Section 1 Anatomy and physiology

Chapter 1

Functional anatomy of the hypothalamic–pituitary–gonadal axis and the male reproductive tract

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Anatomy of reproductive function

The reproductive functional axis of the male can be divided into three major subdivisions: (1) the hypothalamus, (2) the pituitary gland, and (3) the testis. Each level elaborates a signal, or transmitter molecule, that stimulates or inhibits the subsequent level of the axis. The end result is the production and expulsion of semen that contains spermatozoa. This chapter examines the hypothalamic–pituitary–gonadal (HPG) axis, and reviews the functional anatomy of the testis, epididymis, vas deferens, seminal vesicles, prostate, and penis.

Hypothalamus and anterior pituitary gland

The control of male sexual and reproductive function begins with secretion of gonadotropin-releasing hormone (GnRH) by the hypothalamus (Fig. 1.1). This hormone in turn stimulates the anterior pituitary gland to secrete two downstream hormones (termed gonadotropins). These hormones are luteinizing hormone (LH) and follicle-stimulating hormone (FSH). LH is the primary stimulus for the testicular secretion of testosterone, while FSH mainly stimulates spermatogenesis.

Gonadotropin-releasing hormone (GnRH)

The neuronal cells of the arcuate nuclei of the hypothalamus secrete GnRH, a 10-amino-acid peptide. The endings of these neurons terminate in the median eminence of the hypothalamus, where they release GnRH into the hypothalamic–hypophysial portal vascular system. The GnRH is transported to the anterior pituitary gland via the hypophysial portal blood and stimulates the release of the two gonadotropins, LH and FSH [1]. The output of GnRH is influenced by three types of rhythmicity: seasonal, on a timescale of

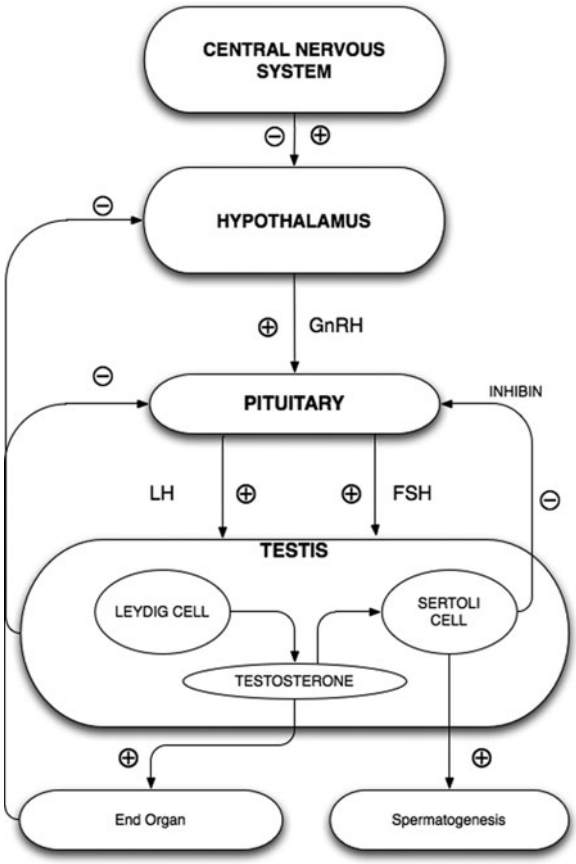

Figure 1.1. Feedback regulation of the hypothalamic–pituitary–gonadal (HPG) axis in males. Positive (stimulatory) effects are shown by + and inhibitory (negative feedback) effects by –. GnRH, gonadotropin-releasing hormone; LH, luteinizing hormone; FSH, follicle-stimulating hormone.

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months and peaking in the spring; circadian, resulting in highest testosterone levels during the early morning hours; and pulsatile, with peaks occurring every 90–120 minutes on average [2]. The intensity of this hormone's stimulus is determined (1) by the frequency of the cycles of secretion and (2) by the quantity of GnRH released with each cycle. LH secretion by the anterior pituitary gland is also cyclical. LH follows the pulsatile release of GnRH. On the other hand, FSH secretion changes slowly with the fluctuation of GnRH secretion over a period of many hours.

Gonadotropic hormones: LH and FSH

Luteinizing hormone and follicle-stimulating hormone are glycoproteins that are secreted by gonadotropic cells in the anterior pituitary gland. In the absence of GnRH secretion from the hypothalamus, the gonadotropes in the pituitary gland secrete essentially no LH or FSH. They exert their effects on their target tissues in the testes via the cyclic adenosine monophosphate (cAMP) second messenger system. This, in turn, activates specific enzyme systems in the respective target cells.

Testosterone and LH

Testosterone is secreted by the Leydig cells in the interstitium of the testes in response to stimulation by LH from the anterior pituitary gland. The quantity of testosterone secreted is nearly directly proportional to the level of LH stimulation. Mature Leydig cells are normally found in a child's testes for a few weeks after birth, but then involute until puberty. The secretion of LH at puberty causes testicular interstitial cells that look like fibroblasts to evolve into functional Leydig cells.

Negative feedback of testosterone

The testosterone secreted by the testes in response to LH inhibits the secretion of LH from the anterior pituitary. The bulk of this inhibition is most likely from the direct effect of testosterone on the hypothalamus to decrease the secretion of GnRH. A decrease in GnRH secretion results in a parallel decrease in secretion of both LH and FSH by the anterior pituitary. This decrease in LH, in turn, decreases the secretion of testosterone by the testes. Hence, whenever serum level of testosterone exceeds the body's preset homeostatic level, the automatic negative feedback effect, operating through the hypothalamus and anterior pituitary gland, reduces the testosterone secretion back toward the desired operating level (see Chapter 30). On the contrary, a testosterone-poor environment allows the hypothalamus to secrete large amounts of GnRH, with a corresponding increase in LH and FSH from the anterior pituitary and an increase in testicular testosterone secretion.

Testosterone and FSH

In the seminiferous tubules, both FSH and testosterone are necessary for the maintenance of spermatogenesis. Specific FSH-dedicated receptors on the Sertoli cells induce Sertoli cell growth and elaboration of various spermatogenic substances. Simultaneously, the paracrine action of testosterone and dihydrotestosterone from the interstitial Leydig cells stimulates and supports spermatogenesis in the seminiferous tubule.

Inhibin

Inhibin is a glycoprotein, like both LH and FSH. It has a molecular weight of 36 000 daltons. Inhibin is dimeric in structure, and the two monomers are linked together by a single disulfide bond. The monomers are termed α and β subunits. The α subunit is conserved in the different types of inhibin, but the β subunit varies. In humans, the Sertoli cells secrete inhibin B ($\alpha\beta_B$). Inhibin B selectively suppresses FSH secretion in the anterior pituitary gland by inhibiting transcription of the gene encoding the β subunit of FSH [3]. Additionally, inhibin has a slight effect on the hypothalamus to inhibit secretion of GnRH. Inhibin is released from the Sertoli cells in response to robust, rapid spermatogenesis. The end result is to diminish the pituitary secretion of FSH. Conversely, when the seminiferous tubules fail to produce sperm, inhibin production diminishes, resulting in a marked increase in FSH secretion. This potent inhibitory feedback effect on the anterior pituitary gland provides an important negative feedback mechanism for control of spermatogenesis, operating simultaneously with and in parallel to the negative feedback mechanism for control of testosterone secretion.

Testis

Embryologically, the testes develop at the urogenital ridge and descend into the scrotum via the inguinal canal at birth. These two paired organs are suspended

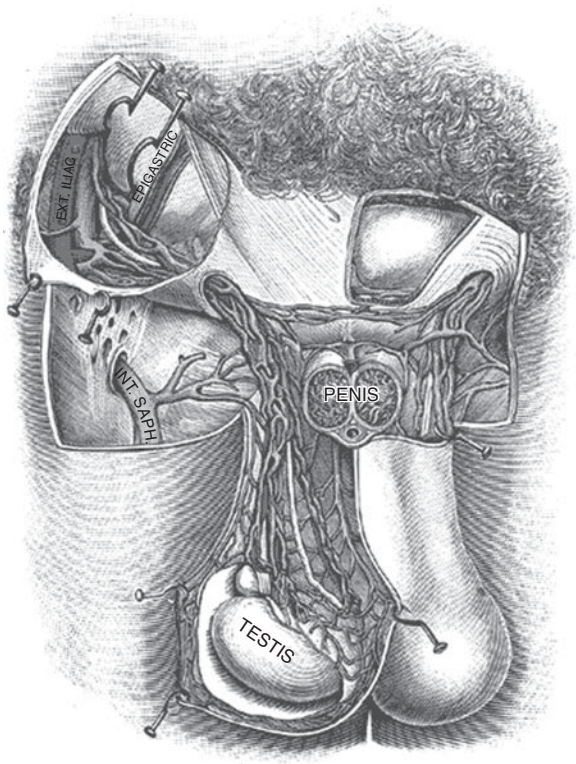

Figure 1.2. Vascular anatomy of the spermatic cord and testis. (Reproduced from Gray H. *Anatomy of the Human Body.* Philadelphia, PA: Lea & Febiger, 1918; Bartleby.com, 2000.) *See color plate section.*

on the spermatic cords and are covered by numerous layers of tissue. Upon emerging from the inguinal ring in utero, they are covered by the tunica vaginalis, internal spermatic fascia, cremasteric muscle, external spermatic fascia, dartos fascia, and skin.

Arterial and venous supply

The arterial supply of the testis is derived from three different sources (Fig. 1.2). The testicular artery arises from the aorta. The artery of the vas deferens (vasal artery) originates from the internal iliac artery. Lastly, the cremasteric artery (external spermatic artery) arises from the inferior epigastric artery [4].

The testicular artery becomes part of the countercurrent exchange phenomenon when it associates with a network of veins known as the pampiniform plexus. Several veins (pampiniform plexus) surround the convoluted testicular artery. The surrounding venous blood cools down arterial blood arriving at the testis. The accepted explanation for the pampiniform plexus is that it functions to efficiently maintain the optimal temperature for spermatogenesis, which is below body temperature. Skandhan and Rajahariprasad hypothesized that the process of spermatogenesis results in a large amount of heat, which has to be regulated [5]. The pampiniform plexus and the human scrotal skin act as a radiator for the robust heat generation. The scrotal skin is devoid of subcutaneous fat, and the presence of high sweat-gland density enables heat transmission. Upon exposure to cold temperatures, the scrotal surface is minimized by contraction, preventing temperature loss, and cremaster muscles retract the testes closer to the abdomen, for temperature maintenance.

The rich anastomoses between the testicular (internal spermatic) and vasal arteries allow maintenance of testicular viability if the internal spermatic artery is transected. In the testis, the artery gives rise to centrifugal arteries that pierce the testicular parenchyma. Further branches divide into arterioles that bring in blood to peritubular and intertubular capillaries [6]. In some men, up to 90% of testicular blood supply derives from the testicular artery.

Testicular venous drainage is through the pampiniform plexus, which in the region of the internal inguinal ring gives origin to the testicular vein [7]. The left testicular vein discharges into the left renal vein at a right angle, whereas the right testicular vein discharges directly into the inferior vena cava at an oblique angle. All testicular veins have valves. In the region of the fourth lumbar vertebra the testicular veins divide into two trunks, one lateral and one medial [7,8]. The lateral trunk is anastomosed with retroperitoneal veins, mainly colonic and renal capsular veins, and the medial trunk is anastomosed with ureteral veins [7,8].

Testicular organization

The interior of the testis can be divided into compartments (Fig. 1.3). Within each compartment, are seminiferous tubules and interstitial tissue. The seminiferous tubules are long, looped structures that house spermatozoa production. The length of the uncoiled seminiferous tubules is approximately 240 meters (800 feet) [9,10]. The seminiferous tubules drain into the rete testis. Before draining into the epididymis, the tubules of the rete testis unite into 6–12 ductuli efferentes.

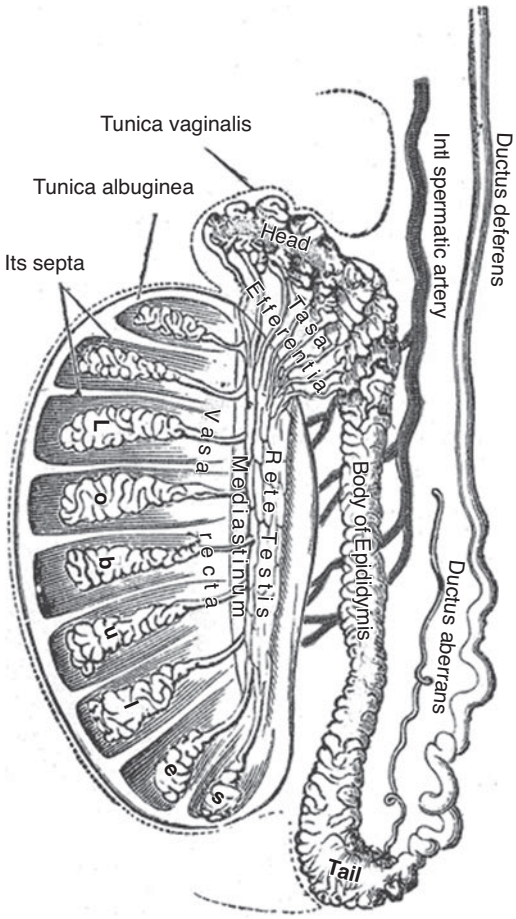

Figure 1.3. Internal structure of the testis and epididymis. (Reproduced from Gray H. *Anatomy of the Human Body*. Philadelphia, PA: Lea & Febiger, 1918; Bartleby.com, 2000.) *See color plate section.*

The seminiferous tubules contain two types of cells, spermatogenic cells and Sertoli cells, which have several functions in support of spermatogenesis. Stem cells (spermatogonia) develop from primordial germ cells that arise from the yolk sac and enter the testes during the fifth week of development (see Chapter 2). In the embryonic testes, the primordial germ cells differentiate into spermatogonia, which remain dormant during childhood and actively begin producing sperm at puberty. Toward the lumen of the seminiferous tubule are layers of progressively more mature cells. In order of advancing maturity, these are primary spermatocytes, secondary spermatocytes, spermatids, and spermatozoa. After a spermatozoon has formed, it is released into the lumen of the seminiferous tubule.

Large Sertoli cells are embedded among the spermatogenic cells in the seminiferous tubules. These "sustentacular cells" extend from the basement membrane to the lumen of the tubule. Internal to the basement membrane and spermatogonia, tight junctions join neighboring Sertoli cells to one another. These junctions form the blood–testis barrier. This barrier isolates the developing gametes from the blood and prevents an immune response against the spermatogenic cell's surface antigens, which are recognized as alien by the immune system.

Sertoli cells support and protect developing spermatogenic cells in several ways. They (1) nourish spermatocytes, spermatids, and sperm, (2) phagocytize excess spermatid cytoplasm, (3) control movements of spermatogenic cells and the release of sperm into the lumen of the seminiferous tubule, and (4) produce fluid for sperm transport, secrete inhibin, and regulate the effects of testosterone and FSH.

Spermatogenesis

In humans, spermatogenesis takes 74 days. It begins with the spermatogonia, which contain the diploid ($2n$) number of chromosomes. Spermatogonia are a variety of stem cell; when they undergo mitosis, some spermatogonia remain near the basement membrane of the seminiferous tubule in an undifferentiated state to serve as a reservoir of cells for future cell division and subsequent sperm production. The rest of the spermatogonia lose contact with the basement membrane, squeeze through the tight junctions of the blood–testis barrier, undergo developmental changes, and differentiate into primary spermatocytes. Primary spermatocytes are diploid ($2n$) and have 46 chromosomes. Shortly after it forms, the primary spermatocyte replicates its DNA in preparation for meiosis. The two cells formed by meiosis I are secondary spermatocytes. Each secondary spermatocyte is haploid (n) and has 23 chromosomes. Each chromosome within a secondary spermatocyte has two chromatids (two copies of DNA). Next, the secondary spermatocytes undergo meiosis II. In meiosis II, the two chromatids of each chromosome separate. The four haploid cells resulting from meiosis II are called spermatids. Thus, a single primary spermatocyte produces four spermatids via two rounds of cell division (meiosis I and meiosis II).

As spermatogenic cells proliferate, they fail to complete cytoplasmic separation (cytokinesis). The cells remain in contact via cytoplasmic bridges through

their entire development. This allows for the synchronized production of sperm in any given area of seminiferous tubule. The final stage of spermatogenesis is called spermiogenesis. It is the transformation of spermatids (*n*) into sperm. In spermiogenesis, no cell division occurs. The spermatid becomes a single spermatozoon. During this process, spherical spermatids are transformed into elongated, slender sperm. During this time, mitochondria multiply, and an acrosome and a flagellum develop. Sertoli cells dispose of the excess cytoplasm. Lastly, spermatozoa enter into the lumen of the seminiferous tubule as they are released from their connections to Sertoli cells in a process called spermiation. Fluid secreted by Sertoli cells pushes sperm toward the ducts of the testes. At this point, sperm are immobile and will complete maturation in the epididymis.

Epididymis

The epididymis is a tightly coiled structure, which when unfurled can be 6 meters long. Anatomically, the epididymis can be divided into three regions: the head (caput), the body (corpus), and the tail (cauda). The epididymal head consists of 8–12 efferent ducts and the initial segment of the ductus epididymis. As we move from the head to the tail of the epididymis, the lumen of the epididymis is first large and asymmetrical. It then narrows as the body of the epididymis is approached. When the tail of the epididymis is encountered, the lumen enlarges significantly (Fig. 1.3).

The epididymis is lined with pseudostratified columnar epithelium and encircled by layers of smooth muscle [11]. The free surfaces of the columnar cells contain stereocilia that increase the surface area for the reabsorption of degenerated sperm. Around the caput epididymis, a wispy layer of contractile cells encircles the tubule. In the cauda epididymis, smooth muscle cells can be seen organized in three distinct layers. Connective tissue around the muscle layers attaches the loops of the ductus epididymis and carries blood vessels and nerves.

Innervation

The innervation of the human epididymis is a product of the pelvic plexus and the hypogastric plexus. These give rise to the inferior and intermediate spermatic nerves [12]. The density of the nerve fibers increases proportionally along the length of the epididymis, similar to the increase in density of smooth muscle cells [11,13,14]. Van De Velde and Risely postulated that the peristaltic activity of the epididymis could be associated with the increasing density of smooth muscle cells and nerve fibers [15].

Arterial and venous supply

The testicular artery divides into the superior and inferior epididymal branches, which delivers blood to the head and body of the epididymis [16]. The blood supply to the epididymal tail (cauda) is derived from the deferential artery (artery of the vas). As in the testis, the epididymis enjoys a rich anastamotic system through the deferential, cremasteric, and testicular arteries to ensure collateral blood flow.

In his seminal 1954 publication, MacMillan described the vessels draining blood from the body and tail of the epididymis as joining to form the vena marginalis of Haberer. This vein unites with the pampiniform plexus, the cremasteric vein, or the deferential vein [16].

Lymphatic drainage of the caput and corpus epididymis follows the internal spermatic vein and terminates in the preaortic nodes. The lymph from the cauda epididymis drains into the external iliac nodes.

Epididymal function

The function of the epididymis can be divided into three broad categories: (1) sperm storage, (2) sperm maturation, and (3) sperm transport.

Storage of sperm

The two testes of the human adult form up to 120 million sperm each day. An average of 215 million spermatozoa are stored in each epididymis [17]. Approximately half of the total number of epididymal spermatozoa is stored in the caudal region. They can remain stored, maintaining their fertility, for at least a month. During this time, they are kept in a deeply suppressed inactive state by multiple inhibitory substances in the secretions of the ducts. Conversely, with a high level of sexual activity and ejaculations, storage may be no longer than a few days [18]. After ejaculation, the sperm become motile, and they also become capable of fertilizing the ovum. The Sertoli cells and the epithelium of the epididymis secrete a special nutrient fluid that is ejaculated along with the sperm. This fluid contains hormones (including both testosterone

and estrogens), enzymes, and special nutrients that are essential for sperm maturation.

Maturation of sperm

After formation in the seminiferous tubules, the sperm require several days to pass through the 6-meter-long tubule of the epididymis. Sperm removed from the seminiferous tubules and from the early portions of the epididymis are non-motile, and they cannot fertilize an ovum [19]. However, after the sperm have been in the epididymis for some 18–24 hours they develop the capability of motility, even though several inhibitory proteins in the epididymal fluid still prevent final motility until after ejaculation [20–23].

The normal motile, fertile sperm are capable of flagellated movement though the fluid medium at velocities of 1–4 mm/min. The activity of sperm is greatly enhanced in a neutral and slightly alkaline medium, as exists in the ejaculated semen, but it is greatly depressed in a mildly acidic medium. A strong acidic medium can cause rapid death of sperm. The activity of sperm increases markedly with increasing temperature, but so does the rate of metabolism, causing the life of the sperm to be considerably shortened. Although sperm can live for many weeks in the suppressed state in the genital ducts of the testes, life expectancy of ejaculated sperm in the female genital tract is only 1–2 days.

Transport of sperm

Sperm transport from the caput epididymis to the cauda epididymis takes between 2 and 12 days [17,24]. Transit of sperm through the cauda can be variable, and it is affected by sexual activity [25]. Movement of the sperm through the epididymis is influenced by motile cilia and the muscular contraction of the ductuli efferentes. As previously mentioned, the density of smooth muscle cells increases proportionally along the length of the epididymis, which is responsible for the spontaneous rhythmic contractions of the epididymis.

Vas deferens and ejaculatory duct

In its caudal portion, the epididymis becomes less convoluted, and its outer diameter increases to 2–3 mm (inner diameter 300–500 μm). Beyond this point, the duct is known as the vas deferens or ductus deferens. The ductus deferens is 45 cm long and travels within the spermatic cord towards the pelvis. In the pelvis it runs superior to the ureter at the level of the bladder

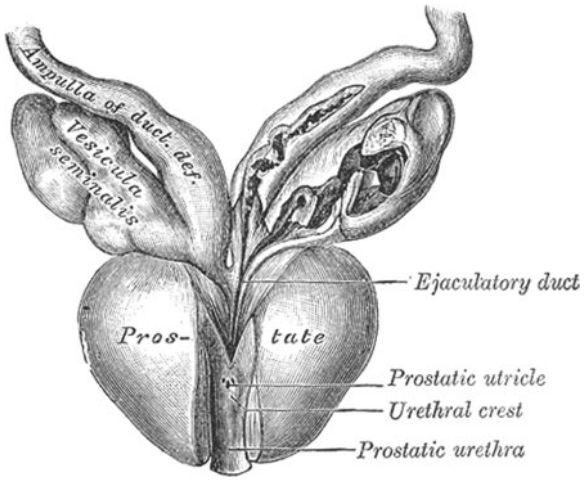

Figure 1.4. Prostate, seminal vesicles, vas deferens and ejaculatory ducts and prostatic urethra. (Reproduced from Gray H. *Anatomy of the Human Body*. Philadelphia, PA: Lea & Febiger, 1918; Bartleby.com, 2000.)

and travels in an inferior medial direction to enter the superior-posterior surface of the prostate. The ejaculatory duct then continues within the prostate gland.

The blood supply of the vas deferens is derived from the inferior vesicle artery via the deferential artery [26]. The vas deferens has both parasympathetic and sympathetic input. However, the dominant source of innervation is from the sympathetic adrenergic system.

The mucosa of the vas deferens consists of pseudostratified columnar epithelium and lamina propria [27]. The vas deferens is composed of three layers of smooth muscle: an inner and outer longitudinal layer, and a middle circular layer.

The primary function of the vas deferens and ejaculatory duct is to transport mature sperm to the prostatic urethra. Similar to the epididymis, the vas deferens exhibits a sperm storage capacity for several months.

Seminal vesicles

The seminal vesicles lie posterior to the base of the urinary bladder and anterior to the rectum (Fig. 1.4). The arterial supply of the seminal vesicles is derived from the inferior vesical artery and the middle rectal artery. Venous drainage is through the inferior vesical and middle rectal veins. Lymphatic drainage is directed to the internal iliac lymph nodes.

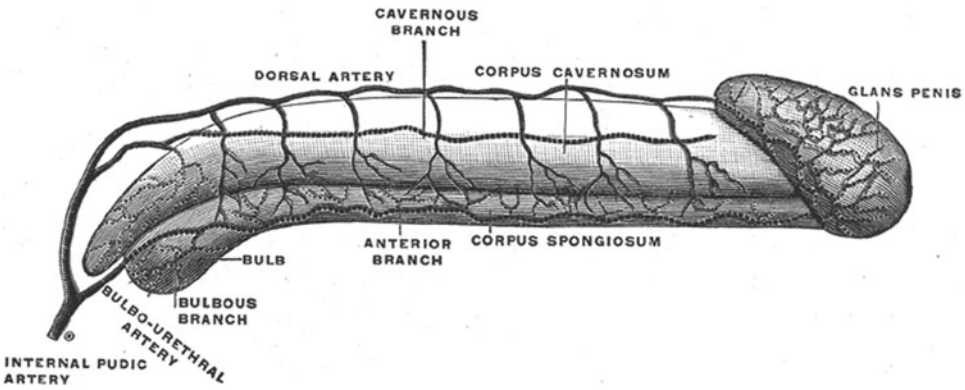

Figure 1.5. Arterial anatomy of the penis. (Reproduced from Gray H. *Anatomy of the Human Body.* Philadelphia, PA: Lea & Febiger, 1918; Bartleby.com, 2000.) *See color plate section.*

The embryonic origin of the seminal vesicles is the Wolffian duct. Its convoluted structure houses a secretory epithelial lining. Fluid secreted by the seminal vesicles normally constitutes about 80% of the volume of semen. The fluid is an alkaline, viscous fluid that contains fructose, prostaglandins, and clotting proteins. The alkaline nature of the seminal fluid helps to neutralize the acidic secretions of the female reproductive tract that otherwise would inactivate and kill sperm. The fructose is an important energy source for the sperm. Prostaglandins may contribute to sperm motility and viability [28]. The clotting proteins help semen coagulate after ejaculation, but the semen is subsequently liquefied by prostatic proteases.

Prostate

The prostate is a walnut-sized gland that lies at the base of the bladder (Fig. 1.4). It measures about 4 × 3 × 2 cm. The arterial supply of the prostate is derived from branches of the internal iliac artery: the inferior vesical artery, the internal pudendal artery, and the middle rectal artery. The prostatic venous plexus drains into the internal iliac veins. Lymphatic vessels terminate mainly in the internal iliac nodes.

Prostatic secretions constitute approximately 25–30% of the fluid volume of the ejaculate. The fluid is a milky, slightly acidic fluid that contains several substances such as citric acid, prostate-specific antigen, pepsinogen, lysozyme, amylase, hyaluronidase, and acid phosphatase. These substances are presumed to contribute to sperm motility and viability.

Bulbourethral glands

The bulbourethral glands (sometimes called Cowper's glands) are about the size of peas. They lie posterolateral to the membranous urethra within the muscles of the pelvic floor. Their ducts open into the spongy urethra. During sexual arousal, these glands secrete a fluid that acts to lubricate the urethra and the penile glans. The fluid is slightly alkaline and plays a role in neutralizing residual urethral urine.

Penis

The functional unit of the penis consists of the corpora cavernosa. These dual cylindrical erectile bodies form the basis of the erection. They are connected to each other for the distal two-thirds of their length. There are robust fenestrations within the corpora cavernosa that allow cross-talk between the corpora. Proximally, they are connected to the undersurface of the inferior pubic rami. A thick fibrous covering called the tunica albuginea surrounds each corpus cavernosum. As a result of cavernous nerve signals, the spongy sinusoidal spaces fill with blood and expand against the tunica albuginea, compressing the subtunical venous plexuses, decreasing venous outflow. The sinusoidal spaces (lacunar spaces) are lined by vascular endothelium. The walls of these spaces are referred to as trabeculae and are composed of smooth muscle and collagen.

Arterial and venous supply

The internal iliac artery supplies vascular inflow to the corpus cavernosum (Fig. 1.5). This artery splits into the

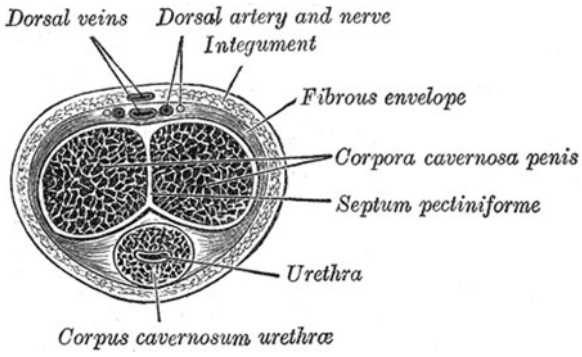

Figure 1.6. Cross-section of the penis. (Reproduced from Gray H. *Anatomy of the Human Body*. Philadelphia, PA: Lea & Febiger, 1918; Bartleby.com, 2000.) *See color plate section.*

inferior gluteal and the internal pudendal artery just proximal to the coccygeus muscle. The internal pudendal runs beneath the sacrospinous ligament and over the sacrotuberous ligament where it enters Alcock's canal. As the artery exits the canal, it gives off the perineal artery before piercing the urogenital diaphragm. The perineal artery continues its course anteriorly and superiorly to deliver blood to the ischiocavernosus muscle, aspects of the bulbospongiosus muscle, and the posterior surface of the scrotum.

After the internal pudendal artery emerges from Alcock's canal, it is referred to as the common penile artery. The common penile artery then branches into the artery of the penile bulb, urethral artery, dorsal penile artery, and the deep artery of the penis (cavernosal artery). The paired cavernosal arteries enter the tunica albuginea at the base of the penis. They travel centrally within each corpus, sprouting helicine arteries at regular intervals. These small serpentine vessels terminate directly into the sinusoidal spaces. Neuromediated relaxation of the trabeculae (walls of the sinusoidal spaces) allows expansion of these sinusoids and the subsequent initiation and maintenance of erection (Fig. 1.6).

Venous drainage of the penis loosely mirrors the arterial supply. Blood leaves the penis via three paths: deep, middle, and superficial venous system. The deep system drains the proximal third of the penis. Emissary veins emerge from this region of the penis and link with the cavernosal, bulbar, and crural veins. Blood from this region drains into the internal pudendal vein.

The middle drainage system receives blood from the glans and corpus spongiosum, as well as the distal two-thirds of the penile shaft. Blood draining the sinusoidal (lacunar) spaces is directed into a rich network of subtunical veins called the subtunical plexus. This plexus sends emissary veins through the tunica albuginea, where they anastamose with circumflex veins. The circumflex veins drain into the deep dorsal vein and then the retrocoronal venous plexus before continuing to the dorsal venous complex in the pelvis.

The superficial drainage system is largely composed of the paired superficial penile veins. They accept blood from numerous surface veins. Blood from this system ultimately ends up in the saphenous system.

Neuroanatomy

Innervation from the sacral parasympathetic (pelvic), thoracolumbar sympathetic, and somatic (pudendal) nerves is required for the generation of erection and ensuing detumescence [29–33]. Parasympathetic neurons originate in the sacral spinal cord (S2–S4). They provide the major excitatory input to the penis. Excitatory signals leave the intermediolateral nuclei and travel via the pelvic nerve (or nervi erigentes) to the pelvic plexus. Here, the preganglionic fibers relay their information to the short, postganglionic cavernosal nerve. The cavernosal nerve courses along the posterolateral aspect of the prostate before exiting the pelvis [34]. As the nerves leave the pelvis, they are intimately related to the urethra. Before entering the corpus cavernosum at the crus, the cavernous nerve sends branches to the corpus spongiosum [29,34].

Sympathetic innervation of the penis originates in the intermediolateral columns of the thoracolumbar spinal cord. Fibers pass through in the sympathetic chain before descending to the inferior mesenteric and superior hypogastric plexuses. The nerve fibers then coalesce to form the hypogastric nerve en route to the pelvic plexus. From there, the sympathetic fibers reach the penis via the cavernous nerves. Additionally, sympathetic input may be accomplished through the pelvic nerve and the pudendal nerve [35].

Additionally, sympathetic innervation is responsible for ejaculation. This reflex is initiated by stimulation of the postganglionic fibers of the lumbar spinal cord and results in the contraction of the bladder neck with simultaneous contraction of the ejaculatory duct. Prior to ejaculation, emission occurs. During emission, the epididymis, vas deferens, seminal vesicles,

and prostate contract to force semen into the posterior urethra. Somatic contractions of the bulbospongiosus, ischiocavernosus, and superficial transverse perineus muscles assist in semen propulsion.

The third component of penile neuroanatomy is the somatic system [29,30,36]. The afferent fibers transmit tactile information from the genitalia to the central nervous system [29]. Efferent fibers carry impulses to skeletal muscles [36]. The pudendal nerve conveys motor and sensory impulses. The cell bodies originate in the spinal segments S2–S4. The nerve courses through Alcock's canal before giving off inferior rectal, perineal, and posterior scrotal nerves. The last branch of the pudendal nerve is the dorsal nerve of the penis. It provides motor innervation for the ischiocavernosus and bulbospongiosus muscle. In the penis, this paired nerve runs laterally to the dorsal artery and communicates sensory information from the glans penis and the penile shaft to the sacral cord.

Erection and detumescence: cavernosal smooth muscle physiology

Relaxation of the cavernosal smooth muscle cell is the biological event responsible for the erection [37–39]. As previously mentioned, the trabeculae between the lacunar spaces are occupied by smooth muscle and collagen, in a ratio of 1 : 1 [37,39,40]. The smooth muscle cells are composed of thin, intermediate, and thick filaments [40–42]. The most important of these are the thin (actin) and thick (myosin) filaments [41,42].

The cavernous nerve releases nitric oxide that stimulates the conversion of guanosine triphosphate (GTP) to cyclic guanosine monophosphate (cGMP). cGMP and cAMP cause the potassium channels to open, resulting in cellular hyperpolarization. The calcium channels close, causing the endoplasmic reticulum to sequester intracellular calcium, leaving a Ca^{2+}-poor microenvironment [43]. The calcium–calmodulin complex (which is bound to myosin light chain kinase [MLCK] in the contractile state) disassociates, causing decoupling of the myosin–actin cross-bridges [41,42]. Smooth muscle relaxation ensues, resulting in filling of sinusoidal spaces and penile rigidity [40,43].

Sympathetic-mediated release of norepinephrine and epinephrine sets a second messenger system in motion that increases intracellular concentration of calcium ions. The higher Ca^{2+} stimulates the formation of a calcium–calmodulin complex that binds to and activates MLCK, allowing the chain reaction for smooth muscle contraction to occur, leading to detumescence after orgasm.

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