
- Efferent ductules
- Leydig cell
- Mediastinum testis
- Myoid cell
- Rete testis
- Sertoli cell
- Sperm flagella
- Spermatid
- Spermatocyte
- Spermatogenesis
- Spermatogonial stem cell
- Spermiogenesis
- Tubuli recti
- Tunica albuginea
- Tunica vaginalis

Introduction

The male reproductive system includes the testes, genital ducts, accessory reproductive glands, and penis. The testes, epididymis and initial portion of the ductus (vas) deferens are located within the scrotal sac. The paired testes serve as a site for spermatogenesis and hormone production. Sperm are propelled toward the accessory glands passively and actively (by peristaltic contraction) within the male genital ductal system. Along the way, the prostate gland, seminal vesicles, and bulbourethral glands contribute their
secretory products to produce semen. The penis serves as the conduit for transmission of semen into the female reproductive tract during sexual intercourse.

Structure of the Testis

Paired testes are each located in the scrotal sac outside of the abdominal cavity. This location assures a reduced temperature for the normal development of sperm. The epididymis is associated with the posterior aspect of the testis. A thick layer of connective tissue, the tunica albuginea, surrounds the testis and in the region where the rete testis is located the former is thickened even further to form the mediastinum of the testis. Fibrous septae extend from the region of the mediastinum into the testicular mass and subdivide the testis into 250 individual lobules (see Figure next page).

Within each lobule there are 1-4 seminiferous tubules. The seminiferous tubule has a U-shaped configuration with each end being continuous with the rete testis. Each seminiferous tubule is approximately 40-80 cm in length and roughly 150 µm in diameter. They end at the end at the mediastinum testis by straightening out, forming tubuli recti. These ducts consist of a specialized epithelium and a basal lamina. Products generated by the epithelium of the seminiferous tubules are conveyed to the rete testis. The gland consists of the following layers:

A. Tunica Albuginea

Thick, connective tissue capsule of the testis

Mediastinum Testis

- thickened, posterior portion of the tunica albuginea
- gives rise to connective tissue septa which extend into the parenchyma,
- divides the testis into incomplete compartments (about 250 lobules)
- blood vessels, lymphatic channels, and efferent ductules pass through the mediastinum as they enter/exit the testis

Tunica Vasculosa

- inner layer of tunica albuginea
- loose connective tissue with abundant blood vessels
- its vessels penetrate septa to reach and supply the lobular tissue

B. Tunica Vaginalis
Serous sac embryologically derived from peritoneum

C. Lobuli Testis
- pyramidal shaped compartments; form the structural unit of the testis
- bounded by connective tissue septae each lobule is comprised of 1-4 seminiferous tubules positioned within a loose connective tissue stroma

Seminiferous Tubules

The specialized epithelium lining the seminiferous tubules is composed primarily of two distinct cell types surrounded by a basement membrane. The two primary cell types are somatic Sertoli cells and germinal spermatogenic cells. The latter include spermatogonia, spermatocytes and spermatids. The wall of the seminiferous tubule contains collagen fibers, fibroblasts, and contractile cells termed myoid cells.

Contractions of myoid cells are responsible for moving non-motile sperm from the lumen of the seminiferous tubules to the rete testis. The space between the loops of the
seminiferous tubules contains blood vessels, lymphatic channels, macrophages and androgen-producing cells known as **interstitial cells of Leydig**.

Histologic features of the seminiferous epithelium include (see Figure below):

- complex stratified epithelium
- rests on a basal membrane that conveys signals to gonial stem cells
- organized into poorly-defined layers
- lines the lumen of each seminiferous tubule
- site of spermatogenesis (occurs in waves along the length of tubules)
- consists of 2 principal cell types: **Spermatogenic (germline cells) and Sertoli cells**

**Interstitial Tissue of the Testis**

- lamina propria/fibrous connective tissue stroma
- surrounds the seminiferous tubules
- houses neural and vascular elements (capillary endothelial cells)
- fibroblasts and myoid cells
- interstitial cells of **Leydig** (these cells produce **androgens**)

**Leydig Cells**

The Leydig cells, arranged in aggregates, are located within the space surrounding the seminiferous tubules. These are steroid-producing cells and as such contain lipid droplets, a well-developed smooth ER and mitochondria with tubular cristae. Leydig cells respond to LH by synthesizing **testosterone**. Approximately 95% of the testosterone in the blood is synthesized by the Leydig cells, while the remainder is derived from the adrenal cortex.
Testosterone is maintained in high concentrations in proximity to the seminiferous tubules by Androgen-Binding Protein (ABP) which is synthesized and secreted by Sertoli cells into the lumen of seminiferous tubules.

**Sertoli Cells**

Prior to puberty the Sertoli cells represent the principal cell type within the seminiferous epithelium. Once puberty occurs, these cells represent only 10% of cells in the seminiferous epithelium. Sertoli cells become the predominant cell type in this epithelium when the patient becomes elderly.

Sertoli cells have a characteristic columnar appearance and extend from the basal lamina to the lumen of the seminiferous tubule. The plasma membrane of these Sertoli cells has an irregular outline as they provide crypts in which developing spermatogenic cells, in various stages of differentiation, are housed. The nuclear membrane of the Sertoli cell often displays indentations and heterochromatin is typically associated with its nucleolus.

**Key Point:** Adjacent Sertoli cells are united near their basal aspect by **occluding junctions** (tight junctions) and thus separate the seminiferous tubule into basal and adluminal compartments. This specific arrangement represents the **blood-testis barrier**. Histological and biological features of Sertoli cells include the following:

- nondividing (post-mitotic) cell
- columnar cell, rests on basal lamina
- large, pale oval to triangular nucleus with large, dense nucleolus
- nutritive cell; supports developing spermatogenic cells
- phagocytoses (engulfs) extruded residual body cytoplasm during spermiogenesis

**Zonulae occludentes** (tight junctions) between adjacent Sertoli cells serve to:

- establish the **blood-testis barrier**
- spare spermatogenic cells from auto-immunologic destruction
- compartmentalize the seminiferous epithelium

**Sertoli Cell Functions**

Sertoli cells support, protect and nourish developing spermatogenic cells. They also **phagocytose residual bodies** which have been discarded by spermatids near the end of spermiogenesis. In addition to secreting fluid rich in proteins and ions into the tubule lumen, Sertoli cells also facilitate the release of mature spermatids into the tubule lumen during a process known as spermiation.

Sertoli cells also synthesize and secrete **androgen-bonding protein** (ABP) in response to stimulation by FSH. **Inhibin** and **activin** subunits are also synthesized and secreted by
the Sertoli cells. Fetal and neonatal Sertoli cells synthesize **mullerian-inhibiting substance**, which inhibits development of paired paramesonephric ducts (i.e., inhibits formation of fallopian tubes and the uterus).

**Spermatogenic (Germinal) Cells**

Spermatogenic cells replicate by mitosis and differentiate by way of meiotic divisions into mature haploid sperm that are released into the lumen. Spermatogenesis does not occur synchronously in all seminiferous tubules. As they progress through specific stages, maturing cells gradually move through the epithelial layers towards the lumen.

- Spermatogonia (Type A are true stem cells and Type B are progenitor cells)
- Primary spermatocytes
- Secondary spermatocytes
- Spermatids
- Spermatozoa

**Spermatogonia** are in direct contact with the basal lamina of the seminiferous tubule wall and lie outside of the blood-testis barrier. These cells are derived from successive mitotic divisions of spermatogonial stem cells starting at puberty.

Spermatogonia differentiate into **primary spermatocytes** that yield two **secondary spermatocytes** following the first meiotic division. The second meiotic division results in the formation of two **spermatids** from each secondary spermatocyte. It takes days for the first meiotic division to be completed while the second meiotic division takes only minutes. Hence, primary spermatocytes are the most prevalent cell type present within the seminiferous epithelium. Spermatocytes and spermatids are connected by **intracellular bridges** that allow free passage of mRNA and protein between differentiating cells. These bridges are lost from spermatozoa prior to their release.

**Spermatids and Spermiogenesis**

The spermatids lie in the adluminal compartment and within crypts of the Sertoli cell plasma membrane. **Spermiogenesis** is the process by which spermatids differentiate into sperm. This process is characterized by three major events: (1) development of a flagellum, (2) development of an **acrosome** and (3) nuclear condensation.

**Mature sperm**

The mature sperm consists of a **head** and **tail** united by a **connecting piece**. The tail is further subdivided into three regions: **middle piece**, **principal piece** and **end piece**. A **condensed nucleus** and an **acrosome** comprise the head of the sperm. The latter contains a number of enzymes necessary for the process of fertilization. A microtubular **axoneme**, and outer dense fibers surrounded by **helically arranged mitochondria** characterize the
middle piece. The longest portion of the tail is the principal piece consisting of the centrally located axoneme surrounded by seven outer dense fibers and a fibrous sheath. Only the axoneme is present within the very short end piece of the tail.

Genital Ducts (Tubuli Recti, Rete Testis and Ductuli Efferentes)

A long intricate system of ducts convey sperm, testosterone, and fluid through the male pelvis. The male genital ductal system is divided into 2 groups of ducts that have unique embryologic origins: the intra-testicular ducts (tubuli recti and rete testis) and the extra-testicular (excretory) ducts.

**Tubuli Recti**
- located in lobuli testis
- short, straight tubules
- termination of seminiferous tubule
- lined by simple epithelium composed of Sertoli cells

**Rete Testis**
- located in mediastinum testis
- labyrinthine plexus of anastomosing ducts
- lined by simple cuboidal epithelium

Sperm pass from the seminiferous tubules through the **tubuli recti** to the rete testis. The tubuli recti are lined by simple cuboidal epithelium with occluding junctions at the apical ends of the cells. The **rete testis** is comprised of irregular anastomosing networks lined by simple cuboidal epithelium.

After passing through the rete testis, sperm enter the **ductuli efferentes** lined by a simple cuboidal epithelium that functions to absorb fluid from the lumen. Ciliated cells are also present and help transport sperm. The identifying characteristic of the ductuli efferentes
is the **scalloped-appearance** of its epithelium. Some **smooth muscle cells** surround the epithelium and its basal lamina.

Histologic features of the ductuli efferentes are summarized below:

- located in head of the epididymis
- about 15 tubules
- drain sperm from rete testis into ductus epididymis
- lined by simple cuboidal and columnar epithelium, with some ciliated cells
- lumen has a highly scalloped appearance

**Epididymis**

Spermatozoa mature within the confines of the epididymis, a highly coiled tube 4-6 cm in length. It is subdivided into **head**, **body** and **tail** regions. The epididymis is lined by a **pseudostatified columnar epithelium** possessing long, branching microvilli termed **stereocilia**. The epithelium is taller in the head region and shorter in the tail. Columnar cells and rounded basal cells constitute the primary cell types of the epithelial lining.

The epithelium of the epididymis also contains **intraepithelial lymphocytes**. Sperm transport is facilitated by contraction of smooth muscle cells in the epididymis wall that are arranged in outer longitudinal and inner circular layers. Histologic features of the epididymis are summarized below:

- lined by pseudostratified columnar epithelium with **stereocilia (long microvilli)**
- two cell types: short basal cells (with round nuclei) and tall columnar cells (with oval nuclei)

**Ductus Deferens (Vas Deferens)**

Like the epididymis, its epithelium is **pseudostatified columnar**. The smooth muscle cells of its wall are arranged in inner and outer longitudinal layers with a **middle circularly-arranged layer** between them.

As the ductus deferens approaches the prostate gland it enlarges to form the **ampulla**. On each side, the ductus deferens unites with the **seminal vesicle** to form the **ejaculatory duct** that passes through the substance of the prostate gland to enter the **prostatic urethra**. Histologic features of the vas deferens are summarized below:

- thick walled muscular tube
- location: **spermatic cord** (inguinal canal, abdominal cavity)
- pseudostatified columnar epithelium
- muscular wall has 3 layers of smooth muscle: inner longitudinal layer, middle circular layer, and outer longitudinal layer
Seminal Vesicles

There are 3 male accessory sex glands: paired seminal vesicles, prostate gland, and bulbourethral glands. Their secretions contribute to the fluid of semen, which aids in gamete transport and function. Each seminal vesicle is composed of an outer connective tissue layer and a middle layer of circularly and longitudinally arranged smooth muscle. This organ is a highly coiled blind tube that is lined by an epithelium that ranges from simple cuboidal to pseudostratified columnar.

Epithelial cells of the seminal vesicles secrete a fluid rich in fructose that accounts for 50% to 70% of the volume of the ejaculate. The open end of the seminal vesicle joins the ductus deferens to form the ejaculatory duct.

Histologic features of the seminal vesicle are summarized below:

- long, narrow convoluted gland
- mucosa = pseudostratified columnar epithelium
- connective tissue core of mucus membrane thrown into extensive folds
- adventitia = fibroelastic connective tissue
- secretory product: rich nutritive, yellow fluid

Prostate Gland

The prostate gland is a large gland located between the urinary bladder and the root of the penis. It houses the prostatic portion of the urethra and its wall is traversed by the ejaculatory ducts as they obtain the lumen of the prostatic urethra. The prostate is composed of 30-50 branched tubuloalveolar glands lined by simple or pseudostratified columnar type epithelium. Secretory products of these glandular elements are ultimately delivered to prostatic urethra as the glands open into the prostatic sinuses on each side of the midline crest located along its posterior wall.

The prostatic gland is typically arranged into 3 regions: (a) transition zone - periurethral mucosal glands, (b) central zone - submucosal glands, and (c) peripheral zone - main glands. Cells of the prostatic glands secrete prostate-specific acid phosphatase, prostate-specific antigen, amylase and fibrinolysin. In elderly individuals the lumen of the prostatic glands contains prostatic concretions, known as corpora amylacea that are rich in glycoproteins and may become calcified. The prostatic urethra is lined by transitional epithelium.

Histologic features of the prostate gland are summarized below:

- largest accessory gland
- multiple glands ensheathed in single capsule
- branched tubuloalveolar units
- arranged in 3 layers: transitional, central, peripheral
simple or pseudostratified columnar epithelium

**corpora amylacea** (prostatic concretions) found in prostatic lumina

thick fibroelastic capsule gives rise to connective tissue stroma (with accompanying smooth muscle and vasculature)

secretory products: thin, white fluid containing prostatic acid phosphatase and other proteolytic enzymes

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**Penis**

The penis is composed of three cylindrical masses of **erectile tissue**: paired **corpora cavernosa** and the ventrally-located **corpus spongiosum**. The latter contains a portion of the urethra. Each of the erectile masses is surrounded by a dense layer of connective tissue termed the **tunica albuginea**. The distal aspect of the corpus spongiosum expands to form the **glans penis** that in turn covers the distal aspect of each corpora cavernosum.

Each erectile tissue mass is composed of irregular, interconnected vascular spaces (sinusoids) supplied by an artery and drained by numerous venous channels. The sinusoids fill with blood during erection and compression of the venous channels helps to maintain the erect state by preventing blood from exiting via the venous channels.

**Bulbourethral (Cowper’s) glands** are small, paired glands that empty their secretions into the penile urethra. They are lined by a mucous-secreting glandular epithelium. This secretion serves as lubrication during sexual intercourse. The epithelial lining of the penile and membranous urethra is composed of **pseudostratified columnar epithelium**. Some stratified columnar epithelium may also be present. Histologic features of Cowper’s glands are summarized below:

- simple cuboidal or columnar epithelium
- thin fibroelastic capsule - gives rise to septa which subdivides the gland
- secretory product - mucus released into urethra