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Erectile Dysfunction

(Impotence; ED)

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Erectile dysfunction is the inability to attain or sustain an erection satisfactory for sexual intercourse. Most erectile dysfunction is related to vascular, neurologic, psychologic, and hormonal disorders; drug use can also be a cause. Evaluation typically includes screening for underlying disorders and measuring testosterone levels. Treatment options include oral phosphodiesterase inhibitors, intraurethral or intracavernosal prostaglandins, vacuum erection devices, and surgical implants.

(See also Overview of Male Sexual Dysfunction.)

Erectile dysfunction (ED—formerly called impotence) affects up to 20 million men in the US. The prevalence of partial or complete ED is > 50% in men aged 40 to 70, and prevalence increases with aging. Most affected men can be successfully treated.

Etiology

There are 2 types of erectile dysfunction (ED):

Primary ED, the man has never been able to attain or sustain an erection

Secondary ED, acquired later in life by a man who previously was able to attain erections

Primary ED is rare and is almost always due to psychologic factors or clinically obvious anatomic abnormalities.
Secondary ED is more common, and > 90% of cases have an organic etiology. Many men with secondary ED develop reactive psychologic difficulties that compound the problem.
Psychologic factors, whether primary or reactive, must be considered in every case of ED. Psychologic causes of primary ED include guilt, fear of intimacy, depression, or anxiety. In secondary ED, causes may relate to performance anxiety, stress, or depression. Psychogenic ED may be situational, involving a particular place, time, or partner.
The **major organic causes of ED** are physiologic (organic)

Vascular disorders

Neurologic disorders

These disorders often stem from atherosclerosis or diabetes.
The most common **vascular cause** is atherosclerosis of cavernous arteries of the penis, often caused by smoking, endothelial dysfunction, and diabetes. Atherosclerosis and aging decrease the capacity for dilation of arterial blood vessels and smooth muscle relaxation, limiting the amount of blood that can enter the penis (see Overview of Male Sexual Function: Erection). Endothelial dysfunction is a disease of the endothelial lining of the small arterioles that reduces the ability to vasodilate when needed to increase blood flow. Endothelial dysfunction appears to be mediated by reduced levels of nitric oxide and can result from smoking, diabetes, and/or low testosterone levels. Veno-occlusive dysfunction permits venous leakage, which results in inability to maintain erection.
Priapism, usually associated with trazodone use, cocaine abuse, and sickle cell disease, may cause penile fibrosis and lead to ED by causing fibrosis of the corpora cavernosa and thus impairment of the penile blood flow necessary for erection.
Neurologic causes include stroke, partial complex seizures, multiple sclerosis, peripheral and autonomic neuropathies, and spinal cord injuries. Diabetic neuropathy and surgical injury are particularly common causes.
Complications of pelvic surgery (eg, radical prostatectomy [even with nerve-sparing techniques], radical cystectomy, rectal cancer surgery) are other common causes. Occasionally, transurethral resection of the prostate is a cause. Other causes

include hormonal disorders, drugs, pelvic radiation, and structural disorders of the penis (eg, Peyronie disease). Prolonged perineal pressure (as occurs during bicycle riding) or pelvic or perineal trauma can cause ED.

Any endocrinopathy or aging associated with testosterone deficiency (hypogonadism) may decrease libido and cause ED. However, erectile function only rarely improves with normalization of serum testosterone levels because most affected men also have neurovascular causes of ED.

Numerous drug causes are possible (see table Commonly Used Drugs That Can Cause Erectile Dysfunction). Alcohol can cause temporary ED.

Diagnosis

Clinical evaluation

Screening for depression

Testosterone level

Evaluation should include history of drug (including prescription drugs and herbal products) and alcohol use, pelvic surgery and trauma, smoking, diabetes, hypertension, and atherosclerosis and symptoms of vascular, hormonal, neurologic, and psychologic disorders. Satisfaction with sexual relationships should be explored, including evaluation of partner interaction and partner sexual dysfunction (eg, atrophic vaginitis, dyspareunia, depression).

It is vital to screen for depression, which may not always be apparent. The Beck Depression Scale or, in older men, the Yesavage Geriatric Depression Scale (see table Geriatric Depression Scale [Short Form]) is easy to administer and may be useful.

Examination is focused on the genitals and extragenital signs of hormonal, neurologic, and vascular disorders. Genitals are examined for anomalies, signs of hypogonadism, and fibrous bands or plaques (Peyronie disease). Poor rectal tone, decreased perineal sensation, or abnormal bulbocavernosus reflexes may indicate neurologic dysfunction. Diminished peripheral pulses suggest vascular dysfunction.

A psychologic cause should be suspected in young healthy men with abrupt onset of erectile dysfunction (ED), particularly if onset is associated with a specific emotional event or if the dysfunction occurs only in certain settings. A history of ED with spontaneous improvement also suggests psychologic origin (psychogenic ED). Men with psychogenic ED usually have normal nocturnal erections and erections upon awakening, whereas men with organic ED often do not.

Commonly Used Drugs That Can Cause Erectile Dysfunction

Class	Drugs
Antihypertensives	Beta-blockers, clonidine, loop diuretics (probably), spironolactone, thiazide diuretics
Central nervous system drugs	Alcohol, anxiolytics, cocaine, monoamine oxidase inhibitors, opioids, selective serotonin reuptake inhibitors, tricyclic antidepressants
Others	Amphetamines, 5-alpha-reductase inhibitors, antiandrogens, cancer chemotherapy drugs, anticholinergics, cimetidine, estrogens, luteinizing hormone–releasing hormone agonists and antagonists

Testing

Laboratory assessment should include measurement of morning testosterone level; if the level is low or low-normal, prolactin and luteinizing hormone (LH) should be measured. Evaluation for occult diabetes, dyslipidemias, hyperprolactinemia, thyroid disease, and Cushing syndrome should be done based on clinical suspicion.

Currently, duplex ultrasonography after intracavernous injection of a vasoactive drug such as a mixture of prostaglandin E1, papaverine, and phentolamine (available commercially as a combination product) is most often used to evaluate penile vasculature. Normal values include a peak systolic flow velocity > 25 cm/sec and a resistive index > 0.8. Resistive index is the difference between peak systolic velocity and end-diastolic velocity divided by peak systolic velocity. Rarely, in selected patients for whom penile revascularization surgery is being considered after pelvic trauma, pelvic arteriography, dynamic infusion cavernosography, and cavernosometry may be done. Several sleep-entrained erectile episodes occur in healthy men. These erectile events, measured by nocturnal penile tumescence monitors, may help differentiate between organic and psychogenic etiology of erectile dysfunction. Its current use, however, is primarily in medico-legal settings.

Treatment

- Treatment of underlying causes
- Drugs, usually oral phosphodiesterase inhibitors (see table Oral Phosphodiesterase Type 5 Inhibitors for Erectile Dysfunction)
- Vacuum erection device or intracavernosal or intraurethral prostaglandin E1 (2nd-line treatment)
- If other treatments fail, surgical implantation of penile prosthesis

Underlying organic disorders (eg, diabetes, prolactin-secreting pituitary adenoma, hypogonadism, Peyronie disease) require appropriate treatment. Drugs that are temporally related to onset of erectile dysfunction (ED) should be stopped or replaced. Depression may require treatment. For all patients, reassurance and education (including of the patient's partner whenever possible) are important. Clinicians should use this encounter to discuss behavior modification (eg, dietary changes and weight loss).

For further therapy, an oral phosphodiesterase inhibitor is tried first. If necessary, another noninvasive method, such as a vacuum erection device or intracavernosal or intraurethral (suppository) prostaglandin E1 is tried next. Invasive treatments are used when noninvasive methods fail. All drugs and devices should be tried ≥ 5 times before being considered ineffective.

Drugs for erectile dysfunction

First-line treatment of ED is usually an oral phosphodiesterase inhibitor. Other drugs used include intracavernosal or intraurethral prostaglandin E1. However, because almost all patients prefer oral drug therapy, oral drugs are used unless they are contraindicated or not tolerated.

Oral phosphodiesterase inhibitors selectively inhibit cyclic guanosine monophosphate (cGMP)–specific phosphodiesterase type 5 (PDE5), the predominant phosphodiesterase isomer in the penis. These drugs include sildenafil, vardenafil, avanafil, and tadalafil (see table Oral Phosphodiesterase Type 5 Inhibitors for Erectile Dysfunction). By preventing the hydrolysis of cGMP, these drugs promote the cGMP-dependent smooth muscle relaxation that is essential for normal erection. Although vardenafil and tadalafil are more selective for the penile vasculature than sildenafil, clinical responses and adverse effects of these drugs are similar. In comparative clinical trials, these drugs show comparable efficacy (60 to 75%).

Oral Phosphodiesterase Type 5 Inhibitors for Erectile Dysfunction

Drug	Dose*	Onset of Action	Comments
Avanafil	50, 100, or 200 mg	30 minutes	Can be taken 15 minutes before intercourse
Sildenafil	Initial: 50 mg Maintenance: 25–100 mg (most men respond best to 100 mg)	60 minutes	Duration of action: ≈ 4 hours; take on empty stomach
Tadalafil	10–20 mg	60 minutes	Duration of action: 24–36 hours
Tadalafil, low-dose	2.5–5 mg	60 minutes	For daily use, taken at about the same time each day, without regard to timing of sexual activity For daily use in patients who also need treatment of benign prostatic hyperplasia
Vardenafil	10–20 mg	60 minutes	Duration of action: ≈ 4 hours
Vardenafil, orally disintegrating form	10 mg	30 minutes	Can be taken 30 minutes before intercourse

* PDE5 inhibitors should be taken on an empty stomach at least 1 hour before sexual intercourse except as noted. Maximum frequency is once a day unless otherwise noted.

PDE5 = phosphodiesterase type 5.

All PDE5 inhibitors cause direct coronary vasodilation and potentiate the hypotensive effects of other nitrates, including those used to treat coronary artery disease as well as recreational amyl nitrate ("poppers"). Thus, the concomitant use of nitrates and PDE5 inhibitors can be dangerous and should be avoided. Patients who only occasionally use nitrates (eg, for rare bouts of angina) should discuss the risks, selection, and proper timing of possible PDE5 inhibitor use with a cardiologist.

Adverse effects of PDE5 inhibitors include flushing, visual abnormalities, hearing loss, dyspepsia and headache. Sildenafil and vardenafil may cause abnormal color perception (blue haze). Tadalafil use has been linked with myalgias. Rarely, nonarteritic ischemic optic neuropathy (NAION) has been associated with PDE5 inhibitor use, but a causal relationship has not been established. All PDE5 inhibitors should be administered cautiously and at lower initial dosages to patients receiving alpha-blockers (eg, prazosin, terazosin, doxazosin, tamsulosin) because of the risk of hypotension. Patients taking an alpha-blocker should wait at least 4 hours before using a PDE5 inhibitor. Rarely, PDE5 inhibitors cause priapism.

Alprostadil (prostaglandin E1), self-administered via intraurethral insertion or intracavernosal injection, can produce erections with a mean duration of 30 to 60 minutes. Intracavernous alprostadil may be compounded with papaverine and phentolamine for increased efficacy when necessary. Excessive dosing may cause priapism in ≤ 1% of patients and genital or pelvic pain in about 10%. Office teaching and monitoring by the physician helps achieve optimal and safe use, including minimizing the risk of prolonged erection. Intraurethral therapy is less effective at producing satisfactory erection (up to 60% of men) than intracavernosal injection (up to 90%). Combination therapy with a PDE5 inhibitor and intraurethral alprostadil may be useful for some patients who fail to respond to oral PDE5 inhibitors alone.

Mechanical devices for erectile dysfunction

Men who can develop but not sustain an erection may use a constriction ring to help maintain erection; an elastic ring is placed around the base of the erect penis, preventing early loss of erection. Men who cannot achieve erection can first use a vacuum erection device that draws blood into the penis via suction, after which an elastic ring is placed at the base of the penis to maintain the erection. Bruising of the penis, coldness of the tip of the penis, and lack of spontaneity are some drawbacks to this modality. These devices can also be combined with drug therapy if needed.

Surgery for erectile dysfunction

If drugs and vacuum devices fail, surgical implantation of a penile prosthesis can be considered. Prostheses include semi-rigid silicone rods and saline-filled multicomponent inflatable devices. Both models carry the risks of general anesthesia, infection, and prosthesis erosion or malfunction. In the hands of experienced surgeons, the long-term rate of infection or malfunction is well below 5% and the rate of patient and partner satisfaction is > 95%. The advantages of surgical prosthesis implantation are obvious: erections are produced immediately and spontaneously, erections last until the patient deflates his device and sexual activity may occur as frequently as the couple wishes. Thus when satisfaction rates are compared among all treatment options, the penile prosthesis shows the highest couple satisfaction rate. Low-intensity extracorporeal shock wave therapy (Li-ESWT) is not approved but is undergoing clinical testing in the US.

Key Points

Vascular, neurologic, psychologic, and hormonal disorders and sometimes drug use can compromise achievement of satisfactory erections.

Evaluate all men with ED for hormonal, neurologic, and vascular disorders and depression.

Measure testosterone levels and consider other testing based on clinical findings.

Treat underlying disorders and use an oral PDE5 inhibitor if necessary.

If those measures are ineffective, consider intracavernosal or intraurethral prostaglandin E1 or use of a vacuum device; surgical implantation of a penile prosthesis is the final line of treatment.