

Erectile dysfunction: When to treat and when to refer

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~50% of males over age 40 report some sexual dysfunction; primary care physicians can offer options to older men seeking treatment

Although sexual potency is maintained in some men into late decades, the myth that potency is the norm in aging human males is exactly that – a myth. It is a myth perpetuated by popular culture, not scientific evidence. Some primary care physicians believe that sexual potency in older males is the norm, and that if it is lacking, it is “all in the head.” Yet one study reveals that nearly 50% of men over age 40 complain of sexual dysfunction.¹ The myths that surround the problems of impotence, or erectile dysfunction (ED), confound the attempts of patients to receive treatment and the attempts of physicians to help them.

Because sexuality training is lacking in most medical schools, another obstacle that makes it difficult for older males to receive treatment is the belief that older patients are indifferent to sexual activity or sexual functioning. Although for some men in all age groups this may be true, it would be incorrect to assume that most older men do not have an interest in continuing their sexual intimacy. With the aging of the Baby Boomers, it is important that physicians keep the door open to older patients who may want to discuss their concerns regarding sexual intimacy. If patients make inquiries about this subject, physicians owe them sincere attention and a commitment to help them in ways that are appropriate. This paper presents a practical approach to the evaluation and treatment of erectile dysfunction.

Incidence and pathophysiology

Erectile dysfunction (ED) is defined as the consistent inability to obtain or maintain an erection for satisfactory sexual relations. It can also be expressed as a condition whereby penile erection sufficient for vaginal penetration is not achievable by normal physiologic means.²

In 1948, Kinsey et al³ reported an age-related incidence of ED in their sample of 12,000 American men: 20% in the normal population age 30 to 40, 30% in the population age 40 to 50, and 35% age 50 to 60. More contemporary data from the Massachusetts Male Aging Study (MMAS)¹ has indicated that the prevalence of ED of any degree is 39% at age 40, and 67% at age 70. The MMAS study emphasized that 52% of men age 40 to 70 have some degree of ED.

By these accounts, it is clear that ED is widespread and has a strong age-dependence. With the increasingly uninhibited approach of patients to address this subject with their physicians, primary care physicians can expect to see ever-larger numbers of ED cases in the future.

Physiology of erectile response

Penile erection is a complex hemodynamic function. The neurophysiologic events of erection involve multiple levels of the central and peripheral nervous systems, as well as mechanical, hydraulic, and hormonal aspects.

Five physiologic areas are critical to a normal erectile response:

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Increased arterial inflow, which leads to vasodilatation of the penile arterial bed, is critical for males to achieve erection. In order for the penis to become rigid enough for vaginal penetration, there must be relaxation of the smooth muscle cells in the corporal bodies of the penis with an increase in its blood supply, followed by passive occlusion of corporal venous outflow. With the gradual compression of the emissary veins that drain the cavernosal spaces of the penis against a nondistensible tunica albuginea, more blood enters the penis than leaves the corporal bodies, resulting in an erection.

Causes of ED

Approximately 90% of ED in men over age 50 is due to physical causes, medications, or both; the remaining 10% is due to psychological etiologies.⁸

Arterial disease, such as arteriosclerosis affecting hypogastric or pudendal vessels, as well as the small arteries of the corpora cavernosa, can interfere with proper erectile function. Fibrosis, calcification and obliteration of the small cavernosal vessels occur with aging, and early changes can be identified in men as young as age 30.⁴ It is estimated that atherosclerosis is the cause of approximately 40% of ED in men over age 50.

Among the most commonly recognized associated risk factors are hypertension, dyslipidemia, diabetes, and cigarette smoking. In men with diabetes, irrespective of type, prevalence of ED is approximately 50% (range 20% to 75%) depending on patient age, duration, and severity of the diabetes. Any condition that results in oxidative stress leads to endothelial dysfunction and can be a contributor to ED.⁵

Another common cause of ED is corporal veno-occlusive dysfunction. This is sometimes present in younger individuals, but more common in pa-

Table 1 Indications for urologic referral

- Patients with Peyronie's disease
- Patients with severe sexual dysfunction and severe associated peripheral vascular insufficiency, in whom vasculogenic erectile dysfunction is suspected
- Patients on nitrates who are not candidates for sildenafil citrate
- Patients who fail medical management, ie, failed oral therapy

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tients over age 60, as the effectiveness of the venous closure mechanism deteriorates with age. The emissary veins, which have an oblique course through the tunica albuginea of the corpora cavernosa, tend to lose this obliquity with the aging process.⁶ This reduces the passive compression of the venous outlets, and prevents the trapping of the blood within the corporal bodies of the penis, thereby weakening the erection.

Neurologic disorders causing impotence include peripheral neuropathy, spinal cord lesions, or lesions of the cerebral hemispheres. Peripheral neuropathy can be of diabetic, uremic, toxic, traumatic, or idiopathic origin. CNS injury seen after a cerebrovascular accident can also cause ED.

Endocrine disorders may play a role in the etiology of ED. Testosterone is necessary to maintain the libido or sex drive, and the incidence of hypogonadism as a cause of ED is 3% to 5%.⁷ However, the loss of libido in most men is a result of testosterone deficiency. This diagnosis can be confirmed by obtaining a serum testosterone level.

Other chronic disease states associated with a high prevalence of ED include hepatic failure, Alzheimer's disease, sleep apnea, chronic obstructive pulmonary disease, hyper- and hypothyroidism, Peyronie's disease (plaque formation in the corporal bodies of the penis resulting in angulation or curvature of the penis with erections), pelvic surgery (major prostate, bladder, or bowel operations), pelvic injury, or pelvic radiation.

Medications can contribute to im-

potence, including most notably some that act on the nervous or vascular systems, such as antidepressants (eg, SSRIs), and antihypertensives. Although all antihypertensive medications can be implicated as causes of ED, the ACE inhibitors and the calcium channel blockers are the least likely culprits.

Psychogenic sexual dysfunction can occur in aging males, although its presence is less conspicuous as a cause of sexual dysfunction than among younger men.

Patient history

Physicians need to make an effort to ask patients about their sexuality. The question we suggest, "Are you having any problems with intimacy with your partner?" is a non-threatening way to query patients and lets them know that you would be comfortable discussing this topic with them if they so desired.

It is important to facilitate the dialogue with the patient and make sure the patient expresses himself comfortably on the subject of sexuality. Some patients may want their partner present for the discussion. Physicians need to ask their patients the following:

How long has sexual dysfunction been a problem?

Did it start suddenly or gradually?

Have you had a change in libido?

If so, did the loss of libido precede the sexual dysfunction, or did the loss of sexual interest merely follow the sexual dysfunction?

What is the quality, frequency, and duration of erections?

Is penetration possible?

Also of importance is the partner's

cooperation and the partner's response to the patient's lack of normal erections. Inquire if the patient is experiencing spontaneous nocturnal erections or early morning erections on awakening. Although the absence of nocturnal erections implies a physical problem, the presence of nocturnal erections or early morning erections does not exclude organic causes of ED.

The physical examination

The physical examination relative to an ED complaint involves checking the penis for Peyronie's plaques, phimosis or meatal stenosis, examining the testes for size and consistency, and performing a rectal exam in all men over age 50 to check the prostate gland. Peripheral pulses need to be examined in the lower extremities to evaluate the vascular status.

General laboratory tests are needed to determine the presence of occult, co-morbid systemic medical conditions, vascular risk factors, or endocrine abnormalities.

Systemic medical disorders, such as diabetes, renal insufficiency, or blood dyscrasias, may be screened with routine complete blood counts, BUN, creatinine, serum electrolytes, glucose level, and liver enzymes. Vascular risk factors, such as dyslipidemia, may be determined by a lipid profile.

Since the overall incidence of hypogonadism as an etiologic factor in ED is less than 5%, the measurement of serum testosterone is not a routine test. However, if diminished sexual desire is a concomitant part of the patient's complaint, serum testosterone levels should be obtained. It is recommended that blood be drawn before 10 a.m. when the serum testosterone is at the highest level as a result of the natural circadian rhythm. If testosterone is properly drawn and is decreased or at the lower limit of normal, a second sample should be measured to serve as a confirmation. A serum luteinizing hormone (LH) should also be obtained to evaluate the hypothalamic-pituitary-gonadal axis, and serum prolactin

should be measured, as high prolactin can antagonize the peripheral action of testosterone.

Patients with primary hypogonadotropic hypogonadism usually present with ED, loss of libido, or infertility. Hypogonadotropic hypogonadism is characterized by low levels of testosterone and low to normal LH and follicle-stimulating hormone (FSH) levels. Hypogonadism may also occur as a result of a decrease in the production of testosterone by the Leydig cells in the testes. These patients have low serum testosterone levels and elevated LH levels as a result of loss of the negative feedback on the gonadotropin-releasing hormone (GnRH) in the hypothalamus.

First line therapy for ED

Phosphodiesterase-5 (PDE5) inhibitors are today's first line therapy for ED. Several phosphodiesterase enzymes are distributed in various tissues of the human body. The PDE5 exists in the cavernous tissue of the penis, and achieves enzymatic degradation of cyclic 3' 5' guanosine monophosphate (cGMP), which serves as a messenger for smooth muscle relaxation by nitric oxide. By inhibiting the enzyme PDE5, these drugs potentiate the male erection, as they effectively "inhibit an inhibitor" of the erectile process. These drugs are **contraindicated** in patients who are taking or have taken nitroglycerin or other nitrates, as the additive effect of these drugs can cause blood pressure to plummet and decrease coronary artery perfusion, resulting in MI. Use these drugs with caution patients on alpha blockers.

Sildenafil. Sildenafil (Viagra) has a success rate of 70% to 85% in all groups (mean age 55.7) of patients.⁹

Usual dosage of sildenafil is 50 mg or 100 mg. There is also a 25 mg tablet for patients with severe renal insufficiency. Generally, geriatric patients begin with the 50 mg dosage.

Sildenafil should be taken 30 to 45 minutes prior to the expected time of sexual intimacy. Patients should be ad-

vised to avoid ingesting a fatty meal prior to taking the drug as this may retard the absorption from gastrointestinal tract. Patients should be titrated to the 100 mg dose if the 50 mg dose is ineffective. The maximum dose should be tried 6 to 8 times before concluding that the drug is not effective.

Tadalafil. Tadalafil (Cialis), another PDE5 inhibitor, has a half-life of 17.5 hours and a duration of action of approximately 36 hours. This drug is well tolerated and studies showed that discontinuation rates from side effects were about the same as those from patients taking placebo. The dosage is 10 to 20 mg to be used 30 minutes before engaging in sexual intimacy.

With the exception of once-daily tamsulosin (Flomax) 0.4 mg, tadalafil is contraindicated with all other alpha-blockers.¹⁰

Vardenafil. Vardenafil (Levitra), is the newest PDE5 inhibitor. The profile of this drug is similar to others in its class and has a high efficacy and low adverse events. The dosage of vardenafil is 10 to 20 mg and has an onset of action at 20 minutes. Side effects of vardenafil include headache and facial flushing. This drug should not be used in conjunction with any form of organic nitrates. Because of its mild hypotensive effect, vardenafil should not be taken in conjunction with any alpha-blockers.¹¹

HRT. Hormone replacement therapy is indicated in truly hypogonadal men. Safe and effective treatment can be provided with long-acting intramuscular injections, transdermal patches, or transdermal testosterone-containing gel.¹² Oral testosterone should be avoided because of possible hepatic toxicity with long-term use. The dose of intramuscular testosterone (cypionate or enanthate) is 200 mg IM every 2 weeks. The non-scrotal transdermal patches (Androderm) are available as 2.5 and 5 mg doses and are applied daily. Testosterone containing gels (AndroGel dispensed as 5, 7.5, or 10 g packets and Testim 1% in 5 g packets) are also available and are less likely to

cause skin irritation than the patches. However, it is important that no skin contact with the man's partner take place immediately after application of the gel because of the transfer of the testosterone to others. Patients should have their partners avoid contact at the application site until the gel has been absorbed into the skin and the skin is dry, which is usually in 10 to 15 minutes. All men who use testosterone replacement therapy need to have a digital rectal exam and PSA test at least on an annual basis.

When to refer

Patients who do not respond to oral therapy can be referred to a urologist for additional testing (see Table); treatments such as those discussed below are viable options for older men, but should be handled through referral.

Vacuum devices. Vacuum devices use a transparent plastic cylindrical chamber that fits tightly over the penis and permits the creation of a negative pressure within it in order to attract blood into the erectile bodies. Once the penis is distended with blood, the patient constricts the penile base with an elastic ring to maintain the erection, at which time the negative pressure can be released and the cylinder removed. It is safe to maintain erections up to 30 minutes in this manner. The advantage of this method is that it is effective and safe. A key disadvantage is that the device is rather bulky and some patients find that pumping it and positioning the elastic ring can be cumbersome.

Injections. Vasoactive drugs can be self-injected by the patient into the corpus cavernosum to achieve vasodilatation and smooth muscle relaxation. Five to 10 minutes after an injection the patient should have an erection rigid enough to have sexual intercourse. Prostaglandin E1 (alprostadil, Caverject or Edex) with

or without phentolamine and papaverine can be used if sildenafil is ineffective. The method is effective and safe. The most common side effect is a pain at the injection site in the penile shaft that can persist for several minutes or up to an hour, especially with alprostadil. Other side effects are priapism and penile fibrosis.

Implants. Over the past three decades, mechanical and material design improvements have resulted in marked advancement in the reliability and safety of penile implants. There are semi-rigid and inflatable models. Complication rates range from 7% to 17%,^{13,14} but overall, patients and their partners have been satisfied with the benefit derived from the use of these implanted devices.

Patients who do not respond to oral therapy can be referred to a urologist for additional testing and treatment. For older men who want to engage in sexual intimacy with their partner, help is available. Table 1 is a list of patients who might be referred to a urologist.

Conclusion

Erectile dysfunction is a common condition associated with the aging process. Many older men have disease states that produce oxidative stress on the endothelium resulting in endothelial dysfunction and contribute to ED. Most primary care physicians can successfully treat ED with oral therapy. Patients who do not respond to oral therapy can be referred to a urologist for additional treatment options.

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