Erectile dysfunction (ED) is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual function. It was previously thought that ED was essentially a psychologic disorder. Recently, however, the majority of men with ED have been found to have an underlying organic cause. ED also encompasses disorders in ejaculation and orgasm.

How Common Is It?
Kinsey et al reported the results of a survey conducted on 15,781 men. The survey suggested that the prevalence of ED was less than 1% in men under age 30, 6.7% in men between the ages of 45 to 55, and 25% in men above 65 years.

The Massachusetts Male Aging Study (MMAS) was a cross-sectional community-based random-sample survey in men aged 40 to 70. The study was conducted between 1987 and 1989 in 11 cities around Boston. Although the sample population

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was less than the cohort in Kinsey’s study, the MMAS addressed several pertinent questions related to sexuality in aging men. The study showed that the prevalence of ED in this population was 52%. The projected number of men who will be affected by ED for the year 2005 is more than 50 million men between the ages of 40 and 70.

Another study showed evidence that the prevalence of ED was significantly associated with age (p < 0.001), and correlated with a lower quality of life (P < 0.001).

**Mechanisms of Erection**

**Neuroanatomy.** The neural mechanisms responsible for erections in men are still poorly understood. It is known, however, that there are two kinds of penile erections: reflexogenic and psychogenic.

Peripherally, the penis is innervated by both divisions of the autonomic nervous system, as well as the somatic sensory nerves through the pudendal nerve. The pudendal nerve arises from the S2-S4 segments of the spinal cord in Onuf’s nucleus, and supplies the skin of the dorsal, and the lateral aspects of the shaft and the glans. Other sensory contribution comes from the ilioinguinal nerve; this nerve particularly affects the skin of the ventral base of the penis and the anterior part of the scrotum. The parasympathetic innervation to the penis originates as preganglionic fibers from the intermediolateral nuclei in the S2-S4 spinal segments. Nerve fibers form a plexus that courses laterally in the endopelvic fascia close to the hypogastric vessels, terminating beside the rectum into the pelvic plexus. Branches from the plexus innervate the urinary bladder, lower ureter, seminal vesicles, prostate, rectum and urethra.

Two critical branches (called the cavernous nerves) have been implicated in the mechanisms of erection. The cavernous nerves travel along the posterolateral aspects of the prostate to the corpora cavernosa. At the base of the prostate, the cavernous nerves are located lateral to the capsule of the prostate. Distally, the cavernous nerves are at the five and seven o’clock position near the apex of the prostate. The sympathetic innervation of the penis is derived from the tho-
Erectile Dysfunction

The efferent fibers run through the retroperitoneum towards the hypogastric plexus. These nerves contribute to the pelvic plexus and the cavernous nerves, and are responsible for emission and ejaculation.

The arterial supply of the penis is derived from the internal pudendal artery. This artery branches from the ischiopudendal trunk of the internal iliac artery, which contributes to the vascular supply of the prostate.

Hemodynamics of Erection

The past decade had witnessed a surge in the understanding of the physiology of erection. This knowledge has tremendously aided researchers who are investigating methods to treat ED, and has helped design some treatment options, particularly vasoactive drugs.

Extensive investigations in animal models and human volunteers have settled some of the controversy regarding the mechanism of erection (see sidebar). During erection, there is an increase in arterial blood-flow, sinusoidal relaxation and venous resistance, resulting in turgidity of the corpora cavernosa and corpus spongiosum (i.e., vascular or full-erection phase). Subsequent contraction of the bulbocavernous and ischiocavernous muscles either spontaneously or reflexively compresses the proximal corpora, culminating in cavernosal rigidity and further engorgement of the glans penis; this is commonly seen during masturbation or intercourse (i.e., skeletal muscle or rigid-erection phase). In full erection, the pressure in the corpora cavernosa is approximately 90 mmHg to 100 mmHg, while the pressure in the glans penis is 40 mmHg to 50 mmHg. In the rigid-erection phase, compression of the blood-distended corpora can increase the intracavernous pressure well above the systolic pressure.

In the flaccid state, the arterioles are constricted and the sinusoids are contracted; together, they exert maximum resistance against arterial flow, allowing only a small amount of blood to enter the corpora for nutritional purposes. The venules in the periphery of the corpora run between the corpora and the adjacent sinusoidal wall, while the larger intermediary venules run between the sinusoidal wall and the tunica albuginea for some distance before exiting as the emissary veins. When the sinusoids are contracted (in the flaccid state), these venules drain freely to the extra penile veins. During erection, the smooth muscles of the sinusoids and arterioles relax, increasing sinusoidal compliance and causing peripheral resistance to decrease to a minimum; this results in a sudden increase in the arterial flow, dilation of the arterial tree and a filling of the sinusoids. Dilation of the arterial tree allows blood to rush in, and permits transmission of about 80% of the systolic pressure to the sinusoidal spaces. This high intracavernous pressure converts a soft flaccid organ to a blood-distended erect penis.

Distension of the sinusoids within a limited space (because of a relatively indistendable tunica albuginea) results in a compression of the small venules between the sinusoids. Further expansion of the sinusoids during full erection compresses the intermediary venules between the sinusoidal wall and the
The tunica albuginea. Stretching of the tunica albuginea also compresses the emissary veins. These actions reduce the venous capacity to a minimum, efficiently obtaining and maintaining erection in the corpora cavernosa without diverting too much cardiac output for penile erection. In contrast, the glans penis (with no tunica albuginea) remains flaccid during the erection.

**The Six Phases of Penile Erection**

Based on the actions of the arterial, venous and sinusoidal systems, Lue et al described six phases of penile erection (Figure 1). Flaccid phase. In the flaccid state, only a minimal amount of blood flow enters the corpora cav-

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**Figure 1.** Arterial blood flow and intracavernous pressure changes during the different phases of penile erection in experimental animals.
ernosa for nutritional purposes. The pH, PCO₂ and PO₂ of blood from the corpora cavernosa are at levels maintained in venous blood. High-resolution ultrasound and doppler study in humans show that the paired cavernous arteries at the base of the penis have an average inner diameter of 0.05 cm. Peak velocity of blood flow is usually 15 cm/second, or is not detectable.

**Latent (filling) phase.** There is increased blood flow in the internal pudendal artery during both the systolic and the diastolic phases, without an increase in intracavernous pressure. The penis shows slight elongation and fullness. The highest blood-flow rate occurs during this phase, with a peak flow velocity over 30 cm/second and a two-fold dilation of the cavernous arteries.

**Tumescence phase.** The penis rapidly expands and elongates to its maximum capacity. The intracavernous pressure continues to increase, and, subsequently, blood inflow decreases.

**Full-erection phase.** During this phase, the intracavernous pressure can rise to as much as 85% of the systolic pressure, and becomes more steady. Blood flow in the internal pudendal artery is less than the blood flow during the tumescence phase. Although the venous channels are mostly compressed, the venous flow is slightly higher than what it is during the flaccid state, and blood gases of the intracavernous blood are maintained at the same level as in the arterial side.

**Skeletal or rigid-erection phase.** As a result of the contraction of the ischiocavernosus muscles, the intracavernous pressure rises well above the systolic pressure, causing rigid erection. During this phase, there is almost no blood flow through the cavernous artery. The short duration of this phase, however, prevents the development of ischemia.

**Detumescence phase.** After ejaculation or the cessation of erotic stimuli, sympathetic tonic discharge resumes, resulting in the contraction of the smooth muscles around the sinusoids and arterioles. The blood flow diminishes to the level it had during the flaccid phase, and a large portion of blood is expelled from the sinusoidal spaces. The penis returns to its flaccid length and girth.

**Why Erectile Dysfunction?**

Penile erection is a complex physiologic response that is dependent on the integration of psychogenic, endocrine, vascular and neurogenic mechanisms. Disturbance of one or more of these mechanisms will result in erectile dys-

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Psychogenic Factors: How Important are They?

In the past, psychogenic factors were considered to be very important in causing ED; more than 90% of impotent patients were diagnosed to be psychogenic. Increasingly, sophisticated med-
Erectile Dysfunction

ical examinations are now able to determine physical causes for dysfunctions that, in the past, would have been diagnosed as having a psychogenic base. In a systematic, multidisciplinary, multidimensional assessment of a large number of impotent men, an organic cause was found in 35.9% of men, a psychogenic cause was found in 38.3%, and multiple or indeterminate causes in 28.8% of men.15

Men with primary psychogenic impotence often come from sexually repressed backgrounds, where sex was not discussed or was treated as sinful and immoral. Generally, anxiety and depression are believed to be the major causes of psychogenic sexual dysfunction. These emotions may be the result of nonsexual concerns, or may be specific to the sexual situation. The presence of anxiety and depression may be a result of impotence, as well as a precipitating factor for ED.16 It must be stressed that identifying a possible psychologic factor does not mean that this factor is the sole cause of impotence.

Psychologic evaluation is important in both the diagnosis and treatment of sexual dysfunction. The interview and the questionnaire are two tools typically used for this evaluation. It is helpful to interview the couple together as well as apart, in case there is information one would rather not share with the other.16 Some studies have shown that interviewing the partner of the individual with ED confirmed the diagnosis in 82% of cases, and changed the diagnosis in 18% of the cases. Studies regarding the partner’s impact on treatment showed that in 42% of the cases, there was no change in the chosen treatment modality, in 18% of the cases, there was a change of treatment due to a change in diagnosis and in 40% of the cases, there was a change in the chosen treatment modality, even though the diagnosis was confirmed.17

The Endocrine Factor

The prevalence of endocrine disorders in a population of impotent men is not clear, but is estimated to be between 5% and 35%.18 Many hormones may affect sexual performance, but androgens and prolactin play the most important role.19

Testosterone, the principal androgen in the male, is secreted primarily by the testicular Leydig cells. The adrenals also secrete some testosterone. Testosterone secreted by Leydig cells is regulated by the hypothalamus and the pituitary gland through the hypothalamic pituitary gonadal axis. Testosterone affects its target tissues either directly or after it has been intracellularly converted to dihydrotestosterone (DHT). Although the effects of both androgens (testosterone and DHT) are well established, their role and the level required for normal erectile physiology and sexual behavior are still being investigated.20

Some studies have demonstrated that castrated and hypogonadal men were able to maintain sexual activity. It was found that androgen replacement in hypogonadal individuals had a significant effect on sexual behavior and activity that was dose-dependent, and could not be reproduced by placebo. Hypogonadal men who received an androgen replacement experienced a return of libido, mood elevation and restoration of ejaculation. For men with erectile potency, the situation is more complex. It appears that the physiologic capacity for
Erection is less sensitive to androgen withdrawal than are sexual interest and sexual activity. Androgen-dependent spontaneous erection (diurnal and nocturnal) is markedly suppressed in hypogonadism, and is restored by androgen replacement. In contrast, erections in response to erotic films are unaffected by androgen replacement, despite the marked effects of androgen on sexual interest and behavior. The central process leading to spontaneous erections is androgen-dependent, whereas the mechanism leading to erection in response to a certain type of external erotic stimuli remains intact despite androgen deficiency. Although the importance of androgens for normal sexual interest and activity has been established, the amount of androgens required for both basal and optimal function is still unknown, and may have vary by individual. Not only may the circulating level of testosterone be important, but there may also be more basic physiologic mechanisms working at the molecular level (i.e., receptor site activation).21

Prolactin has a complex relationship with gonadotropins. In men with hyperprolactinemia and testosterone deficiency, serum Luteinizing hormone (LH) levels are inappropriately low, indicating the failure of the hypothalamic pituitary axis to respond to a reduced amount of testosterone. Prolactin also appears to inhibit gonadotropin-releasing hormone (GnRH). Individuals with prolactin-secreting tumors respond to an infusion of GnRH by increasing the level of LH. In addition, GnRH may have a direct effect on the central nervous system. Some of the most common causes of hyperprolactinemia include pituitary tumors, primary hypothyroidism and drug-related and idiopathic factors.22

Abnormalities in the thyroid hormone may alter the hypothalamic pituitary gonadal axis, resulting in ED. Hypothyroidism causes both an increase in the estradiol production rate and a decrease in its metabolic clearance, resulting in an elevation of serum estradiol. The Leydig cells may be inhibited by the high estradiol levels and/or by circulating antibodies to thyroid-stimulating hormone. The decreased libido seen in patients with hyperthyroidism may be due to the hypermetabolic effects of thyroxine or the increased level of circulating estrogen.23 Individuals with hyperthyroidism also com-
plain of sexual dysfunction. In these patients, testosterone secretion is decreased, and the metabolic transformation of testosterone shifts towards etiocholanolone rather than androsterone. The elevated serum prolactin levels in individuals with primary hypothyroidism (mediated by the feedback-induced thyrotropin-releasing hormone [TRH]) may also contribute to impotence.

The incidence of decreased libido and potency in acromegalic individuals with elevated levels of growth hormone is as high as 50%, due to hypothalamic pituitary dysfunction and increased serum prolactin.21

Peripheral Vascular Disease: A Leading Cause of ED

Erection is essentially a hemodynamic process; vascular diseases are therefore the leading causes of erectile dysfunction. In the majority of cases, intervention is successful. Alteration in the flow of blood to (arterial) and from (venous) the penis are the two mechanisms by which vascular impotence occurs. Decreased arterial flow to the penis may be due to various causes. The most well known cause is Leriche’s syndrome, or thrombotic obliteration of the aortic bifurcation, with resultant pain and claudication of the hips and thighs, and, in males, impotence. Atherosclerotic and traumatic arterial occlusive diseases of the hypogastric cavernous arterial bed can decrease the perfusion pressure and the arterial flow to the lacunar spaces, thus decreasing the rigidity of the erect penis and increasing the time to maximal erection. Fibrosis, calcification and obliteration of the small cavernous vessels (which may occur with aging) have the same effect. Common risk factors associated with arterial insufficiency include hypertension, hyperlipidemia, cigarette smoking, diabetes mellitus, blunt perineal or pelvic trauma and pelvic irradiation.24

Veno-occlusive disorders or venogenic impotence could be defined as occurring when the penile arterial inflow is less than venous outflow. When tests such as dynamic infusion cavernosometry and cavernosography are performed on men with vasculogenic impotence, about 55% to 88% of the men are found to have a venous leak. For practical purposes, however, venogenic impotence could be defined as occurring only when excessive venous outflow prevents full erection in the presence of normal arterial blood flow.25

Neurologic Factors

Neurologic impotence is said to exist if a neuropathic process (either central or peripheral) results in failure to initiate the arteriolar and lacunar smooth-muscle relaxation that facilitates the hemodynamic alteration associated with penile erection. Neurogenic factors have been estimated to be the sole or major contributing factor in 10% to 20% of all organically impotent men. The pelvic cavernous nerve complex is the major pathway for neurologic control of penile erection. Impairment of this pathway or other neurologic pathways that utilize the pelvic cavernous nerve as the final common pathway will result in neurogenic impotence. These pathways include the dorsal-nerve afferent pathway (both peripherally and centrally), as well as the poorly described efferent pathway.26

Neurologic causes of impotence are most commonly peripheral neuropathy, spinal-cord lesions or lesions of the cerebral hemisphere. Peripheral neuropathy may result from a variety of causes; the most important cause is diabetes mellitus. Patients with chronic renal failure (particularly those undergoing hemodialysis) are frequently impotent. Even though uremic neuropathy may
contribute to impotence through Schwan’s cell dysfunction, the hormonal abnormalities associated with uremia are most likely the primary cause. Amyloidosis, with involvement of the autonomic nervous system, can cause neurogenic impotence, especially the familial type. Multiple sclerosis is characterized by a loss of myelin in the white matter of the brain, brain stem and spinal cord. The impact of MS on potency is variable, affecting 35% to 43% of MS patients. The severity of impotence is directly related to the duration of the disease, but in several patients, sexual potency tended to remit and relapse. Other causes of spinal-cord lesions that can affect potency include those accompanying syphilis (tabes dorsalis), spina bifida, syringomyelia, amyotrophic lateral sclerosis and compression from a herniated disk or tumor.

**Diabetes Mellitus (DM) and Erectile Function**

The prevalence of erectile dysfunction in men with DM ranges from 35% to 75%, and is two to five times higher than the prevalence of ED in healthy control subjects. ED occurs 10 to 15 years earlier in diabetic patients than in nondiabetic ones, and is often an early complication of DM. Some studies report that impotence may often be the only symptom that leads to the discovery of unrecognized DM.27

**Evaluation for Erectile Dysfunction**

**History and physical examination.** When taking a patient’s history, the physician should emphasize the following issues (Table 1):

1. **Duration of the ED.** An onset of short duration should always point to the possibility of a psychogenic background. The lack of nocturnal and morning erection signals a more organic cause for the ED. The patient should be asked to describe the problem in his terms: Is it consistent with the same sexual partner or does it vary if more than one partner is involved? The patient should also be encouraged to relate the frequency of the problem and the frequency of sexual encounters that were not satisfactory. One should also ask the patient about his libido and sexual gratification during the orgasm.

2. **Circumstances surrounding the ED.** The subtle onset of ED should always point to the possibility of an organic cause. Physicians should inquire about any changes in the general health of the patient to rule out an associated disease.

3. **Medical history.** Special interest should always be paid to the medication the patient is taking. The majority of antihypertensive drugs are associated with variable degrees of ED. Antipsychotic drugs are also associated with ejaculation disorders, particularly delayed ejaculation and lack of libido. The patient should

**Table 1**

**Evaluation of Erectile Dysfunction**

- Sexual function questionnaire
- Gastrointestinal disease or surgery
- Pelvic or spinal trauma
- Vascular or endocrine diseases
- Neurologic diseases
- Sleep disorders
- Marital and sexual history
- Medications
- Tobacco and alcohol consumption
understand that he should not voluntarily interrupt the treatment because of any side effects he may experience. Every effort should be made to substitute the offending drug with another drug that has fewer side effects.

As previously mentioned, diabetes mellitus is associated with ED.

4. Surgical history. ED usually occurs following extensive pelvic surgery. Radical prostatectomy is notoriously associated with ED in more than 50% of cases. Other pelvic surgeries (e.g., abdomino-perineal resection of the rectum, surgery of the retroperitoneum, extensive fracture for the pelvic girdle) are known to cause ED.

In the physical examination, physicians should emphasize the general habitus and the degree of masculinization of the patient (such as secondary sexual characteristics [e.g., pubic hair, gynecomastia]) as part of the evaluation of the endocrinal status.

Local examination involves an estimation of the consistency, size and location of the testes, looking for any possible anomalies. The penile size and any abnormal fibrosis should be documented. Occasionally, a Polaroid® picture depicting the penis in an erect state is a very effective method to assess the degree of curvature for future reference.

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**What Specific Tests Should Be Performed?**

Laboratory tests are needed only if the diagnosis of hypogonadism cannot be confirmed during the history and the physical examination. These tests should not be ordered indiscriminantly, since they have not been proven to be cost-effective.

Specific tests should be requested if the diagnosis is unclear or if the patient requests a full investigation for a litigation problem.

Color duplex Doppler penile ultrasound is a relatively noninvasive test that can detect changes in the arterial and venous penile blood flow. When performed in conjunction with the intracavernosal injection of a vasoactive agent, this test helps predict the patient response to local therapy.

Diurnal penile tumescence has gained popularity because of its simplicity and reproducibility. This test involves the study of the erection and rigidity by a Rigiscan® under erotic visual stimulation.

Cavernosometry-cavernosography should be performed to diagnose the possibility of a veno-occlusive disease. Currently, these tests are not commonly ordered, due to their invasiveness and poor yield.

Penile electrophysiologic studies such as conduction velocity and cortical-evoked potentials are very sophisticated tests used to uncover any changes in the penile innervation in patients with peripheral neuropathy. These studies are also helpful in medico-legal cases to document any subtle damage to the penile innervation.

Pudendal arteriography is usually reserved for patients with localized arterial blockage, and is often performed prior to surgical arterialization of the penis.

Office injection of a vasoactive drug in a cumulative dose is a very cost-efficient method of assessing the patient’s response. A full rigid erec-
Erectile Dysfunction

Erection after 10 to 15 minutes and lasting 30 minutes is indicative of a vascular disorder that is not major.28

Treatment of Erectile Dysfunction

The treatment of ED has taken a major turn during the last two decades. With a better understanding of the mechanisms of hemodynamics involved in erection, several different methods have been proposed to help restore penile erection.

**Vasoactive local drugs.** The principle behind the application of vasoactive drugs is to induce a sudden decrease in the vascular resistance in the cavernous bodies. The resulting sinusoidal relaxation will enable blood to pool in the corpora cavernosa to induce rigidity.

For practical purposes, there are three drugs available that can be used alone or in combination: papaverine, phentolamine and prostaglandin E1 PGE1.

After the basic examination and tests have been conducted, intracavernosal administration of these drugs should be presented to the patient as a treatment option. The patient should be made aware of the limitations, side effects and long-term complications of this therapy. The recently introduced intraurethral-installed PGE1 (Muse®) has been embraced for its simplicity in delivering the drug. The price and the inconsistency of response are the main drawbacks of the therapy.

**Vacuum constriction device.** The principle behind this device is to create a vacuum around the penis using a specially designed cylinder, resulting in blood pooling in the corpora cavernosa. An elastic band is applied around the base of the penis to maintain the rigidity. Proponents of this device praise its simplicity and efficiency. Complications are usually minor, in the form of local bruising. Use of this device necessitates patient education and support.29

**Systemic oral drugs.** The presence of sildenafil has changed the way ED is treated. Sildenafil is a potent inhibitor to cyclic GMP, and therefore increases the penile response to sexual stimulation. There have been several studies confirming the efficacy and safety of sildenafil in patients with variable etiologies of ED.30,31,32

The main side effects of sildenafil are headache, flushing, dyspepsia and visual disturbances.

**Surgical treatment.** The demand for surgical implantation of a penile prosthesis has declined in the recent years with the introduction of less invasive and efficient ways of restoring erection. Penile implants can be divided into two general types: nonhydraulic (semirigid) and hydraulic. The surgical principle is to dilate the cavernous tissue and to replace it with two cylinders of adequate length and girth. The surgery is invasive and carries a risk of complications. The patient should understand the limitations and the possible complications of penile implants.

Conclusion

Management of ED should include a proper evaluation of the patient’s symptoms. Special investigation tests should be tailored to the individual patient’s needs. Invasive tests should be reserved according to the patient’s desire, and in medicolegal cases. In the majority of cases, treating the underlying cause of ED is not practical or feasible. The treating physician should discuss the different treatment options with the patient and provide the treatment that is acceptable to the patient.
References


