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# Male Sexual Dysfunction

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## I. Definitions

Male sexual dysfunctions are classified into dysfunctions of libido, problems with emission/ejaculation/orgasm, erectile dysfunction, and priapism.

**Erectile dysfunction** (ED), defined as the persistent inability to obtain and maintain an erection sufficient for sexual intercourse, affects over 30 million men in the United States. ED is more prevalent among patients with atherosclerotic peripheral vascular disease, hypertension, diabetes mellitus, hypercholesterolemia, and heart disease and among men who smoke cigarettes. ED is an age-dependent disorder (Fig. 10.1) that affects the diabetic male an average of 10 to 15 years earlier than it does his nondiabetic counterpart.

**Fig. 10.1. Probability of various degrees of erectile dysfunction according to age. (Adapted from data in Feldman et al. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *J Urol* 1994;151:54–61.)**

**Primary ED** refers to ED that is lifelong, whereas **secondary ED** implies the loss of previously normal potency. ED caused exclusively by emotional stress or psychiatric disease is termed **psychogenic ED** and accounts for an estimated 10% to 50% of all cases of ED. **Organic ED**, which is ED caused exclusively by vascular, neurologic, endocrine, or other physical disease, accounts for an estimated 50% to 80% of cases. In the majority of impotent men, erectile impairment has both a psychological and an organic basis, and a complete management program will take this into account. **Priapism** is persistent erection that is not associated with sexual desire; it may be venoocclusive (associated with arterial ischemia and usually painful) or arteriogenic (occurring in high-flow states and painless). Erectile function must be differentiated from libido, ejaculation, orgasm, and fertility. **Libido** is a psychological concept that describes the desire for sexual intercourse. **Ejaculation**, which is neurophysiologically distinct from penile erection, consists of three events: (a) seminal emission (delivery of semen to the posterior urethra), (b) bladder neck closure, and (c) propulsion of semen to the external meatus. **Orgasm** is the cerebral and psychological appreciation of release of sexual tension. **Infertility** is the inability to produce offspring and is usually not due to ED.

## II. Physiology of erection

The bulk of the penis is composed of paired erectile bodies (the corpora cavernosa) (Fig.

10.2). The corpus spongiosum surrounds the urethra and distally expands to form the glans penis.

**Fig. 10.2. Cross-sectional view of penile anatomy, showing corpora cavernosa, corpus spongiosum, urethra, and their fascial coverings.**

The tunica albuginea, a tough layer of fibrous tissue that surrounds the corpus cavernosum, is composed of wavy collagen and elastin that allow erectile tissue to expand and elongate. Formation of tunical fibrotic plaques (Peyronie's disease) can result in loss of tunical compliance, penile curvature, and venoocclusive dysfunction. The interior of the corpus cavernosum contains specialized, widely communicating, endothelium-lined vascular lacunar

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spaces that consist of connective tissue (50% to 55%) and corporal smooth muscle (45% to 50%) (Fig. 10.3).

**Fig. 10.3. Microcirculation of the penis. During erection, cavernosal expansion compresses the subtunical venules against the rigid tunica albuginea, impeding venous outflow from the cavernosal sinuses.**

## *A. Blood supply*

to the penis is from the internal pudendal artery, which enters the perineum through Alcock's canal and gives rise to four terminal branches (dorsal artery, cavernosal artery, bulbar artery, and scrotal artery). Within the corpora, the cavernosal artery branches into the helicine arterioles. These arterial resistance vessels open into the lacunar spaces (Fig. 10.3). There are interconnections between the dorsal penile artery and the cavernosal artery. This communication is responsible for the success of microvascular penile bypass surgery between the inferior epigastric artery (donor vessel) and the dorsal artery (recipient vessel) in patients with cavernosal artery occlusion. Last, accessory pudendal arteries provide additional blood flow to the corpora cavernosa. Injury to these arteries during radical retro-pubic prostatectomy may explain why some patients experience ED following successful nerve-sparing procedures.

## *B. Venous drainage*

### 1. Intracavernosal drainage

from the peripheral lacunar spaces passes into subtunical venules, which lie between the peripheral erectile tissue and the tunica albuginea (Fig. 10.3). A series of subtunical venules coalesce into emissary veins, which pierce the tunica albuginea to join extratunical veins.

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In the flaccid state, lacunar venous blood passes unimpeded from the subtunical to the emissary to the extratunical veins. In the erect state, however, the subtunical venules become stretched and compressed, thus forming the primary site of resistance to venous outflow during penile erection.

### 2. Extracavernosal drainage.

The three routes of extratunical venous drainage are the (a) deep dorsal veins, (b) cavernosal and crural veins, and (c) superficial dorsal vein. The deep dorsal veins accept most of the venous flow from the distal corpora by way of emissary and circumflex veins. The deep dorsal veins empty into Santorini's vesicoprostatic plexus. The proximal corporal bodies are drained by the cavernosal and crural veins, which drain into both Santorini's vesicoprostatic plexus and the internal pudendal vein. The superficial dorsal vein drains blood from the pendulous penile skin and glans and communicates with the deep dorsal vein.

## *C. Vascular physiology*

### 1. Nitric oxide.

The corporal smooth muscle is contracted in the flaccid state and relaxed in the erect state. Following sexual stimulation, initially contracted helicine arteriolar smooth muscle undergoes relaxation through release of neuronal nitric oxide, arterial inflow increases, and nitric oxide is released from endothelial cells. Nitric oxide is a gas that diffuses into the corporal smooth muscle and induces smooth muscle relaxation. This latter process can occur only if the partial pressure of oxygen in the lacunar spaces is above 50 mm Hg, a situation that occurs only after exposure of the lacunar space to systemic arterial blood.

### 2. Venous outflow resistance.

Filling of the lacunar spaces stretches the subtunical venules to create venous outflow resistance and a further increase in intracavernosal pressure.

### 3. Detumescence

is brought about by neuronally mediated smooth muscle contraction, with restoration of corporal venous drainage. The **sympathetic nerves** (T10 to L2), which are responsible for detumescence and maintenance of flaccidity, project to the corpora as well as to the prostate and bladder neck via the hypogastric nerves. Adrenergic tone is crucial in initiating detumescence and in maintaining the flaccid state of the penis, since the smooth muscle of the arteries and cavernosal trabeculae must remain actively contracted. Contraction of cavernosal trabecular smooth muscle in response to norepinephrine is mediated by $\alpha_1$-adrenergic receptors.

## *D. Neurophysiology.*

Erectile function in the penis is regulated by autonomic (parasympathetic and sympathetic)

and somatic (sensory and motor) pathways to the erectile tissues and perineal striated muscles. Three sets of peripheral nerves innervate the penis: the sympathetic nerves (inhibitory), the parasympathetic nerves (excitatory), and the pudendal nerves (sensory).

The **parasympathetic nerves**, originating in the intermediolateral nuclei of the S2 to S4 spinal cord segments, provide the major excitatory input to the penis and are responsible for vasodilation of the penile vasculature and subsequent erection. The efferent pathway is via the pelvic nerves, which are preganglionic parasympathetic nerves originating from S2 through S4.

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The pelvic nerves join the pelvic plexus, which gives rise to the cavernous nerve of the penis. Stimulation of the pelvic nerves causes a marked increase in flow through the pudendal arteries and entrance of blood into the cavernosal spaces. The afferent limb of the erection response is mediated by the dorsal penile nerve (a branch of the pudendal nerve), which transmits sensory impulses to the spinal cord.

Penile erections are elicited by local sensory stimulation of the genital organs (reflexogenic erections) and by central psychogenic stimuli received by or generated within the brain (psychogenic erections). Most cerebral regulatory functions for erection occur in the hypothalamus and limbic system (Table 10.1). The role of the **sympathetic nervous system** in the initiation of penile erection is not clear, but its activation is generally associated with contraction of corpus cavernosal smooth muscle and penile detumescence.

**Table 10.1. Neurologic pathways of the sexual response**

| Response | Afferent | Spinal Cord | Efferent |
|---|---|---|---|
| Erection | | | |
| Reflexogenic | Pudendal nerve | S2–4 sacral | Pelvic nerves |
| Psychogenic | Cerebral | Suprasacral | Pelvic nerves |
| Emission | Pudendal nerve | Lumbosacral | Sympathetic nerves |
| Ejaculation | Pudendal nerve | S2–4 sacral | Pudendal nerve |

The **pudendal nerves** comprise motor efferent and sensory afferent fibers innervating the ischiocavernous and bulbocavernous muscles as well as the penile and perineal skin. Pudendal motor neuron cell bodies are located in Onuf's nucleus of the S2 to S4 segments. The pudendal nerve enters the perineum through the lesser sciatic notch at the posterior border of the ischiorectal fossa and runs in Alcock's canal (pudendal canal) toward the posterior aspect of the perineal membrane. At this point, the pudendal nerve gives rise to the perineal nerve, with branches to the scrotum, and the rectal nerve, supplying the inferior rectal region. The dorsal nerve of the penis emerges as the last branch of the pudendal nerve. It then turns distally along the dorsal penile shaft, lateral to the dorsal artery. Multiple fascicles fan out distally, supplying proprioceptive and sensory nerve terminals to the dorsum of the tunica albuginea and the skin of the penile shaft and glans penis.

## III. Causes of ED

### *A. Vasculogenic ED*

#### 1. Arterial disease.

Atherosclerosis is a common cause of organic ED. Arterial ED is characterized clinically by erections that take longer than usual to develop (diminished spontaneity), have diminished rigidity, and demonstrate poor sustainability (Table 10.2). Arterial ED may be associated with general vascular risk factors such as hypertension, cigarette smoking, diabetes mellitus, and hypercholesterolemia. The



incidence of ED in atheromatous aortoiliac and peripheral vascular disease is about 50%. Blunt trauma to the perineum related to falls, sporting accidents, or bicycle injuries and blunt trauma to the pelvis (pelvic fractures) related to motor vehicle accidents may cause site-specific, nondiffuse arterial-occlusive disease in the common penile or cavernosal artery.

**Table 10.2. Etiology of erectile dysfunction**

| | |
|---|---|
| I. | Psychogenic |
| | |

| | | |
|---|---|---|
| II. | Organic | |
| | a. | **I**nflammatory: prostatitis, urethritis, stricture |
| | b. | **M**echanical: chordee, Peyronie's disease, phimosis |
| | c. | **P**ostoperative: iatrogenic |
| | d. | **O**cclusive: arteriogenic |
| | e. | **T**raumatic: pelvic fracture, urethral rupture |
| | f. | **E**ndurance: chronic and systemic diseases |
| | g. | **N**eurologic: neuropathy, temporal lobe epilepsy, multiple sclerosis |
| | h. | **C**hemical: alcohol, marijuana, prescription drugs |
| | i. | **E**ndocrine: testicular failure, pituitary failure, hyperprolactinemia |

Source: From A. D. Smith, personal communication.

### 2. Venoocclusive ED.

The venous outflow regulatory mechanism depends on the completeness of trabecular smooth muscle relaxation and the expandability of the erectile tissue, defined as the ability to achieve maximal corporal volumes at low intracavernosal pressures. An increase in corporal smooth muscle tone during stress or anxiety may induce a functional venous leak. An increase in the trabecular connective tissue content, which can be secondary to abnormal collagen metabolism induced by chronic ischemia, plays a central role in the pathogenesis of organic venous leak ED. Ultimately, fibrosis of the erectile tissue causes a decreased expandability of erectile tissue, with subsequent poor stretching of the subtunical venules, poor venous outflow resistance, and failure to maintain erection.

## *B. Diabetes mellitus.*

Diabetes mellitus is a common cause of organic ED, affecting up to 75% of diabetic

patients. Patients with insulin-dependent juvenile diabetes commonly have peripheral neuropathic ED. Those with non–insulin-dependent, adult-onset diabetes usually have vasculogenic ED, but a combination of the neuropathic and angiopathic effects of diabetes is probably responsible in most cases. It is hypothesized that cavernosal artery insufficiency, corporal venoocclusive dysfunction, and/or autonomic neuropathy are the major organic pathophysiologic mechanisms leading to persistent erectile impairment in men with diabetes mellitus.

## *C. Renal failure.*

Approximately 50% of dialysis-dependent uremic patients suffer from ED, but improvement after transplantation occurs in many patients—presumably because of reversal of the anemia associated with chronic renal failure or

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improvement in uremic neuropathy. Correction of abnormalities in zinc metabolism may also contribute to restoration of potency following renal transplantation. Hyperprolactinemia secondary to decreased clearance and increased production seen in end-stage renal disease has also been associated with ED.

## *D. Neurologic lesions*

can affect erectile function at many levels:

### 1. Intracerebral

(Parkinson's disease, cerebrovascular disease). Efferent pathways from the medial preoptic area may be affected in addition to higher cortical functions, affecting sexual response.

### 2. Spinal cord

(spinal cord trauma, multiple sclerosis, myelodysplasia). Approximately 80% of patients with cervical spinal cord lesions, 70% with thoracic lesions, and 50% with lumbar lesions are able to have reflex erections. Psychogenic erections may occur in approximately 25% of patients whose spinal cord injury or lesion is below T12. Psychogenic erections are not possible in patients with complete lesions above T12. ED may, in rare cases, be the sole presenting symptom of multiple sclerosis. Sexual dysfunction may be seen in up to 75% of patients with multiple sclerosis.

### 3. Peripheral nerves

[alcoholic neuropathy, diabetic neuropathy (see above), after surgery or trauma]. Damage to the cavernous nerves during radical pelvic surgery such as radical prostatectomy is not uncommon. Diabetic neuropathy is the most frequent cause of peripheral neurogenic ED.

## *E. Endocrine disorders*

are responsible for fewer than 5% of instances of ED. The etiologic significance of the hypothalamic–pituitary–testicular axis in ED is unclear. Androgens influence the growth and

development of the male reproductive tract and secondary sexual characteristics. Their effect on libido and sexual behavior is well established, but the effect of androgens on normal erectile physiology is poorly understood. Isolated testosterone deficiency is rare and is usually accompanied by a marked loss of libido.

### 1. Hypogonadotropic hypogonadism (Prader—Willi and Laurence—Moon—Biedl syndromes).

These syndromes are rare, and patients usually present to the pediatrician or internist with delayed puberty.

### 2. Hypergonadotropic hypogonadism (Klinefelter's syndrome, mumps orchitis, surgical orchiectomy).

These conditions are all characterized by excessive pituitary hormone secretion in an attempt to overcome underlying testicular pathology. Potency may persist despite decreased libido.

### 3. Hyperprolactinemia (pituitary adenoma, craniopharyngioma, drug therapy).

Although prolactin promotes the action of androgens, at pharmacologic doses, it may inhibit luteinizing hormone and testosterone release as well as the peripheral conversion of testosterone to dihydrotestosterone. Hyperprolactinemia is associated with low or low-normal levels of serum testosterone. Androgen replacement therapy without restoration of normal prolactin levels will not restore potency. The effects of hyperprolactinemia on erectile function appear to be centrally mediated. Serum prolactin may be lowered by administering bromocriptine, L-dopa, or



cyproheptadine.

Hyperthyroid states are commonly associated with diminished libido and, less frequently, with ED. ED associated with hypothyroid states has been reported and may be secondary to associated low levels of testosterone secretion and elevated levels of prolactin.

## *F. Trauma*

### 1. Pelvic fracture with ruptured posterior urethra.

Damage to the neurovascular bundle or to the internal pudendal or common penile artery at the time of injury is predominantly responsible for most of the ED seen following these injuries. Primary realignment with immediate repair is associated with a high incidence of ED or decreased rigidity, likely secondary to disruption of the cavernous nerves during manipulation of the hematoma. Suprapubic cystotomy with delayed repair of the urethra has a lower incidence of associated ED, ranging from 13% to 56%.

### 2. Perineal trauma.

Many patients previously thought to have primary psychogenic ED are found to have occlusion of the common penile or cavernosal artery secondary to perineal trauma that occurred before puberty. Bicycle accidents and extensive bicycle riding account for a significant portion of these blunt perineal injuries.

## *G. Postoperative or iatrogenic ED*

### 1. Aortic or peripheral vascular surgery

may impair blood flow through the hypogastric arteries and thus cause arterial ED.

### 2. Renal transplantation

may cause ED, especially if a second contralateral transplantation is performed with end-to-end hypogastric artery anastomosis. In most instances, however, renal transplantation improves sexual function by reversing the anemia and uremic neuropathy associated with chronic renal failure.

### 3. Pelvic irradiation

may cause an accelerated occlusive atherosclerosis of the pelvic vessels, leading to ED. Fibrosis of cavernosal erectile tissue secondary to irradiation of the crural region is also likely to contribute to postirradiation ED.

### 4. Cavernosal–spongiosal shunts

performed for the emergency treatment of priapism (Winter, Quackles, and El Ghorab procedures) can rarely produce a permanent corporal leak ED.

### 5. Neurosurgical procedures.

Surgery such as lumbar laminectomy, sacral rhizotomy, and pudendal neurectomy can produce neurogenic ED, especially if the sacral roots at S2, S3, and S4 are injured.

### 6. Abdominoperineal resection of the rectum.

The incidence of ED is higher if this operation is performed for malignant disease.

### 7. Radical prostatectomy or cystoprostatectomy.

The incidence of ED can be lowered to perhaps 40% to 60% if “nerve-sparing” techniques are used.

### 8. Transurethral sphincterotomy

may lead to ED in rare instances. One should avoid incision at the 3 o'clock and 9 o'clock positions to prevent thermal injury to the cavernosal arteries.

## *H. Drugs.*

Various medications are associated with ED. Please refer to Table 10.3 for a partial list of these agents.

**Table 10.3. Partial list of medications that can cause erectile dysfunction**

| |
|---|
| **Centrally acting agents** |
| Marijuana |
| Reserpine |
| Clonidine |
| α-Methyldopa |
| Tricyclic antidepressants |
| Phenothiazines |
| Ethanol |
| Opioids |
| **Anticholinergic agents** |
| Antimuscarinic agents |
| Antihistamines |
| Tricyclic antidepressants |
| Phenothiazines |
| **Antiandrogenic agents** |

| |
|---|
| Spironolactone |
| Estrogens |
| Cyproterone acetate |
| Disopyramide |
| Ketoconazole |
| Cimetidine |
| **Hyperprolactinemic agents** |
| Estrogen |
| Phenothiazines |
| Haloperidol |
| Metoclopramide |
| Opiates |
| Imipramine |
| Reserpine |
| α-Methyldopa |
| **Sympatholytic agents** |
| α-Adrenergic blockers |
| Bretylium |

| |
|---|
| Reserpine |
| Clonidine |
| Guanethidine |
| β-Adrenergic blockers |
| α-Methyldopa |
| **Agents with unknown mechanism** |
| ε-Aminocaproic acid |
| Naproxen |
| Thiazides |
| Digoxin |

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## IV. Evaluation

### *A. Sexual history.*

The onset, duration, and circumstances of the erection problem are all important. One can distinguish three different types of erections: partner induced, nocturnal, and self-induced (masturbation). Three important qualities are hardness, maintenance, and spontaneity. It is useful to ask the patient questions concerning the qualities of all three types of erection. The degree of axial penile rigidity (hardness) can be quantified by using a scale of 1 to 10, in which 1 denotes the rigidity of a marshmallow and 10 the rigidity of a steel rod. Questions about the degree of maintenance should be asked and compared with prior capabilities. Questions concerning the degree of spontaneity should relate to the work, effort, and concentration required to achieve an erection compared with prior capabilities. Other questions include the following: Are there associated abnormalities in ejaculation,

libido, or orgasm? Some symptoms suggest psychogenic ED, and others suggest organic disease. A psychogenic cause is suggested by the sudden onset of ED or the presence of ED under some circumstances but complete erection at other times. In contrast, gradual deterioration of erectile quality over months or years with preservation of libido suggests organic disease. Most patients with ED can ejaculate despite poor or absent erections.

## *B. Medical history.*

Inquiries should be made about diabetes mellitus, hypertension, smoking, hypercholesterolemia, and hyperlipidemia as well as about liver, renal, vascular, neurologic, psychiatric, and endocrine disease. Is there any history of abdominal, pelvic, or perineal surgery or trauma? The possible use of androgenic substances, whether prescribed or over the counter, mandates inquiries about these agents, as they are associated with decreased serum testosterone levels and decreased libido.

## *C. Psychological evaluation.*

Given the personal, interpersonal, social, and occupational implications of sexual problems, a brief psychosocial history is mandatory for every patient. Current psychological state, self-esteem, and history of sexual trauma/abuse, as well as past and present relationships and social and occupational performance, should be addressed.

A psychological interview with a psychologist or sex therapist may be indicated to assess the presence of personality disorders and anxiety. If possible, the couple should be present for the evaluation to assess their expectations from the planned therapy.

## *D. Physical examination.*

The general body habitus and status of **secondary sexual characteristics** should be assessed. Gynecomastia may be present in patients with androgen deficiency or estrogen excess. Absence of the peripheral pulses in the lower extremities may indicate vascular insufficiency. The penis should be examined carefully for adequacy of length, fibrotic regions of the tunica albuginea (Peyronie's disease), or deformity of the corporal bodies. It is important to stretch the penis to examine for tunical pathology. The dorsal penile pulse should be easily palpable. The presence, size, and consistency of the testes should be determined by palpation. The sensory function of the pudendal nerve can be assessed by pinprick testing of the penile and perineal skin. The integrity of the sacral reflexes is determined by eliciting the bulbocavernosus reflex.

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## *E. Laboratory tests.*

Laboratory testing is strongly recommended. Standard serum chemistries, complete blood cell count, and lipid profiles may elucidate vascular risk factors such as hypercholesterolemia, diabetes, and renal failure. Determinations of serum prostate-specific antigen (PSA) and serum thyroid-stimulating hormone may be indicated in select cases. The integrity of the hypothalamic–pituitary–gonadal axis should be examined in every patient with ED. It is unclear which testosterone assay (total, free, or bioavailable) is

best; however, there is a consensus that at least one of these assays should be performed. Although pituitary adenomas are a rare cause of sexual dysfunction, this potentially life-threatening disease and reversible cause of ED should not be forgotten.

## *F. Specialized diagnostic tests.*

The introduction of sildenafil in 1998 dramatically reduced the need for specialized testing. Diagnostic modalities such as duplex Doppler ultrasound, cavernosometry, caversonography, and selective pudendal arteriography expand the physician's and patient's understanding of the pathophysiologic mechanisms, but disadvantages such as invasiveness, cost, and associated risks and complications have reduced the indications for specialized testing.

### 1. Nocturnal penile tumescence

(NPT) is the assessment of changes in penile circumference that occur during sleep. Such testing may be used to distinguish organic from psychogenic ED, but its ability to evaluate axial rigidity is poor. The accuracy of NPT in distinguishing organic from psychogenic ED is approximately 80%. In the normal postpubertal male, three to five erections occur each night during rapid eye movement stage sleep. Each erection lasts approximately 30 minutes, and these episodes occur every 90 minutes. The number and duration of tumescence episodes decrease gradually with age. Types of NPT techniques include the following:

a. **Penile strain gauge.** A circular strain gauge is placed at the base and tip of the penis. Penile erection results in stretching of the strain gauge, which is recorded. This technique measures only change in circumference, not rigidity.

b. **Snap gauge.** A disposable band is placed around the penis; the band contains three plastic strips that snap on stretching. Each strip has a different tensile strength (approximately 80, 100, and 120 mm Hg). The snap gauge provides a rough measure of rigidity and circumferential change but not a written record.

c. **Rigiscan** is an ambulatory device consisting of two loops placed around the base and tip of the penis that send information to a microcomputer to measure penile circumference and radial rigidity.

### 2. Neurologic testing.

Penile biothesiometry (vibration testing) is used to assess the threshold for vibratory sensation and has proved helpful in the management of diabetic patients with ED. Other specialized tests have been described and include (a) dorsal nerve conduction time for peripheral sensory neuropathy, (b) sacral evoked response for pudendal nerve and sacral cord lesions, and (c) dorsal nerve somatosensory evoked potential testing for peripheral and central nervous system lesions in the sensory (afferent) pudendal pathway.

## 3. Vascular testing

includes office intracavernosal injection testing, duplex Doppler ultrasound, studies of the penile brachial index, penile plethysmography, cavernosal artery systolic occlusion pressure in the erect state, recordings of the change in the diameter of the cavernosal artery in the flaccid and erect state, and selective internal pudendal arteriography in the erect state. The detection rate for suspected vascular pathology has ranged from 33% to 87%.

a. **Penile brachial index testing.** A Doppler stethoscope and a 1.2-cm penile cuff are used to determine penile artery systolic pressures. This value is expressed as a ratio with the systemic blood pressure measured in the arm, and the result is considered abnormal if the ratio is <0.60. This test is still valuable but has been replaced by ultrasound-based testing.

b. **Duplex ultrasonography.** B-Mode images and Doppler values are obtained with a 7.5-MHz transducer during a pharmacologically induced penile erection. This test is performed to assess cavernosal artery diameter and flow velocity; simultaneous functional and anatomic information is thereby obtained. Peak flow velocity, acceleration time, diastolic flow velocity, and resistive index are some of the parameters that can be measured to gather information about the relative status of penile inflow and outflow mechanisms in a minimally invasive fashion. This test is performed after the penis has been maximally relaxed using pharmacologic agents.

c. **Dynamic infusion cavernosometry and cavernosography.** The intracavernosal pressure and volume are measured following injection of intracavernosal vasoactive agents. In healthy persons, the equilibrium intracavernosal pressure is recorded after 10 minutes to approximate the mean systemic arterial blood pressure (90 mm Hg). Subsequently, infusion of saline solution into the corpora is begun through a separate intracavernosal needle. Flow rates for maintenance of various intracavernosal pressures are recorded. Generally, an infusion rate of <5 mL/min is required to maintain a series of intracavernosal pressure values. Once a pressure of 150 mm Hg is reached, the infusion is stopped, and the “pressure decay” is noted after 30 seconds. Normally, the pressure should not drop >45 mm Hg in 30 seconds. Patients suspected of having venous leak ED, based on abnormalities of the flow to maintain and pressure decay studies, undergo infusion of x-ray contrast agent into their corpora to confirm the diagnosis. Radiographic demonstration of contrast agent outside the corpora following administration of intracavernosal papaverine, combined with the inability to sustain intracavernosal pressure, indicates ED caused by “corporal venous leak.” Arterial integrity is assessed in this study by recording the cavernosal artery systolic occlusion pressure and comparing this value with the systemic brachial artery systolic occlusion pressure.

d. **Selective internal pudendal arteriography.** Arteriography is a more invasive test that is indicated if arteriogenic ED is suspected in a candidate for microvascular arterial bypass surgery for ED. Arteriography is usually

performed with intravascular and intracavernosal vasodilators and patient sedation to optimize visualization of the cavernosal vessels.

# V. Treatment

## *A. First-line therapy*

### 1. Sex therapy.

For patients with evidence of psychogenic ED and no discernible organic cause, a short course (6 to 12 weeks) of sex therapy should be prescribed. The details of this therapy are beyond the scope of this chapter. In organic ED, behavioral sex therapy may be combined with various other forms of therapy in selected cases to optimize patient response. Because performance anxiety may continue to play a significant role in a couple's sexual life after medical or surgical treatment, behavioral sex therapy may be useful even in the presence of organic pathology.

### 2. The vacuum erection device (VED)

is one of the mainstays of noninvasive therapy for ED. It consists of a cylindrical component and a suction device that the patient places around the penis to create negative pressure and achieve an erection (Fig. 10.4). Maintenance of erection is then accomplished with an elastic constriction ring placed at the base of the penis. The advantages of VED include simplicity of use, low cost, relative safety, and ability to start treatment immediately. Patients with significant peripheral vascular disease, those receiving anticoagulants, and diabetics are generally not good candidates for the VED.

**Fig. 10.4. Hand-operated vacuum erection device.**

a. **Efficacy.** Patient acceptance and satisfaction with vacuum constrictive devices in all types of ED, including diabetic ED, have been reported to be 68% to 83%. The reasons for discontinuation of this treatment have included



premature loss of penile tumescence and rigidity, penile pain, pain during ejaculation, and inconvenience.

b. **Complications.** Patient compliance with the recommended guidelines for use is mandatory because serious problems may be encountered if the VED is left in place for a long period. To date, the complications from the use of these devices have been minor and self-limited. They have included difficulty with ejaculation, penile pain, ecchymoses, hematomas, and petechiae. Patients taking aspirin or warfarin are more likely to develop complications related to vascular fragility. Many of the devices manufactured have a valve that limits the vacuum pressure (<250 mm Hg), a feature

that might decrease these types of complications.

## 3. Oral agents.

The introduction of **sildenafil citrate** in 1998 revolutionized the management of men with ED. Sildenafil has not only encouraged patients and health care professionals to more openly discuss human sexuality, it has also increased the number of patients using other therapeutic modalities such as intracavernosal injections and penile prostheses.

a. **Sildenafil citrate** is a potent and selective inhibitor of phosphodiesterase type 5 (PDE5). The drug blocks the hydrolysis of cyclic GMP, enhancing the accumulation of cyclic GMP and potentiating the relaxant effects of nitric oxide. After oral administration, the drug is rapidly absorbed and 40% bioavailable. Fatty foods decrease the bioavailability of the drug to 29%. Sildenafil is metabolized in the liver by the cytochrome P450 enzyme system and is excreted in feces (80%) and urine (13%). Sildenafil is effective in treating ED resulting from a variety of organic causes, including diabetes mellitus.

    1. **Dosing.** Sildenafil is used on demand (prn). The recommended initial dose is 50 mg taken 1 hour before sexual activity. After the initial dose, it can be adjusted based on efficacy and tolerability. The maximum recommended dose is 100 mg, no more than once per day, independent of the dosage used. The majority of patients (75%) use 100 mg, and only 2% of patients use 25 mg. The initial dose in patients older than 65 years, in patients with renal or liver insufficiency, or in patients receiving drugs that inhibit cytochrome P450 (erythromycin, cimetidine) is 25 mg.

    2. **Contraindications.** Sildenafil is contraindicated in patients who require nitroglycerine to treat myocardial ischemia. The American College of Cardiologists and the American Heart Association also recommend that sildenafil be used with caution in patients receiving complex antihypertensive regimens; in patients with coronary artery disease, borderline blood pressure, or renal/liver insufficiency; and in patients who use drugs that inhibit cytochrome P450.

    3. **Adverse effects.** The rate of discontinuation of this agent is extremely low (0.4% to 1.2%), most likely because of its low side effect profile and high efficacy. The most common side effects are headaches (16%), facial flushing (10%),



    dyspepsia (7%), nasal congestion (4%), and diarrhea (3%). In addition, at the 100-mg dose, 2% to 3% of men may experience transient alterations in color vision.

b. **Yohimbine hydrochloride** is a natural product derived from the bark of the yohimbe tree that produces a presynaptic $\alpha_2$-adrenergic blocking agent. Peripherally, its effect is to increase cholinergic and decrease adrenergic activity. Yohimbine also

acts as a mood stimulant. Its efficacy rate is only about 20% to 25% overall, and it seems to be most effective in patients with psychogenic ED. Nevertheless, the drug continues to find use as a safe and low-cost alternative to sildenafil. Standard dose is 5.4 mg PO tid. Adverse effects include dizziness, flushing, nausea, and headache.

c. **Vardenafil**, a potent and selective PDE5 inhibitor, is currently in clinical trials and will soon be available in the USA. It offers a slightly quicker onset of action than sildenafil.

d. **Tadalafil** is also a potent and selective PDE5 inhibitor with a long half-life (almost 18 hours) that will soon be available in the USA. Because of its long half-life, it will be administered once daily rather than prn as sildenafil is. The most common adverse events were headache, back pain, myalgia, and dyspepsia. Interestingly, no color vision alterations were observed with tadalafil.

## 4. Androgen replacement

is indicated only in patients with documented androgen deficiency; it should not be used empirically. The cause of androgen deficiency should be thoroughly investigated. Older men should be followed regularly for prostatic enlargement or nodularity while receiving androgen therapy. PSA must be checked annually.

a. **Parenteral testosterone** has a long history as reliable treatment of male hypogonadism. Both testosterone enanthate and testosterone cypionate are very lipophilic, resulting in slow release from the adipose tissue at the injection site. The dose is 200 to 400 mg IM every 2 to 4 weeks.

b. **Oral testosterone** may be given as 10 to 30 mg of methyltestosterone daily or 5 to 20 mg of fluoxymesterone daily but is generally less effective than parenteral therapy. Oral testosterone therapy is associated with cholestatic jaundice (reversible on withdrawal of drug therapy) and hepatocarcinoma. Liver toxicity is caused by 17α-methyl preparations of testosterone. For these reasons, oral testosterone therapy is not recommended.

c. **Transdermal testosterone** therapy that can achieve steady serum levels of testosterone is now available in several forms. Compliance may be significantly improved because of the ease of application.

    1. **Scrotal patch** application is based on the observation that genital skin is the only skin across which sufficient natural testosterone can be absorbed to raise the serum testosterone concentration to normal levels. The patch is applied to the scrotal skin once a day and worn continuously except when bathing. Absorption is better with hairless skin.



    2. **Body skin patch.** A 5-mg patch is applied to the arm, torso, or thigh and delivers 5 mg of testosterone over 24 hours.

3. **Testosterone gel** is supplied in 2.5- and 5.0-g packets. These contain 25 and 50 mg of testosterone, respectively. The dose is 50 to 100 mg qd applied to normal skin. It may take a month for the serum testosterone concentration reach the normal male range.

## *B. Second-line therapy*

### 1. Intracavernous pharmacotherapy.

Most patients suffering from ED, both organic and mixed, may potentially be treated with intracavernous pharmacotherapy. Before intracavernosal pharmacotherapy is instituted as a long-term form of therapy, a diagnostic and therapeutic trial must be performed in the office so that the patient is fully comfortable with the technique of injection and the dosage. Patients are usually advised to inject a maximum of three times per week. The initial acceptance rate for intracavernosal pharmacotherapy is between 65% and 85% in most studies, but there is a nearly 50% 1-year dropout rate. Loss of interest in sexual activity and complications of intracavernosal pharmacotherapy (e.g., pain, dislike of self-injection, recovery of spontaneous erections, other medical conditions) are some of the reasons for the high dropout rate. Agents that have been used in this mode include papaverine, phentolamine, prostaglandin $E_1$, and forskolin in various combinations. Lower doses of vasoactive agents are indicated in spinal cord–injured patients, whereas diabetic individuals usually require higher doses. Onset of erection is usually around 10 minutes from the time of injection, and duration may range from 30 minutes to 6 hours. Intracavernosal pharmacotherapy with vasoactive medications is contraindicated in patients taking monoamine oxidase inhibitors, patients with hypersensitivity to these agents, and those prone to secondary priapism (e.g., sickle cell disease or trait, leukemia, or multiple myeloma).

a. **Papaverine hydrochloride** is a direct smooth muscle relaxant and vasodilator whose action is unrelated to nerve activity. It is supplied as a solution containing 30 mg/mL. The dose varies from patient to patient and must be individualized. The drug is given alone (rare) or in combination with other agents such as phentolamine or phentolamine and alprostadil (tri-mix) (Table 10.4).

**Table 10.4. Vasoactive agents for intracavernous injection**

| Vasoactive Agent(s) | Typical Dose Range |
|---|---|

| | |
|---|---|
| Papaverine HCl | 15–45 mg |
| Prostaglandin $E_1$ | 10–40 µg |
| Papaverine/phentolamine | 30 mg/1 mg |
| Papaverine/phentolamine/prostaglandin $E_1$ | 30 mg/1 mg/10 µg |

b. **Phentolamine mesylate** is a short-acting α-adrenergic blocking agent that is most often combined with

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papaverine or alprostadil. It is supplied in a 1-mL vial containing 5 mg. The intracavernous dose is up to 1 mg.

c. **Alprostadil** alone (usually 10 to 40 µg) or in combination with papaverine and/or phentolamine mesylate may be injected intracavernosally. Most studies show increased efficacy for the three-drug combination regimen compared with monotherapy.

d. **Three-drug regimen solution** consists of 30 mg of papaverine, 1 mg of phentolamine, and 10 µg of prostaglandin $E_1$ per milliliter of solution. The dose is highly individualized, ranging from 0.05 to 1 mL or sometimes more if required to obtain an adequate response. A safe test dose is 0.25 mL.

e. **Forskolin**, a naturally occurring alkaloid that directly activates the catalytic domain of adenylate cyclase, has demonstrated efficacy as an auxiliary vasoactive agent in patients who had previously failed high-volume, high-concentration injection therapy. Forskolin is especially useful in patients with diabetes or post–radical prostatectomy ED who develop significant corporal pain with the use of intracavernosal prostaglandin $E_1$.

f. **Technique of injection** is important in obtaining satisfactory results and reducing the risk of complications. The vasoactive solution selected should be drawn up in a 1-cc syringe with a 27G needle. The needle should penetrate the tunica albuginea at the lateral border near the base of the penis but not go so deep as to injure the cavernosal artery (Fig. 10.5). Firm pressure should be placed on the injection site for 3 minutes after injection to prevent hematoma.

**Fig. 10.5. Technique of injecting vasoactive agents into corpus cavernosum.**

g. **Complications** of intracavernosal pharmacotherapy may include the following:

1. **Local hematoma** can be largely prevented by instructing the patient to compress the injection site manually for at least 3 minutes.

2. **Corporal fibrosis** is the most significant long-term complication of intracavernosal pharmacotherapy and may be related to a number of factors, including drug effect, genetic predisposition, local trauma during intercourse, injection frequency, or a combination of these. It

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may resolve spontaneously in 35% of patients, and intracavernosal pharmacotherapy may be reinstituted. Persistence of corporal fibrosis is not necessarily a reason to stop intracavernosal pharmacotherapy if the degree of fibrosis and deformity is not severe and they are not interfering with intercourse. In more severe cases, insertion of a penile prosthesis and penile straightening will be required. Local induration may be reduced by alternating injection sites and limiting the injections to no more than two or three per week.

3. **Priapism** is a potentially serious complication that can lead to permanent corporal fibrosis. Priapism of <24 hours' duration can usually be managed without surgery by corporal aspiration and intracavernosal injection of α-adrenergic agents.

4. **Pain** may be reported by the patient on intracavernosal pharmacotherapy. The pain may be at the injection site for a short time after injection, but diffuse penile “ache” is more common. Prolonged pain may be experienced in the penile shaft or the perineum in approximately 20% of patients on prostaglandin $E_1$ monotherapy, but this is rare with papaverine or phentolamine.

## 2. Transurethral alprostadil,

a Food and Drug Administration–approved medication for the treatment of men with ED, is a semisolid pellet inserted intraurethrally with an applicator. This compound is the same as that used for intracavernosal injection, but the doses required are significantly larger (125 to 1,000 μg). From the corpus spongiosum, the agent must pass into the corpus cavernosum to initiate the hemodynamic events leading to erection. The most commonly used initial dose is 500 μg. About 65% of patients using transurethral alprostadil report erections sufficient for intercourse, but only one-third report erections with 100% rigidity. The major advantage is ease of delivery compared with intracavernosal injections. The most common side effect is penile pain (10%), with hypotension-related symptoms the next most common (3%). Priapism or penile fibrosis has not been reported. Recent studies suggest that placement of a penile ring may enhance the effectiveness of this mode of

treatment.

## *C. Third-line therapy*

### 1. Surgical prostheses.

Third-line treatment interventions are invasive, irreversible, and associated with many potentially serious complications such as device infection, erosion, and malfunction. Penile prostheses should be viewed only as a last-resort therapy in patients with treatment-refractory ED. Despite their significant cost and potential invasiveness, penile prostheses continue to find application in patients who have failed other forms of therapy.

a. **Historical notes.** Interest in treating ED developed among urologists following the development of a successful intracorporal noninflatable penile prosthesis by Small and Carrion and an inflatable prosthesis by Scott and Bradley in the 1970s. Over the next two decades, further development of penile prostheses proceeded along these two distinct lines:

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the malleable or rigid prosthesis and the multicomponent inflatable prosthesis. More recently, two-component and self-contained inflatable devices have been introduced.

b. **Counseling and selection of prosthesis.** A variety of prostheses are available (Table 10.5). The ideal penile prosthesis would result in a normal-appearing penis when flaccid while providing increased girth and length when erect. This ideal is rarely achieved, and patients should be counseled that penile prostheses will not restore the full length previously achieved by natural erections. Thus, careful counseling and selection of the device most appropriate for the individual patient are very important to patient satisfaction. Considerations include patient anatomy, physical habitus, cosmetic preference, surgeon's preference, and cost of the device. The advantages of the malleable/ semirigid devices are easier placement, less dependence on patient manual dexterity, lesser chance of component failure, and far lower cost. The disadvantages are somewhat higher risk of erosion, more difficult concealment, and lack of change in girth. The malleable/semirigid devices are preferred in patients who have physical problems such as severe arthritis or abdominal obesity. Younger patients with good hand dexterity will often choose the three-piece prothesis (Fig. 10.6). This device is especially appropriate for those concerned about cosmesis in the flaccid state.

**Table 10.5. Types of penile prostheses**

| Type | Manufacturer | Models | Description |
|---|---|---|---|

| | | | |
|---|---|---|---|
| Mechanical | Timm Medical | Dura II | Ball-and-socket articulation |
| Malleable | AMS | 600, 650 | Wire core |
| | Mentor | Malleable, Accuform | Silver wire core |
| Inflatable | | | |
| One piece | AMS | Dynaflex | Proximal reservoir activated by pressure on glans |
| Two piece | AMS | Ambicor | Pump and reservoir combined |
| | Mentor | Mark II | — |
| Three piece | AMS | Ultrex | Full fluid transfer during inflation/deflation |
| | Mentor | Alpha 1 | |

**Fig. 10.6. Typical three-piece inflatable penile prosthesis.**

c. **Preoperative preparation.** The following protocol is recommended prior to implantation of penile prostheses to reduce the risk of device infection:

1. Scrub genitalia and perineum for 10 minutes each day for 7 days prior to surgery with chlorhexidine digluconate soap (Hibiclens).

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2. Prescribe an oral quinolone (e.g., gatifloxacin 400 mg PO) for 3 days prior to the surgery.

3. Give perioperative antibiotics (vancomycin 1 g and gentamycin 80 mg IV 1 hour prior to surgery).
4. Scrub and prep lower abdomen, genitalia, inguinal folds, perineum, and thighs with iodine-containing solution for 15 minutes.
5. Carefully catheterize the bladder with 16F Foley catheter. After draining the bladder, plug the Foley catheter.
6. Change gloves after draping, and put on double gloves.

d. **Postoperative care.** The Foley catheter can be removed on the morning after surgery. For inflatable prostheses, the patient should be sent home with the device semiinflated. Oral antibiotics should given for 14 days. Sexual activity is prohibited until after the first office visit at 6 weeks postoperatively.

e. **Device infection.** The incidence of infection following penile prosthetic surgery ranges between 0.4% and 9%. Following implantation, the time frame for the presentation of infection will vary depending on the organism involved. Infections with more virulent and aggressive bacteria will usually present within the first few postoperative days, with the patient presenting with fever, pain, and swelling overlying the prosthesis accompanied by purulent wound drainage. However, a group of patients will complain of prolonged pain but will not have obvious purulent drainage from the wound. Prolonged pain, fixation of the pump or tubing to the overlying scrotal skin, elevated white blood cell count and sedimentation rate, and hyperglycemia in diabetic patients may all be helpful in suggesting a possible infection by less virulent organisms. Duplex Doppler ultrasound



may also be helpful in cases in which clinical findings are not conclusive.

## 2. Arterial revascularization

may be indicated in the rare patient with a focal arterial lesion that can be identified on arteriography. The best candidates for penile revascularization are patients who are young, nondiabetic, and nonsmokers and who have no underlying neurologic disease.

## 3. Venous surgery.

At present, the available procedures (crural plication, ligation, or excision of the deep dorsal vein of the penis; ligation of cavernosal veins; spongiolysis; or a combination of the above, including the radiologic administration of coils or sclerosing agents) have not demonstrated long-term success in most impotent patients. Complications reported from the various procedures, especially those involving proximal penile dissection, include diminished penile sensation and shortened penile length.

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