Gillenwater, Jay Y., Grayhack, John T., Howards, Stuart S., Mitchell, Michael E.

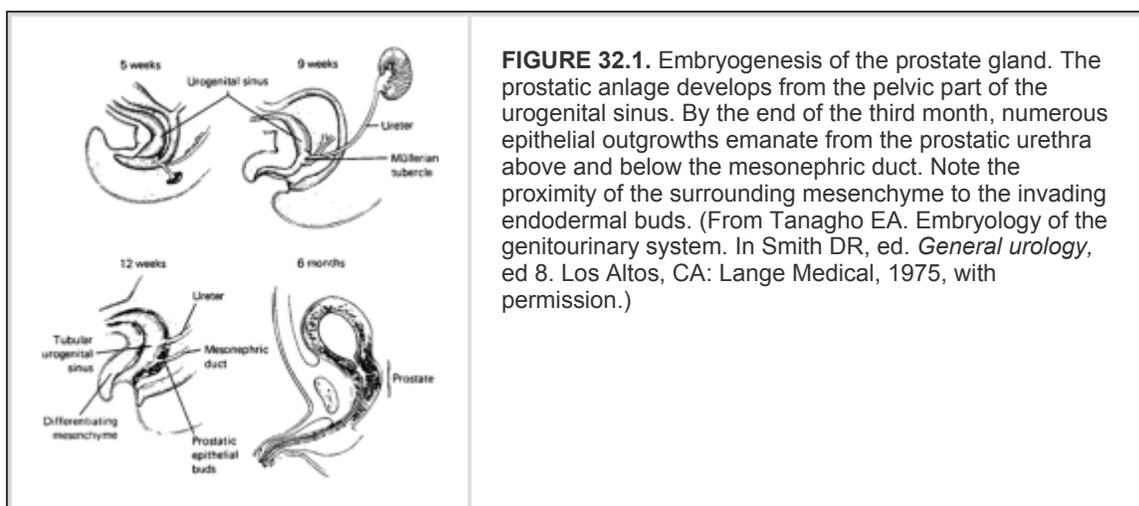Adult & Pediatric Urology, 4th Edition

ANATOMY

Part of "32 - BENIGN PROSTATIC HYPERPLASIA"

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Embryology

The prostate gland develops from the pelvic portion of the urogenital sinus at a fetal crown-rump length corresponding to a 10- to 12-week gestation (12). The prostate arises after the development of numerous endodermal buds, which initially proliferate throughout the entire length of the primitive urethra. Ultimately, the most extensive areas of proliferation into and about the prostatic anlage occur adjacent to the areas of the ejaculatory ducts and the verumontanum. These areas correspond to the points of termination of the mesonephric duct and its müAdullerian counterpart, respectively (194). The endodermal buds next invade the abundant surrounding urogenital sinus mesenchyme, which is responsible for the development of the connective tissue and muscular constituents of the definitive prostate (Fig. 32.1). Although this process continues throughout the life of the fetus, the gland is well differentiated by the end of the fourth month (12). Normal development of the wolffian and müllerian ducts and urogenital sinus-derived structures is dependent on the testosterone and müllerian-inhibiting secretions of the fetal testis. Conversion of testosterone to dihydrotestosterone, which occurs in both stroma and epithelium, is critical for the development of the prostate. An understanding of the role of growth factors and embryonic control mechanisms in organogenesis in general and in the prostate is currently the subject of intense investigation, as is the phenomenon of so-called imprinting (58,288).

FIGURE 32.1. Embryogenesis of the prostate gland. The prostatic anlage develops from the pelvic part of the urogenital sinus. By the end of the third month, numerous epithelial outgrowths emanate from the prostatic urethra above and below the mesonephric duct. Note the proximity of the surrounding mesenchyme to the invading endodermal buds. (From Tanagho EA. Embryology of the genitourinary system. In Smith DR, ed. *General urology,* ed 8. Los Altos, CA: Lange Medical, 1975, with permission.)

Gross Anatomy

General Considerations

The prostate is a compound tubuloalveolar gland whose base abuts the bladder neck and whose apex merges with the membranous urethra to rest on the urogenital diaphragm (386). The intact adult gland resembles a blunted cone, weighs approximately 18 to 20 g, and measures about 4.4 cm transversely across its base, 3.4 cm in length, and 2.6 cm in its anteroposterior diameter (208). The urethra enters the prostate near the middle of its base and exits the gland on its ventral surface above and in front of its apical portion. The ejaculatory ducts enter the base on its posterior aspect and run in an oblique fashion to emerge and terminate adjacent to the verumontanum. The capsule of the prostate gland is an inseparable condensation of stromal elements that is incomplete at the apex; it does not represent a true capsule (13). Fibrous septa emanate from the capsule, pierce the underlying parenchyma, and divide it into multiple lobules (386). These glandular units drain into branched tubules, which lead into 20 to 30 prostatic ducts. Most of these ducts empty their contents into the prostatic urethra adjacent or distal to the verumontanum (235). These and other relationships are depicted in Fig. 32.2 and Fig. 32.3.
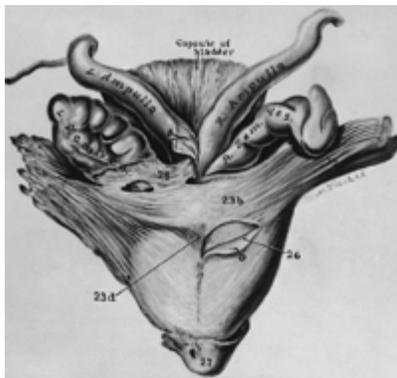

FIGURE 32.2. A dorsal view of the prostate gland, ampulla, seminal vesicles, and bladder. A median sulcus divides the prostate into halves and receives bandlike projections from the retrospermatic branch of the prostatic cord *(23d).* The dorsal capsule of the prostate (26) is synonymous with the anterior layer of Denonvilliers' fascia. Note the caplike investment (27) of the urogenital diaphragm on the apex of the prostate. (From Uhlenhuth E. *Problems in the anatomy of the pelvis: an atlas.* Philadelphia: Lippincott, 1953, with permission.)
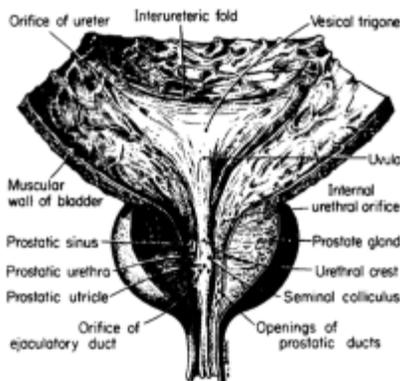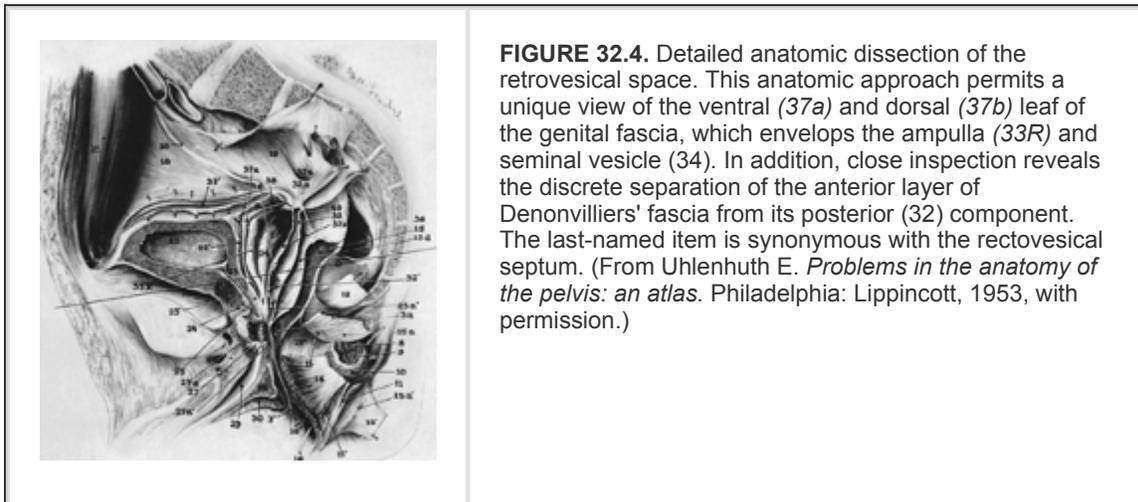

FIGURE 32.3. A frontal view of the bladder and prostate gland. The prostatic utricle sits atop the verumontanum (seminal colliculus) and represents one of two müllerian duct remnants in humans, the other being the appendix testis. Note that the majority of prostatic ducts drain adjacent or distal to the verumontanum. The area extending from the trigone to the termination of the prostatic urethra constitutes the internal urethral sphincter or bladder neck mechanism. (From Woodburne RT. Pelvis. In: Woodburne RT, ed. *Essentials of human anatomy.* New York: Oxford University Press, 1978, with permission.)
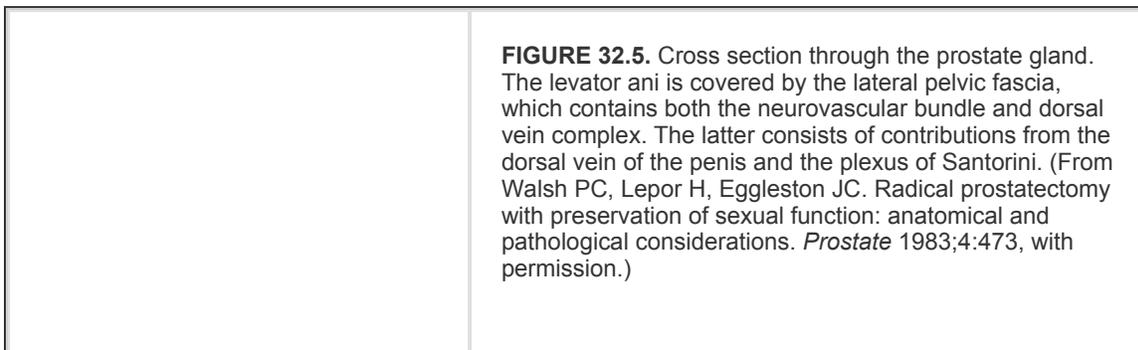
Denonvilliers' fascia is a visceral pelvic fascia formed by a condensation of fused peritoneum; it extends from the anterior peritoneal reflection superiorly to the urogenital diaphragm inferiorly. In its caudal extent, Denonvilliers' fascia envelops the posterior surface of the seminal vesicles and remains affixed to the posterior prostatic capsule (386). We suspect that the disputed existence of grossly identifiable anterior and posterior components of this fascial layer (369) as delineated in Fig. 32.4 is the result of their variably fused anatomic status rather than a misinterpreted rectal fascia propria.

FIGURE 32.4. Detailed anatomic dissection of the retrovesical space. This anatomic approach permits a unique view of the ventral *(37a)* and dorsal *(37b)* leaf of the genital fascia, which envelops the ampulla *(33R)* and seminal vesicle (34). In addition, close inspection reveals the discrete separation of the anterior layer of Denonvilliers' fascia from its posterior (32) component. The last-named item is synonymous with the rectovesical septum. (From Uhlenhuth E. *Problems in the anatomy of the pelvis: an atlas.* Philadelphia: Lippincott, 1953, with permission.)

The endopelvic fascia corresponds to that condensation of extraperitoneal connective tissue that forms a subserous covering for the pelvic viscera and envelops their contiguous neurovascular pedicles. A sheetlike proliferation of the endopelvic fascia contributes to the formation of the puboprostatic ligaments. These avascular facial condensations, varying from a pillarlike to a fan configuration, lie on either side of the prostatic midline. They anchor the anterior and lateral aspect of the prostate to the posterior aspect of the pubis and superior fascia of the pelvic diaphragm (374).

The lateral pelvic fascia, also described as the parietal layer of the endopelvic or prostatic fascia, serves as the fascial envelope to the levator ani muscle and maintains continuity with the capsule of the prostate along its anterior and anterolateral aspects. The tributaries of the dorsal vein complex traverse this fascial layer (Fig. 32.5). Anatomic dissections by Walsh and Donker (372) revealed that the major neurovascular bundles to the prostate are contained posterolaterally within the lateral leaves of this fascia.

FIGURE 32.5. Cross section through the prostate gland. The levator ani is covered by the lateral pelvic fascia, which contains both the neurovascular bundle and dorsal vein complex. The latter consists of contributions from the dorsal vein of the penis and the plexus of Santorini. (From Walsh PC, Lepor H, Eggleston JC. Radical prostatectomy with preservation of sexual function: anatomical and pathological considerations. *Prostate* 1983;4:473, with permission.)

Blood Supply

The prostatovesicular artery, the major arterial supply to the prostate and seminal vesicles, is a branch of the inferior vesical artery that originates from the anterior division of the hypogastric artery and courses medially on the levator muscle to the bladder base. After providing tiny branches to the bladder base, prostate, and tip of the seminal vesicles, its terminal arborizations supply the prostate with its main arterial supply in the form of urethral and capsular branches (208). The urethral branches course along the posterolateral aspect of the vesicoprostatic junction and usually enter the bladder neck and periurethral aspect of the prostate gland at the 5 and 7 o'clock positions (Fig. 32.6). Capsular arteries supply the peripheral portion of the prostatic parenchyma via four to six branches traversing the posterolateral aspect of the gland. Walsh and Donker (372) determined that the nervi erigentes form an extensive plexus enveloping these

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capsular branches that serve as a vascular scaffold and a demonstrable anatomic landmark. The anterior division of the hypogastric artery also supplies the inferior aspect of the prostate, as well as the seminal vesicles and vas deferens, with accessory vessels from the middle hemorrhoidal and internal pudendal arteries (208,386).

Wide, thin-walled veins on the lateral and anterior aspect of the prostate gland merge with veins of the vesical plexus and the deep dorsal vein of the penis to form the plexus of Santorini within the puboprostatic space. This confluence of veins empties into the hypogastric vein. Of importance, these prostatic vessels freely communicate with the plexiform venous arborizations (Batson's plexus) that envelop and enter the lumbosacral spine and the wings of the ilia. The lack of competent valves in this nervous system has been postulated by some to provide direct access for embolic spread of prostate carcinoma to the skeletal system (23).

FIGURE 32.6. Arterial supply to the prostate gland. The anterior division of the hypogastric artery supplies the primary (inferior vesical) and secondary (middle rectal and pudendal) branches to the prostate gland. The prostatovesicular artery (prostatic artery) is a terminal tributary of the inferior vesical branch and arborizes into urethral and capsular components. In addition, it supplies the dorsal aspect of the seminal vesicles and bladder
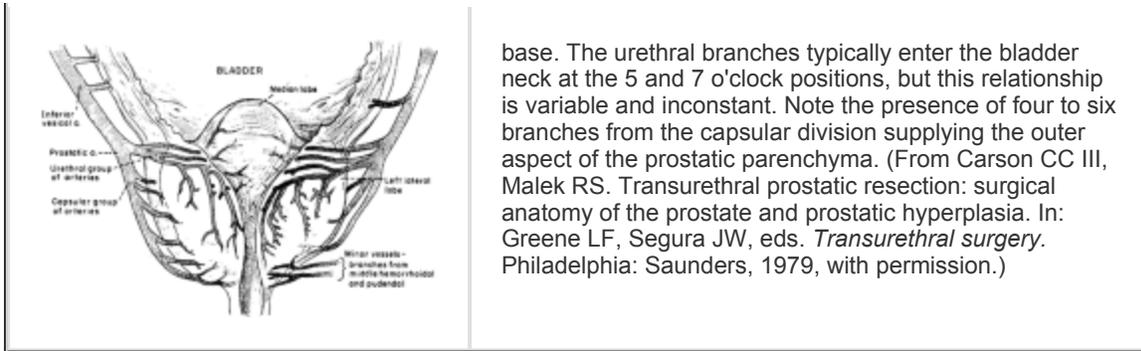
base. The urethral branches typically enter the bladder neck at the 5 and 7 o'clock positions, but this relationship is variable and inconstant. Note the presence of four to six branches from the capsular division supplying the outer aspect of the prostatic parenchyma. (From Carson CC III, Malek RS. Transurethral prostatic resection: surgical anatomy of the prostate and prostatic hyperplasia. In: Greene LF, Segura JW, eds. *Transurethral surgery.* Philadelphia: Saunders, 1979, with permission.)

Nerve Supply

In 1982, Walsh and Donker (372) published landmark observations describing the anatomic relationship of the pelvic (autonomic) plexus and the prostate gland. The prostate, other pelvic organs, and corpora cavernosa receive their autonomic innervation from the pelvic plexus, a fenestrated rectangular plate 4 cm long and 2.5 to 3.0 cm high lying retroperitoneally adjacent to the rectum within the sagittal plane (201). Both the parasympathetic and sympathetic divisions of the autonomic nervous system contribute to the plexus. Parasympathetic visceral efferent preganglionic nerve fibers from the second through fourth levels of the sacral cord enter the plexus by way of the pelvic splanchnic nerve (nervi erigentes). This nerve is a composite of five or six branches rather than a discrete entity. The sympathetic component emanates from the thoracolumbar center (T-11 to L-2) and courses via the hypogastric nerve, arborizations of the sacral sympathetic chain (S-4 to S-5), and branches that originate from the autonomic inferior mesenteric plexus and accompany the superior hemorrhoidal artery to join the plexus (201,215).

As stated previously, the prostatovesicular artery provides the macroscopic landmark and extrinsic support for these delicate nerves (Fig. 32.7). They lie outside of the confines of the prostatic capsule and Denonvilliers' fascia but traverse the lateral pelvic fascia (374). The prostate receives its

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branches from the pelvic plexus through the lateral leaves of this fascial layer (Fig. 32.5). These observations, initially made by dissections performed in fetal and newborn tissue, have been confirmed by studies in the adult male pelvis (201,215).

FIGURE 32.7. Innervation of the prostate, urethra, and corpora cavernosa. The branches to the prostate are contained within the lateral pelvic fascia and maintain an intimate relationship with the vascular scaffold created by the prostatovesicular artery. (From Walsh PC, Lepor H, Eggleston JC. Radical prostatectomy with preservation of sexual function: anatomical and pathological considerations. *Prostate* 1983;4:473, with permission.)

Lymphatics

Small lymphatic vessels surround each prostatic acinus, ultimately forming larger channels that contribute to the periprostatic plexus on the surface of the gland. This network communicates with branches from the perivesical lymph node group. The first major portal of lymphatic drainage from the prostate is to the iliopelvic lymph nodes (312). This lymphatic network can be conveniently divided into three nodal groups: the external iliac, the internal iliac, and the common iliac. The composition of these groups has been clearly summarized by Lieber (209).

The external iliac lymph node system consists of three separate groups. The lateral chain, consisting of one to three lymph nodes, lies along the lateral aspect of the external iliac artery. The most inferior node in this group is designated the lateral crural lymph node. The intermediate node group traverses the area between the external iliac artery and vein. The medial group of lymphatic vessels, the most significant of the three, lies superior to the obturator nerve and medial and posterior to the external iliac vein. The middle node of this medial chain is called the obturator lymph node; the most inferior node, designated the internal retrocrural node, communicates with the node of Cloquet within the femoral canal and with other deep inguinal nodes.

The internal iliac group (hypogastric chain) most often constitutes four to eight lymph nodes affixed to the areolar investment of the hypogastric vessels. This chain is rarely delineated on lymphography (55).
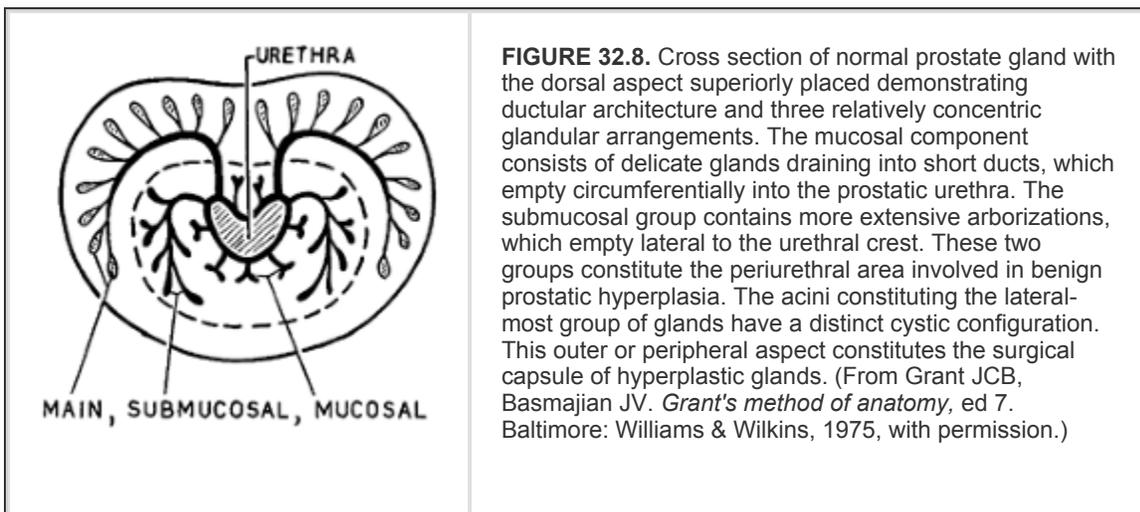
The common iliac lymph node group represents a continuation of the external iliac chain and also possesses lateral, intermediate, and medial groups. The last, by far the most important, usually consists of three to six lymph nodes. It gives rise to the nodes of the sacral promontory, opposite the second and third sacral foramen. The medial chain of the common iliac lymph nodes provides access to the perigastric nodes. Extensive cross-communication exists between right and left common iliac chains. Figure 33.45 depicts the anatomy of the pelvic lymph nodes and their relationship to the retroperitoneal abdominal lymphatics (see Chapter 33).

Normal Internal Architecture

Regionally organized tissue configurations have gained increasing acceptance in principle, if not in specific detail, in the prostate. Nevertheless, the proposed organization of the fetal, newborn, and adult prostate into discrete lobes has been regarded with skepticism (12,128,212,213,388). With a focus on the development of BPH, Franks (100,101) conceptualized a prostate with an inner (urethral) and outer glandular configuration (Fig. 32.8). McNeal (235) argues,
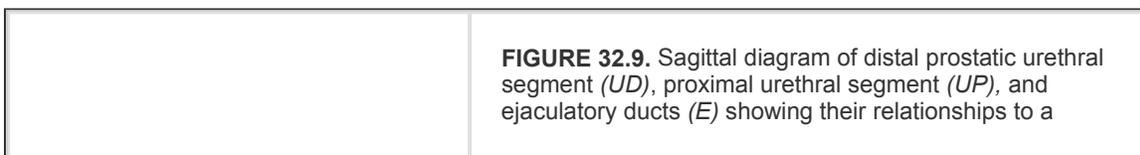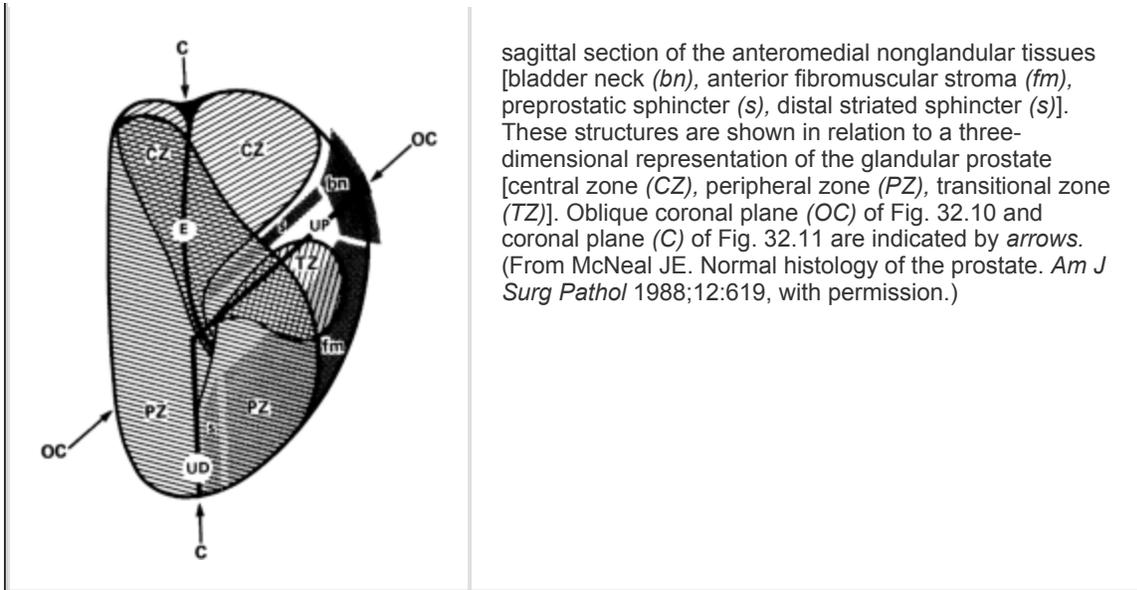
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as did Lowsley, that the urethral (inner) glands be considered separately from the prostate and its intrinsic architecture. However, the major physiologic and biochemical similarities of these glands and those of the prostatic parenchyma weigh against this concept.

FIGURE 32.8. Cross section of normal prostate gland with the dorsal aspect superiorly placed demonstrating ductular architecture and three relatively concentric glandular arrangements. The mucosal component consists of delicate glands draining into short ducts, which empty circumferentially into the prostatic urethra. The submucosal group contains more extensive arborizations, which empty lateral to the urethral crest. These two groups constitute the periurethral area involved in benign prostatic hyperplasia. The acini constituting the lateral-most group of glands have a distinct cystic configuration. This outer or peripheral aspect constitutes the surgical capsule of hyperplastic glands. (From Grant JCB, Basmajian JV. *Grant's method of anatomy,* ed 7. Baltimore: Williams & Wilkins, 1975, with permission.)

McNeal (235,237) has proposed and promoted acceptance of anatomic subdivisions with probable pathophysiologic significance in the adult prostate. In his studies, McNeal emphasized the use of coronal and oblique coronal sections of prostates obtained between puberty and the third decade of life to study normal anatomy. Tisell and Salander (361), who used meticulous dissection techniques, observed subdivisions of the prostate gland that had several similarities to those reported by McNeal, but they interpreted these as evidence for prostatic lobes.

McNeal observed that the urethra separates the prostate into ventral (fibromuscular) and dorsal (glandular) portions. Approximately midway between the apex and base, the posterior wall of the urethra undergoes an acute 35-degree ventral angulation that serves to segregate the urethra into proximal and distal segments. The verumontanum and ejaculatory duct orifices exist exclusively within the distal segment. McNeal separates the glandular prostate thus delineated into four distinct regions: peripheral zone, central zone, transition zone, and periurethral gland region (Fig. 32.9).

FIGURE 32.9. Sagittal diagram of distal prostatic urethral segment *(UD)*, proximal urethral segment *(UP),* and ejaculatory ducts *(E)* showing their relationships to a

sagittal section of the anteromedial nonglandular tissues [bladder neck *(bn)*, anterior fibromuscular stroma *(fm)*, preprostatic sphincter *(s)*, distal striated sphincter *(s)*]. These structures are shown in relation to a three-dimensional representation of the glandular prostate [central zone *(CZ)*, peripheral zone *(PZ)*, transitional zone *(TZ)*]. Oblique coronal plane *(OC)* of Fig. 32.10 and coronal plane *(C)* of Fig. 32.11 are indicated by *arrows.* (From McNeal JE. Normal histology of the prostate. *Am J Surg Pathol* 1988;12:619, with permission.)
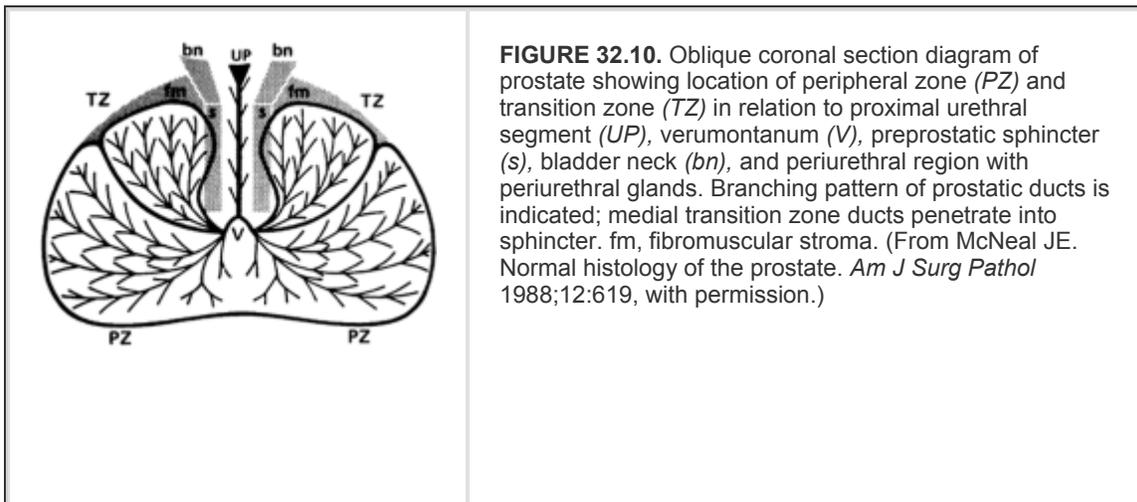
FIGURE 32.10. Oblique coronal section diagram of prostate showing location of peripheral zone *(PZ)* and transition zone *(TZ)* in relation to proximal urethral segment *(UP)*, verumontanum *(V)*, preprostatic sphincter *(s)*, bladder neck *(bn)*, and periurethral region with periurethral glands. Branching pattern of prostatic ducts is indicated; medial transition zone ducts penetrate into sphincter. fm, fibromuscular stroma. (From McNeal JE. Normal histology of the prostate. *Am J Surg Pathol* 1988;12:619, with permission.)
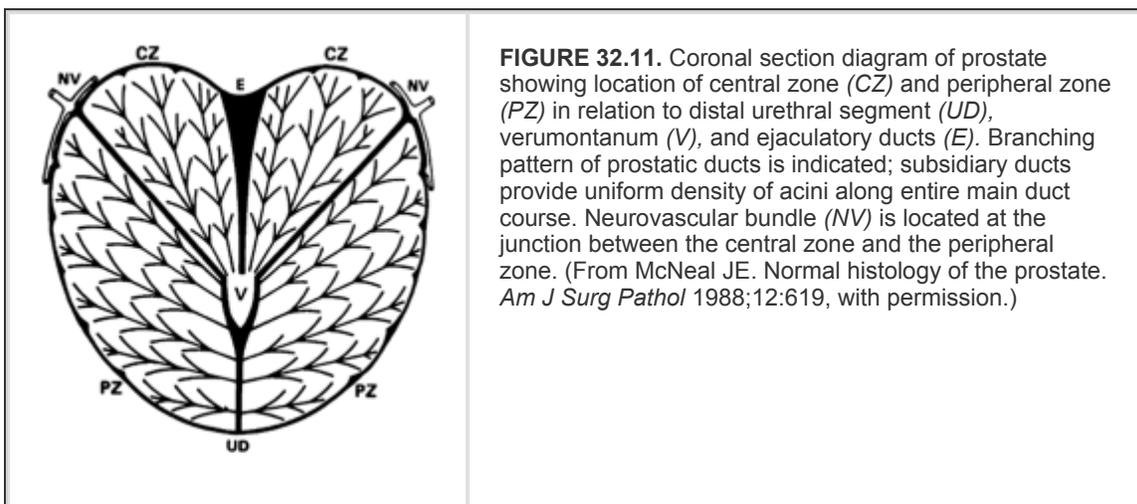

FIGURE 32.11. Coronal section diagram of prostate showing location of central zone *(CZ)* and peripheral zone *(PZ)* in relation to distal urethral segment *(UD)*, verumontanum *(V)*, and ejaculatory ducts *(E)*. Branching pattern of prostatic ducts is indicated; subsidiary ducts provide uniform density of acini along entire main duct course. Neurovascular bundle *(NV)* is located at the junction between the central zone and the peripheral zone. (From McNeal JE. Normal histology of the prostate. *Am J Surg Pathol* 1988;12:619, with permission.)

The peripheral zone constitutes approximately 75% of the glandular prostate. Its ductal system enters the urethra along the posterolateral recesses of the urethra extending from the verumontanum distally to the prostatic apex (Fig. 32.3 and Fig. 32.10).

The wedge-shaped central zone, whose base is positioned superiorly at the bladder neck, occupies approximately 20% of the glandular prostate. Its ductal network closely follows the ejaculatory ducts to the urethra and empties adjacent to orifices of the ejaculatory ducts on the apex of the verumontanum (Fig. 32.11).

The transition zone, accounting for about 4% to 5% of the adult glandular prostate, is not well defined in the prepubertal prostate (234). It consists of two modest lobules of paraurethral tissue anterior to the peripheral zone. Its ducts empty in the posterior lateral recess of the urethra just proximal to peripheral zone ducts. The transition zone is lateral to McNeal's preprostatic sphincter, a smooth muscle cylinder enveloping the proximal urethra from the bladder neck to the base of the verumontanum (Fig. 32.9). The last anatomically discrete area within the glandular prostate is the periurethral gland region, representing less than 1% of the total volume of the glandular prostate. Its ductal network represents a more proximal extension of those of the peripheral and transition zone areas. These various regions have differing acinar, stromal, and cellular configurations. McNeal postulates that the anatomic and histologic similarities of the peripheral and transition zones and periurethral gland region are attributable to a common urogenital sinus embryonic origin. In distinction, he postulates that the close association between the central glandular zone, the ejaculatory ducts, and the seminal vesicles may reflect a common wolffian duct embryonic origin (235).

Last, the anterior or ventral fibromuscular stroma forms an apron that extends distally, covers the entire anterolateral aspect of the glandular prostate, and is responsible for the anterior convexity of the prostate gland. It represents approximately one-third of the tissue within the prostate capsule (237). This unusually distinct area, composed predominantly of smooth muscle fibers, maintains continuity proximally with the detrusor muscle fibers of the bladder neck.

As noted, the so-called capsule of the prostate is a condensation of stromal elements that envelopes the underlying parenchyma in a rather uniform manner (Fig. 32.12) except at the apex. Periodically, distinct septa emanate from the capsular sheath and penetrate the interior of the gland,

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segregating it into lobules. The peripheral aspect of the capsule consists predominantly of fibroblasts, collagen, and elastic fibers. The septations differ from the bulk of the capsule in that they contain abundant smooth muscle cells (SMCs). The resulting epithelial folds and papillae are buttressed by the union of capsular septa and filamentous stromal branches. A complex network of lymphatics, blood vessels, and nerves courses through these branches. The capsular septa and stroma represent a dynamic scaffolding system for the underlying parenchyma. As a unit, they constitute 25% to 30% of the total volume of the prostate gland (7,246,252).

FIGURE 32.12. Transverse section of normal prostate
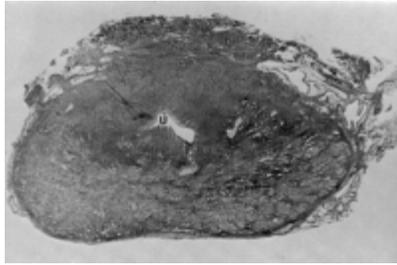
gland. The fibrovascular constitution of the capsule surrounding otherwise normal, peripherally distributed acinar elements is well illustrated. Note the absence of hyperplastic tissue in the periurethral area. (From Kirchheim D. Histochemistry. In: Hinman F Jr, ed. *Benign prostatic hypertrophy.* New York: Springer-Verlag, 1983, with permission.)

Prostatic stroma consists predominantly of SMCs and fibroblasts arranged in close proximity to the distinct basal lamina of the epithelium. However, the fibroblasts tend to be organized parallel to the long axis of these tubulosaccular glands and form a more predictable relationship with the basement membrane (252). The smooth muscle surrounds individual glands and is thought to play a pivotal role in the release of glandular secretions. Furthermore, contraction of the circular smooth muscle of the bladder neck and preprostatic sphincter assists in the elimination of secretions within the prostatic urethra; this smooth muscle probably forms the major working element of the internal urethral sphincter. The anterior and anterolateral aspects of the prostate contain smooth and skeletal muscle, which joins the fibers of the external sphincter, augmenting urinary control in that region (223).

The excretory ducts are lined by simple or pseudostratified columnar epithelium for most of their course, but transitional epithelium is noted distally as they enter the floor and lateral surfaces of the urethra adjacent or distal to the verumontanum. From a teleologic standpoint, these ducts are inefficiently arranged. As noted previously, rather than a single main excretory duct, there are 16 to 32 separate ducts with distinct urethral orifices. Moreover, the ducts have an irregular branching pattern with numerous cystic outgrowths. This serpiginous pattern seems likely to restrict rather than promote the transit of secretions. The ductal network possesses both columnar and basal cells. However, neither has a secretory capability. Analysis of their ultrastructure reveals a few randomly distributed organelles. The generous investment of the ductal compartment by SMCs admixed with nerve axons is noteworthy. These elements appear to be integrally related to emptying the ducts (see Secretory Mechanisms) (84,339).

Blood capillaries that traverse the stromal labyrinth consist of both continuous and fenestrated subtypes. These vessels and their associated nerves probably play an active role in both the elaboration and propagation of the gland's secretions (84).

The acinar epithelium consists of two well-recognized cell types: (a) a tall, columnar glandular secretory cell that is luminal in orientation, and (b) a nonsecretory basal cell that is flattened, cuboidal, and abuts a distinct eosinophilic basement membrane approximately 0.07 to 0.12 mm thick.

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Both cell types make direct contact with the latter (Fig. 32.13). The predominating

glandular secretory cells possess a variety of distinctive light and electron microscopic features (Fig. 32.14), including the following:
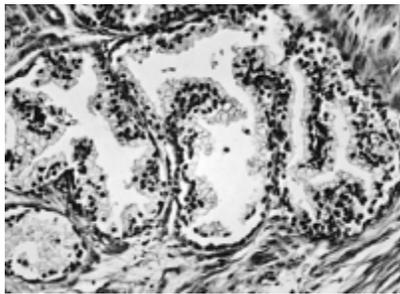

FIGURE 32.13. Photomicrograph of normal prostatic acini demonstrating double cell layers. The latter consists of basal cells and adluminal (secretory) cell components (×200). (From Mostofi FK, Price EB. *Tumors of the male genital system,* series 2, fascicle 8, *Atlas of tumor pathology.* Washington, DC: Armed Forces Institute of Pathology, 1972, with permission.)
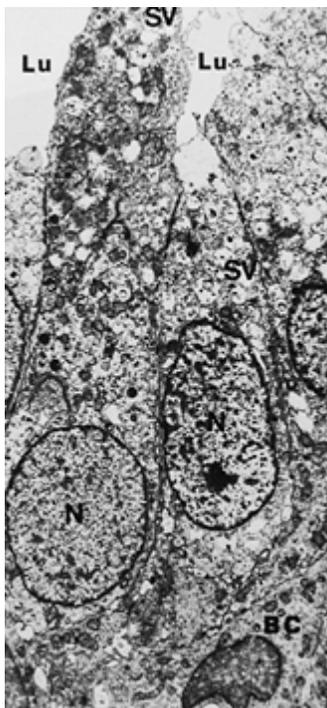

FIGURE 32.14. Electron micrograph of normal prostatic epithelial cells. The adluminal cells contain prominent nuclei *(N)* with mitochondria, lipid droplets, and secretory vesicles *(SV)* easily demonstrated. Apocrine secretion (release of secretory products plus a portion of the cell wall) is reflected by the loss of the villous extension apparent in the center of the field. Merocrine secretion (release of secretory product through the intact cell) is also demonstrated in the prostate. The basal cell *(BC)* abuts a distinctive basement membrane (not shown) and contains a prominently serrated nucleus. Lu, lumen acinus. (From Kirchheim D. Histochemistry. In: Hinman F Jr, ed. *Benign prostatic hypertrophy.* New York: Springer-Verlag, 1983, with permission.)

1. Although typically tall and columnar in profile, the cell may appear compact in areas with high cellular density.

2. Nuclei are located in a dependent position with a long axis paralleling that of the cell.

3. Nucleoli are rarely encountered; they are separated from a double nuclear membrane

by punctate areas of delicate heterochromatin.

4. The basal cytoplasm harbors free ribosomes, rough endoplasmic reticulum (RER), and some short mitochondria.

5. The supranuclear area is characterized by the presence of a Golgi apparatus consisting of aggregates of small vesicles and elongated lacunae, RER, some lipid droplets, and secretory granules and vacuoles with a solitary limiting membrane.

6. Active lysosomes and different types of dense bodies, the most prominent of which contains lipofuscin, are present within the apical cytoplasm.

7. The apical cytoplasm contains numerous villiform extensions that project from glandular cells into the acinar lumina that vary in prominence depending on the secretory status of the cell.

8. Glandular cells react with monoclonal antibodies to prostate-specific antigen (PSA), prostate-binding protein, and acid phosphatase. Acid phosphatase is noted predominantly within the secretory vacuoles and lysosomes; in contrast, aminopeptidase and PSA are located in the apical cell border and cytoplasm, respectively.

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9. A distinct lateral plasma membrane exists; cell-to-cell contact is accomplished through apical junctional complexes and numerous desmosomes (184,252,339). Cytokeratins (CKs) 8 and 18 appear to be specific for the prostate secretory cell (331).

The basal or nonsecretory cell subpopulation also possesses distinctive histologic and ultrastructural characteristics, including the following (Fig. 32.13 and Fig. 32.14):

1. Basal cells are polygonal in orientation and possess a relatively large nucleus with a serrated border. As with glandular cells, the long axis of the nucleus parallels that of the cell itself.

2. Extension of these cells never appears to reach the lumen of the gland.

3. Their cytoplasm, lacking secretory granules, is more electron dense than that of glandular cells.

4. In addition to lacking secretory granules, basal cells reveal an inconspicuous array of mitochondria, endoplasmic reticulum, and free ribosomes and possess a much abbreviated Golgi apparatus.

5. Despite possessing linear attachments, basal and columnar cells are commonly separated by lacunae containing cytoplasmic projections.

6. Basal cells possess a number of intracytoplasmic filaments, some of which may serve a contractility function (or functions); others are CKs. CKs 5 and 15 appear to

be basal-cell specific (331).

7. Pinocytotic vesicles that may facilitate transfer of materials between the glandular and stromal compartments are present.

8. The basal cell compartment appears more prominent in the inner than in peripheral prostatic glands.

9. Basal cells do not react with monoclonal antibodies directed against acid phosphatase, PSA, and prostate-binding protein (PBP).

10. The basal cell compartment is thought to function as reserve or stem cells and to be primarily responsible for tissue repair.

Although cytokeratin characterization distinguishes adult basal and adluminal epithelial cells (22,329,331), Xue and associates (390) identified intermediately located cells with mixed basal and adluminal cell cytokeratins in the developing prostate; they postulate that these may facilitate a transition between basal and adluminal cells. Interestingly, no apparent qualitative differences in CK expression were found between central and peripheral zone tissues (329).

The prostate contains two groups of cells: the neuroendocrine (NE) or endocrine-paracrine (EP) cells, native to the prostate, and inflammatory cells that have the potential to secrete recognized growth factors and other potential growth-modifying agents. With regard to the latter, macrophages and mast cells are encountered in normal prostates; lymphocytic infiltrates are common in BPH (252,342,358). The absence of granulocytes suggests that these infiltrates are not a response to infection; flow cytometric analysis identified T cells (60% to 70%), B cells (15%), and macrophages (15%) in them (103). These cells have been shown to produce potent growth factors. For example, T cells infiltrating human prostate cancers have been shown to produce vascular endothelial growth factor (VEGF), and tumor-derived lymphocytes produce breast tumor and stromal cell–stimulating heparin-binding epidermal growth factor (HB-EGF) and bFGF/FGF$_2$ (basic fibroblastic growth factor/fibroblast growth factor 2) (281). These cells could provide potent mitogenic stimuli for prostate stromal or epithelial growth (103) and contribute to the pathogenesis of BPH (342).

Neuroendocrine cells rest on the basal cell layer between sensory cells and establish contact with nerves or other NE

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cells through open-type dendritic cells. NE cells secrete a range of products varying from serotonin, neuron-specific enolase, bombesin, and somatostatin to human chorionic gonadotropin–like and thyroid-stimulating hormone–like peptides (73). They are present in all areas of the prostate and urethra and in benign and malignant tissue in varying concentrations. NE cells are most numerous in the main periurethral prostatic ducts and are reduced in number in BPH acini (74). Defining the role of NE cells in normal and abnormal prostate growth remains an elusive challenge.

As noted, prostatic stroma is heterogeneous, consisting of fibroblasts (FBs) and SMCs that are arranged in both periacinar and interacinar configurations (70). The fibroblasts tend to

be organized parallel to the long axis of tubulosaccular glands and smooth muscle elements surround individual glands and blend with the adjacent stroma. SMCs and FBs comprising the stroma can be readily distinguished *in vivo* and *in vitro* by monoclonal antibodies; for example, smooth muscle α-actin and myosin for SMCs and prolyl-4-hydroxylase and ASO2 (Dianova) for fibroblasts (170,325). Proliferation can be induced in both by growth factors such as platelet-derived growth factor (PDGF), basic fibroblast growth factor (bFGF), transforming growth factor-β (TGF-β), insulin-like growth factors I and II (IGF-I, IGF-II), and others (103,343,349). Adult SMCs commonly achieve a highly differentiated contractile phenotype *in vivo.* However, these cells can assume an activated synthetic phenotype with a fibroblast-like appearance, proliferate rapidly, and secrete unique extracellular matrix (ECM) and thrombospondin and tenascin (220) as well as collagen in a developing organism and *in vitro.* Human prostate-derived fibroblasts synthesize bFGF *in vitro* (330,345) but lack an identifiable mechanism to secrete this growth factor. Steroid hormone receptors and expression of 5α-reductase type 2 activity have been documented in prostate stroma (66,70,190,332), as has the secretion of factors such as keratinocyte growth factor, a mitogen for human prostatic epithelial cells *in vitro* (171,177,189).

Overall, accumulating *in vivo* and *in vitro* observations indicate greater qualitative and quantitative diversity in epithelial and stromal components of the prostate than has been appreciated. Traditional phenotypic characterization of cells may fail to identify significant physiologic differences. The dynamic interaction of these cells seems to play a major role in the degree and character of cellular and organ growth. More exact characterization of the cellular components of the internal architecture of the prostate will almost certainly add significantly to our ability to understand and alter pathologic growths of the prostate.