Male Reproductive System

Introduction

Given the large number of genetically engineered mouse models generated and studied as models for human prostate carcinoma, it is important for researchers and pathologists to know the normal anatomy and histology of both the mouse and the human male urogenital tract and to understand the anatomical differences between mouse and human. Genetically engineered mouse models can exhibit changes not seen in the human. The prostate gland exemplifies this point. The mouse prostate is divided into four lobes, where each lobe is histologically distinct. Conversely, the human prostate is a single organ without lobes. The mouse also contains additional accessory sex glands that are not found in the human. Consequently, these glands in mouse should not be interpreted as an abnormal finding. Histologic characteristics are important to understanding the phenotype of mouse models of human disease. A basic understanding of the normal histology of the urogenital organs of mouse and human is essential for proper interpretation and characterization of mouse models of disease.

Anatomy and Histology of the Human and Mouse Male Urogenital Tract

In the mouse, the male reproductive system consists of paired testes; extratesticular ducts, which include the efferent ducts, epididymis, and vas deferens; and the accessory sex glands, which consist of seminal vesicles, prostate gland, bulbourethral glands, ampullary glands, and preputial glands and the urethra and penis. The ampullary glands and preputial glands are unique to the mouse (Table 1 and Figure 1).

In the human, the male reproductive system consists of the paired testes; a system of ducts consisting of ductuli efferentes, epididymis, ductus deferens, and the ejaculatory duct; and exocrine glands, which include the paired seminal vesicles,
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#### FIGURE 1 The male mouse reproductive system
The reproductive tract consists of paired testes, epididymis, vas deferens, and the accessory sex glands which consist of paired seminal vesicles, prostate lobes, ampullary glands, bulbourethral glands, preputial glands, and the penis. Source: Adapted with permission from Anatomy of a Laboratory Mouse, Cook, M.J., 1965, with permission from Elsevier.

#### Need-to-know
- Mice have ampullary and preputial glands.

#### FIGURE 2 The male human reproductive system

#### Need-to-know
- Humans lack ampullary and preputial glands.
Male Reproductive System

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Lawrence True
University of Washington School of Medicine, Seattle, WA, USA

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prostate gland, and the bulbourethral glands of Cowper; and the penis (Table 1 and Figure 2).

**Testes**

**Gross Anatomy**

The paired testes produce and release the male gametes, spermatozoa. The sex cord/stromal cells synthesize and secrete hormones (i.e., the androgenic steroid testosterone). In the mouse and human, the paired testes are located within the scrotum, covered by the tunica albuginea and tunica vaginalis, which also line the inner surface of the scrotum. The mouse is unique in that the testes communicate with the abdominal cavity through patent inguinal canals, which remain open throughout life. The inguinal canals are occupied by the epididymal fat body when the testes are in the scrotum. Out of the scrotum, each testis is surrounded by the epididymis and adipose tissue (the epididymal fat body) (Figure 3).

In the human, the inguinal canals are normally closed after descent of the testes during development. During development, the testes descend from the retroperitoneum within the abdomen into the scrotum. As the testes descend, they carry a layer of peritoneum so that once in the scrotum, they are surrounded by a double layer of mesothelium, the tunica vaginalis. The tunica vaginalis consists of visceral and parietal layers. The capsule of the testis is composed of a visceral layer of tunica vaginalis and a dense, fibrous tunica albuginea (Figure 4). The epididymis lies on the posterior aspect of each testis in both species.

**FIGURE 3 Mouse testes.** In this dissection, the testes outside scrotum and inguinal canal. Each mouse testis (T) is surrounded by the capsule (tunica albuginea) and juxtaposed to the epididymis on the posterior aspect. The epididymis has a head (H) and a tail (t) and is surrounded by adipose tissue (A).

**FIGURE 4 The human testes.** The paired human testes are located within the scrotum. Each testis is surrounded by a fibrous capsule (tunica albuginea). Fibrous septae partition the testis into lobules. The seminiferous tubules of the lobules connect to the segments of the ductal system—the rete testis, ductus efferentes, epididymis, and, within the spermatic cord, the vas deferens. Source: © Elsevier, Inc., www.netterimages.com.

- **Need-to-know**
  - The mouse paired testes can communicate with the abdominal cavity through open inguinal canals.
  - Humans have closed inguinal canals.
Histology

In the mouse, the bulk of each testis is composed of arrays of convoluted seminiferous tubules (Figures 5–11). The seminiferous tubules form loops at either end that end in tubuli recti, which lead to the rete testis and then over to a collecting chamber to efferent ducts and the head of the epididymis. The tubuli recti are confluent with the rete testis. The rete testis is located directly under the tunica albuginea. The tunica albuginea is a dense fibrous capsule that covers the testis and is continuous with the interlobular septa in the human.

The tubuli recti and rete testis are lined by a simple cuboidal epithelium without the germ cell complement, which should not be mistaken for atrophic or abnormal seminiferous tubules (Figure 9). The seminiferous tubules are lined by Sertoli cells and germ cells, and they are surrounded by a basement membrane. Within the

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FIGURE 6  Human testes. As in the mouse, each human testis is composed of convoluted seminiferous tubules (S) and interstitial or Leydig cells (L).

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interstitium between the seminiferous tubules are Leydig cells, rare inflammatory cells, and vessels. The Leydig cells have an abundant, eosinophilic cytoplasm and large, round nuclei with large nucleoli. Leydig cells produce testosterone under the regulation of pituitary luteinizing hormone. In the human, the Leydig cells contain elongated, intracytoplasmic crystals called the crystals of Reinke. They may be seen under light microscopy and are only found in humans and bush rats. Their function remains unknown.

As in mice, the human testis is composed of coiled seminiferous tubules (Figure 6). Three or four seminiferous tubules are grouped by fibrous septae into lobules. The seminiferous tubules connect, in sequence, to the segments of the ductal system—the rete testis, ductus efferentes, epididymis, and, within the spermatic cord, the vas deferens (Figures 10 and 11).

In the mouse and human, the seminiferous tubules are composed of Sertoli cells and germ cells, which are arranged in layers. Spermatogonia, which are the earliest stage of germ cell maturation, are located at the base of the tubules. During spermatogenesis, germ cells move to the lumina of the tubules as they proceed through stages of maturation from spermatogonia to spermatocytes, spermatids, and mature spermatozoa (Figures 7 and 8). In the human, spermatogenesis occurs in 70 days. Final maturation of spermatozoa occurs in the epididymis. In the mouse, spermatogenesis occurs in 35 days.

In the mouse and human, spermatogenic staging has been extensively reviewed. Sertoli cells, which have relatively scant cytoplasm and oblong nuclei with small nucleoli, are interspersed with the developing germ cells; these cells function to support and nurture the developing spermatozoa. The maturing elongated spermatids are attached to the cell membrane of Sertoli cells. Each Sertoli cell can support up to 50 germ cells.

Need-to-know

- The germ cell types, from basal location (immature) to luminal location (mature), are, respectively, spermatogonia, spermatocytes, spermatids, and spermatozoa in both the mouse and the human.
- In the mouse, it takes approximately 35 days for spermatogonia to develop into spermatozoa.
- In the human, it takes approximately 70 days for spermatogonia to develop into spermatozoa.
**Figure 9** Mouse rete testis. In mice, the dilated tubules of the rete testis (RT) are located under the tunica albuginea (TA) and lined by a simple epithelium.

**Figure 10** Human rete testis. The rete testis (RT), which drains the seminiferous tubules (SM), is a complex of ducts, lined by a flat cuboidal epithelium (E). The rete connects with the ductuli efferentes.

**Figure 11** Human rete testis. The human rete connects with the ductuli efferentes, which are a complex of ducts, lined by a short columnar epithelium, that have a serrated configuration. The ducts of the ductuli efferentes are surrounded by smooth muscle (SM), which helps move the sperm into the epididymis. The human convoluted ducts (D) of the ductuli efferentes are lined by a single layer of epithelial cells (E) and surrounded by smooth muscle. Each duct of the ductuli efferentes is lined by an epithelium, which varies from tall columnar and ciliated (C) to short and nonciliated with a layer of basal reserve cells (B). Each ductulus is surrounded by a band of smooth muscle. The ciliated cells and smooth muscle help propel spermatozoa toward the epididymis. Seminiferous tubule (T) is indicated.

**Need-to-know**

- The dilated tubules of the mouse rete testis are lined by only a simple epithelium and should not be mistaken for atrophic seminiferous tubules.
- The epithelium of the human rete testis is cuboidal.
Epididymis

Gross Anatomy

The major function of the epididymis is the accumulation, maturation, and storage of mature spermatozoa. In both species, the paired epididymides are structurally similar, consisting of a head, body, and tail. The epididymis lies on the posterior aspect of the testis, with the head at the upper pole and tail at the lower pole. In the mouse, the head of the epididymis is surrounded by the epididymal fat body (Figures 3 and 4).

Histology

In both mouse and human, the epididymal ducts are composed of a smooth muscle wall and a columnar to cuboidal epithelium. The tubules are smallest and have the tallest epithelium (pseudostratified columnar) in the head, whereas tubules are largest and the epithelium is the shortest (cuboidal to simple columnar) in the tail. Long microvilli, stereocilia, characterize epididymal epithelial cells. The head of the epididymis is connected to the ductuli efferentes; the epididymal tail, which stores the mature spermatozoa, is connected to the vas deferens (Figures 12–19).

In mice, the epididymis often forms spermatoceles and spermatic granulomas. A sperm granuloma forms when spermatozoa penetrate interstitial tissues and incite an inflammatory reaction. The sperm granuloma should not be misinterpreted as a neoplastic process because neoplasia is rare in the mouse epididymis. Blockage of the lumen of the secretory ductal system may result in sterility. In the human, basal cells and occasional lymphocytes may be seen within the epididymal epithelium.

FIGURE 12  Mouse epididymis. The mouse paired epididymides consist of a head, body, and tail. Histologically, the epididymal ducts are lined by columnar to cuboidal epithelium and smooth muscle.

FIGURE 13  Mouse epididymal tubules. The tubules are smallest and have the tallest epithelium (columnar) in the head.

FIGURE 14  Mouse epididymal tubules. The tubules are largest and epithelium the lowest (cuboidal) in the tail. The lumina contain mature spermatozoa.
**Ductulus Efferens**

The ductuli efferentes collect, store, and conduct spermatozoa from the testis to the head of the epididymis. In the human, the ductuli efferentes drain from the rete testis into the head of the epididymis. These ducts are lined by a single layer of epithelial cells that vary from tall columnar and ciliated to short, nonciliated cells. A minority of epithelial cells contain a yellow-brown pigment. Cilia propel spermatozoa into the epididymis. The nonciliated cells are thought to reabsorb some of the testicular fluid. Each ductulus is surrounded by smooth muscle.

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**FIGURE 15** The human rete testis. Rete testis (RT) drains into the head of the epididymis (E) via the ducts of the ductuli efferentes.

**FIGURE 16** Human epididymal tubules. The tubules are lined by smooth muscle (SM) and pseudostratified epithelium (E).

**FIGURE 17** Human epididymal tubules. The tubules are smallest and have the tallest epithelium (E; columnar) in the head (shown here), whereas tubules are largest and epithelium the lowest (cuboidal) in the tail. The principal epithelial cells have very long microvilli (MV) called stereocilia. SM, smooth muscle.

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**Need-to-know**

- In the aged male mouse, the epithelium lining the epididymis and vas deferens frequently contains cells with large, polyploid nuclei. This is an incidental finding.
- In both mouse and human, the epididymal tubules are smallest and have the tallest epithelium (columnar) in the head, and the tubules are largest and epithelium the lowest (cuboidal) in the tail. The lumen contains mature spermatozoa.
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**Epididymis**

**Gross Anatomy**

The major function of the epididymis is the accumulation, maturation, and storage of mature spermatozoa. In both species, the paired epididymides are structurally similar, consisting of a head, body, and tail. The epididymis lies on the posterior aspect of the testis, with the head at the upper pole and tail at the lower pole. In the mouse, the head of the epididymis is surrounded by the epididymal fat body (Figures 3 and 4).

**Histology**

In both mouse and human, the epididymal ducts are composed of a smooth muscle wall and a columnar to cuboidal epithelium. The tubules are smallest and have the tallest epithelium (pseudostratified columnar) in the head, whereas tubules are largest and the epithelium is the shortest (cuboidal to simple columnar) in the tail. Long microvilli, stereocilia, characterize epididymal epithelial cells. The head of the epididymis is connected to the ductuli efferentes; the epididymal tail, which stores the mature spermatozoa, is connected to the vas deferens (Figures 12–19).

In mice, the epididymis often forms spermatoceles and spermatic granulomas. A sperm granuloma forms when spermatozoa penetrate interstitial tissues and incite an inflammatory reaction. The sperm granuloma should not be misinterpreted as a neoplastic process because neoplasia is rare in the mouse epididymis. Blockage of the lumen of the secretory ductal system may result in sterility. In the human, basal cells and occasional lymphocytes may be seen within the epididymal epithelium.
The ductuli efferentes collect, store, and conduct spermatozoa from the testis to the head of the epididymis. In the human, the ductuli efferentes drain from the rete testis into the head of the epididymis. These ducts are lined by a single layer of epithelial cells that vary from tall columnar and ciliated to short, nonciliated cells. A minority of epithelial cells contain a yellow-brown pigment. Cilia propel spermatozoa into the epididymis. The nonciliated cells are thought to reabsorb some of the testicular fluid. Each ductulus is surrounded...
FIGURE 18  **Mouse vas deferens.** The vas deferens is lined by ciliated columnar epithelium (E) with a thick middle circular smooth muscle layer (C) and inner (I) and outer longitudinal smooth muscle layers (L) and adventitia (A). A layer of sperm (S) is noted in the lumen.

- **Need-to-know**
  - The thick layers of smooth muscle around the vas deferens are used for expelling sperm.
  - In older mice, the epithelium frequently has a crowded appearance and surface blebbing.
  - The vas deferens and associated blood vessels and nerves form the spermatic cord.
  - In mouse and human, the dilated end of the vas deferens is the ampulla.

FIGURE 19  **Human vas deferens.** The vas deferens is also lined by a ciliated columnar epithelium (E) with a very thick muscle wall with a circular layer (C), inner (I) and outer (O) layers, and adventitia (A).
by a thin band of smooth muscle that aids in propelling the spermatozoa toward the epididymis (Figure 11).

**Vas Deferens**

In the mouse and the human, the vas deferens, which is paired, conducts spermatozoa from the tail of the epididymis to the urethra.

**Gross Anatomy**

In the mouse, the vas deferens leads from the tail of the epididymis into the ampulla, which opens into the urethra at the level of the colliculus seminalis.

In the human, the vas deferens (ductus deferens) is connected to the tail of the epididymis at the ampulla. The ampulla of the vas connects to a short duct draining the seminal vesicle within the prostate to form an ejaculatory duct. The ejaculatory ducts from each side connect to the prostatic urethra.

**Histology**

Histologically in the mouse and human, the paired vas deferentia are lined by ciliated columnar epithelium that is surrounded by inner and outer layers of longitudinally oriented smooth muscle and adventitia (Figures 18 and 19). The thick layers of smooth muscle conduct and expel spermatozoa during ejaculation. The spermatic cord is composed of the vas deferens and associated blood vessels and nerves. In the mouse, the epithelium often appears crowded. Within the epithelium of epididymis and...
vas deferens of aged male mice are cells with large, polyploidy nuclei (Figures 18 and 19).

**ACCESSORY SEX GLANDS**

**Seminal Vesicles**

- **Gross anatomy**

In mouse and human, the seminal vesicles are large, bilateral, sacculated glands dorsolateral to the urinary bladder (Figures 1, 2, and 20–23). In the mouse, the anterior lobe (coagulating gland) of the prostate is bilaterally attached to the lesser curvature of the seminal vesicles (Figure 24). In the mouse, the ducts of the seminal vesicles open at the seminal collicle. The combined secretions of the seminal vesicles, prostate, and bulbourethral glands form the copulatory plug. In the human, the seminal fluid is composed of the combined secretions of the seminal vesicles and prostate.

**FIGURE 22** Human seminal vesicle. Each seminal vesicle is composed of a prominent muscular wall (1) and consists of a lumen into which complex outpouchings of folded mucosa (2) secrete eosinophilic, mucinous product (3). The epithelium contains folds (2) that give a honeycombed appearance at low magnification.

**FIGURE 23** Human seminal vesicle. The epithelium (E) consists of pseudostratified tall columnar, secretory cells that contain intracytoplasmic lipid droplets, and it is surrounded by a prominent muscular wall (M). Epithelial cells often have yellow/brown lipofuscin granules (L) and variably sized nuclei (N).

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  - In the mouse, the branching of the mucosal folds is normal and should not be confused with hyperplasia.
  - The lumen contains characteristic, intensely eosinophilic secretions.
  - The human epithelial cells often contain lipofuscin granules.
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When the gland is distended with secretory material, the folds stretch and shorten. The seminal vesicles of aged B6 mice may retain secretions and enlarge, either unilaterally or bilaterally. They may also become blocked and distended in mouse models of prostatic cancer. This dilatation may result in abdominal distention. Contraction (atrophy) of one or both seminal vesicles is also common. Mice may present with dilatation of one seminal vesicle and contraction of the other seminal vesicle.

The human seminal vesicles develop as diverticula of the ductus deferentia. They consist of a lumen into which complex outpouchings of mucosa secrete a mucinous product. The pseudostratified epithelium consists of tall, columnar cells, some of which have a yellow-brown cytoplasmic pigment and variably sized nuclei. The smooth muscle wall of the seminal vesicles is arranged as an inner circular layer and an outer longitudinal layer. The muscle conducts secretions into the urethra during ejaculation (Figures 22 and 23).

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The mouse prostate is divided grossly into four distinct lobes: anterior, dorsal, ventral, and lateral (Figure 24). Dorsal and lateral lobes are sometimes grouped together as the dorsolateral lobe. The lobes surround the urethra and are invested in a membrane. They can be difficult to identify without the aid of a dissecting scope; however, once the entire tract is removed, and the surrounding membrane is removed, each has a characteristic shape and location if viewed under a dissecting scope. The dorsal lobe is around the urethra. It has a butterfly shape. On the ventral aspect of the tract, the ventral lobe appears clear, gelatinous, and leaf-shaped and is located above the urethra and toward midline. It is flanked by both lateral lobes, which start dorsally and then incompletely wrap around the urethra ventrally. The anterior prostate is also known as the coagulating gland. The coagulating glands are located cranial to the other lobes and are attached to the lesser curvature of the seminal vesicles. They are tubular in shape and grossly appear clear and gelatinous.
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The human prostate gland is situated between the base of the urinary bladder and the rectum. The urethra, into which the ductal system of the prostate and the ejaculatory ducts drain, passes through the prostate. In contrast to the multilobed mouse prostate, the human prostate is a single organ that is organized as histologically similar zones by the pattern of branching of the prostate ducts (Figures 25 and 27). The zones have a complex three-dimensional structure. The central zone surrounds the urethra. The transition zone, which is the site of the benign condition termed nodular hypertrophy, is predominantly anterior to the urethra. Conversely, the peripheral
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### Need-to-know
- The human prostate is a single alobular structure.
- The mouse prostate is composed of four paired lobes located circumferentially around the urethra and caudal to the urinary bladder.
**Histology**

In the mouse, the seminal vesicle is lined by smooth muscle and a tall columnar epithelium that forms characteristic branching mucosal folds. The branching of the mucosal folds is normal and should not be confused with hyperplasia. The lumen contains characteristic, intensely eosinophilic secretions (Table 2, Figures 20 and 21).

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**FIGURE 25** Human prostate. The gross human prostate is a single alobular structure with three zones. The transition zone (TZ) is demarcated from the peripheral zone (PZ) by fibrous tissue (arrow). Note the urethra (UR). The central zone is located in the posterior and medial aspect of the prostate (not pictured).

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FIGURE 26 Mouse prostate. The prostate is divided into histologically distinct lobes that surround the urethra (Ur): seminal vesicle (SV), anterior prostate (AP), dorsal (DP), lateral prostate (LP), and ventral (VP) prostate lobes.

zone, which is the site of the majority of cases of prostate carcinoma, is located posterior to the urethra (Figure 27). Separated from the rectum by no more than a thin fibromuscular stroma, the peripheral zone is relatively accessible for transrectal biopsies to sample the prostate for prostatic adenocarcinoma.

**Histology**

Histologically, the lobes of the mouse prostate are separated from one another by a mesothelium-lined thin, delicate capsule. The glandular prostate is separated from the mesothelial-lined capsule by loose fibroadipose tissue that contains major vessels, nerves, and ganglia. The mouse ductules that constitute each lobe are surrounded by a few layers of spindle cells (a mix of fibroblasts and smooth muscle cells) and eosinophilic collagen. Overall, the mouse prostate has a modest stromal component compared to that of the human prostate.

The individual lobes of the mouse prostate have distinctive histological characteristics. The dorsal prostate is lined by columnar epithelium with moderate infolding, and it contains granular cytoplasm with homogeneous, eosinophilic secretions. Individual glands are surrounded by a thin fibromuscular stroma. It has centrally to basally located uniform nuclei. The lateral prostate is lined by mostly cuboidal to low columnar epithelium with sparse infolding, and it contains granular cytoplasm with amorphous, particulate, eosinophilic secretions and small, uniform, basally located nuclei. The lateral lobes are surrounded by peripheral loose connective tissue. The ventral prostate is lined by mostly
Chapter 18  Male Reproductive System

FIGURE 27  Human prostate. The prostate is alobular, but it is divided into three concentric zones. The central zone (CZ) encircles the ejaculatory ducts (ED), the transition zone (TZ) surrounds the prostatic part of the urethra (Ur), and the peripheral zone (PZ) makes up the bulk of the gland. The human prostate is surrounded by a capsule (C).

- **Need-to-know**
  - The mouse prostate is divided into four histologically distinct lobes.
  - The human prostate is divided into zones that are not clearly demarcated from one another but may be characterized by specific predisposition to disease.
  - The human prostate is surrounded by a capsule, whereas the mouse prostate. Lobes are invested and separated by a thin mesothelial-lined capsule/membrane.

### TABLE 2  Mouse Prostate Lobes and Accessory Sex Glands

<table>
<thead>
<tr>
<th>Acini</th>
<th>Dorsal Prostate</th>
<th>Lateral Prostate</th>
<th>Ventral Prostate</th>
<th>Anterior Lobe (Coagulating Gland)</th>
<th>Seminal Vesicle</th>
<th>Ampullary Gland</th>
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<tbody>
<tr>
<td>Cuboidal epithelium with sparse infolding and focal tufting, and it contains abundant, homogeneous, pale, serous secretions and small, uniform, basally located nuclei. The anterior prostate lobes (coagulating gland) are lined by a cuboidal to columnar epithelium with a papillary or cribriform growth pattern, and they contain eosinophilic, granular cytoplasm with centrally located nuclei and abundant, homogeneous, eosinophilic secretions. (Table 2 and Figure 28). The height of the epithelium of the glands within the various lobes varies with the stages of the secretory cycle from cuboidal (quiescent) to columnar (active). Histologically, prostatic glands (or acini) are irregularly shaped and embedded in a fibromuscular stroma (Figures 29–31). Similar to the mouse, the human prostatic glands consist of cuboidal to columnar epithelium composed of a luminal secretory cell layer subjacent to which is a layer of basal cells. Rare basal cells, which have a neuroendocrine phenotype, represent less than 1% of prostate epithelial cells. These three cell types have distinct immunophenotypes: luminal secretory cells—KLK3/prostate-specific antigen and KRT8 (keratin 8); basal cells—KRT 5/6, KRT 10, KRT 14 (keratins 5/6, 10, and 14, respectively), and TP63/p63; and neuroendocrine...</td>
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FIGURE 28  Mouse prostate lobes. The four prostate lobes are histologically distinct. (A) Dorsal prostate: lined by columnar epithelium, with moderate infolding; contains granular cytoplasm with homogeneous, eosinophilic secretions. Individual glands are surrounded by a thin fibromuscular stroma (arrows). Centrally to basially located uniform nuclei. Surrounded by peripheral loose connective tissue. (B) Lateral prostate: lined by mostly cuboidal to low columnar epithelium with sparse infolding; contains granular cytoplasm with amorphous, particulate, eosinophilic secretions. Small, uniform, basally located nuclei. Surrounded by peripheral loose connective tissue. (C) Ventral prostate: lined by mostly cuboidal epithelium with sparse infolding and focal tufting (arrows); abundant luminal spaces contain homogeneous, pale, serous secretions. Small, uniform, basally located nuclei. (D) Anterior prostate (coagulating gland): The epithelium is cuboidal to columnar with a papillary or cribriform growth pattern (arrows). Contains eosinophilic, granular cytoplasm with centrally located nuclei and abundant, homogeneous, eosinophilic secretions.

- Need-to-know

- Loose connective tissue surrounds individual glands in both dorsal and lateral lobes.
- The dorsal prostate glands are surrounded by a fibromuscular stroma.
- There is contractile fibromuscular stroma surrounding all of the gland lobules in the human prostate.
FIGURE 29 Human prostate. The prostate is composed of branching glands (G) that are irregularly shaped and surrounded by a dense stroma (S) composed of fibroblasts, collagen, and smooth muscle. The epithelium forms branching folds (F) that give a papillary appearance.

FIGURE 30 Human prostate. The prostatic glands are irregularly shaped and lined by an epithelium composed of a luminal secretory layer (S) of tall columnar cells and a basal cell layer (B) that lies on a basement membrane.

- Need-to-know
  - It is common to find lamellated corpora amylacea and prostatic concretions that increase with age.
  - The basal cell layer is difficult to detect on H&E.
  - The basal cells produce a characteristic high-molecular-weight keratin.
  - The basal cell layer is often absent in malignant glands and may be a useful indication of malignancy.

FIGURE 31 Human prostate gland. Pseudostratified epithelium, consisting of columnar cells and small basal cells, lines a secretory alveolus. A prostatic concretion (arrow) is in the alveolar lumen. A prominent fibromuscular stroma is in adjacent areas.
cells—neurosecretory granule-associated proteins CHGB/chromogranin B and SYP/synaptophysin. Lamellated variably calcified eosinophilic aggregates of protein, termed corpora amylacea, can be found within some gland lumina. These may obstruct ducts and, quite rarely, predispose to prostatitis (Figure 31). Corpora amylacea are not seen in the mouse prostate.

**Bulbourethral Glands (Cowper’s Glands)**

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Histologically, the bulbourethral glands in mice are multilobular. Each lobule is composed of acini that open into a centrally located canal. A thin capsule of fibrous connective tissue surrounds and separates the acini. The acini are composed of epithelial cells. In the secretory state, the epithelium has abundant, foamy cytoplasm, and in the resting state, the cytoplasm is eosinophilic and finely granular. The secretory cells are found mainly in the body, and the resting cells are found in the tail (Figure 32). The ductular epithelium is cuboidal. Older mice may develop cystic bulbourethral glands. Cystic glands result in swelling of the perineal region and impaired reproductive performance. Bacterial infections with *Staphylococcus aureus* and *Pasteurella pneumotropica* are also common.

In humans, mucin-expressing bulbourethral glands (Cowper’s glands) are situated adjacent to and drain into the membranous urethra. These glands consist of closely juxtaposed acini composed of polygonal epithelial cells with abundant clear cytoplasm. Although the Cowper’s glands are virtually never the site of pathological changes in human, expression of transgenes in genetically engineered mouse models may produce pathological changes in the mouse bulbourethral glands.

**Preputial Glands**

- **Gross anatomy**

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connective tissue capsule that surrounds large, cavernous ducts lined by stratified squamous epithelium and acini (Figure 34). The acini are composed of eosinophilic, pale, foamy, secretory sebaceous cells with dark nuclei and peripheral, flat, elongated basal cells (Figure 35). The preputial glands are prone to bacterial infection and subsequent abscessation. Marked enlargement of the glands due to ductal ectasia, hyperkeratosis, and cyst formation may also occur. The incidence in these changes increases with age.

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Male Reproductive System

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Periurethral glands (glands of Littré) are small mucus-secreting glands that drain into the urethra. In the human, they are adjacent to and drain into the penile urethra. In the mouse,
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they are located in the suburethral tissue of the membranous urethra distal to the prostatic ducts. They may be found within samples of mouse prostate and other mouse accessory tissues. Some mouse strains contain a urethral diverticulum that is located near the posterior aspect of the pelvic canal and is lined by transitional epithelium. This should not be confused with the bulbourethral glands, which are located at the same anatomic level. In the male mouse, the membranous urethra lies in close proximity to the prostate, seminal vesicles, coagulating glands, and vas deferens, and it can be seen in en bloc sections (Figure 37).

In the mouse, the combined secretions of the seminal vesicles, coagulating glands (anterior prostate), and bulbourethral glands form a coagulum or copulatory plug that can be found...
incidentally in any part of the urethra or urinary bladder of the male and also in the vagina of the female. This plug prevents the outflow of semen from the vagina and thus aides in fertilization. It is composed of homogeneous, amorphous to granular, eosinophilic secretory material that often contains mature sperm (Figure 41).

In the human, the urethra has two segments—the prostatic urethra and the penile urethra. Transitional epithelium (urothelium) and nonkeratinizing stratified squamous epithelium, which becomes more prominent in the distal urethra, line the urethra (Figures 39 and 40). The urethral meatus at the distal penis is lined by...
FIGURE 42 Mouse penis. Cross section of the mouse penis within the prepuce (P). Penile urethra (UR) and corpora cavernosa (CC) are shown. Note the dorsal vessels (DV) and nerves (N). This particular section shows an arteritis of the dorsal small to medium arteries, which is a common background change.

FIGURE 43 Mouse penis. A cross section with the os penis (OP) below the penile urethra (UR).

FIGURE 44 Human penis. The penis consists of three cylindrical masses of erectile tissue. The dorsal aspect is composed of the corpora cavernosa penis, and the midline consists of the corpus cavernosum urethrae (corpus spongiosum) that surrounds and supports the penile urethra. The cavernous bodies are surrounded and invested by fibroelastic tissue, the tunica albuginea, which is continuous with a loose hypodermis. Source: © Elsevier, Inc., www.netterimages.com.

Need-to-know
- The mouse penis has an os penis.
- The penis is a site for polyarteritis in the mouse.
- The mouse penile glans is enclosed within a prepuce.
- The human penis does not have an os penis.
stratified squamous epithelium. The paraurethral glands (glands of Littré) and the bulbourethral glands (Cowper’s glands) lubricate the urethra with mucoid secretions.

**Penis**

In both mouse and human, the penis consists of the root, body, and glans. In the mouse, the penis is composed of the penile or distal portion of the urethra, vascular erectile tissue (the bulbous cavernosum and bulbous spongiosum), and the orifice of the penis (Figures 42 and 43). The mouse penis also contains the os penis (Figure 43). The glans is enclosed in a loose sheath, the prepuce, which is lined by stratified squamous epithelium that contains hair follicles.

In the mouse, focal aggregates of lymphocytes are relatively common in the organs of the male reproductive tract; however, these inflammatory cells are not considered functionally significant. This is in contrast to arteritis and periarteritis that may occur in the small to medium-sized arteries in various organ systems, including the testes, penis, and prostate. The condition consists of an accumulation of inflammatory cells around arteries (perivasculitis) or expanding the vascular wall (arteritis) and may be accompanied by hyalinization and/or degeneration and necrosis of the vascular wall (Figures 42 and 43).

The human penis is lined by skin and contains three cylindrical portions of erectile tissue—paired corpora cavernosa and a corpus spongiosum that partially surrounds the penile urethra (Figure 44).

**FURTHER READING**


Lymph Nodes

The lymph nodes are peripheral organs that house a major subset of mature lymphoid cells. The lymph nodes serve a similar function in the mouse and human and are critical in mediating immune reactions to exogenous and endogenous stimuli.

Distribution

Lymph node distribution in mice has been well described (Figure 1). There can be inter- and intrastrain differences in the numbers of nodes per mouse. Nodes are generally very small (1–4 mm) and difficult to visualize within fat or other tissues. They are usually grayish in color and elongated or round. The largest lymph nodes are generally the mesenteric and mandibular nodes. Other nodes commonly used for histopathology studies include popliteal (in fat behind the knee), axillary, and subiliac. Human lymph nodes are present in typical external locations, including neck (cervical), axillae, and inguinal regions, and also internal locations, including thoracic, paraaortic, and mesenteric regions (Figure 2). Human lymph nodes vary in size from 0.5 to 2 cm. Even in healthy humans, external lymph nodes are often palpable.

Anatomy

The lymph nodes are important components of the immune system, and their macroanatomy is similar in mice and humans. A three-dimensional schematic of a typical lymph node is outlined in Figure 3. Afferent lymphatics enter the lymph node on the convex edge, and efferent lymphatics exit on the concave edge. A fibrous capsule surrounds the exterior of the lymph node. Blood supply is provided by arterioles and venules, typically entering the node near the efferent lymphatics. Within the node is a cortex, composed of lymphoid nodules, and a medullary sinus, containing cords of lymphocytes and plasma cells with associated macrophages. Lymph flows from the afferent lymphatics into the subcapsular...
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