UNIT
Nine

Alterations in the Male and Female Reproductive Systems

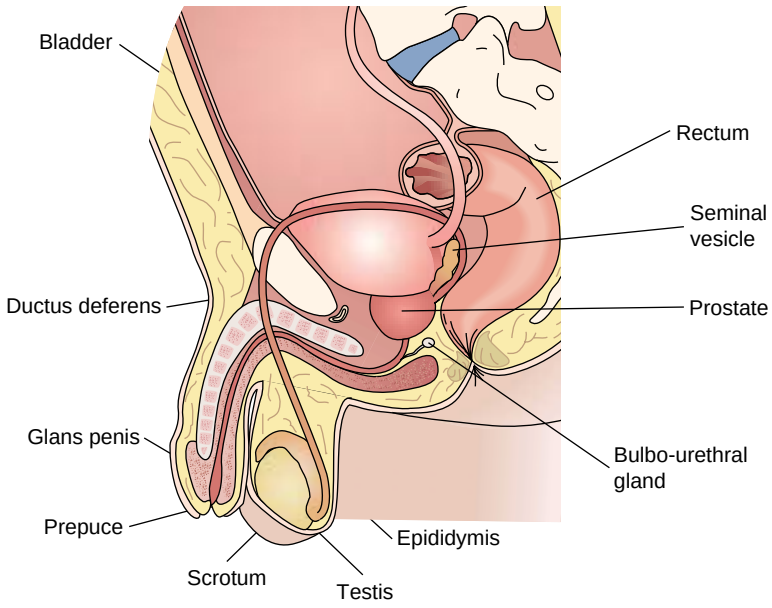
CHAPTER
33

Alterations in the Male Reproductive System

The male genitourinary system is subject to structural defects, inflammation, and neoplasms, all of which can affect urine elimination, sexual function, and fertility. This chapter focuses on spermatogenesis and hormonal control of male reproductive function; neural control of sexual function and erectile dysfunction; disorders of the penis, scrotum, testes, and prostate; disorders of the male reproductive system in children; and changes in function as a result of the aging process.

PHYSIOLOGIC BASIS OF MALE REPRODUCTIVE FUNCTION

The male genitourinary system is composed of the paired gonads, or testes, genital ducts, accessory organs, and penis (Fig. 33-1). The dual function of the testes is to produce male sex androgens (*i.e.*, male sex hormones), mainly testosterone, and spermatozoa (*i.e.*, male germ cells). The internal accessory organs produce the fluid constituents of semen, and the ductile system aids in the storage and transport of spermatozoa. The penis functions in urine elimination and sexual function.



■ **FIGURE 33-1** ■ The structures of the male reproductive system, including the testes, the scrotum, and the excretory ducts.

Spermatogenesis

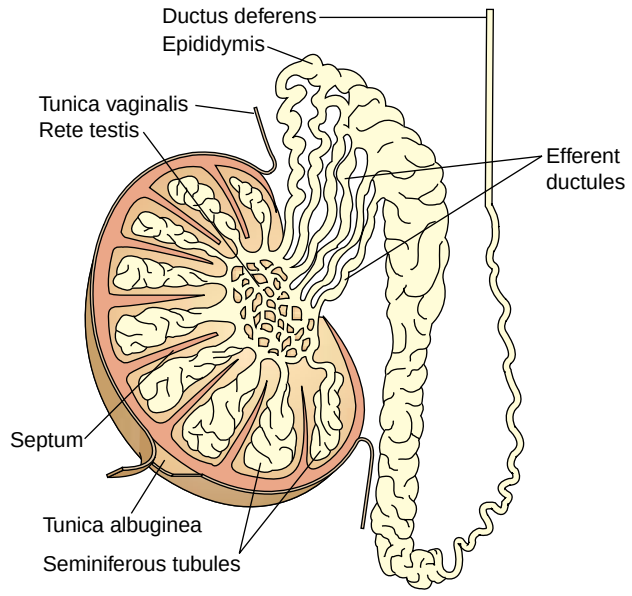
Spermatogenesis refers to the generation of spermatozoa or sperm. It begins at an average age of 13 years and continues throughout the reproductive years of a man's life. Spermatogenesis occurs in the seminiferous tubules of the testes (Fig. 33-2). Internally, the testes are composed of several hundred compartments or lobules. Each lobule contains one or more coiled seminiferous tubules. The outer layer of the seminiferous tubules is made up of connective tissue and smooth muscle; the inner lining is composed of Sertoli's cells, which are embedded with sperm in various stages of development (Fig. 33-3). Sertoli's cells secrete a special fluid that contains nutrients to bathe and nourish the immature germ cells; they provide digestive enzymes that play a role in spermiation (*i.e.*, converting the spermatocytes to sperm); and they are thought to play a role in shaping the head and tail of the sperm. Sertoli's cells also secrete several hormones, including the principal feminizing sex hormone, estradiol, which seems to be required in the male for spermatogenesis, and inhibin, which controls the function of Sertoli's cells through feedback inhibition of follicle-stimulating hormone (FSH) from the anterior pituitary gland.

After the spermatozoa are formed in the seminiferous tubules, they travel through the efferent tubules to the epididymis, which is the final site for sperm maturation. Because the spermatozoa are not motile at this stage of development,

KEY CONCEPTS

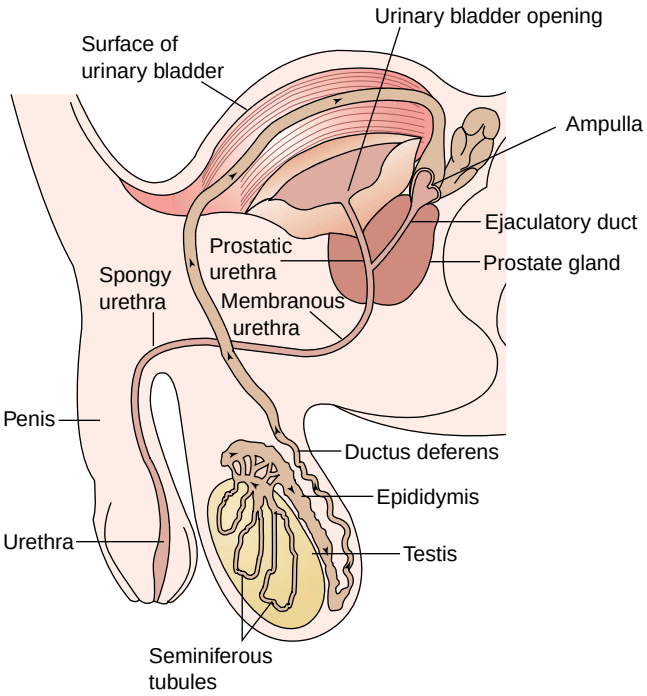
MALE REPRODUCTIVE SYSTEM

- The male genitourinary system functions in both urine elimination and reproduction.
- The testes function in both production of male germ cells (spermatogenesis) and secretion of the male sex hormone, testosterone.
- The ductile system (epididymides, vas deferens, and ejaculatory ducts) transports and stores sperm and assists in their maturation, and the accessory glands (seminal vesicles, prostate gland, and bulbourethral glands) prepare the sperm for ejaculation.
- Sperm production requires temperatures that are 2° to 3°C below body temperature. The position of the testes in the scrotum and the unique blood flow-cooling mechanisms provide this environment.
- The urethra, which is enclosed in the penis, is the terminal portion of the male genitourinary system. Because it conveys both urine and semen, it serves both urinary and reproductive functions.



■ **FIGURE 33-2** ■ The parts of the testes and epididymis.

■ **FIGURE 33-3** ■ (**A**) Cross-section of seminiferous tubule and (**B**) stages of development of spermatozoa.



■ **FIGURE 33-4** ■ The excretory ducts of the male reproductive system and the path that sperm follows as it leaves the testis and travels to the urethra.

peristaltic movements of the ductal walls of the epididymis aid in their movement.[1] The spermatozoa continue their migration through the ductus deferens, also called the *vas deferens*. The ampulla of the vas deferens serves as a storage reservoir for sperm. Sperm are stored in the ampulla until they are released through the penis during ejaculation (Fig. 33-4). Spermatozoa can be stored in the genital ducts for as long as 42 days and still maintain their fertility. Surgical disconnection of the vas deferens in the scrotal area (*i.e.*, vasectomy) serves as an effective method of male contraception. Because sperm are stored in the ampulla, men can remain fertile for 4 to 5 weeks after performance of a vasectomy.

The seminal vesicles, the prostate gland, and the bulbourethral glands form the accessory reproductive structures of the male genitourinary system. The spermatozoa plus the secretions from the genital ducts and accessory organs make up the semen (from the Latin word meaning *seed*). The seminal vesicles consist of two highly tortuous tubes that secrete fluid for the semen. Each of the paired seminal vesicles is lined with secretory epithelium containing an abundance of fructose, prostaglandins, and several other proteins. The fructose secreted by the seminal vesicles provides the energy for sperm motility. The prostaglandins are thought to assist in fertilization by making the cervical mucus more receptive to sperm and by causing reverse peristaltic contractions in the uterus and fallopian tubes to move the sperm toward the ovaries. Each seminal vesicle joins its corresponding vas deferens to form the ejaculatory duct, which enters the posterior part of the prostate and continues through until it ends in the prostatic portion of the urethra. During the emission phase of coitus, each vesicle empties fluid into the ejaculatory duct, adding bulk to the semen. Approximately 70% of the ejaculate originates in the seminal vesicles.

Hormonal Control of Male Reproductive Function

The male sex hormones are called *androgens*. The testes secrete several male sex hormones, including *testosterone*, *dihydrotestosterone*, and *androstenedione*.[2] Testosterone, which is the most abundant of these hormones, is considered the main testicular hormone. The adrenal cortex also produces androgens, although in much smaller quantities (<5% of the total male androgens) than those produced in the testes. The testes also secrete small quantities of estradiol and estrone.

Testosterone is produced and secreted by the interstitial Leydig's cells in the testes. It is metabolized in the liver and excreted by the kidneys. In the bloodstream, testosterone exists in

a free (unbound) or a bound form. The bound form is attached to plasma proteins, including albumin and the sex hormone-binding protein produced by the liver. Only approximately 2% of circulating testosterone is unbound and therefore able to enter the cell and exert its metabolic effects. Much of the testosterone that becomes fixed to the tissues is converted to dihydrotestosterone, especially in certain target tissues such as the prostate gland. Some of the actions of testosterone depend on this conversion, whereas others do not. Testosterone also can be aromatized or converted to estradiol in the peripheral tissues.

Testosterone exerts a variety of biologic effects in the male (Chart 33-1). In the male embryo, testosterone is essential for the appropriate differentiation of the internal and external genitalia, and it is necessary for descent of the testes in the fetus. Testosterone is essential to the development of primary and secondary male sex characteristics during puberty and for the maintenance of these characteristics during adult life. It causes growth of pubic, chest, and facial hair; it produces changes in the larynx that result in the male bass voice; and it increases the thickness of the skin and the activity of the sebaceous glands, predisposing to acne.

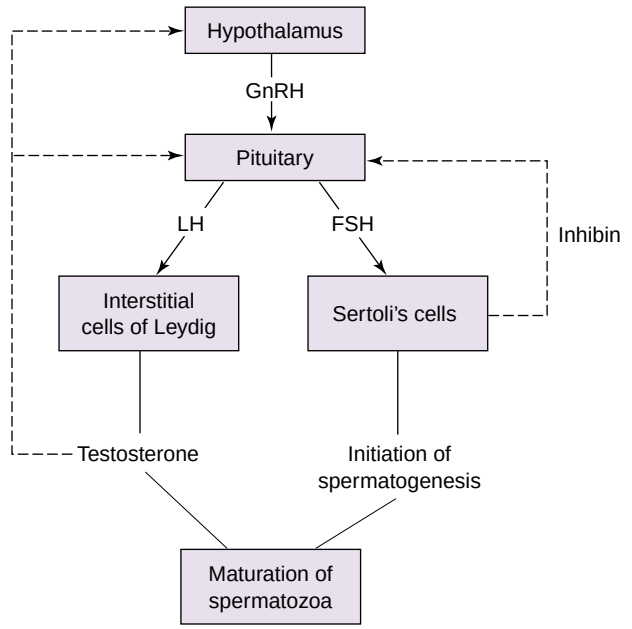
All or almost all of the actions of testosterone and other androgens result from increased protein synthesis in target tissues. Androgens function as anabolic agents in males and females to promote metabolism and musculoskeletal growth. Testosterone and the androgens have a great effect on the development of increasing musculature during puberty, with boys averaging approximately 50% more of an increase in muscle mass than do girls.

Action of the Hypothalamic and Anterior Pituitary Hormones

The hypothalamus and the anterior pituitary gland play an essential role in promoting spermatogenic activity in the testes and maintaining the endocrine function of the testes by means of the gonadotropic hormones. The synthesis and release of the gonadotropic hormones from the pituitary gland are regulated by gonadotropin-releasing hormone (GnRH), which is synthesized by the hypothalamus and secreted into the hypothalamo-hypophysial portal circulation (Fig. 33-5).

CHART 33-1 Main Actions of Testosterone

- Induces differentiation of the male genital tract during fetal development
- Induces development of primary and secondary sex characteristics
  - Gonadal function
  - External genitalia and accessory organs
  - Male voice timbre
  - Male skin characteristics
  - Male hair distribution
- Anabolic effects
  - Promotes protein metabolism
  - Promotes musculoskeletal growth
  - Influences subcutaneous fat distribution
- Promotes spermatogenesis (in FSH-primed tubules) and maturation of sperm



■ **FIGURE 33-5** ■ Hypothalamic-pituitary feedback control of spermatogenesis and testosterone levels in the male. The *dashed line* represents negative feedback.

Two gonadotropic hormones are secreted by the pituitary gland: FSH and luteinizing hormone (LH). In the male, LH also is called *interstitial cell-stimulating hormone*. The production of testosterone by the interstitial cells of Leydig is regulated by LH. FSH binds selectively to Sertoli's cells surrounding the seminiferous tubules, where it functions in the initiation of spermatogenesis. Under the influence of FSH, Sertoli's cells produce androgen-binding protein, plasminogen activator, and inhibin. Androgen-binding protein binds testosterone and serves as a carrier of testosterone in Sertoli's cells and as a storage site for testosterone. Although FSH is necessary for the initiation of spermatogenesis, full maturation of the spermatozoa requires testosterone. Androgen-binding protein also serves as a carrier of testosterone from the testes to the epididymis. Plasminogen activator, which converts plasminogen to plasmin, functions in the final detachment of mature spermatozoa from Sertoli's cells.

Circulating levels of the gonadotropic hormones are regulated in a negative feedback manner by testosterone. High levels of testosterone suppress LH secretion through a direct action on the pituitary and an inhibitory effect on the hypothalamus. FSH is thought to be inhibited by a substance called *inhibin*, produced by Sertoli's cells. Inhibin suppresses FSH release from the pituitary gland. The pituitary gonadotropic hormones and Sertoli's cells in the testes form a classic negative feedback loop in which FSH stimulates inhibin and inhibin suppresses FSH. Unlike the cyclic hormonal pattern in the female, in the male, FSH, LH, and testosterone secretion and spermatogenesis occur at relatively unchanging rates during adulthood.

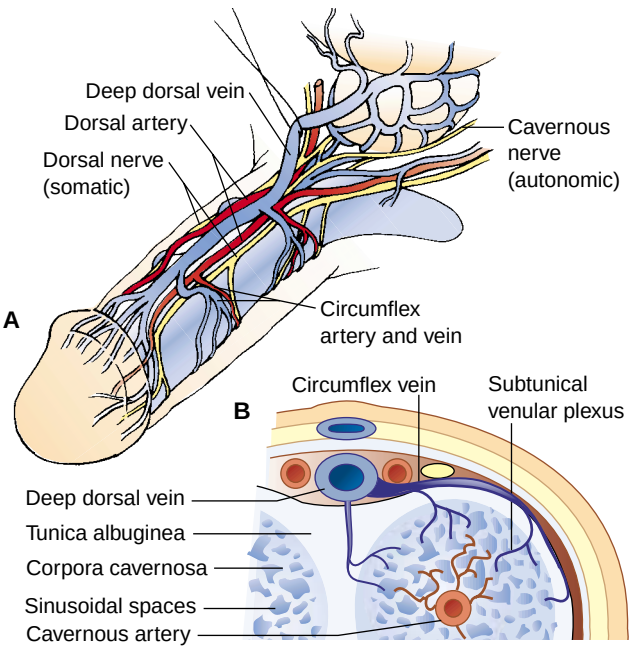
Neural Control of Sexual Function

The penis is the male external genital organ through which the urethra passes. It functions both as a sexual organ and as an organ of urine elimination. Anatomically, the external penis

consists of a shaft that ends in a tip called the *glans* (Fig. 33-1). The loose skin of the penis shaft folds to cover the glans, forming the prepuce, or foreskin. The glans of the penis contains many sensory nerves, making this the most sensitive portion of the penile shaft. The cylindrical body or shaft of the penis is composed of three masses of erectile tissue held together by fibrous strands and covered with a thin layer of skin (Fig. 33-6). The two lateral masses of tissue are called the *corpora cavernosa*. The third, ventral mass is called the *corpus spongiosum*. The corpora cavernosa and corpus spongiosum are cavernous sinuses that normally are relatively empty but become engorged with blood during penile erection.

The physiology of the male sex act involves a complex interaction between autonomic-mediated spinal cord reflexes, higher neural centers, and the vascular system. It involves erection, emission, ejaculation, and detumescence. Erection involves increased inflow of blood into the corpora cavernosa and penile rigidity. Ejaculation represents the expulsion of the sperm from the urethra. Detumescence, or penile relaxation, results from outflow of blood from the corpora cavernosa.

Erection is a neurovascular process involving the autonomic nervous system, neurotransmitters and endothelial relaxing factors, the vascular smooth muscle of the arteries and veins supplying the penile tissue, and the trabecular smooth muscle of the sinusoids of the corpora cavernosa (Fig. 33-6). The penis is innervated by both the autonomic and somatic nervous systems. In the pelvis, the sympathetic and parasympathetic components of the autonomic nervous system merge to form what are called the *cavernous nerves*.[3] Erection is under the control of the parasympathetic nervous system, and ejaculation and detumescence (penile relaxation) are under the control of the sympathetic nervous system. Somatic innervation, which occurs through the pudendal nerve, is responsible for penile sensation and contraction and relaxation of the extracorporeal striated muscles (bulbocavernous and ischiocavernous).[3]



■ **FIGURE 33-6** ■ Anatomy and mechanism of penile erection. (**A**) Innervation and arterial and venous blood supply to penis. (**B**) Cross-section of the sinusoidal system of the corpora cavernosa.

KEY CONCEPTS

DISORDERS OF PENILE ERECTION

- Erection is a neurovascular process involving the autonomic nervous system, the somatic nervous system by way of the pudendal nerve, the vascular system, and the sinusoidal spaces of the corpora cavernosa.
- Parasympathetic innervation through the pelvic nerves initiates relaxation of the trabecular smooth muscle of the corpora cavernosa through the action of nitric oxide, the inflow of arterial blood, and cessation of venous outflow.
- Erectile failure can result from disorders in one or a combination of the neural, vascular, or chemical mediator aspects of the erectile process.

Penile erection is the first effect of male sexual stimulation, whether psychological or physical. It involves increased inflow of blood into the corpora cavernosa due to relaxation of the trabecular smooth muscle that surrounds the sinusoidal spaces and compression of the veins controlling outflow of blood from the venous plexus. Erection is mediated by parasympathetic impulses that pass from the sacral segments of the spinal cord through the pelvic nerves to the penis. Parasympathetic stimulation results in release of nitric oxide, a nonadrenergic-noncholinergic neurotransmitter, which causes relaxation of trabecular smooth muscle of the corpora cavernosa. This relaxation permits inflow of blood into the sinuses of the cavernosa at pressures approaching those of the arterial system. Because the erectile tissues of the cavernosa are surrounded by a nonelastic fibrous covering, high pressure in the sinusoids causes ballooning of the erectile tissue to such an extent that the penis becomes hard and elongated. At the same time, contraction of the somatic-innervated ischiocavernous muscles forcefully compresses the blood-filled corpora cavernosa, producing a further increase in intercavernous pressures. During this phase of erection, inflow and outflow of blood cease.

Parasympathetic innervation must be intact and nitric oxide synthesis must be active for erection to occur. Nitric oxide activates guanyl cyclase, an enzyme that increases the concentration of cyclic guanosine monophosphate (cGMP), which in turn causes smooth muscle relaxation. Other smooth muscle relaxants (*e.g.*, prostaglandin E_1 analogs and α-adrenergic antagonists), if present in high enough concentrations, can independently cause sufficient cavernosal relaxation to result in erection.[3] Many of the drugs that have been developed to treat erectile dysfunction act at the levels of these mediators.

Detumescence or penile relaxation is largely a sympathetic nervous system response. It can result from a cessation of neurotransmitter release, the breakdown of second messengers such as cGMP, or sympathetic discharge during ejaculation. Contraction of the trabecular smooth muscle opens the venous

channels so that the trapped blood can be expelled and penile flaccidity return.

Erectile Dysfunction

"Erectile dysfunction is defined as the inability to achieve and maintain an erection sufficient to permit satisfactory sexual intercourse."[4] It has been estimated that the disorder affects 20 to 30 million men in the United States.[5] Erectile dysfunction is commonly classified as psychogenic, organic, or mixed psychogenic or organic.[5,6] The latter is the most common.

Psychogenic causes of erectile dysfunction include performance anxiety, a strained relationship with a sexual partner, depression, and overt psychotic disorders such as schizophrenia. Depression is a common cause of erectile dysfunction.[5]

Organic causes span a wide range of pathologies. They include neurogenic, hormonal, vascular, drug-induced, and cavernous impairment etiologies. Neurogenic disorders such as Parkinson's disease, stroke, and cerebral trauma often contribute to erectile dysfunction by decreasing libido or preventing the initiation of erection. In spinal cord injury, the extent of neural impairment depends on the level, location, and extent of the lesion. Somatosensory involvement of the genitalia is essential to the reflex mechanisms involved in erection; this becomes important with aging and conditions such as diabetes that impair peripheral nerve function.

Hormonal causes of erectile dysfunction include a decrease in androgen levels. Androgen levels may be decreased because of aging. Hypoprolactinemia from any cause interferes with both reproduction and erectile function. This is because prolactin acts centrally to inhibit dopaminergic activity, which is a stimulus for release of the hypothalamic GnRH that controls the release of pituitary gonadotropic hormones.

Common risk factors for generalized penile arterial insufficiency include hypertension, hyperlipidemia, cigarette smoking, diabetes mellitus, and pelvic irradiation.[5] In hypertension, erectile function is impaired not so much by the increased blood pressure as by the associated stenotic arterial lesions. Focal stenosis of the common penile artery most often occurs in men who sustained blunt pelvic or perineal trauma (*e.g.*, from bicycling accidents). Failure of the veins to close completely during an erection (veno-occlusive dysfunction) may occur in men with large venous channels that drain the corpora cavernosa. Other disorders that impair venous occlusion are degenerative changes involving the tunica albuginea, as in Peyronie's disease. Poor relaxation of the trabecular smooth muscle may accompany anxiety with excessive adrenergic tone.

Many drugs are reported to cause erectile dysfunction, including antidepressant, antipsychotic, and antihypertensive medications. Cigarette smoking can induce vasoconstriction and penile venous leakage because of its effects on cavernous smooth muscle.[5] Alcohol in small amounts may increase libido and improve erection; however, in large amounts it can cause central sedation, decreased libido, and transient erectile dysfunction.

Aging is known to increase the risk of erectile dysfunction.[7] Many of the pathologic processes that contribute to erectile dysfunction are more common in older men, including diabetes, hyperlipidemia, vascular disease, and the long-term effects of cigarette smoking. Age-related declines in testosterone also may play a role. Psychosocial problems such as depression, esteem issues, partner relationships, history of substance abuse, and anxiety and fear of performance failure also may contribute to erectile dysfunction in older men.

A diagnosis of erectile dysfunction requires careful history (medical, sexual, and psychosocial), physical examination, and laboratory tests aimed at determining what other tests are needed to rule out organic causes of the disorder.[6] Because many medications, including prescribed, over-the-counter, and illicit drugs, can cause erectile dysfunction, a careful drug history is indicated.

Treatment methods include psychosexual counseling, androgen replacement therapy, oral and intracavernous drug therapy, vacuum constriction devices, and surgical treatment (prosthesis and vascular surgery).[6] Among the commonly prescribed drugs are sildenafil, yohimbine, alprostadil, and phentolamine. Sildenafil (Viagra) is a selective inhibitor of phosphodiesterase type 5, the enzyme that inactivates cGMP. Yohimbine, an α_2-adrenergic receptor antagonist, acts at the adrenergic receptors in brain centers associated with libido and penile erection. Both sildenafil and yohimbine are taken orally. Alprostadil, a prostaglandin E analog, acts by producing relaxation of cavernous smooth muscle. It is either injected directly into the cavernosa or placed in the urethra as a minisuppository. Phentolamine, an α_2-adrenergic receptor antagonist, also is administered by intracavernous injection.

In summary, spermatogenesis occurs in the Sertoli's cells of the seminiferous tubules of the testes. After formation in seminiferous tubules, the spermatozoa travel through the efferent tubules to the epididymis, then to the ductus deferens, and on to the ampulla, where they are stored until released through the penis during ejaculation. The male accessory organs consist of the seminal vesicles, prostate gland, and bulbourethral glands. Secretions from the genital ducts and accessory organs combine with the spermatozoa to form the semen.

The function of the male reproductive system is under the negative feedback control of the hypothalamus and the anterior pituitary gonadotropic hormones FSH and LH. Spermatogenesis is initiated by FSH, and the production of testosterone is regulated by LH. Testosterone, the major male sex hormone, is produced by the interstitial Leydig's cells in the testes. In addition to its role in the differentiation of the internal and external genitalia in the male embryo, testosterone is essential for the development of secondary male characteristics during puberty, the maintenance of these characteristics during adult life, and spermatozoa maturation.

The male sex act involves erection, emission, ejaculation, and detumescence. The physiology of these functions involves a complex interaction between autonomic-mediated spinal cord reflexes, higher neural centers, and the vascular system. Erection is mediated by the parasympathetic nervous system and emission and ejaculation by the sympathetic nervous system. Erectile dysfunction is defined as the inability to achieve and maintain an erection sufficient to permit satisfactory sexual intercourse. It can be due to psychogenic factors, organic disorders, or mixed psychogenic and organic conditions.

DISORDERS OF THE PENIS, THE SCROTUM AND TESTES, AND THE PROSTATE

Disorders of the Penis

Disorders of the penis include congenital defects (discussed in Disorders in Childhood), acute and chronic inflammatory conditions, Peyronie's disease, priapism, and neoplasms.

Inflammation and Infection

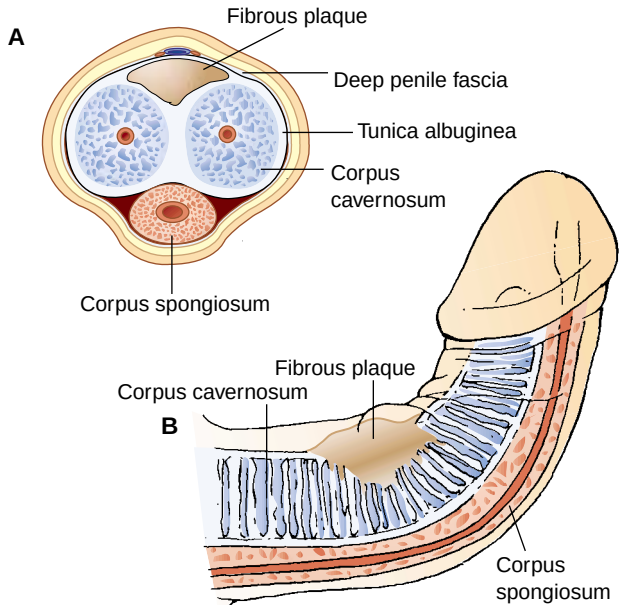
Balantitis and Balanoposthitis. *Balanitis* is an acute or chronic inflammation of the glans penis. *Balanoposthitis* refers to inflammation of the glans and prepuce. It usually is encountered in males with phimosis (a tight foreskin) or a large, redundant prepuce that interferes with cleanliness and predisposes to bacterial growth in the accumulated secretions and smegma (*i.e.*, debris from the desquamated epithelia). If left untreated, the condition may cause ulcerations of the mucosal surface of the glans; these ulcerations may lead to inflammatory scarring of the phimosis and further aggravate the condition.

Acute superficial balanoposthitis is characterized by erythema of the glans and prepuce. An exudate in the form of malodorous discharge may be present. Extension of the erythema and edema may result in phimosis. The condition may result from infection, trauma, or irritation. Infective balanoposthitis may be caused by a wide variety of organisms. Chlamydiae and mycoplasmas have been identified as causative organisms in this disease. The inflammatory reaction is nonspecific, and correct identification of the specific agent requires bacterial smears and cultures.

Balanitis xerotica obliterans is a chronic white, patchy lesion that originates on the glans and usually progresses to involve the meatus. It is clinically and histologically similar to the lichen sclerosus that is seen in females. It commonly is observed in middle-aged diabetic men. Treatment measures include topical or intralesional injections of corticosteroids.[8]

Peyronie's Disease

Peyronie's disease involves a localized and progressive fibrosis of unknown origin that affects the tunica albuginea (*i.e.*, the tough, fibrous sheath that surrounds the corpora cavernosa) of the penis. It is named after Francois de la Peyronie, who wrote in 1743, describing a patient who had "rosary beads of scar tissue to cause upward curvature of the penis during erection."[9] The disorder is characterized initially by an inflammatory process that results in dense fibrous plaque formation. The plaque usually is on the dorsal midline of the shaft, causing upward bowing of the shaft during erection (Fig. 33-7). Some men may develop scarring on both the dorsal and ventral aspects of the shaft, causing the penis to be straight but shortened or have a lateral bend.[9] The fibrous tissue prevents lengthening of the involved area during erection, making intercourse difficult and painful. The disease usually occurs in middle-aged or elderly men. Although the cause of the disorder is unknown, the dense microscopic plaques are consistent with findings of severe vasculitis. As many as 47% of men with Peyronie's disease have another condition associated with fascial tissue fibrosis, such as Dupuytren's contracture (fibrosis of the palmar fascia).[9]



■ **FIGURE 33-7** ■ Peyronie's disease. (**A**) Penile cross-section showing plaque between the corpora. (**B**) Penile curvature.

The manifestations of Peyronie's disease include painful erection, bent erection, and the presence of a hard mass at the site of fibrosis. Approximately two thirds of men report pain as a symptom. The pain is thought to be generated by inflammation of the adjacent fascial tissue and usually disappears as the inflammation resolves.[10] During the first year or so after formation of the plaque, while the scar tissue is undergoing the process of remodeling, penile distortion may increase, remain static, or resolve and disappear completely.[9] In some cases, the scar tissue may progress to calcification and formation of bone-like tissue.

Diagnosis is based on history and physical examination. Doppler ultrasonography may be used to assess causation of the disorder. Although surgical intervention can be used to correct the disorder, it often is delayed, because in many cases the disorder is self-limiting.[10] Less invasive treatments include the administration of oral agents with antioxidant properties (*e.g.*, vitamin D, potassium aminobenzoate, and colchicine).

Priapism

Priapism is an involuntary, prolonged, abnormal and painful erection that is not associated with sexual excitement. Priapism is a true urologic emergency because the prolonged erection can result in ischemia and fibrosis of the erectile tissue with significant risk of subsequent impotence. Priapism can occur at any age, in the newborn as well as other age groups. Sickle cell disease or neoplasms are the most common cause in boys between 5 and 10 years of age.

Priapism is due to impaired blood flow in the corpora cavernosa of the penis. Two mechanisms for priapism have been proposed: low-flow (ischemic) priapism, in which there is stasis of blood flow in the corpora cavernosa with a resultant failure of detumescence, and high-flow (nonischemic) priapism, which involves persistent arterial flow into the corpora cavernosa.[11] In high-flow priapism, there is no hypoxia of local tissue, the penis is less rigid, the pain is less than in stasis

priapism, and permanent corporal fibrosis and cellular damage are rare.[11]

Priapism is classified as primary (idiopathic) or secondary to a disease or drug effect. Primary priapism is the result of conditions such as trauma, infection, and neoplasms. Secondary causes include hematologic conditions such as leukemia, sickle cell disease, and thrombocytopenia; neurologic conditions such as stroke, spinal cord injury, and other central nervous system lesions; and renal failure. Between 6% and 12% of males with sickle cell disorders are affected by priapism.[11] The relative deoxygenation and stasis of cavernosal blood during erection is thought to increase sickling. Various medications, such as antihypertensive drugs, anticoagulant drugs, antidepressant drugs, alcohol, and marijuana, can contribute to the development of priapism. Androstenedione, sold as an over-the-counter drug to enhance muscle building and athletic performance, has been implicated in the disorder.[12] Currently, intracavernous injection therapy for erectile dysfunction is one of the more common causes of priapism.

The diagnosis of priapism usually is based on clinical findings. Doppler studies of penile blood flow, penile ultrasonography, and computed tomography (CT) scans may be used to determine intrapelvic pathology.

Initial treatment measures include analgesics, sedation, and hydration. Urinary retention may necessitate catheterization. Local measures include application of ice packs and irrigation of the corpus cavernosum with plain or heparinized saline, or instillation of α-adrenergic drugs. If less aggressive treatment does not produce detumescence, a temporary surgical shunt may be established between the corpus cavernosum and the corpus spongiosum.

The prognosis for whether fibrosis or erectile failure will occur is determined by the severity and duration of blood stasis. In high-flow priapism, the damaging effects of decreased oxygen tension and intracavernal blood pressure are less pronounced than in stasis priapism. Normal erectile potency can be restored even after a long duration of high-flow priapism. In contrast, persistent stasis priapism is known to result in impaired erectile function and tissue fibrosis unless resolved within 24 to 48 hours of onset.[11]

Cancer of the Penis

Squamous cell cancer of the penis is most common in men between 45 and 60 years of age. In the United States, it accounts for less than 1% of male genital tumors; however, in other countries, it accounts for 10% to 20% of male cancers.[13,14] When it is diagnosed early, penile cancer is highly curable. The greatest hindrance to early diagnosis is a delay in seeking medical attention.

The cause of penile cancer is unknown. Several risk factors have been suggested, including poor hygiene, human papillomavirus (HPV) infections, ultraviolet radiation exposure, and immunodeficiency states. There is an association between penile cancer and poor genital hygiene and phimosis. One theory postulates that smegma accumulation under the phimotic foreskin may produce chronic inflammation, leading to carcinoma. The HPVs have been implicated in the genesis of several genital cancers, including cancer of the penis.[13] Ultraviolet radiation also is thought to have a carcinogenic effect on the penis. Males who were treated for psoriasis with ultraviolet A or B therapies (*i.e.*, PUVA or PUVB) have had a reported increased incidence of genital squamous cell carcinomas.[13] Because of this observation, it is suggested that men should shield their genital area when using tanning salons. Immunodeficiency states also may play a role in the pathogenesis of penile cancer. Approximately 18% of men with acquired immunodeficiency syndrome (AIDS)-related Kaposi's sarcoma have lesions of the penis or genitalia.[13]

Dermatologic lesions with precancerous potential include balanitis xerotica obliterans (discussed earlier) and giant condylomata acuminata.[14] Giant condylomata acuminata are cauliflower-like lesions arising from the prepuce or glans that result from HPV infection.

Approximately 95% of penile cancers are squamous cell carcinoma.[13] It is thought to progress from an in situ lesion to an invasive carcinoma. Bowen's disease and erythroplasia of Queyrat are penile lesions with histologic features of carcinoma in situ.[14] Bowen's disease appears as a solitary, thickened, gray-white, opaque plaque with shallow ulceration and crusting. It commonly involves the skin of the shaft of the penis and the scrotum. Erythroplasia of Queyrat involves the mucosal surface of the glans or prepuce. It is characterized by single or multiple shiny red, sometimes velvety, plaques.[14] These lesions require careful follow-up because of their potential to progress to invasive carcinoma.

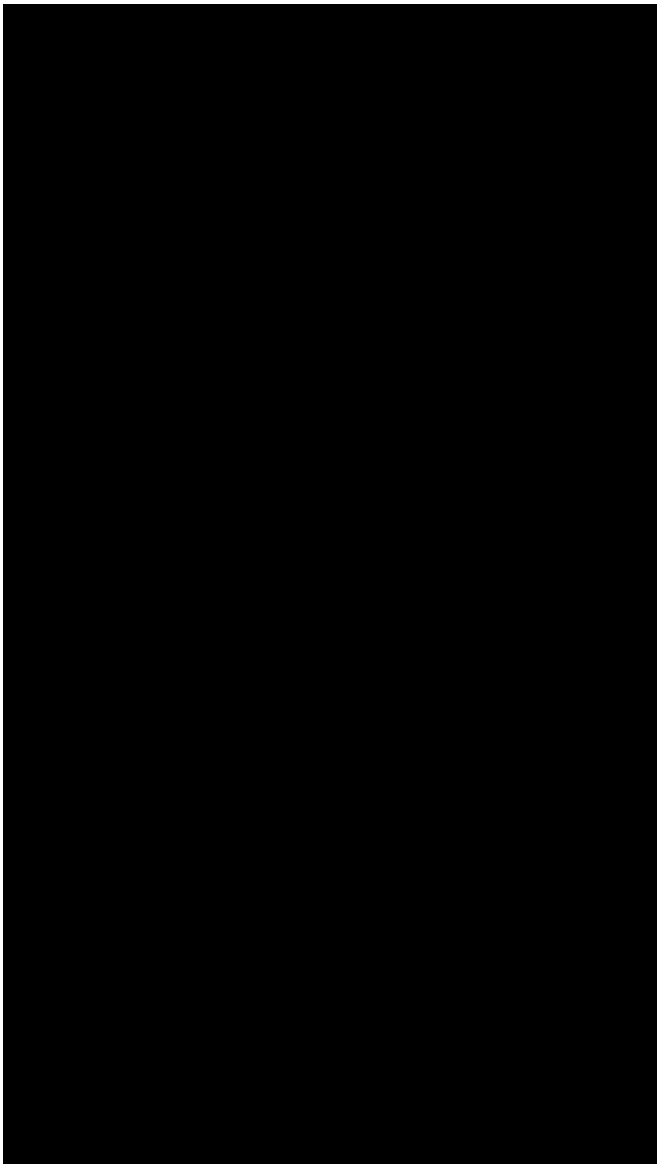
Invasive carcinoma of the penis begins as a small lump or ulcer. If phimosis is present, there may be painful swelling, purulent drainage, or difficulty urinating. Palpable lymph nodes may be present in the inguinal region. Diagnosis usually is based on physical examination and biopsy results. CT scans, penile ultrasound studies, and magnetic resonance imaging (MRI) may be used in the diagnostic workup.

Treatment options vary according to stage, size, location, and invasiveness of the tumor. Carcinoma in situ may be treated conservatively with fluorouracil cream application or laser treatment.[14] Surgery remains the mainstay of treatment for invasive carcinoma. Partial or total penectomy is indicated for invasive lesions.

Disorders of the Scrotum and Testes

The testes, or male gonads, are two egg-shaped structures located outside the abdominal cavity in the scrotum. Embryologically, the testes develop in the abdominal cavity and then descend through the inguinal canal into a pouch of peritoneum (which becomes the tunica vaginalis) in the scrotum during the seventh to ninth months of fetal life. As they descend, the testes pull their arteries, veins, lymphatics, nerves, and conducting excretory ducts with them. These structures are encased by the cremaster muscle and layers of fascia that constitute the spermatic cord (Fig. 33-8A). The descent of the testes is thought to be mediated by testosterone, which is active during this stage of development.

After descent of the testes, the inguinal canal closes almost completely. Failure of this canal to close predisposes to the development of an inguinal hernia later in life (Fig. 33-8B). An inguinal hernia or "rupture" is a protrusion of the parietal peritoneum and part of the intestine through an abnormal opening from the abdominal cavity. A loop of small bowel may become incarcerated in an inguinal hernia (strangulated hernia), in which case the lumen may become obstructed, and the vascular supply compromised (see Chapter 27).



The testes and epididymis are completely surrounded by the tunica vaginalis, a serous pouch derived from the peritoneum during fetal descent of the testes into the scrotum. The tunica vaginalis has an outer parietal layer and a deeper visceral layer that adheres to the dense fibrous covering of the testes, the tunica albuginea. The tunica albuginea protects the testes and gives them their ovoid shape. A space exists between these two layers that typically contains a few milliliters of clear fluid. The cremaster muscles, which are bands of skeletal muscle arising from the internal oblique muscles of the trunk, elevate the testes. The testes receive their arterial blood supply from the long testicular arteries, which branch from the aortic artery. The spermatic veins, which drain the testes, arise from a venous network called the *pampiniform plexus* that surrounds the spermatic artery. The testes are innervated by fibers from both divisions of the autonomic nervous system. Associated sensory nerves transmit pain impulses, resulting in excruciating pain, especially when the testes are hit forcibly.

The scrotum, which houses the testes, is made up of a thin outer layer of skin that forms rugae, or folds, and is continuous with the perineum and outer skin of the groin. Under the outer skin lies a thin layer of fascia and smooth muscle (*i.e.*, dartos muscle). This layer contains a septum that separates the two testes. The dartos muscle responds to changes in temperature. When it is cold, the muscle contracts, bringing the testes closer to the body, and the scrotum becomes shorter and heavily wrinkled. When it is warmer, the muscle relaxes, allowing the scrotum to fall away from the body.

The location of the testes in the scrotum is important for sperm production, which is optimal at 2°C to 3°C below body temperature. Two systems maintain the temperature of the testes at a level consistent with sperm production. One is the pampiniform plexus of spermatic veins that surround the spermatic artery. This plexus absorbs heat from the arterial blood, cooling it as it enters the testes. The other is the cremaster muscles, which respond to decreases in testicular temperature by moving the testes closer to the body. Prolonged exposure to elevated temperatures, as a result of prolonged fever or the dysfunction of thermoregulatory mechanisms, can impair spermatogenesis. Some tight-fitting undergarments hold the testes against the body and are thought to contribute to a decrease in sperm counts and infertility by interfering with the thermoregulatory function of the scrotum. Cryptorchidism, the failure of the testes to descend into the scrotum, also exposes the testes to the higher temperature of the body.

Disorders of the Testicular Tunica

Hydrocele. A hydrocele forms when excess fluid collects between the layers of the tunica vaginalis (Fig. 33-9). It may be unilateral or bilateral and can develop as a primary congenital defect or as a secondary condition. Acute hydrocele may develop after local injury, epididymitis or orchitis, gonorrhea, lymph obstruction, or germ cell testicular tumor, or as a side effect of radiation therapy. Chronic hydrocele is more common. Fluid collects about the testis, and the mass grows gradually. Its cause is unknown, and it usually develops in men older than 40 years.

Most cases of hydrocele in male infants and children are due to a patent processus vaginalis, which is continuous with the peritoneal cavity. In many cases they are associated with an indirect inguinal hernia.[15] Most hydroceles of infancy close spontaneously; therefore, they are not usually repaired before the age of 1 year. Hydroceles that persist beyond 2 years of age may require surgical treatment.

Hydroceles are palpated as cystic masses that may attain massive proportions. If there is enough fluid, the mass may be mistaken for a solid tumor. Transillumination of the scrotum (*i.e.*, shining a light through the scrotum for the purposes of visualizing its internal structures) or ultrasonography can help to determine whether the mass is solid or cystic and whether the testicle is normal.[16] A dense hydrocele that does not illuminate should be differentiated from a testicular tumor. If a hydrocele develops in a young man without apparent cause, careful evaluation is needed to exclude cancer or infection.

In an adult male, a hydrocele is a relatively benign condition. The condition often is asymptomatic, and no treatment is necessary. When symptoms do occur, the feeling may be that of heaviness in the scrotum or pain in the lower back. In cases of secondary hydrocele, the primary condition is treated. If the hydrocele is painful or cosmetically undesirable, surgical correction is indicated. Surgical repair may be done inguinally or transcrotally.

■ **FIGURE 33-9** ■ (**A**) Normal testis and appendages, (**B**) varicocele, and (**C**) hydrocele.

Hematocele. A hematocele is an accumulation of blood in the tunica vaginalis, which causes the scrotal skin to become dark red or purple. It may develop as a result of an abdominal surgical procedure, scrotal trauma, a bleeding disorder, or a testicular tumor.

Spermatocele. A spermatocele is a painless, sperm-containing cyst that forms at the end of the epididymis. It is located above and posterior to the testis, is attached to the epididymis, and is separate from the testes. Spermatoceles may be solitary or multiple and usually are less than 1 cm in diameter. They are freely movable and should transilluminate. Spermatoceles rarely cause problems, but a large one may become painful and require excision.

Varicocele. A varicocele is characterized by varicosities of the pampiniform plexus, a network of veins supplying the testes (Fig. 33-9). The left side is more commonly affected because the left internal spermatic vein inserts into the left renal vein at a right angle, whereas the right spermatic vein usually enters the inferior vena cava. Incompetent valves are more common in the left internal spermatic veins, causing a reflux of blood back into the veins of the pampiniform plexus. The force of gravity resulting from the upright position also contributes to venous dilatation. If the condition persists, there may be damage to the elastic fibers and hypertrophy of the vein walls, as occurs in formation of varicose veins in the leg. Sperm concentration and motility are decreased in 65% to 75% of men with varicocele because of changes in testicular temperature resulting from altered blood flow.[16]

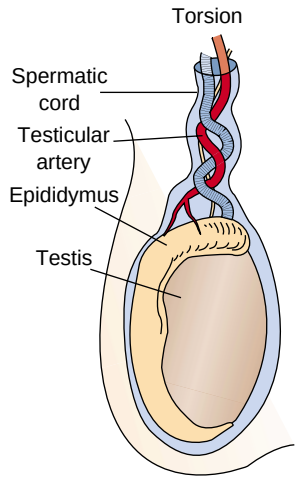
Varicoceles rarely are found before puberty, and the incidence is highest in men between 15 and 35 years of age. Symptoms of varicocele include an abnormal feeling of heaviness in the left scrotum, although many varicoceles are asymptomatic. Usually, the varicocele is readily diagnosed on physical examination with the patient in the standing and recumbent positions. Typically, the varicocele disappears in the lying position because of venous decompression into the renal vein. Scrotal palpation of a varicocele has been compared to feeling a "bag of worms."

Treatment options include surgical ligation or sclerosis using a percutaneous transvenous catheter under fluoroscopic guidance. It has been shown that 40% of men with abnormalities in their semen and a varicocele show some degree of improvement in fertility after obliteration of the dilated veins.[16] Aside from improving fertility, other reasons for surgery include the relief of the sensation of "heaviness" and cosmetic improvement.

Testicular Torsion

Testicular torsion is a twisting of the spermatic cord that suspends the testis (Fig. 33-10). It is the most common acute scrotal disorder in the pediatric and young adult population. Testicular torsion can be divided into two distinct clinical entities, depending on the level of spermatic cord involvement: extravaginal and intravaginal torsion.[17]

Extravaginal torsion, which occurs almost exclusively in neonates, is the less common form of testicular torsion. It occurs



■ **FIGURE 33-10** ■ Testicular torsion with twisting of the spermatic cord that suspends the testis and the spermatic vessels that supply the testis with blood.

when the testicle and the fascial tunicae that surround it rotate around the spermatic cord at a level well above the tunica vaginalis. *Intravaginal torsion* is considerably more common than extravaginal torsion. It occurs when the testis rotates on the long axis in the tunica vaginalis. In most cases, congenital abnormalities of the tunica vaginalis or spermatic cord exist.[17] The tunica vaginalis normally surrounds the testes and epididymis, allowing the testicle to rotate freely in the tunica. Although anomalies of suspension vary, the epididymal attachment may be loose enough to permit torsion between the testis and the epididymis. More commonly, the testis rotates about the distal spermatic cord. Because this abnormality is developmental, bilateral anomalies are common.

Intravaginal torsion occurs most frequently between the ages of 8 and 18 years and rarely is seen after 30 years of age. Males usually present in severe distress within hours of onset and often have nausea, vomiting, and tachycardia. The affected testis is large and tender, with pain radiating to the inguinal area. Extensive cremaster muscle contraction causes a thickening of the spermatic cord.

Testicular torsion must be differentiated from epididymitis, orchitis, and trauma to the testis. On physical examination, the testicle often is high in the scrotum and in an abnormal orientation. These changes are due to the twisting and shortening of the spermatic cord. The degree of scrotal swelling and redness depends on the duration of symptoms. The testes are firm and tender. The cremasteric reflex, normally elicited by stroking the medial aspect of the thigh and observing testicular retraction, frequently is absent.[17] Color Doppler ultrasonography is increasingly used in the evaluation of suspected testicular torsion.[17]

Intravaginal testicular torsion is a true surgical emergency, and early recognition and treatment are necessary if the testicle is to be saved. Treatment includes surgical detorsion (repositioning and fixation) and orchiectomy. Orchiectomy is carried out when the testis is deemed nonviable after surgical detorsion. Testicular salvage rates are directly related to the duration of torsion. Because the opposite testicle usually is affected by the same abnormal attachments, prophylactic fixation of that testis often is performed.

Inflammation and Infection

Epididymitis. Epididymitis is an inflammation of the epididymis. There are two major types of epididymitis: sexually transmitted infections associated with urethritis and primary nonsexually transmitted infections associated with urinary tract infections and prostatitis. Most cases of epididymitis are caused by bacterial pathogens.

In primary nonsexual infections, the pressure associated with voiding or physical strain may force pathogen-containing urine from the urethra or prostate up the ejaculatory duct and through the vas deferens and into the epididymis. Infections also may reach the epididymis through the lymphatics of the spermatic cord. In rare cases, organisms from other foci of infection reach the epididymis through the bloodstream. In children, the disorder usually is associated with congenital urinary tract abnormalities and infection with gram-negative rods.

Sexually transmitted acute epididymitis occurs mainly in young men without underlying genitourinary disease and is most commonly caused by *Chlamydia trachomatis* and *Neisseria gonorrhoeae* (singly or in combination). In men older than 35 years, epididymitis often is associated with pathogens such as *Escherichia coli*, *Pseudomonas*, and gram-positive cocci.

Epididymitis is characterized by unilateral pain and swelling, accompanied by erythema and edema of the overlying scrotal skin that develops during a period of 24 to 48 hours. Initially, the swelling and induration are limited to the epididymis. However, the distinction between the testis and epididymis becomes less evident as the inflammation progresses, and the testis and epididymis become one mass. There may be tenderness over the groin (spermatic cord) or in the lower abdomen. Fever and reports of dysuria occur in approximately one half of cases. Whether urethral discharge is present depends on the organism causing the infection; it usually accompanies gonorrheal infections, is common in chlamydial infections, and is less common in infections caused by gram-negative organisms.

Laboratory findings usually reveal an elevated white blood cell count. Urinalysis and urine culture are important in the diagnosis of epididymitis, with bacteriuria and pyuria suggestive of the disorder. Treatment during the acute phase (which usually lasts for 3 to 4 days) includes bed rest, scrotal elevation and support, and antibiotics.[18] Bed rest with scrotal support improves lymphatic drainage. The choice of antibiotics is determined by age, physical findings, urinalysis, Gram's stain results, cultures, and sexual history. Oral analgesics and antipyretics usually are indicated. Sexual activity or physical strain may exacerbate the infection and worsen the symptoms and should be avoided.

Orchitis. Orchitis is an infection of the testes. It can be precipitated by a primary infection in the genitourinary tract, or the infection can be spread to testes through the bloodstream or the lymphatics. Epididymitis with subsequent infection of the testis is commonly related to genitourinary tract infections (cystitis, urethritis, genitoprostatitis) that travel to the epididymis and testis through the vas deferens or the lymphatics of the spermatic cord.

Orchitis can develop as a complication of a systemic infection, such as parotitis (*i.e.*, mumps), scarlet fever, or pneumonia. Probably the best known of these complications is orchitis caused by the mumps virus. Mumps orchitis does not occur in prepubertal boys. However, approximately 20% to 35% of adolescent boys and young men with mumps develop this form of orchitis.[18] The onset of mumps orchitis is sudden; it usually occurs approximately 3 to 4 days after the onset of the parotitis and is characterized by fever, painful enlargement of the testes, and small hemorrhages into the tunica albuginea. Unlike epididymitis, the urinary symptoms are absent. The symptoms usually run their course in 7 to 10 days. The residual effects seen after the acute phase include hyalinization of the seminiferous tubules and atrophy of the testes. Spermatogenesis is irreversibly impaired in approximately 30% of testes damaged by mumps orchitis.[18] If both testes are involved, permanent sterility results, but androgenic hormone function usually is maintained.

Cancer of the Scrotum and Testes

Tumors can develop in the scrotum or the testes. Benign scrotal tumors are common and often do not require treatment. Carcinoma of the scrotum is rare and usually is associated with exposure to carcinogenic agents. Almost all solid tumors of the testes are malignant.

Scrotal Cancer. Cancer of the scrotum was the first cancer directly linked to a specific occupation when, in the 1800s, it was associated with chimney sweeps.[19] Studies have linked this cancer to exposure to tar, soot, and oils. Most squamous cell cancers of the scrotum are linked to poor hygiene and chronic inflammation. Exposure to ultraviolet A radiation (*e.g.*, PUVA) or HPV also has been associated with the disease. The mean age of presentation with the disease is 60 years, often preceded by 20 to 30 years of chronic irritation.

In the early stages, cancer of the scrotum may appear as a small tumor or wartlike growth that eventually ulcerates. The thin scrotal wall lacks the tissue reactivity needed to block the malignant process; more than one half of the cases seen involve metastasis to the lymph nodes. Because this tumor does not respond well to chemotherapy or irradiation, the treatment includes wide local excision of the tumor with inguinal and femoral node dissection.[20]

Testicular Cancer. Testicular cancer accounts for 1% of all male cancers and 3% of male urogenital cancers. Although relatively rare, it is the most common cause of cancer in the 15- to 34-year-old age group.[20,21] In the past, testicular cancer was a leading cause of death among males entering their most productive years. However, since the late 1970s, advances in therapy have transformed an almost invariably fatal disease into one that is highly curable. With appropriate treatment, the prognosis for men with testicular cancer is excellent. The 5-year survival rate for patients with early disease exceeds 95%. Even patients with more advanced disease have excellent chances for long-term survival.

Although the cause of testicular cancer is unknown, several predisposing influences may be important: cryptorchidism, genetic factors, and disorders of testicular development.[22] The strongest association has been with cryptorchid or undescended testes. The higher the location of the undescended testis, the greater the risk.[22] Genetic predisposition also appears to be important. Family clustering of the disorder has been described, although a well-defined pattern of inheritance has not been established. Men with disorders of testicular development, including those with Klinefelter's syndrome and testicular feminization, have a higher risk of germ cell tumors.

Approximately 95% of malignant tumors arising in the testis are germ cell tumors.[21,23] Germ cell tumors can be classified as seminomas and nonseminomas based on their origin in primordial germ cells and their ability to differentiate in vivo. Because these tumors derive from germ cells in the testis, they are multipotential (able to differentiate into different tissue types) and often secrete polypeptide hormones or enzymes representing earlier stages of development (see Chapter 5). *Seminomas* are the most common type of testicular tumors. They account for approximately 50% of germ cell tumors and occur most frequently during the fourth decade of life.[21] Seminomas are thought to arise from the seminiferous epithelium of the testes and are the type of germ cell tumor most likely to produce a uniform population of cells.

The *nonseminoma tumors* include embryonal carcinoma, teratoma, choriocarcinoma, and yolk cell carcinoma derivatives. Nonseminoma tumors usually contain more than one cell type and are less differentiated than seminomas. Embryonal carcinomas are the least differentiated of the tumors, with totipotential capacity to differentiate into other nonseminomatous cell types. They occur most commonly in the 20- to 30-year-old age group. Choriocarcinoma is a rare and highly malignant form of testicular cancer that is identical to tumors that arise in placental tissue. Yolk sac tumors mimic the embryonic yolk sac histologically. They are the most common type of testicular tumors in infants and children to 3 years of age, and in this age group are associated with a very good prognosis.[22] Teratomas are composed of somatic cell types from two or more germ-line layers (ectoderm, mesoderm, or endoderm). They constitute less than 2% to 3% of germ cell tumors and can occur at any age from infancy to old age. They usually behave as benign tumors in children; in adults, they often contain minute foci of cancer cells.

Often the first sign of testicular cancer is a slight enlargement of the testicle that may be accompanied by some degree of discomfort. This may be an ache in the abdomen or groin or a sensation of dragging or heaviness in the scrotum. Frank pain may be experienced in the later stages, when the tumor is growing rapidly and hemorrhaging occurs. Testicular cancer can spread when the tumor may be barely palpable. Signs of metastatic spread include swelling of the lower extremities, back pain, cough, hemoptysis, or dizziness. Gynecomastia (breast enlargement) may result from human chorionic gonadotropin (hCG)-producing tumors.

Early diagnosis of testicular cancer is important because a delay in seeking medical attention often results in presentation with a later stage of the disease and decreased treatment effectiveness. Recognition of the importance of prompt diagnosis and treatment has resulted in the development of a procedure for testicular self-examination and an emphasis on public education programs about this type of cancer. The American Cancer Society strongly advocates that every young adult male examine his testes at least once each month as a means of early detection of testicular cancer.

The diagnosis of testicular cancer requires a thorough urologic history and physical examination. A painless testicular mass may be cancer. The examination for masses should include palpation of the testes and surrounding structures, transillumination of the scrotum, and abdominal palpation. Testicular ultrasonography can be used to differentiate testicular masses. CT scans and MRI are used in assessing metastatic spread.

Tumor markers, which measure protein antigens produced by malignant cells, provide information about the existence of a small or undetected tumor and the type of tumor present. Three tumor markers are useful in evaluating the tumor response: α-fetoprotein, a glycoprotein that normally is present in fetal serum in large amounts; hCG, a hormone that normally is produced by the placenta in pregnant women; and lactate dehydrogenase (LDH), a cellular enzyme normally found in muscle, liver, kidney, and brain. The reappearance in the adult of these protein markers suggests activity normally present in the embryo.

The basic treatment of all testicular cancers includes orchiectomy, which is done at the time of diagnostic exploration. Dependent on the histologic characteristics of the tumor and the clinical stage of the disease, radiation or chemotherapy may used after orchiectomy. Rigorous follow-up in all men with testicular cancer is necessary to detect recurrence, which most often occurs within the first year.[23]

Disorders of the Prostate

The prostate is a fibromuscular and glandular organ lying just inferior to the bladder. The prostate gland secretes a thin, milky, alkaline fluid containing citric acid, calcium, acid phosphate, a clotting enzyme, and a profibrinolysin. During ejaculation, the capsule of the prostate contracts, and the added fluid increases the bulk of the semen. Both vaginal secretions and the fluid from the vas deferens are strongly acidic. Because sperm mobilization occurs at a pH of 6.0 to 6.5, the alkaline nature of the prostatic secretions is essential for successful fertilization of the ovum. The bulbourethral glands (Fig. 33-1) lie on either side of the membranous urethra and secrete an alkaline mucus, which further aids in neutralizing acids from the urine that remain in the urethra.

The prostate gland, which forms a fibrous capsule that surrounds the urethra where it joins the bladder, also functions in the elimination of urine. The segment of urethra that travels through the prostate gland is called the *prostatic urethra*. The prostatic urethra is lined by a thin layer of smooth muscle that is continuous with the bladder wall. This smooth muscle represents the true involuntary sphincter of the male posterior urethra. Because the prostate surrounds the urethra, enlargement of the gland can produce urinary obstruction.

The prostate gland is made up of many secretory glands arranged in three concentric areas surrounding the prostatic urethra, into which they open. The component glands of the prostate include the (1) small mucosal glands associated with the urethral mucosa, (2) the intermediate submucosal glands that lie peripheral to the mucosal glands, and (3) the large main prostatic glands that are situated toward the outside of the gland. It is the overgrowth of the mucosal glands that causes benign prostatic hyperplasia in older men.

Prostatitis

Prostatitis refers to a variety of inflammatory disorders of the prostate gland, some of which are bacterial and some are not. It may occur spontaneously, as a result of catheterization or instrumentation, or secondary to other diseases of the male genitourinary system. As an outcome of 1995 and 1998 consensus conferences, the National Institutes of Health has established a classification system with four categories of prostatitis syndromes: asymptomatic inflammatory prostatitis, acute bacterial prostatitis, chronic bacterial prostatitis, and chronic prostatitis/pelvic pain syndrome.[24] Men with asymptomatic inflammatory prostatitis have no subjective symptoms and are detected incidentally on biopsy or examination of prostatic fluid.

Acute Bacterial Prostatitis. Acute bacterial prostatitis often is considered a subtype of urinary tract infection. The most likely etiology of acute bacterial prostatitis is an ascending urethral infection or reflux of infected urine into the prostatic ducts. The most common organism is *E. coli*. Other frequently found species include *Pseudomonas*, *Klebsiella*, and *Proteus*. Less frequently, the infection is caused by *Staphylococcus aureus*, *Streptococcus faecalis*, *Chlamydia*, or anaerobes such as *Bacteroides* species.[25,26]

The manifestations of acute bacterial prostatitis include fever and chills, malaise, myalgia, arthralgia, frequent and urgent urination, dysuria, and urethral discharge. Dull, aching pain often is present in the perineum, rectum, or sacrococcygeal region. The urine may be cloudy and malodorous because of urinary tract infection. Rectal examination reveals a swollen, tender, warm prostate with scattered soft areas. Prostatic massage produces a thick discharge with white blood cells that grows large numbers of pathogens on culture.

Acute prostatitis usually responds to appropriate antimicrobial therapy chosen in accordance with the sensitivity of the causative agents in the urethral discharge. Depending on the urine culture results, antibiotic therapy usually is continued for at least 4 weeks. Because acute prostatitis often is associated with anatomic abnormalities, a thorough urologic examination usually is performed after treatment is completed.

A persistent fever indicates the need for further investigation for an additional site of infection or a prostatic abscess. CT scans and transrectal ultrasonography of the prostate are useful in the diagnosis of prostatic abscesses. Prostatic abscesses, which are relatively uncommon since the advent of effective antibiotic therapy, are found more commonly in males with diabetes mellitus. Because prostatic abscesses usually are associated with bacteremia, prompt drainage by transperitoneal or transurethral incision followed by appropriate antimicrobial therapy usually is indicated.[25]

Chronic Bacterial Prostatitis. In contrast to acute bacterial prostatitis, chronic bacterial prostatitis is a subtle disorder that is difficult to treat. Men with the disorder typically have recurrent urinary tract infections with persistence of the same strain of pathogenic bacteria in prostatic fluid and urine. Organisms responsible for chronic bacterial prostatitis usually are the gram-negative enterobacteria (*E. coli*, *Proteus*, or *Klebsiella*) or *Pseudomonas*. Occasionally, a gram-positive organism such as *S. faecalis* is the causative organism. Infected prostatic calculi may develop and contribute to the chronic infection.

The symptoms of chronic prostatitis are variable and include frequent and urgent urination, dysuria, perineal discomfort, and low back pain. Occasionally, myalgia and arthralgia accompany the other symptoms. Secondary epididymitis sometimes is associated with the disorder. Many men develop relapsing lower or upper urinary tract infections because of recurrent invasion of the bladder by the prostatic bacteria. Bacteria may exist in the prostate gland even when the prostatic fluid is sterile.

The most accurate method of establishing a diagnosis is by urine cultures. Even after an accurate diagnosis has been established, treatment of chronic prostatitis often is difficult and frustrating. Unlike their action in the acutely inflamed prostate, antibacterial drugs penetrate poorly into the chronically inflamed prostate. Long-term therapy (3 to 4 months) with an appropriate low-dose oral antimicrobial agent often is used to treat the infection. Transurethral prostatectomy may be indicated when the infection is not cured or adequately controlled by medical therapy, particularly when prostate stones are present.

Chronic Prostatitis/Chronic Pelvic Pain Syndrome. Chronic prostatitis/pelvic pain syndrome is both the most common and least understood of the prostatitis syndromes.[27] The category is divided into two types, inflammatory and noninflammatory, based on the presence of leukocytes in the prostatic fluid. The inflammatory type was previously referred to as *nonbacterial prostatitis*, and the noninflammatory type as *prostatodynia*.

Men with nonbacterial prostatitis have inflammation of the prostate with an elevated leukocyte count, inflammatory cells

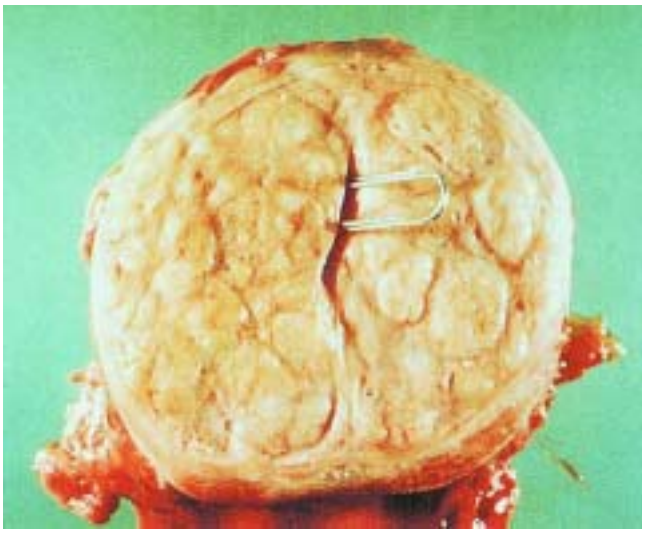
in their prostatic secretions, but no evidence of bacteria. The cause of the disorder is unknown, and efforts to prove the presence of unusual pathogens (*e.g.*, mycoplasmas, chlamydiae, trichomonads, viruses) have been largely unsuccessful. It also is thought that nonbacterial prostatitis may be an autoimmune disorder. Manifestations of *inflammatory prostatitis* include pain along the penis, testicles, and scrotum; painful ejaculation; low back pain; rectal pain along the inner thighs; urinary symptoms; decreased libido; and impotence.

Men with noninflammatory prostatitis have symptoms resembling those of nonbacterial prostatitis but have negative urine culture results and no evidence of prostatic inflammation (*i.e.*, normal leukocyte count). The cause of noninflammatory prostatitis is unknown, but because of the absence of inflammation, the search for the cause of symptoms has been directed toward extraprostatic sources. In some cases, there is an apparent functional obstruction of the bladder neck near the external urethral sphincter; during voiding, this results in higher than normal pressures in the prostatic urethra that cause intraprostatic urine reflux and chemical irritation of the prostate by urine. In other cases, there is an apparent myalgia (*i.e.*, muscle pain) associated with prolonged tension of the pelvic floor muscles. Emotional stress also may play a role.

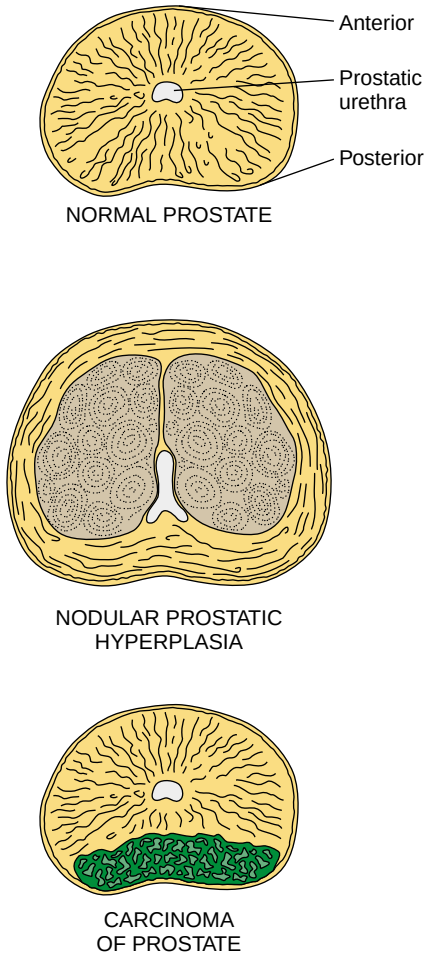
Treatment methods for chronic prostatitis/pelvic pain syndrome are highly variable. Antibiotic therapy is used when an occult infection is suspected. Sitz baths and nonsteroidal antiinflammatory agents may provide some symptom relief. In men with irritative urination symptoms, anticholinergic agents or α-adrenergic–blocking agents may be beneficial.

Benign Prostatic Hyperplasia

Benign prostatic hyperplasia (BPH) is an age-related, nonmalignant enlargement of the prostate gland (Fig. 33-11). It is characterized by the formation of large, nodular lesions in the periurethral region of the prostate, rather than the peripheral zones, which commonly are affected by prostate cancer (Fig. 33-12). BPH is one of the most common diseases of aging men. It has been reported that 25% of men older than 55 years of age and 50% of men older than 75 years of age experience symptoms of BPH.[28]



■ **FIGURE 33-11** ■ Nodular hyperplasia of the prostate. Cut surface of a prostate enlarged by nodular hyperplasia shows numerous, well-circumscribed nodules of prostatic tissue. The prostatic urethra (*paper clip*) has been compressed to a narrow slit. (Rubin E., Farber J.L. [1999]. *Pathology* [3rd ed., p. 955]. Philadelphia: Lippincott Williams & Wilkins)



■ **FIGURE 33-12** ■ Normal prostate, nodular benign prostatic hypertrophy, and cancer of the prostate. (Rubin E., Farber J.L. [1999]. *Pathology* [3rd ed., p. 954]. Philadelphia: Lippincott Williams & Wilkins.) (Artist: Dimitri Karetnikov)

The exact cause of the BPH is unknown. Potential risk factors include age, family history, race, ethnicity, and hormonal factors. The incidence of BPH increases with advancing age, is highest in African Americans, and is lowest in native Japanese. Men with a family history of BPH are reported to have had larger prostates than those of control subjects, and higher rates of BPH were found in monozygotic twins than in dizygotic twins.[28]

Both androgens (testosterone) and estrogens appear to contribute to the development of BPH. Dihydrotestosterone (DHT), the biologically active metabolite of testosterone, is thought to be the ultimate mediator of prostatic hyperplasia, with estrogen serving to sensitize the prostatic tissue to the growth-producing effects of DHT. Free plasma testosterone enters prostatic cells, where at least 90% is converted into DHT by

KEY CONCEPTS

HYPERPLASIA AND CANCER OF THE PROSTATE

- The prostate gland surrounds the urethra, and periurethral enlargement will cause manifestations of urinary obstruction.
- Benign prostatic hyperplasia is an age-related enlargement of the prostate gland with formation of large, discrete lesions in the periurethral region of the prostate. These lesions compress the urethra and produce symptoms of dysuria or difficulty urinating.
- Prostatic cancer begins in the peripheral zones of the prostate gland and usually is asymptomatic until the disease is far advanced and the tumor has eroded the outer prostatic capsule and spread to adjacent pelvic tissues or metastasized.

the action of 5α-reductase. The discovery that DHT is the active factor in BPH is the rationale for use of 5α-reductase inhibitors in the treatment of the disorder. Although the exact source of estrogen is uncertain, small amounts of estrogen are produced in the male. It has been postulated that a relative increase in estrogen levels that occurs with aging may facilitate the action of androgens in the prostate despite a decline in the testicular output of testosterone.

The anatomic location of the prostate at the bladder neck contributes to the pathophysiology and symptomatology of BPH. There are two prostatic components to the obstructive properties of BPH and the development of lower urinary tract symptoms: dynamic and static.[28,29] The static component of BPH is related to an increase in prostatic size and gives rise to symptoms such as a weak urinary stream, postvoid dribbling, frequency of urination, and nocturia. The dynamic component of BPH is related to prostatic smooth muscle tone. The α_1-adrenergic receptors are the main receptors for the smooth muscle component of the prostate. The recognition of the role of α_1-adrenergic receptor on neuromuscular function in the prostate is the basis for use of α_1-adrenergic–receptor blockers in treating BPH. A third component, detrusor instability and impaired bladder contractility, may contribute to the symptoms of BPH independent of the outlet obstruction created by an enlarged prostate (see Chapter 25).[29,30] It has been suggested that some of the symptoms of BPH might be related to a decompensating or aging bladder, rather than being primarily related to outflow obstruction. An example is the involuntary contraction that results in urgency and an attempt to void that occurs because of small bladder volume.[29]

Clinical Course. The clinical significance of BPH resides in its tendency to compress the urethra and cause partial or complete obstruction of urinary outflow. As the obstruction increases, acute retention may occur with overdistention of the bladder. The residual urine in the bladder causes increased frequency of urination and a constant desire to empty the bladder, which becomes worse at night. With marked bladder distention, overflow incontinence may occur with the slightest increase in intra-abdominal pressure. The resulting obstruction to urinary flow can give rise to urinary tract infection, destructive changes of the bladder wall, hydroureter, and hydronephrosis. Hypertrophy and changes in bladder wall structure develop in stages. Initially, the hypertrophied fibers form trabeculations and then herniations, or sacculations; finally, diverticula develop as the herniations extend through the bladder wall (Chapter 25, Fig. 25-4). Because urine seldom is completely emptied from them, these diverticula are readily infected. Back pressure on the ureters and collecting system of the kidneys promotes hydroureter, hydronephrosis, and eventual renal failure.

It is now thought that the single most important factor in the evaluation and treatment of BPH is the man's own experiences related to the disorder. The American Urological Society Symptom Index consists of seven questions about symptoms regarding incomplete emptying, frequency, intermittency, urgency, weak stream, straining, and nocturia.[31,32] Each question is rated with a score of 0 (mild) to 7 (severe). A maximum score of 35 indicates severe symptoms. Total scores below 7 are considered mild; those between 8 and 20, moderate; and scores over 20, severe. A final question relates to quality of life related to urinary problems.

Diagnosis of BPH is based on history, physical examination, digital rectal examination, urinalysis, blood tests for serum creatinine and prostate-specific antigen (PSA), and urine flow rate. Blood and urine analyses are used as adjuncts to determine BPH complications. Urinalysis is done to detect bacteria, white blood cells, or microscopic hematuria in the presence of infection and inflammation. The serum creatinine test is used as an estimate of the glomerular filtration rate and kidney function. The PSA test is used to screen for prostatic cancer. These evaluation measures, along with the symptom index, are used to describe the extent of obstruction, determine if other diagnostic tests are needed, and establish the need for treatment.

Transabdominal or transrectal diagnostic ultrasonography can be used to evaluate the kidneys, ureters, and bladder. Abdominal radiographs may be used to reveal the size of the gland. Urethrocystoscopy is indicated in men with a history of hematuria, stricture disease, urethral injury, or prior lower urinary tract surgery. It is used to evaluate the length and diameter of the urethra, the size and configuration of the prostate, and bladder capacity. It also detects the presence of trabeculations, bladder stones, and small bladder cancers. CT scans, MRI studies, and radionuclide scans are reserved for rare instances of tumor detection.

Treatment of BPH is determined by the degree of symptoms that the condition produces and complications due to obstruction. When a man develops mild symptoms related to BPH, a "watch and wait" stance often is taken. The condition does not always run a predictable course; it may remain stable or even improve. Until the 1980s, surgery was the mainstay of treatment to alleviate urinary obstruction due to BPH. Currently, there is an emphasis on less invasive methods of treatment, including use of pharmacologic agents. However, when more severe signs of obstruction develop, surgical treatment (*e.g.*, transurethral resection of the prostate [TURP]) usually is indicated to provide comfort and avoid serious renal damage. For men who have heart or lung disease or a condition

that precludes major surgery, a stent may be used to widen and maintain the patency of the urethra.

Pharmacologic management includes the use of 5α-reductase inhibitors and α_1-adrenergic–blocking drugs.[28,29] The 5α-reductase inhibitors such as finasteride reduce prostate size by blocking the effect of androgens on the prostate. The presence of α-adrenergic receptors in prostatic smooth muscle has prompted the use of α_1-adrenergic–blocking drugs to relieve prostatic obstruction and increase urine flow.

Cancer of the Prostate

Prostatic cancer is the most common male cancer in the United States and is second to lung cancer as a cause of cancer-related death in men. The American Cancer Society estimates that during 2002, approximately 189,000 men in the United States received a diagnosis of prostate cancer, and 32,200 men died of the disorder.[33] The increase in diagnosed cases is thought to reflect earlier diagnosis because of the widespread use of PSA testing since the early 1990s.[34] The incidence of prostate cancer varies markedly from country to country and varies among races in the same country.[33] African-American men have the highest reported incidence for prostate cancer at all ages, and Asians and Native American men have the lowest rate. Prostate cancer also is a disease of aging. The incidence increases rapidly after 50 years of age; more than 80% of all prostate cancers are diagnosed in men older than 65 years of age.[33]

The precise cause of prostatic cancer is unclear. As with other cancers, it appears that the development of prostate cancer is a multistep process involving genes that control cell differentiation and growth (see Chapter 5). Several risk factors, such as age, race, heredity, and environmental influences, are suspected of playing a role.[35,36] Male hormone levels also may play a role. There is insufficient evidence linking socioeconomic status, infectious agents, smoking, vasectomy, sexual behavior, or BPH to the pathogenesis of prostate cancer.

The incidence of prostate cancer appears to be higher in relatives of men with prostate cancer. Diet may also play a role. It has been suggested that a diet high in fats may alter the production of sex hormones and increase the risk of prostate cancer. Supporting the role of dietary fats as a risk factor for prostate cancer has been the observation that the diet of Japanese men, who have a low rate of prostate cancer, is much lower in fat content than that of U.S. men, who have a much higher incidence.

In terms of hormonal influence, androgens are believed to play a role in the pathogenesis of prostate cancer.[35] Evidence favoring a hormonal influence includes the presence of steroid receptors in the prostate, the requirement of sex hormones for normal growth and development of the prostate, and the fact that prostate cancer almost never develops in men who have been castrated. The response of prostatic cancer to estrogen administration or androgen deprivation further supports a correlation between the disease and testosterone levels.

Prostatic adenocarcinomas, which account for 98% of all primary prostatic cancers, are commonly multicentric and located in the peripheral zones of the prostate[36] (see Fig. 33-12). The high frequency of invasion of the prostatic capsule by adenocarcinoma relates to its subcapsular location. Invasion of the urinary bladder is less common and occurs later in the clinical course. Metastasis to the lung reflects lymphatic spread through the thoracic duct and dissemination from the prostatic venous plexus to the inferior vena cava. Bony metastases, particularly to the vertebral column, ribs, and pelvis, produce pain that often presents as a first sign of the disease.

Most men with early-stage prostate cancer are asymptomatic. The presence of symptoms often suggests locally advanced or metastatic disease. Depending on the size and location of prostatic cancer at the time of diagnosis, there may be changes associated with the voiding pattern similar to those found in BPH. These include urgency, frequency, nocturia, hesitancy, dysuria, hematuria, or blood in the ejaculate. On physical examination, the prostate is nodular and fixed. Bone metastasis often is characterized by low back pain. Pathologic fractures can occur at the site of metastasis. Men with metastatic disease may experience weight loss, anemia, or shortness of breath.

Screening. Because early cancers of the prostate usually are asymptomatic, screening tests are important. The screening tests currently available are digital rectal examination, PSA testing, and transrectal ultrasonography. PSA is a glycoprotein secreted into the cytoplasm of benign and malignant prostatic cells that is not found in other normal tissues or tumors. However, a positive PSA test indicates only the possible presence of prostate cancer. It also can be positive in cases of BPH and prostatitis. The American Cancer Society and the American Urological Association recommend that men 50 years of age or older should undergo annual measurement of PSA and rectal examination for early detection of prostate cancer.[33] Men at high risk for prostate cancer, such as blacks and those with a strong family history, should undergo annual screening beginning at 45 years of age.[33]

Diagnosis. The diagnosis of prostate cancer is based on history and physical examination and confirmed through biopsy methods. Transrectal ultrasonography, a continuously improving method of imaging, is used to guide a biopsy needle and document the exact location of the biopsied tissue. It also is used for providing staging information.[28] Newly developed small probes for transrectal MRI have been shown to be effective in detecting the presence of cancer in the prostate. Radiologic examination of the bones of the skull, ribs, spine, and pelvis can be used to reveal metastases, although radionuclide bone scans are more sensitive. Excretory urograms are used to delineate changes due to urinary tract obstruction and renal involvement.

Cancer of the prostate, like other forms of cancer, is graded and staged (see Chapter 5). Prostatic adenocarcinoma commonly is classified using the Gleason grading system.[35,36] Well-differentiated tumors are assigned a grade of 1, and poorly differentiated tumors a grade of 5. Two tumor markers, PSA and serum acid phosphatase, are important in the staging and management of prostatic cancer. In untreated cases, the level of PSA correlates with the volume and stage of disease.[37] A rising PSA after treatment is consistent with progressive disease, whether it is locally recurring or metastatic. Measurement of PSA is used to detect recurrence after total prostatectomy. Because the prostate is the source of PSA, levels of the antigen should drop to zero after surgery; a rising PSA indicates recurring disease. Serum acid phosphatase is less sensitive than PSA and is used less frequently. However, it is more predictive of metastatic disease and may be used for that purpose.

Treatment. Cancer of the prostate is treated by surgery, radiation therapy, and hormonal manipulations.[28,38,39] Chemotherapy has shown limited effectiveness in the treatment of prostate cancer. Treatment decisions are based on tumor grade and stage and on the age and health of the man. Expectant therapy (watching and waiting) may be used if the tumor is not producing symptoms, is expected to grow slowly, and is small and contained in one area of the prostate. This approach is particularly suited for men who are elderly or have other health problems. Most men with an anticipated survival greater than 10 years are considered for surgical or radiation therapy.[39] Radical prostatectomy involves complete removal of the seminal vesicles, prostate, and ampullae of the vas deferens. Radiation therapy can be delivered by a variety of techniques, including external beam radiation therapy and transperineal implantation of radioisotopes.

Metastatic disease often is treated with androgen deprivation therapy. Androgen deprivation may be induced at several levels along the pituitary-gonadal axis using a variety of methods or agents. Orchiectomy or estrogen therapy often is effective in reducing symptoms and extending survival. The GnRH analogs (*e.g.*, leuprolide, buserelin, nafarelin) block luteinizing hormone release from the pituitary and reduce testosterone levels without orchiectomy or estrogen therapy. When given continuously and in therapeutic doses, these drugs desensitize GnRH receptors in the pituitary, thereby preventing the release of luteinizing hormone. The antiandrogens block the uptake and actions of androgens in the target tissues. Complete androgen blockade can be achieved by combining an antiandrogen with a GnRH agent or orchiectomy.

In summary, disorders of the penis include balanitis, an acute or chronic inflammation of the glans penis, and balanoposthitis, an inflammation of the glans and prepuce. Peyronie's disease is characterized by the growth of a band of fibrous tissue on top of the penile shaft. Priapism is prolonged, painful, and nonsexual erection that can lead to thrombosis with ischemia and necrosis of penile tissue. Cancer of the penis accounts for less than 1% of male genital cancers in the United States. Although the tumor is slow growing and highly curable when diagnosed early, the greatest hindrance to successful treatment is a delay in seeking medical attention.

Disorders of the scrotum and testes include hydrocele, hematocele, spermatocele, varicocele, and testicular torsion. Inflammatory conditions can involve the scrotal sac, epididymis, or testes. Tumors can arise in the scrotum or the testes. Scrotal cancers usually are associated with exposure to petroleum products such as tar, pitch, and soot. Testicular cancers account for 1% of all male cancers and 3% of cancers of the male genitourinary system. With current treatment methods, a large percentage of men with these tumors can be cured. Testicular self-examination is recommended as a means of early detection of this form of cancer.

The prostate is a firm, glandular structure that surrounds the urethra. Inflammation of the prostate occurs as an acute or a chronic process. Chronic prostatitis probably is the most common cause of relapsing urinary tract infections in men. BPH is a common disorder in men older than 50 years. Because the prostate encircles the urethra, BPH exerts its effect through obstruction of urinary outflow from the bladder. Advances in the treatment of BPH include laser surgery, balloon dilatation, prostatic stents, and pharmacologic treatment.

Prostatic cancer is the most common male cancer in the United States and is second to lung cancer as a cause of cancer-related death in men. A recent increase in diagnosed cases is thought to reflect earlier diagnosis because of widespread use of PSA testing. Most prostate cancers are asymptomatic and are incidentally discovered on rectal examination. Cancer of the prostate, like other forms of cancer, is graded according to the histologic characteristics of the tumor and staged clinically using the TNM system. Treatment, which is based on the extent of the disease, includes surgery, radiation therapy, and hormonal manipulation.

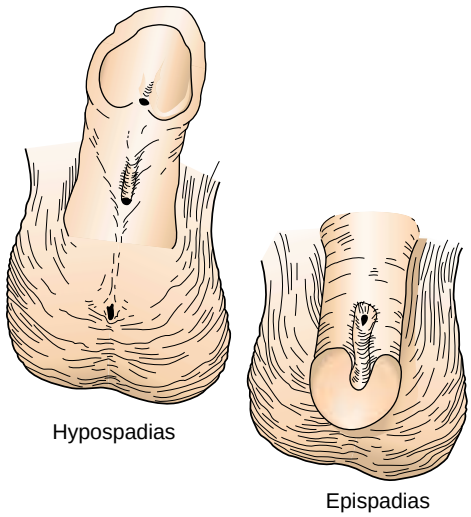
DISORDERS IN CHILDHOOD AND AGING CHANGES

Disorders of Childhood

Disorders of the male reproductive system that present in childhood include hypospadias, epispadias, phimosis and paraphimosis, and cryptorchidism.

Hypospadias and Epispadias

Hypospadias and epispadias are congenital disorders of the penis resulting from embryologic defects in the development of the urethral groove and penile urethra (Fig. 33-13). In hypospadias, which affects approximately 1 in 300 male infants, the termination of the urethra is on the ventral surface of the penis.[34,40] The testes are undescended in 10% of boys born with hypospadias and chordee (*i.e.*, ventral bowing of the penis), and inguinal hernia also may accompany the disorder. In the newborn with severe hypospadias and cryptorchidism (undescended testes), the differential diagnosis should consider ambiguous genitalia and masculinization



■ **FIGURE 33-13** ■ Hypospadias and epispadias.

that is seen in females with congenital adrenal hyperplasia (see Chapter 31). Because many chromosomal aberrations result in ambiguity of the external genitalia, chromosomal studies often are recommended for male infants with hypospadias and cryptorchidism.[34]

Surgery is the treatment of choice for hypospadias.[34] Circumcision is avoided because the foreskin is used for surgical repair. Factors that influence the timing of surgical repair include anesthetic risk, penile size, and the psychological effects of the surgery on the child. In mild cases, the surgery is done for cosmetic reasons only. In more severe cases, surgical repair becomes essential for normal sexual functioning and to prevent the psychological effects of having malformed genitalia. When indicated, surgical repair is usually done between the ages of 6 to 12 months.

Epispadias, in which the opening of the urethra is on the dorsal surface of the penis, is a less common defect. Although epispadias may occur as a separate entity, it often is associated with exstrophy of the bladder, a condition in which the abdominal wall fails to cover the bladder. The treatment depends on the extent of the developmental defect.

Phimosis and Paraphimosis

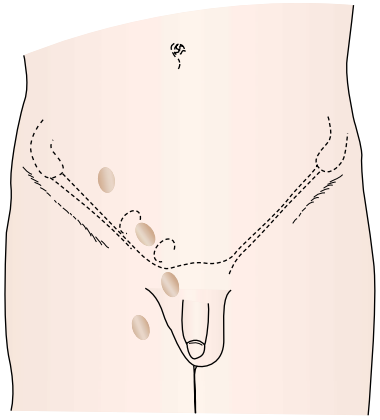
Phimosis refers to a tightening of the prepuce or penile foreskin that prevents its retraction over the glans. Embryologically, the foreskin begins to develop during the eighth week of gestation as a fold of skin at the distal edge of the penis that eventually grows forward over the base of the glans.[40] By the 16th week of gestation, the prepuce and the glans are adherent. Only a small percentage of newborns have a fully retractable foreskin. With growth, a space develops between the glans and foreskin, and by 3 years of age, approximately 90% of male children have retractable foreskins.

Because the foreskin of many boys cannot be fully retracted in early childhood, it is important that the area be cleaned thoroughly. There is no need to retract the foreskin forcibly because this could lead to infection, scarring, or paraphimosis. As the child grows, the foreskin becomes retractable, and the glans and foreskin should be cleaned routinely. If symptomatic phimosis occurs after childhood, it can cause difficulty with voiding or sexual activity. Circumcision is then the treatment of choice.

In a related condition called *paraphimosis*, the foreskin is so tight and constricted that it cannot cover the glans. A tight foreskin can constrict the blood supply to the glans and lead to ischemia and necrosis. Many cases of paraphimosis result from the foreskin being retracted for an extended period, as in the case of catheterized uncircumcised males.

Cryptorchidism

Cryptorchidism, or undescended testes, occurs when one or both of the testicles fail to move down into the scrotal sac. The condition is bilateral in 10% to 20% of cases. The testes develop intra-abdominally in the fetus and usually descend into the scrotum through the inguinal canal during the seventh to ninth months of gestation.[40] The undescended testes may remain in the lower abdomen or at a point of descent in the inguinal canal (Fig. 33-14).



■ **FIGURE 33-14** ■ Possible locations of undescended testicles.

The incidence of cryptorchidism is directly related to birth weight and gestational age; infants who are born prematurely or are small for gestational age have the highest incidence of the disorder. Up to one third of premature infants and 3% to 5% of full-term infants are born with undescended testicles.[35,41] The cause of cryptorchidism in full-term infants is poorly understood. Most cases are idiopathic, but some may result from genetic or hormonal factors.[29]

The major manifestation of cryptorchidism is the absence of one or more of the testes in the scrotum. The testis either is not palpable or can be felt external to the inguinal ring. Spontaneous descent often occurs during the first 3 months of life, and by 6 months of age the incidence decreases to 0.8%.[34,41] Spontaneous descent rarely occurs after 6 months of age.

In children with cryptorchidism, histologic abnormalities of the testes reflect intrinsic defects in the testicle or adverse effects of the extrascrotal environment. The undescended testicle is normal at birth, but pathologic changes can be demonstrated at 6 to 12 months.[34] There is a delay in germ cell development, changes in the spermatic tubules, and reduced number of Leydig cells. These changes are progressive if the testes remain undescended. When the disorder is unilateral, it also may produce morphologic changes in the contralateral descended testis.

The consequences of cryptorchidism include infertility, malignancy, and the possible psychological effects of an empty scrotum. Indirect inguinal hernias usually accompany the undescended testes but rarely are symptomatic. Recognition of the condition and early treatment are important steps in preventing adverse consequences. The risk of malignancy in the undescended testis is four to six times higher than in the general population.[34,41] The increased risk of testicular cancer is not significantly affected by orchiopexy, hormonal therapy, or late spontaneous descent after the age of 2 years. However, orchiopexy does allow for earlier detection of a testicular malignancy by positioning the testis in a more easily palpable location.

As a group, males with unilateral or bilateral cryptorchidism usually have decreased sperm counts, poorer-quality sperm, and lower fertility rates than do men whose testicles descend normally. The likelihood of decreased fertility increases when the condition is bilateral. Unlike the risk of testicular cancer,

there seems to be some advantage to early orchiopexy for protection of fertility.[34,41]

Diagnosis is based on careful examination of the genitalia in male infants. Undescended testes due to cryptorchidism should be differentiated from retractable testes that retract into the inguinal canal in response to an exaggerated cremaster muscle reflex. Retractable testes usually are palpable at birth but become nonpalpable later. They can be brought down with careful palpation in a warm room. Retractable testes usually assume a scrotal position during puberty. They have none of the complications associated with undescended testicles due to cryptorchidism.[34]

Improved techniques for testicular localization include ultrasonography (*i.e.*, visualization of the testes by recording the pulses of ultrasonic waves directed into the tissues), gonadal venography and arteriography (*i.e.*, radiography of the veins and arteries of the testes after the injection of a contrast medium), and laparoscopy (*i.e.*, examination of the interior of the abdomen using a visualization instrument).

The treatment goals for the child with cryptorchidism include measures to enhance future fertility potential, placement of the gonad in a favorable place for cancer detection, and improved cosmetic appearance. Regardless of the type of treatment used, it should be carried out between 6 months and 2 years of age.[34,41] Treatment modalities for children with unilateral or bilateral cryptorchidism include initial hormone therapy with hCG or luteinizing hormone-releasing hormone (LHRH), a hypothalamic hormone that stimulates production of the gonadotropic hormones by the anterior pituitary gland. For children who do no respond to hormonal treatment, surgical placement and fixation of the testes in the scrotum (*i.e.*, orchiopexy) have proved effective. Approximately 95% of infants who have orchiopexy for a unilateral undescended testis will be fertile, compared with a 30% to 50% fertility rate in uncorrected males.[41]

Treatment of males with undescended testis should include lifelong follow-up, considering the sequelae of testicular cancer and infertility. Parents need to be aware of the potential issues of infertility and increased risk of testicular cancer. On reaching puberty, boys should be instructed in the necessity of testicular self-examination.

Aging Changes

Like other body systems, the male reproductive system undergoes degenerative changes as a result of the aging process; it becomes less efficient with age. The declining physiologic efficiency of male reproductive function occurs gradually and involves the endocrine, circulatory, and neuromuscular systems.[42] Compared with the marked physiologic change in aging females, the changes in the aging male are more gradual and less drastic. Gonadal and reproductive failure usually are not related directly to age because a man remains fertile into advanced age; 80- and 90-year-old men have been known to father children.

As the male ages, his reproductive system becomes measurably different in structure and function from that of the younger male. Male sex hormone levels, particularly of testosterone, decrease with age, with the decline starting later on average than in women. The term *andropause* has been used to describe an ill-defined collection of symptoms in aging men, typically those older than 50 years, who may have a low androgen level.[43]

The sex hormones play a part in the structure and function of the reproductive system and other body systems from conception to old age; they affect protein synthesis, salt and water balance, bone growth, and cardiovascular function. Decreasing levels of testosterone affect sexual energy, muscle strength, and the genital tissues. The testes become smaller and lose their firmness. The seminiferous tubules, which produce spermatozoa, thicken and begin a degenerative process that finally inhibits sperm production, resulting in a decrease of viable spermatozoa. The prostate gland enlarges, and its contractions become weaker. The force of ejaculation decreases because of a reduction in the volume and viscosity of the seminal fluid. The seminal vesicle changes little from childhood to puberty. The pubertal increases in the fluid capacity of the gland remain throughout adulthood and decline after the age of 60 years. After age 60 years, the walls of the seminal vesicles thin, the epithelium decreases, and the muscle layer is replaced by connective tissue. Age-related changes in the penis consist of fibrotic changes in the trabeculae in the corpus spongiosum, with progressive sclerotic changes in arteries and veins. Sclerotic changes also follow in the corpora cavernosa, with the condition becoming generalized in 55- to 60-year-old men.

Erectile dysfunction in the elderly male often is directly related to the general physical condition of the person. Diseases that accompany aging can have direct bearing on male reproductive function. Various cardiovascular, respiratory, hormonal, neurologic, and hematologic disorders can be responsible for secondary impotence. For example, vascular disease affects male potency because it may impair blood flow to the pudendal arteries or their tributaries, resulting in loss of blood volume with subsequent poor distention of the vascular spaces of erectile tissue. Other diseases affecting potency include hypertension, diabetes, cardiac disease, and malignancies of the reproductive organs. In addition, certain medications can have an effect on sexual function.

Testosterone and other synthetic androgens may be used in older males with low androgen levels to improve muscle strength and vigor. Preliminary studies of androgen replacement in aging males with low androgen levels show an increase in lean body mass and a decrease in bone turnover. Before testosterone replacement therapy is initiated, all men should be screened for prostate cancer. Testosterone is available as an injectable form that is administered every 2 to 3 weeks or as a transdermal patch or gel. Side effects of replacement therapy may include acne, gynecomastia, and reduced HDL levels. It also may contribute to a worsening of sleep apnea in men who are troubled by this problem.

In summary, childhood disorders of the male reproductive system include congenital disorders in which the urethral opening is located on the ventral surface of the penis (hypospadias) or on the dorsal surface (epispadias). Phimosis is the condition in which the opening of the foreskin is too tight to permit retraction over the glans. Disorders of the scrotum and testes include cryptorchidism or undescended testicles. Early diagnosis and treatment is important because of the risk of malignancy and infertility.

Like other body systems, the male reproductive system undergoes changes as a result of the aging process. The changes occur gradually and involve parallel changes in endocrine, circulatory, and neuromuscular function. Testosterone levels decrease, the size and firmness of the testes decrease, sperm production declines, and the prostate gland enlarges. There usually is a decrease in frequency of intercourse, intensity of sensation, speed of attaining erection, and force of ejaculation.

REVIEW QUESTIONS

- Describe the structure and function of the male reproductive system and hormones and relate to the process of spermatogenesis.
- Relate the development and descent of testes to the pathogenesis of inguinal hernia and cryptorchidism.
- Compare the pathophysiology of cancer of the penis, scrotum, and testes.
- Compare the cause, appearance, and significance of hydrocele, hematocele, spermatocele, and varicocele.
- State the difference between extravaginal and intravaginal testicular torsion.
- Compare the pathology and symptoms of acute bacterial prostatitis, chronic bacterial prostatitis, and chronic prostatitis/pelvic pain syndrome.
- Describe the urologic manifestations and treatment of benign prostatic hyperplasia.
- List the methods used in the diagnosis and treatment of prostatic cancer.
- Describe the autonomic nervous system control of erection, emission, and ejaculation and relate to the pathogenesis of erectile dysfunction and priapism.
- State the difference between hypospadias and epispadias.
- Describe changes in the male reproductive system that occur with aging.

connection

Visit the Connection site at connection.lww.com/go/porth for links to chapter-related resources on the Internet.

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