AMERICAN ASSOCIATION OF CLINICAL ENDOCRINOLOGISTS MEDICAL GUIDELINES FOR CLINICAL PRACTICE FOR THE EVALUATION AND TREATMENT OF MALE SEXUAL DYSFUNCTION: A COUPLE'S PROBLEM–2003 UPDATE

AACE Male Sexual Dysfunction Task Force

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Abbreviations:

AACE = American Association of Clinical Endocrinologists; **AIDS** = acquired immunodeficiency syndrome; **CVA** = cerebrovascular accident; **DHT** = dihydrotestosterone; **FDA** = Food and Drug Administration; **LH** = luteinizing hormone; **NO** = nitric oxide; **NOS** = nitric oxide synthase; **PBI** = penile brachial index; PGE_1 = prostaglandin E_1

MISSION STATEMENTS

Guidelines Mission Statement

The purpose of these guidelines is to present a framework for the evaluation, treatment, and follow-up of the patient—indeed, of the couple—who presents with sexual dysfunction. The conventional focus on male erectile dysfunction is incomplete because whenever a man experiences erectile difficulties, his wife or sexual partner suffers as well. Furthermore, disruption in other aspects of the male sexual response cycle, such as diminished libido and delayed or premature ejaculation, also may impair the couple's sexual gratification. Thus, these guidelines also discuss the cause and, when possible, the available treatments to recognize and rectify disorders of sexual desire, orgasm, and ejaculation. Erectile dysfunction is often compounded by sexual difficulties in the partner or relationship issues. Male sexual dysfunction is most appropriately viewed as a chronic disease with medical, psychologic, and behavioral components that must not be treated in a mechanical and purely medicinal manner. The patient and his sexual partner must be active participants in the full continuum of care. These guidelines address the complexity involved in diagnosing the various aspects of the disorder and offer an organized system of care for the couple. In this way, the outcome can be a cost-effective improvement. The American Association of Clinical Endocrinologists (AACE) believes that, although a multidisciplinary approach may be required in many cases, the clinical endocrinologist is the most appropriate specialist to lead and coordinate the evaluation of the problem, to decide on multispecialty consultations, and to provide follow-up care.

Public Service Mission Statement

According to a recent survey, the Massachusetts Male Aging Study, 52% of men beyond 40 years of age may have some degree of erectile failure. For various reasons, only a small percentage of men seek medical help. This situation is unfortunate because advances in the understanding of male sexual chemistry have led to the development of a wide range of options to help men reclaim their inherent sexual capacity.

Sexual problems can affect men of any age but seem to become more common as men advance in years. Normal male sexual function requires an integrated response between central and local stimuli. Neural signals originating in the brain are transmitted to a thoracolumbar erection center and trigger the psychogenic erection associated with either fantasy or viewing erotic material. This process works in tandem with a reflex erection involving scrotal or genital stimulation, which activates neural impulses in the pudendal nerve that, when transmitted to S4-5 spinal cord sites, stimulate a reflexogenic erection.

Although neural signals are crucial, the vigor of a man's erection is ultimately determined by vascular events governing the flow of blood into the corpora cavernosa. The force with which blood flows into the corpora cavernosa is mediated by an intriguing intracavernosal chemistry sequence involving the enzyme nitric oxide synthase (NOS), nitric oxide (NO), and a second enzyme (adenylate cyclase), which helps generate the cyclic guanosine monophosphate needed to maximize intracavernosal blood flow and increase the pressure within the corpora cavernosa.

The role of testosterone in male sexual function remains complex and controversial. Men acquire full sexual and reproductive competence at adolescence when, in response to pulsatile pituitary luteinizing hormone (LH) secretion, Leydig cell testosterone production surges to adult levels as coincidental pulsatile pituitary follicle-stimulating hormone (FSH) secretion initiates and maintains the orderly process of spermatogenesis in testicular Sertoli cells. Thereafter, the role of testosterone becomes unclear. Some men with below-normal testosterone levels can still have nocturnal erections, but for fully satisfactory sexual and erectile function, a "normal" quotient of testosterone must be present in the bloodstream. As testos-

terone levels decline, so does a man's sexual function. Two actions of testosterone—one central and the other peripheral—are thought to be critical. Testosterone is the main hormonal mediator of a man's libido. As testosterone levels decline, sexual desire decreases. Testosterone also has a critical role in stabilizing the levels of intracavernosal NOS, the enzyme responsible for triggering the NO cascade required to have an erection. Thus, the man with inadequate circulating testosterone will have a dampened libido and suboptimal erectile function. Anything that interferes with hypothalamic pulsatile LH release or reduces the number of Leydig cells available to respond to LH will result in decreased production of testosterone.

As men age, the absolute number of Leydig cells decreases by about 40%, and the vigor of pulsatile LH release is dampened. In association with these events, the free testosterone level declines approximately 1.2% per year and may be associated with commensurate increases in serum LH levels. Most aging men with subnormal levels of testosterone, however, have low or inappropriately normal levels of LH. Some clinicians believe that age-appropriate but lowered levels of free testosterone (in comparison with those in young men) are not contributory to sexual dysfunction. Nevertheless, some clinical studies have substantiated positive responses to testosterone therapy in men with borderline low levels of free testosterone.

In the absence of comorbid conditions, treatment designed to achieve normal testosterone levels will allow the restoration of completely normal erectile function. Thus, several factors—neural activity, vascular events, intracavernosal NOS, and androgens—must work in harmony to maintain normal male sexual function. When a man's sexual function falters, some aspect of these various factors may be malfunctioning. In addition, other disruptive influences (psychologic, emotional, or pharmacologic factors, individually or collectively) may impair a man's sexual function. For example, in depressed men, sexual problems—diminished libido, erectile dysfunction, and premature ejaculation—are common, but the antidepressant medications routinely prescribed to counter the manifestations of depression are themselves associated with a range of adverse effects on sexual function (see subsequent section on drug-related causes of erectile dysfunction).

Libido problems may be related to hypogonadism, hyperprolactinemia, depression, fear of sexual failure, certain medications, or systemic illness. Ejaculatory difficulties can be attributed to either organic or psychogenic problems and are manifested by retarded ejaculation, anejaculation, or premature ejaculation. Medication effects and nerve damage are common organic causes. Relationship difficulties may affect ejaculatory function as well.

Therefore, AACE has developed a systematic medical approach for assessment of each couple and all potential risk factors in the sexual relationship (see Appendix). This approach allows formulation of a plan to diagnose and treat the difficulties and achieve long-term correction. This outcome can be accomplished only with the contin-

ued cooperative efforts of the endocrinologist and both partners.

The aging man's sexual function is a quality-of-life issue. These guidelines will educate physicians about sexual dysfunction, enhance the care and management of affected patients, and thereby provide an important public service.

ROLE OF THE ENDOCRINOLOGIST IN TREATING MALE SEXUAL DYSFUNCTION

The endocrinologist is ideally positioned to identify and evaluate the full range of medical, physical, and psychiatric problems responsible for disrupting an individual man's sexual function. With the full diagnostic array outlined, the endocrinologist can offer a rational and comprehensive treatment tailored to each man's needs and can maximize opportunities to restore normal sexual function.

A man's sexual function is inextricably linked to his sexual body chemistry. The treatment of erectile dysfunction can best be managed by those who understand man's body chemistry, particularly his sexual body chemistry.

Endocrinologists are body chemistry experts, singularly equipped to understand and cope with the alterations in sexual body chemistry responsible for the diminution of sexual function in previously sexually active men. Furthermore, because endocrinologists are trained in the cognitive sciences, they routinely scan the complete diagnostic horizon in search of specific individual factors, or a coalition of factors, that may impair an individual man's sexual function. Often, a combined therapeutic approach, with use of resources from several disciplines, is necessary. Although impotence, or erectile dysfunction, may be the consequence of specific vascular, pharmacologic, hormonal, neurologic, or psychiatric contributions, causality is not always unifocal. Indeed, sometimes multiple problems coexist and collectively contribute to cripple a man's sexual function. For effective treatment, all impediments to normal sexual function must be identified and then managed both individually and collectively.

TYPES OF SEXUAL DYSFUNCTION

Sexual dysfunction may reflect problems with the following factors:

- Libido
- Ejaculation
- Erectile function
- A combination of the above factors

Reduced libido can result from organic or psychologic causes. It often accompanies low levels of serum testosterone or increased levels of serum prolactin, and these changes may be either primary or secondary. It can also be associated with psychologic problems, relationship difficulties, medical illnesses, and use of certain drugs.

Ejaculatory difficulties can consist of premature, retarded, absent, or retrograde ejaculation. Premature

ejaculation is more common in young men than in older men. It can disappear or diminish with increasing age and sexual experience. Men who have erectile dysfunction often complain of premature ejaculation. The exact definition of premature ejaculation is controversial, but ejaculation before or within 2 minutes after vaginal penetration would be a working definition. Psychologic or medical factors (or both) must be considered. Adrenergic agents, especially decongestants, are common causes of premature ejaculation, as is endogenous epinephrine produced by anxiety. Retarded ejaculation or anejaculation also can be due to psychologic, neurologic, or medical causes or some combination of these factors. Retrograde ejaculation often occurs in patients with neurologic disorders, especially diabetic neuropathy, or as a complication of transurethral resection of the prostate.

Erectile dysfunction is the most common problem, afflicting 80 to 85% of the patients seeking medical help for sexual dysfunction. Erectile dysfunction is defined as the inability to achieve or maintain an erection of sufficient duration and firmness to complete satisfactory intercourse through vaginal penetration. In their definition of erectile dysfunction, Masters and Johnson included the fact that such failure must occur in more than 25% of sexual attempts. This criterion highlights the fact that any normal man can occasionally have erectile failure.

The loss of erectile capacity is important to most men. Sexual function serves deeply felt, personal needs and reinforces the permanence of pair-bonding in couples, which aids in the stability of society in general. Sexual function can also be viewed as a status symbol and a psychologic boost. Sexual dysfunction may cause substantial emotional concerns. With the man demonstrating age-related decreased sexual desire, and possibly function, the partner may have emotional concerns as well, manifested by doubts about attractiveness or questions about the man's faithfulness.

ERECTILE DYSFUNCTION

Erectile Physiology

Adrenergic impulses maintain tonic contraction of the smooth muscle of the corpora cavernosa in the flaccid state. Penile erections are the result of enhanced blood flow, caused by arteriolar vasodilatation and cavernosal relaxation attributable to nerve stimulation. Various stimuli trigger the higher centers of the brain, and nerve impulses flow down the spinal cord to the thoracolumbar ganglia (Fig. 1). This process causes nerve impulses (especially from nonadrenergic, noncholinergic nerve fibers) to activate. The main neurotransmitter produced seems to be NO, the endothelium-derived relaxing factor (Fig. 2). This agent causes relaxation of the arterioles and cavernosal smooth muscle of the penis, which allows increased blood flow and increases the intracorporeal pressure to approximate the systolic pressure. The dilated corpora compress the venous outflow channels against the elastic tissue of the tunica albuginea, an action that prevents venous leakage and further increases the intracavernosal pressure to

above systolic pressure. Just before ejaculation, the ischio-cavernosal and pubocavernosal muscles contract to increase intracavernosal pressure further; the response is ejaculation. Tactile stimulation of the penile shaft activates parasympathetic fibers, which travel in the pudendal nerve and function through the spinal reflex arc from S2 to S4. This process further enhances relaxation of the cavernous smooth muscle, which increases blood flow to the penis and, subsequently, intracavernosal pressure. Usually, both mechanisms are at work to cause erections, but as men age, they derive less stimulation from the higher centers and need to rely more on direct penile stimulation—hence, the requirement of aging men to practice extended foreplay. The mechanisms involved are complex and may be related to decreased production of or responsiveness to NOS, the enzyme that produces NO.

Aging-Related Erectile Changes

Before the causes of erectile dysfunction are discussed, the normal aging-related changes in erectile function should be reviewed. Some men seeking help need only reassurance that their symptoms merely represent the expected age-related physiologic changes in function.

In young men, the higher centers of the brain are easily stimulated by fantasizing or thinking about sex, which seems to cause an erection nearly at will. With aging, this ability decreases. Ability to reach arousal with suggestive photographs also becomes less effective, although arousal by viewing a suggestive video may remain longer. Increased interaction of the couple, especially with foreplay, is needed to achieve a satisfactory erection.

Another aging-related change is an increase in the refractory period—that is, the time from ejaculation to the next erection. This interval may range from 30 minutes in a young man to several days in an octogenarian, according to the work of Masters and Johnson.

Erections, once achieved through fantasy and foreplay, are more fragile as men age. Older men must maintain their focus; if they become distracted by thinking of work or other activities, detumescence may occur. The telephone ringing may be enough to cause detumescence. In addition, men may occasionally experience detumescence without ejaculation for no apparent reason.
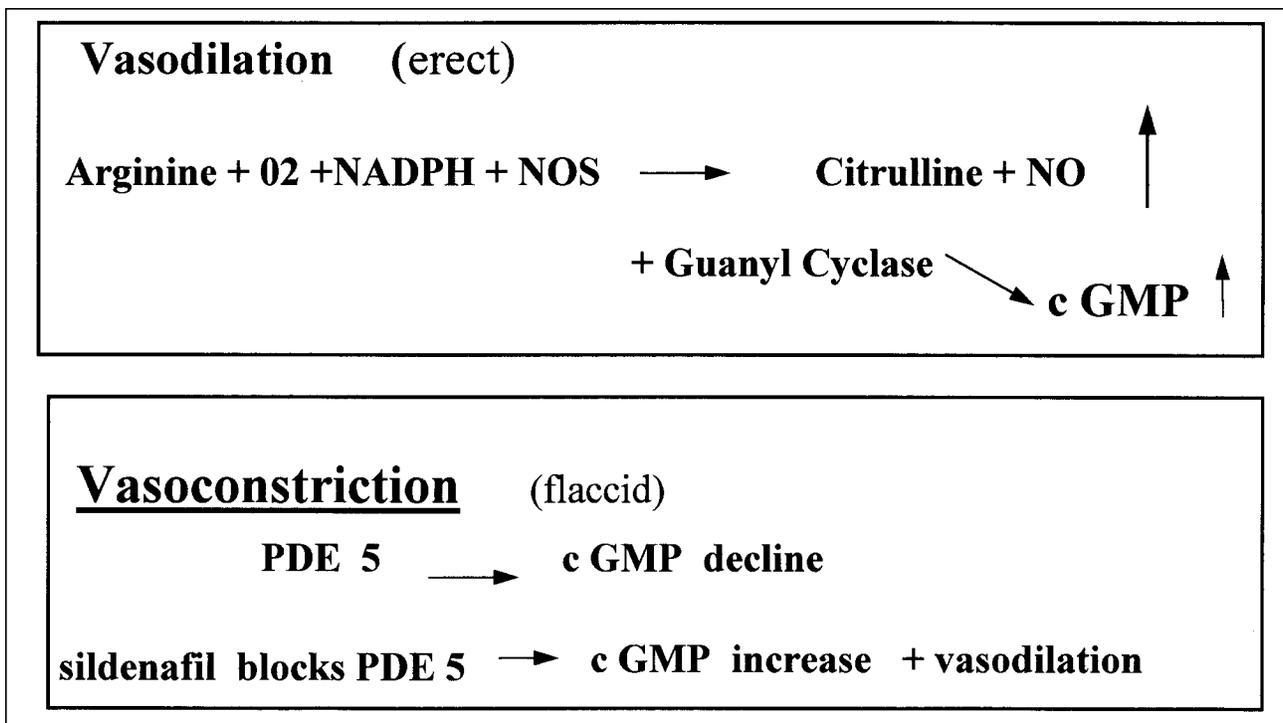
Causes of Erectile Dysfunction

The two main categories of erectile dysfunction are psychologic and organic. Often the dysfunction is of "mixed" etiologic origin, inasmuch as both factors are important. Every man who has some problem with erectile function develops performance anxiety, and determining whether psychologic factors are the main problem or merely a minor accompaniment may be difficult.

Organic causes can be vascular, neurologic, hormonal, medical, or pharmacologic, and some men have multiple etiologic factors. Most of these causes affect the intrapenile vasculogenic mechanisms, whether arterial or venous. Another common finding is a decrease in local NO, which is thought to be the main neurotransmitter in initiating the erectile process. Fibrosis may also be present
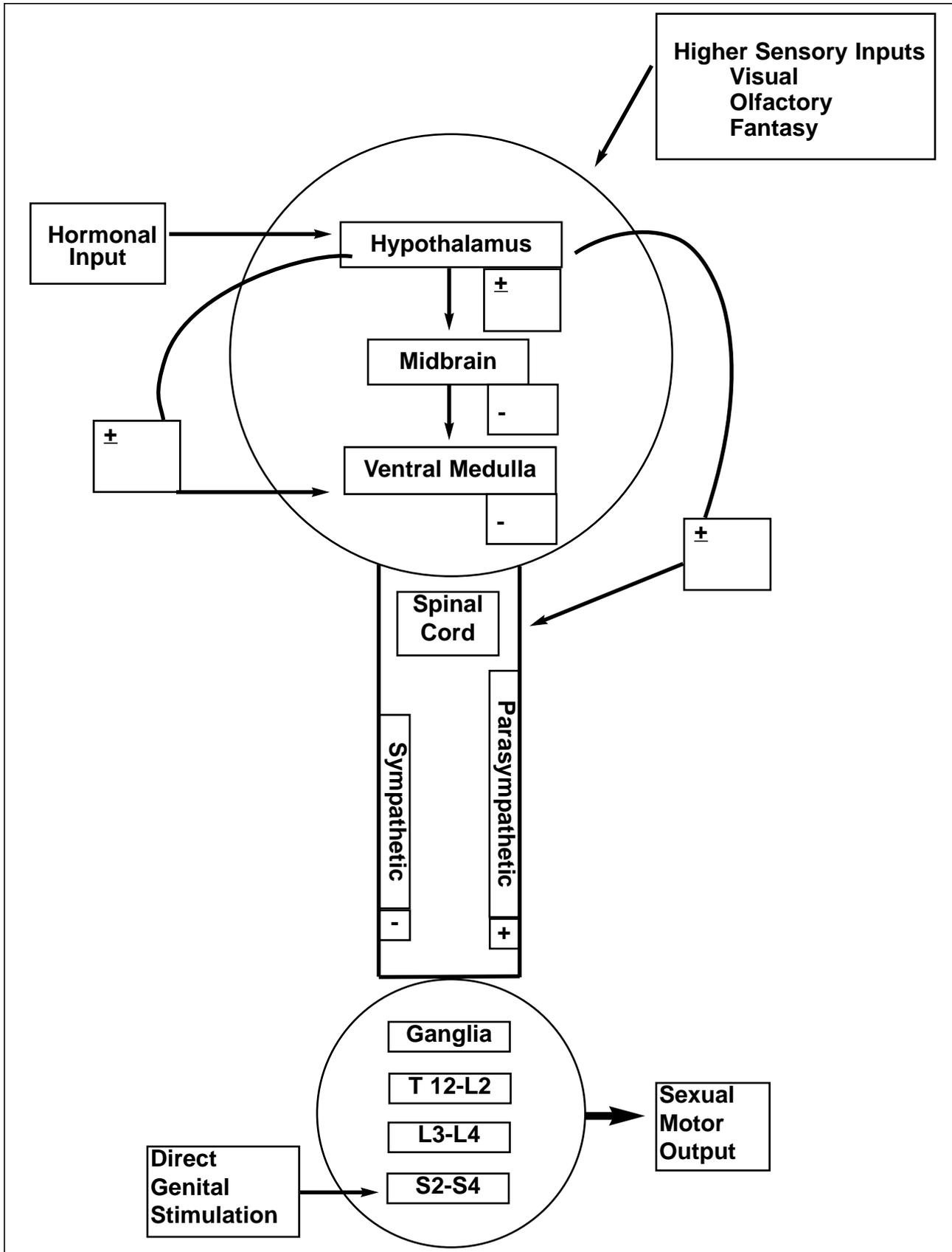
Fig. 1. Neural mechanisms that produce penile erections. (Adapted from Betts TA. Disturbances of sexual behavior. *Clin Endocrinol Metab.* 1975;4:619-641 and Giuliano F, Allard J. Dopamine and sexual function. *Int J Impot Res.* 2001;13[Suppl 3]:S18-S28.)

Vasodilation (erect)

$$Arginine + O_2 + NADPH + NOS \longrightarrow Citrulline + NO$$

$$+ Guanyl\ Cyclase \searrow c\ GMP$$

<u>Vasoconstriction</u> (flaccid)

$$PDE\ 5 \longrightarrow c\ GMP\ decline$$

$$sildenafil\ blocks\ PDE\ 5 \longrightarrow c\ GMP\ increase\ +\ vasodilation$$

Fig. 2. The nitric oxide (*NO*) cascade, underlying penile erection. *cGMP* = cyclic guanosine monophosphate; *NADPH* = reduced form of nicotinamide adenine dinucleotide phosphate; *NOS* = nitric oxide synthase; *PDE* = phosphodiesterase. (From Spark RF. *Sexual Health in Men: The Complete Guide*. Cambridge, MA: Perseus Publishing, 2000:105.)

within the corpora cavernosa, which can limit their expandability, prevent the venules from compressing against the tunica albuginea, and thereby allow venous leakage from the penis.

Vascular Causes

If the corpora cavernosa cannot expand and fill with blood, decreased erectile firmness occurs. Although atherosclerotic plaques, or damage by trauma or irradiation, may decrease blood flow to the penis, vascular causes of erectile dysfunction are more often due to a failure of neural, muscular, or chemical factors. Venous leakage occurs when incomplete filling of the corpora, or intracavernosal fibrosis, causes failure of the veins to be pressed shut against the tunica albuginea.

Neurologic Causes

Erectile function can be impaired as a result of a cerebrovascular accident (CVA or stroke), demyelinating diseases, or even seizure disorders. Tumors or trauma to the spinal cord can also be causative factors of erectile dysfunction. Autonomic and peripheral sensory nerves may be damaged by trauma or transurethral resection of the prostate. A common cause of impaired erectile and ejaculatory function is nerve damage attributable to diabetic autonomic neuropathy. The prevalence of this disorder increases with the duration of disease in both type 1 and type 2 diabetes, and it is more likely to develop when the plasma glucose is poorly controlled.

Hormonal Abnormalities

Hormonal perturbations may contribute to sexual dysfunction, especially erectile dysfunction. Most such problems revolve around dysfunction of the hypothalamic-pituitary-gonadal axis and are associated with either excess prolactin or decreased testosterone levels. Other endocrine disorders that may be associated with impairment of libido or erectile function include hypothyroidism, hyperthyroidism, adrenal insufficiency, or excessive levels of adrenal corticosteroids. In such cases, patients may experience a generalized fatigue or weakness from the effects of the illness. Tumors of the hypothalamic-pituitary area may cause hypogonadism by mass effect, destruction of normal pituitary tissue, or oversecretion of prolactin, which may suppress gonadotropins and cause secondary hypogonadism. Postreceptor action of increased prolactin levels may also result in erectile problems, even in the presence of a normal testosterone level.

Hyperprolactinemia, which can be due to medications, hypothyroidism with increased thyrotropin, chest wall injuries, or compression of the pituitary stalk, can result in sexual problems. Rarely, a patient may demonstrate an excess of a variant large prolactin molecule, macroprolactin, which is biologically inert and therefore incapable of causing sexual dysfunction.

Any major medical illness or surgical procedure can suppress the central axis and cause secondary hypogonadism. Primary hypogonadism due to autoimmune destruction of the testicles occurs in some men as they age. A related

cause is unilateral mumps orchitis occurring during the early adult years, with later failure of the "good testis." Congenital causes include Klinefelter's syndrome, Kallmann's syndrome, and myotonic dystrophy. The incidence of hypogonadism in patients with acquired immunodeficiency syndrome (AIDS) is quite high.

Hypogonadism is defined as a free testosterone level that is below the lower limit of normal for young adult control subjects. Previously, age-related decreases in free testosterone were accepted as "normal," but this concept has been challenged. Similarly, several clinical conditions that were once accepted as normal age-related disorders are now thought to lead to medical problems—for example, hypertension, osteoporosis, and menopause. No agreement exists on the physiologically appropriate level of testosterone as men age or the serum testosterone level at which a man begins to experience impairment of his sexual function. The definition of relative hypogonadism is also uncertain. Many men have normal sexual function even if their testosterone levels decline into the age-adjusted lower normal range. Patients with borderline testosterone levels warrant a clinical trial of testosterone. The threshold of response to testosterone therapy, and thus the necessary dosage, varies—especially in the younger decades of life. If LH is increased and the testosterone level is low, the patient will have decompensated primary testicular failure. In this setting, testosterone replacement therapy is essential.

Men with testicular failure may have the entire spectrum of hypogonadism, which includes osteoporosis, anemia, muscle weakness, depression, and lassitude, as well as sexual dysfunction. The sexual dysfunction, especially decreased libido and decreased erectile capacity, often reverses with testosterone replacement therapy. The variability of response in some patients may be related to comorbid medical illnesses, vascular dysfunction at the penile level, or psychologic factors.

Medical Conditions

Any medical condition that can cause general debility has the potential to decrease sexual desire and performance. Pain, shortness of breath, angina, muscle weakness, or a CVA may be responsible for the dysfunction. The most common medical conditions associated with sexual difficulties are diabetes mellitus and hypertension, possibly because of the microvascular and neurovascular changes that are inherent in these conditions. In patients with diabetes, these factors may lead to a decrease in penile nerve stimulation and in generation of NO. Some investigators have found hypogonadism to be commonly associated with diabetes mellitus. Poorly controlled plasma glucose levels add a separate risk factor, as does the presence of diabetic neuropathy. Not only is hypertension a separate risk factor for sexual problems but hypertension and diabetes often coexist in a patient. Generalized atherosclerosis and peripheral vascular disease may impede blood flow to the penis, as may a damaged vessel attributed to pelvic injury or radiation therapy to the groin.

Recently, a cardiologist reported an assessment of 50 men who presented with erectile dysfunction but who had no history of cardiac disease. Most men had multiple cardiac risk factors, and 56% had asymptomatic ischemic changes on a treadmill test, consistent with silent ischemia. Because erectile dysfunction and cardiovascular disease share common risk factors, erectile dysfunction may be a predictor of future cardiovascular disease. A search for cardiovascular risk factors was suggested as part of the evaluation in men with sexual difficulties.

Cigarette smoking can cause vascular insufficiency as well as a decrease in intrapenile NO levels. Excessive consumption of alcohol or use of other recreational drugs may cause sexual dysfunction, either by a direct effect on the penile neurovascular system or by causing increased prolactin, decreased testosterone production, or both. In Peyronie's disease, collagen tissue is converted to fibrous tissue for unknown reasons; hence, a palpable fibrous plaque is created in the tunica albuginea. The usual manifestation is a bending of the penis to one side during erection, which can occasionally be painful.

Drug-Related Causes

Both prescription and over-the-counter medications have been shown to be the cause of erectile problems in as many as 25% of cases (Table 1). Although single medications can induce erectile dysfunction, the adverse effects of medications are often additive. This situation is particularly frequent in older men who are taking multiple medications, and partial or complete erectile dysfunction often results. A psychologic component can make partial erectile dysfunction progress to complete erectile dysfunction. Some medications can affect libido, whereas others affect erectile function or ejaculation. Nonprescription medications, such as antihistamines or decongestants, may also impair erectile function.

Most psychotropic drugs can affect libido or erectile function, either through a direct action or by increasing prolactin or decreasing testosterone levels. Although antidepressants may cause erectile dysfunction in susceptible patients, they may also be beneficial in improving libido in depressed men. Antihypertensive medications may cause erectile dysfunction either by drug-specific effects or by decreasing the systolic blood pressure and thereby decreasing the intracavernosal penile pressure. This effect is especially prevalent in patients with diabetes or hypertension who have underlying microvascular disease. Ketoconazole, aminoglutethimide, and similar drugs actually decrease the production of testosterone. Most of the earlier antihypertensive agents—such as reserpine, guanethidine, and hydralazine—caused sexual dysfunction. Some β-adrenergic blocking agents may cause sexual problems, but dysfunction with angiotensin-converting enzyme inhibitors or calcium channel blockers is less common. Some drugs (spironolactone, cimetidine, flutamide, or cyproterone acetate) may block the peripheral androgen receptors. Cimetidine may assume a greater importance because it can now be purchased without a

Table 1
Sexual Side Effects of Common Prescription Medications

Type of drug and generic name	Brand name	Sexual side effects
Antihypertensive medications		
Diuretics		
Spironolactone	Aldactone	Decreased libido, breast swelling, impotence
Thiazides	Diuril, HydroDIURIL, Naturetin, Naqua, many others	Impotence
Furosemide	Lasix	None
Centrally acting agents		
Methyldopa	Aldomet	Decreased libido, impotence
Clonidine	Catapres	Impotence
Reserpine	Serpasil, Raudixin, Ser-Ap-Es	Decreased libido, impotence, depression
α-Adrenergic blockers		
Prazosin	Minipress	"Dry" (retrograde) ejaculation
Terazosin	Hytrin	"Dry" (retrograde) ejaculation
β-Adrenergic blockers		
Propranolol	Inderal	Impotence, decreased libido
Metoprolol	Lopressor	Impotence, decreased libido
Combined α- and β-adrenergic blockers		
Labetalol	Normodyne, Trandate	Inhibited ejaculation
Nonadrenergic vasodilator		
Hydralazine	Apresoline	None
Sympathetic nerve blocker		
Guanethidine	Ismelin	Impotence, "dry" (retrograde) ejaculation
Angiotensin-converting enzyme inhibitors		
Captopril	Capoten	None
Enalapril	Vasotec	None
Lisinopril	Zestril	Impotence in a small percentage (1%) of cases
Psychiatric medications		
Antidepressants		
Tricyclics:		
Amitriptyline	Elavil	Inhibited ejaculation, impotence
Amoxapine	Asendin	Decreased libido, impotence
Desipramine	Norpramin	Inhibited ejaculation
Doxepin	Sinequan	Inhibited ejaculation, impotence
Imipramine	Tofranil	Inhibited ejaculation, impotence
Maprotiline	Ludiomil	Inhibited ejaculation
Nortriptyline	Aventyl, Pamelor	Inhibited ejaculation
Protriptyline	Vivactil	Inhibited ejaculation, impotence
Atypical agent:		
Trazodone	Desyrel	Priapism
Monoamine oxidase inhibitors:		
Isocarboxazid	Marplan	Inhibited ejaculation
Phenelzine	Nardil	Inhibited ejaculation, decreased libido
Tranylcypromine	Parnate	Inhibited ejaculation
Antipsychotic medications		
Phenothiazine group:		
Thioridazine	Mellaril	Inhibited ejaculation, priapism, decreased libido
Chlorpromazine	Thorazine	Inhibited ejaculation
Mesoridazine	Serentil	Inhibited ejaculation, decreased libido
Fluphenazine	Prolixin	Inhibited ejaculation, decreased libido
Serotonin reuptake inhibitors:		
Fluoxetine (and others in this class)	Prozac	Anorgasmy (8%)
Perphenazine	Trilafon	Inhibited ejaculation
Trifluoperazine	Stelazine	Inhibited ejaculation

Table 1 (continued)
Sexual Side Effects of Common Prescription Medications

Type of drug and generic name	Brand name	Sexual side effects
Thioxanthene group:		
Chlorprothixene	Taractan	Inhibited ejaculation
Thiothixene	Navane	Inhibited ejaculation, impotence
Butyrophenone:		
Haloperidol	Haldol	Inhibited ejaculation
Antimania medication		
Lithium carbonate	Eskalith, Lithobid	Possible impotence
Antiulcer medications		
Cimetidine	Tagamet	Decreased libido, impotence, gynecomastia
Ranitidine	Zantac	None
Famotidine	Pepcid	None

From Spark RF. *Male Sexual Health: A Couple's Guide.* Yonkers, NY: Consumer Reports Books, 1991: 117-118.

prescription. Drugs such as α-methyldopa, spironolactone, digoxin, and metoclopramide may raise prolactin levels. Thiazide diuretics, finasteride, anticholinergic agents, and pain medications can cause erectile dysfunction.

EVALUATION OF SEXUAL DYSFUNCTION

An algorithm for suggested evaluation of erectile dysfunction is shown in Figure 3.

Evaluation of the Couple

The initial assessment of a male patient with sexual dysfunction and his partner is best performed by a physician who has the training, experience, and interest to conduct an extensive evaluation of the relevant medical, psychologic, and hormonal factors. Accordingly, the clinical endocrinologist is the physician best suited to direct the evaluation and treatment of this problem by a multidisciplinary team.

Ideally, the couple should undergo assessment together at the first visit or soon thereafter. A discussion about the partner is important. Is the patient married, single, divorced, or widowed? Because newer relationships may have adjustment problems, the duration of the relationship is important, as is the age disparity between the partners. The health of the partner is very important; 15% of men report a decreased sexual frequency or ability because of health problems that their partners are experiencing, and the men are infrequently aware of this connection. The question of whether a couple is still sexually active in other ways is more revealing: do they practice alternative sexual techniques even if intravaginal penetration is not possible? This adjustment highlights their relationship in general and how comfortable they are with each other. The interviewer should determine whether any relationship problems exist between the partners or whether external stresses may be a predominant factor. The dynamics between the partners should be carefully observed. Relationship problems may be due to intrinsic philosophic differences between the two, and expectations about sexual fulfillment may also vary. Occasionally, the level of commitment to each other differs. Stresses may be present strictly because of performance anxiety or because of work problems, financial worries, or perhaps problems with children or other relatives. Oftentimes, inadequate communication between the couple, which may be attributable to embarrassment, may be mistaken for lack of caring. The couple may begin to avoid contact and drift apart because of isolation or frustration. Even before sex therapy is considered, one or both parties may require stress management, or the couple might consider marital counseling before sexual counseling.

Sexual History

The examiner must evaluate the symptoms carefully because the sexual history is of considerable importance. Many men have only aging-related sexual changes, and reassurance is all that is necessary. With erectile dysfunction, the most common complaint is attainment of only partial erections that may not achieve vaginal penetration, or if the initial erections penetrate, early detumescence occurs without ejaculation. These problems may coexist in many patients. When organic factors cause the erectile dysfunction, the patient can also develop a fear of failure, which may then lead to a decrease in sexual interest and even avoidance of the partner. Total loss of all penile rigidity is uncommon. The duration of the problem is useful to know because patients who have had sexual difficulties for years tend to have more psychologic adjustments to make, even with successful therapy. If nocturnal or morning erections are present and strong, it will direct the evaluation toward psychologic causes, or it may simply mean that a certain medication might have decreased its concentration (and its adverse effect) during the night.
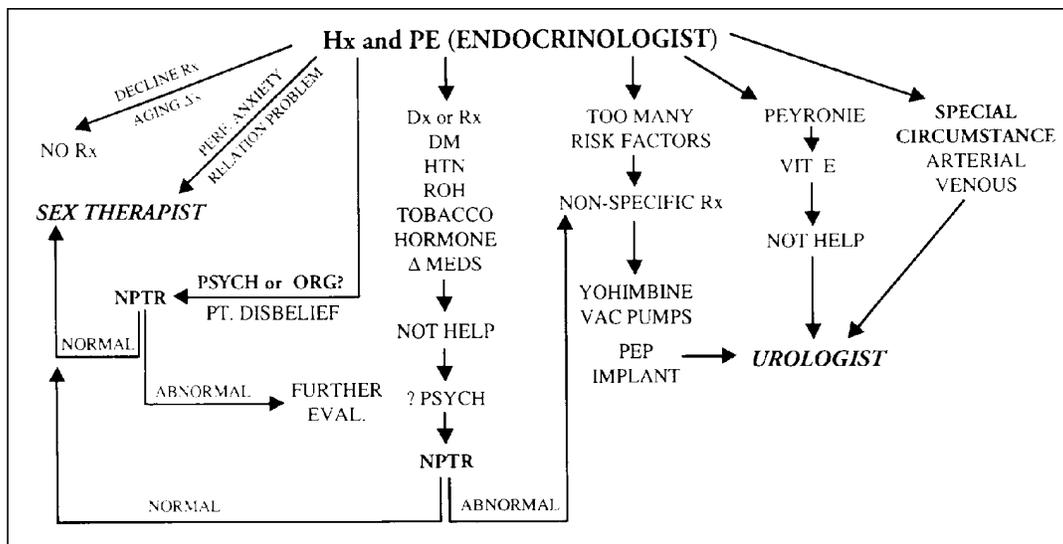
Fig. 3. Algorithm for office evaluation of erectile dysfunction. *DM* = diabetes mellitus; *Dx* = diagnosis; *EVAL* = evaluation; *HTN* = hypertension; *Hx* = history; *MEDS* = medications; *NPTR* = nocturnal penile tumescence and rigidity testing; *ORG* = organic; *PE* = physical examination; *PEP* = pharmacologic erection program (penile injections); *PERF* = performance; *PSYCH* = psychologic; *PT* = patient; *ROH* = alcohol; *Rx* = treatment; *Sx* = symptoms; *VAC* = vacuum; *VIT* = vitamin. (From Guay AT. The endocrinologist as the focus in a multidisciplinary approach to management of erectile dysfunction. *Endocr Pract.* 1997;3:1-8.)

The absence of nocturnal erections can mean that the patient is no longer experiencing rapid eye movement sleep, during which time most erections occur, and it does not necessarily mean that the patient has organic erectile dysfunction.

Medical History

In determining the medical risk factors that might be related to sexual dysfunction, both prescription and over-the-counter medications should be reviewed. (For efficiency, the patient should prepare a list of medications in advance.) The patient should be asked about tobacco and alcohol use as well as use of other recreational drugs. The presence of high-risk medical disorders—diabetes mellitus, hypertension, coronary artery disease, hyperlipidemia, and peripheral vascular disease—must be reviewed. Loud snoring should prompt an evaluation for sleep disorders. Conditions such as sleep apnea, nocturnal myoclonus, or restless legs may directly affect the higher sexual centers or cause secondary hypogonadism. CVA or seizure disorders (and seizure medications) are occasionally associated with sexual dysfunction from central nervous system mechanisms. Any severe debilitating disease can be a potential cause of sexual dysfunction.

A history of emotional illness or surgical procedures, especially of the colon and prostate, should be elicited. Transurethral resection of the prostate is associated with a substantial risk of damage to the penile nerves.

As the patient ages, the possibility of multiple factors causing erectile dysfunction increases. If one adds concurrent performance anxiety and stresses of daily living, the situation is often difficult to assess. Educating the patient and his mate about the interrelationships of the multiple factors, however, helps to eliminate the barriers to successful treatment.

Physical Examination

A comprehensive physical examination is necessary for assessment of blood pressure, secondary sex characteristics, gynecomastia, thyroid abnormalities, femoral pulses, scrotal formation, urethral position, and fibrous plaques in the penile shaft. The testicles should be evaluated for size, consistency, and nodules. Linear measurements (length and width) may be used, but a more accurate determination can be obtained with the Prader orchidometer—a series of elliptical spheres of various volumes to assess testicular size (in different reports, the lower limit of normal volume has varied from 15 to 18 cc).

Sensory adequacy of the penile shaft and perineum can be evaluated roughly by touch and pinprick. A more sophisticated bioesthesiometry apparatus may be used, but the investigator must be aware that nerve conduction and penile sensation normally decrease with age. The bulbocavernosus reflex and rectal sphincter tone must be assessed because both are mediated by the S2-4 spinal reflex arc. The bulbocavernosus reflex is tested with the physician's finger in the rectum directed laterally to where the muscle is inserted. A moderate squeeze on the glans penis will cause the bulbocavernosus muscle to contract if the reflex arc is intact. A screening neurologic examination is necessary.

Diagnostic Tests

Diagnostic testing may be categorized as follows:

- Blood tests
- Vascular assessment
- Sensory studies
- Nocturnal penile tumescence and rigidity testing

Blood Tests

Chemistry testing should evaluate for anemia, increased plasma glucose levels, or impaired renal function. Thyroid testing should be done if clinically indicated. Other hormone screening should include serum testosterone and prolactin levels. The "normal" range for testosterone is controversial. The Massachusetts Male Aging Study confirmed that free testosterone decreases 1.2% per year and bioavailable testosterone decreases 1.0% per year, while the sex hormone-binding globulin increases 1.2% per year, between the ages of 40 and 70 years. For this reason, free or bioavailable testosterone assays are preferred over measurement of the total testosterone level. The free fraction of testosterone may be assessed by equilibrium dialysis or by ultrafiltration. It may also be calculated after total testosterone and sex hormone-binding globulin levels are determined. Because of the diurnal variation of testosterone secretion, obtaining several morning samples or pooling of multiple samples is advisable. A minimum of two subnormal values should be obtained before treatment. Libido and erectile function are usually maintained until the testosterone level is slightly below the normal range unless the patient has comorbid disease. These and other recommendations have been elucidated fully in the AACE clinical practice guidelines for evaluation and treatment of hypogonadism in adult male patients. If the testosterone level is low, or even borderline, a serum LH level should be obtained to distinguish primary from secondary hypogonadism. Compensated primary hypogonadism is present when the testosterone level is normal but the LH level is increased. Further testicular failure can be anticipated. Whether to establish a follow-up schedule for the patient or to initiate treatment is an individual clinical decision.

Vascular Assessment

Vascular flow to the corpora cavernosa may be quantified with the use of a penile Doppler examination. By measuring both penile and brachial blood pressure, a ratio called the penile brachial index (PBI) is determined. Interestingly, investigators have suggested that a low PBI, which should indicate decreased penile blood flow, correlates better with coronary artery disease than it does with erectile dysfunction. Routine measurement is not recommended. The one instance in which the PBI may be of value is in the pelvic steal syndrome. A minor blockage of a small artery may not cause symptoms in the relatively inactive state of foreplay; thus, an erection may be normal. After penetration and pelvic thrusting, however, shunting of the blood to the pelvic musculature may cause detumescence prematurely. This condition is diagnosed by obtaining a PBI before and after exercise on a treadmill or with multiple deep knee bends; a PBI decrease of 0.15 or more is presumptive evidence of the pelvic steal syndrome.

A screening office examination may be done to assess the effect of a penile injection with 10 μg of prostaglandin E_1 (PGE_1) or 10 mg of papaverine, with or without visual sexual stimulation. If an erection capable of penetration is obtained, a physiologically significant vascular deficiency is excluded. If necessary, the erection can be reversed by a penile injection of 0.2 to 0.4 mg of phenylephrine. A more sophisticated evaluation can be achieved by using color duplex ultrasonography, which measures cavernous artery diameter and in-flow pressure, along with the end-diastolic pressure, which assesses venous leakage. This procedure is performed after a similar penile injection of prostaglandin or papaverine. It has also been suggested that endogenous epinephrine, generated by a patient's embarrassment, fear, or anxiety, can affect the validity of the test results. Venous leakage is tested by the intracavernous infusion of saline and radiopaque dye at various rates of flow and pressure.

Sensory Studies

Bioesthesiometry testing was mentioned previously for penile sensory testing. A more sophisticated testing method might involve the use of electromyography, especially in patients with diabetic neuropathy. Various other tests can screen for autonomic neuropathy. Recently, investigators have attempted to use pelvic evoked potentials, but experience with this technique is limited. No currently available test can assess the penile stimulating nerves clinically.

Nocturnal Penile Tumescence and Rigidity Testing

Occasionally, the measurement of nocturnal penile tumescence and rigidity is useful, especially to distinguish between psychologic and organic erectile dysfunction. This technique was developed in sleep laboratories several decades ago. This type of testing is expensive, and some results are questionable because of the unfamiliar surroundings, the startle response, and the embarrassment when the patient is awakened for measurement of the buckling pressure to determine rigidity. It is still regarded by some, however, to be the "gold standard" for distinguishing psychogenic from organic erectile dysfunction.

A Velcro strap around the penis, called a "snap gauge," can determine whether plastic strands of different tensile strength might be broken at night during nocturnal penile activity. Unfortunately, this technique measures only one episode of penile tumescence but not rigidity.

A portable monitor for home use, called the RigiScan monitor, measures both penile rigidity and tumescence. It can be set up easily in the office of any interested physician. The test can help distinguish between organic and psychologic erectile dysfunction, either in the initial assessment of the patient or after organic medical factors have been corrected but the difficulty persists. Severe psychoses may be associated with abnormal nocturnal penile activity, as may sleep apnea or nocturnal myoclonus.

TREATMENT OF SEXUAL DYSFUNCTION

Some men simply require reassurance that their concerns reflect aging changes and that their sexual function is indeed what is expected for their age. Some men refuse treatment. They only wish to be reassured that their sexual deficiency is not a symptom of a more serious illness.

Most men, and indeed couples, prefer a diagnostic evaluation and therapeutic counseling. After discussion of the therapeutic options, some couples do not wish any treatment for erectile problems directed toward intravaginal penetration and would prefer just to engage in alternative sexual techniques such as mutual masturbation.

Psychologic Treatment

The couple should be emotionally compatible. Both partners should be willing to participate and cooperate with therapy. Major relationship problems should be addressed before therapy is introduced. Similarly, major stresses with work, finances, or family will need to be evaluated and corrected first. Performance anxiety, specifically related to fear of sexual failure, is best evaluated and treated by a qualified sex therapist (psychologist or psychiatrist). At times, minor relationship problems manifest after organic causes of sexual dysfunction have been corrected. These minor problems may be caused by fear of failure, fear of frustration, or embarrassment. Decreased libido may be psychologic in origin and may necessitate sexual therapy and possibly pharmacologic treatment. Ejaculation problems can be either organic or psychologic, and the sex therapist will help patients with premature ejaculation as well as with problems involving anejaculation or retarded ejaculation. At times, a female partner might not be knowledgeable about, and may be reluctant to participate in, the increased foreplay that men require to obtain erections as they age. The therapist can reaffirm the need and teach the techniques.

Medical Treatment

If organic problems seem to be dominant, the first step is to identify the medical risk factors and correct them, if possible. Plasma glucose must be regulated in men with poorly controlled diabetes. Medications for hypertension must be optimized. Cessation of tobacco abuse is important. Hyperlipidemia must be treated aggressively. Intake of alcohol should be decreased or discontinued. Use of illicit drugs must be discontinued. Anticipated improvement in sexual function can be a motivational tool to increase patient compliance in treatment of chronic disease.

Hormonal Treatment

Benign prostatic hyperplasia, prostate cancer, sleep apnea, and polycythemia must be evaluated before and after initiation of testosterone therapy for hypogonadal men. A baseline digital rectal examination of the prostate, a prostate-specific antigen level, and a hematocrit should be determined before treatment; if any prostate-related abnormalities are detected, the patient should be referred to a urologist for further evaluation. Any patient treated with replacement androgens should be reassessed within 1 to 3 months after initiation of therapy and then at 6- to 12-month intervals to ensure that clinical problems have not developed or worsened during such treatment. Prostate cancer and breast cancer are contraindications to androgen therapy, whereas sleep apnea, peripheral edema, erythrocytosis (hematocrit >52%), and benign prostatic hyperplasia are relative contraindications that may respond to adjustments in the medication or specific treatments (for example, use of continuous positive airway pressure or weight reduction).

Testosterone replacement for hypogonadism may also correct sexual dysfunction, unless the patient has other comorbid illnesses. For decades, the standard has been a depot intramuscular injection of testosterone enanthate or cypionate every 2 or 3 weeks (200 mg or 300 mg, respectively). Smaller doses and more frequent injections, however, are better at maintaining circulating testosterone levels in the normal range (that is, 50 to 150 mg of testosterone enanthate or cypionate intramuscularly at 7- to 14-day intervals). An alternative approach is to administer 100 mg on days 1, 11, and 21 of each month, while allowing some flexibility of injection days. If testosterone levels are measured, they should be in the normal range just before the next injection. Other forms of intramuscular testosterone preparations are also being evaluated. Implantable testosterone pellets, which are used in other countries, are now available in the United States, but they are infrequently prescribed. Currently available tablets for oral administration have generally not been used because of potential liver toxicity. A newer oral capsule, testosterone undecanoate, has been used for more than a decade in Europe but has not yet been approved for use in the United States. Although the safety is not questioned, multiple daily doses are required, and the absorption is erratic. Other orally and sublingually administered testosterone tablets are being evaluated.

Testosterone scrotal and nonscrotal dermal patches have now been approved by the US Food and Drug Administration (FDA). Testosterone absorption is greater through scrotal skin. The scrotal patch was the first to be introduced. These patches are placed on the scrotal skin and are changed daily, in the morning. For many patients, weekly shaving of the scrotum is necessary. The patch increases testosterone levels to the low-normal range, with peak levels achieved 3 to 5 hours after application of the patch. Because 5α-reductase in scrotal skin is high, the dihydrotestosterone (DHT) level in serum becomes quite high. The role of DHT is currently being investigated. The nonscrotal patch (Androderm), applied daily in the evening, may be worn in various sites on the skin. The manufacturer recommends that it not be used over bony prominences. The levels remain stable in the middle of the normal range, and the DHT levels remain normal. Skin irritation may develop and often responds to application of corticosteroid cream. In a certain small percentage of patients, therapeutic blood levels of testosterone may not be achieved. Another nonscrotal patch, Testoderm, was associated with less skin irritation but was more likely to fall off; it has recently been withdrawn from the market.

A 1% testosterone gel has recently been approved by the FDA for use in the United States. It is more expensive than the testosterone patches. The blood levels of testosterone associated with use of the gel are dose dependent and vary less than with the testosterone patches. Care must

be exercised because the testosterone can be transferred to another person if skin-to-skin contact occurs.

With any form of testosterone treatment, the patient may have a slow but steady increase in libido and erectile ability during a course of months. If no improvement is noted after 3 months, the hormone deficiency is probably not the only cause of the sexual dysfunction. A comorbid medical illness might be present, or perhaps performance anxiety is dominant.

The hypothalamic-pituitary-gonadal axis has been shown to decrease functioning temporarily after acute medical events or surgical procedures; such an occurrence can cause low gonadotropin and testosterone levels. Similarly, a temporary decrease in testosterone levels may occur as a result of less serious circumstances, such as anxiety, excessive intake of alcohol, use of multiple medications, or uncontrolled diabetes. Patients with these causes are less likely to respond to testosterone replacement. Stimulation of gonadotropins with clomiphene citrate and the subsequent increase in testosterone levels emphasize the functional and reversible nature of this phenomenon; short-term therapy with clomiphene citrate may help some patients. If the testicles are intact, testosterone can be stimulated by injections of human chorionic gonadotropin, but this technique is cumbersome and rarely used. Low testosterone levels can also be caused by suppressed gonadotropins attributable to an increased prolactin level. This situation can be reversed by treatment with bromocriptine, pergolide, or cabergoline. If an increased prolactin level is due to use of a psychotropic drug, however, discontinuing the medication may be all that is needed.

Treatment of other endocrine disorders, such as hypothyroidism or hyperthyroidism, reverses the decreased libido or erectile dysfunction that can accompany these conditions. Uncontrolled diabetes mellitus may respond to improved plasma glucose control, especially in patients with recently diagnosed diabetes. Even patients who have had diabetes for more than 10 years may respond to better glycemic control if a major neuropathy is absent. Hypogonadism is common in patients with diabetes, many of whom may respond to testosterone treatment.

Current Nonspecific Therapies
for Erectile Dysfunction

Some patients do not respond to the aforementioned corrective measures and wish to try nonspecific therapy for erectile dysfunction (Table 2). This scenario might especially exist in older men and those with numerous medical risk factors. The major options to consider at the present time are yohimbine tablets, vacuum pump devices, venous constriction rings, corpora cavernosal injections of various chemicals, intraurethral drug suppositories, intrapenile arterial or venous surgical procedures, penile implants, or orally administered phosphodiesterase inhibitors. Trials with sublingually administered apomorphine and vasodilators are ongoing.

Sildenafil has recently been approved by the FDA. It inhibits phosphodiesterase type 5, which predominates in the penile tissue (Fig. 2). This action prevents the breakdown of cyclic guanosine monophosphate, which, therefore, increases smooth muscle relaxation in the corpora cavernosa and enhances penile rigidity. Three doses are available—25 mg, 50 mg, and 100 mg. If the patient does not have hypogonadism and has no contraindications to use of this drug, a clinical trial with sildenafil is indicated. Treatment is usually initiated with the 50-mg tablet, which is then decreased to 25 mg if major side effects are noted or increased to 100 mg if there is lack of efficacy. The tablet is taken 1 hour before sexual activity, and sexual stimulation is necessary. Sildenafil is contraindicated in patients taking nitrates in any form, inasmuch as severe hypotension and resultant syncope have occurred. Side effects are generally mild and tolerable: headaches, hot flashes, heartburn, diarrhea, myalgias, hypotension, and dizziness. The drug may inhibit phosphodiesterase type 6 in the eye, with resultant difficulty in discriminating blue from green, bluish tones in vision, or difficulty seeing in dim light. Whether any adverse effect occurs in diabetic retinopathy or other eye diseases is yet to be determined.

Yohimbine, a derivative of the African yohimbe tree, has been available for several decades. This α_2-antagonist is effective in some cases of psychologic or organic erectile dysfunction, but its efficacy is controversial. A tablet is available in one strength, 5.4 mg (1/12 gr), and the standard dosage is one tablet three times a day. If the patient has a response, it will generally occur within the first 4 weeks. A short course of two tablets three times a

Table 2
The Most Commonly Used
Nonspecific Treatments
for Erectile Dysfunction

Yohimbine tablets

Venous constriction rings

Vacuum devices

Pharmacologic erection program
    Intracavernosal injections
        Papaverine-phentolamine
        Papaverine-phentolamine-prostaglandin E_1
        Prostaglandin E_1
        Potassium channel openers (?)
    Intraurethral suppositories
        Prostaglandin E_1

Penile microvascular arterial bypass operation

Penile venous ligation surgical procedure

Penile implants
    Flexible rods
    Inflatable cylinders

Orally administered phosphodiesterase inhibitors
    Sildenafil
    Tadalafil (approval pending)
    Vardenafil (approval pending)

day may be tried, but the increase in responders will be small. Several reports have described a positive response over placebo in patients with psychologic erectile dysfunction. A response can occur in patients with organic conditions, but this evidence is weaker. If a patient has noted a positive response, the dosage is then adjusted because many patients respond to one or two tablets 1 hour before sexual activity is desired. Major side effects are uncommon, but minor symptoms, including headaches, dizziness, insomnia, and anxiety, may occur in 25% of cases during the first week of treatment. Patients who have blood pressure that is difficult to control might notice a pressure increase. The addition of trazodone to the treatment regimen has increased the number of responders but also increased the number of potential side effects. Trazodone has been shown to be useful alone, especially in men without known organic causes for erectile dysfunction, in dosages of 25 to 200 mg/day. The increased nocturnal penile activity seen with this regimen provides objective evidence of improvement unrelated to any potential placebo effect.

Treatment directed to the skin of the penile shaft has been attempted. Nitroglycerin paste increased penile rigidity but rarely enough to allow penetrability. Furthermore, absorption into the female partner often caused headaches. The use of a nitroglycerin patch decreased this side effect but did not enhance the therapeutic response. Topically applied minoxidil, alone or in combination with a transdermal enhancing compound, did not improve erections enough to warrant its general use. Various topical preparations of PGE_1 are being studied in clinical trials.

Patients who have good rigidity of their penile erections but who have early detumescence, perhaps due to venous leakage, can benefit from the use of rubber constriction rings. These devices are placed around the base of an erect penis to prevent the blood from leaving. Various kits are available with multiple-sized rings, and the patient tries them in decreasing order of size until the blood remains in the penis while causing no discomfort. A newer adjustable soft latex ring has been developed that is considerably less expensive. All these devices should be used in accordance with the manufacturer's directions.

Another form of therapy is the use of a vacuum pump and a plastic cylinder into which the penis is inserted. Air is pumped out of the cylinder, and the negative pressure draws blood into the penis to create an erection. Then a rubber ring is secured at the base of the penis to prevent exit of the blood; the ring can be worn for a maximum time of 30 minutes. This technique is safe but mechanical, and the erection is composed mainly of venous rather than arterial blood; thus, the penis is cooler and appears somewhat cyanotic. Older men with long-standing relationships tend to accept this form of therapy more than do younger men, who may not have a steady partner. In certain conditions in which intrapenile fibrosis is present (Peyronie's disease), use of the vacuum pump may help to break up adhesions.

Intrapenile injections were introduced in the early 1980s. Papaverine and phentolamine were commonly used together to cause intrapenile vasodilatation and muscle relaxation of the corpora cavernosa. Some physicians added alprostadil (PGE_1) to the mixture, but the amount had to be limited because of penile discomfort from the alcohol in the solution. Alprostadil used alone has been approved by the FDA; it remains the only officially approved drug for intracavernosal injection. PGE_1 is available in powder form, which is dissolved by the addition of bacteriostatic water. This medicine occasionally causes discomfort after the injection. The correct dose is found by beginning with the injection of 5 μg in the office. If necessary, the dosage may be cautiously increased at 48-hour, or longer, intervals. The medicine is injected at the base of the penis, along the dorsolateral penile shaft (at the 2-o'clock and 10-o'clock positions), to avoid the dorsal midline blood vessels and nerves as well as the ventral urethra. An erection occurs within 10 minutes with normal foreplay and may last 30 to 90 minutes. The major side effects, which occur in 3 to 10% of patients, are penile pain, cavernosal scarring, or priapism. An orally administered adrenergic compound, such as ephedrine, pseudoephedrine, or terbutaline, is given if the erection lasts longer than 1 hour and can be administered hourly if needed. If this measure is unsuccessful in causing detumescence by 3 hours, treatment with intracavernosal injection of phenylephrine or norepinephrine in the physician's office or an emergency department is then recommended. Intracavernosal lavage by a urologist may be necessary in refractory cases, inasmuch as permanent damage to the corpora cavernosa may occur if priapism goes untreated for more than 6 hours.

Other substances have been used, or proposed, for penile injections. Potassium channel openers are currently being evaluated. Forskolin, a plant derivative that stimulates intrapenile cyclic adenosine monophosphate, is also being assessed in clinical trials. These agents may be useful when other compounds have failed, and they may cause fewer side effects.

A PGE_1 intraurethral suppository has been approved by the FDA for general use. For many patients, this form of treatment is more acceptable than penile injections. Four doses are available, which should be titrated, from 125 mg to 1,000 μg. The pellet (2 to 3 by 1 mm) is inserted into the urethra with the aid of a plastic applicator. Absorption is 80% complete within 10 minutes. An erection similar to that seen with intracavernosal injection will last between 15 and 60 minutes. The response rate is said to be 65%, but some clinicians believe it may be lower. The difference in results might depend on how the medication is dispensed and whether adequate discussion has taken place in the physician's office, including an initial supervised trial. Although transient penile discomfort may occur, 5 to 10% of patients will have substantial pain that will preclude any further use of the medication. Priapism may occur but seems to be uncommon. Many clinicians give patients adrenergic agents to use (pseudoephedrine, ephedrine, or terbutaline) in the event that an erection lasts longer than 2 hours. If an erection persists after 4 hours, more aggressive treatment is necessary.

In the past, rearterialization of the penis or venous ligation for venous leakage was performed. After review of the high rate of failure for these procedures, a National Institutes of Health Consensus Conference, published in 1993, suggested that these procedures be done only as part of strict research protocols. Special cases such as destruction of an artery after trauma to the pelvis or common penile artery in the perineum or after radiation therapy, especially in younger patients, deserve consideration for rearterialization of the penis. Bypass surgical procedures for generalized atherosclerotic disease are discouraged because of the low success rate.

If the foregoing forms of therapy are unsuccessful or unacceptable to the patient, another option is the use of penile implants—either permanent flexible rods or inflatable cylinders. Treatment failures attributable to infection, extrusion, or mechanical failure, especially in patients with diabetes, previously were as high as 36%, but better equipment and techniques have reduced these complications. If a patient requests more details, particularly about the involved surgical procedure, failure rate, and risks, he should be referred to an experienced urologist.

CONCLUSION

Sexual dysfunction, especially erectile dysfunction, necessitates a comprehensive medical and psychologic evaluation involving both partners. All possible risk factors should be outlined and corrected, when feasible. Psychologic factors and relationship problems should be referred to a qualified sex therapist, and surgical options should be addressed by a urologist. Ideally, however, the endocrinologist should be the evaluating physician who supervises the medical and hormonal treatment and who refers the patient, as necessary, to other members of the multidisciplinary team.

DISCLAIMER

These guidelines are intended as a general outline but not meant to dictate or delineate any specific treatments for patients. The area of treatment of sexual dysfunction, and especially erectile dysfunction, is a relatively new discipline. Basic physiologic and pathologic data have recently been elucidated, but many controversial issues remain. Whenever possible, we have presented a majority opinion, while describing various other possibilities. New advances in technology and treatment will keep this field dynamic and in a state of evolution. Thus, modification of ideas will be necessary as new data become available.

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APPENDIX
System of Care for Male Sexual Dysfunction

Step 1: Accurate history (preferably with the couple)
   A. Make sure concerns are not simply aging-related changes
   B. Inquire about relationship problems
   C. Question about performance anxiety
      Action: Reassure if A
            Refer to sex therapist if B or C
            Do nocturnal penile test if uncertain
   D. Outline medical risk factors and medications
      Action: Change or discontinue medications
            Stop any substance abuse

Step 2: General examination
   A. Blood pressure
   B. Breasts for gynecomastia
   C. Secondary sex characteristics
   D. Peripheral circulation
   E. Genital examination
         Especially for penile fibrosis, testicular atrophy, bulbocavernosal reflex
   F. Rectal examination
         Especially assess prostate
         Action: Follow-up on abnormal findings—that is, cardiovascular findings, suspected endocrine
                  diseases, or abnormal prostate

Step 3: Laboratory tests
   A. Plasma glucose
   B. Prolactin
   C. Free testosterone
   D. Luteinizing hormone and follicle-stimulating hormone if testicular atrophy suspected
   E. Thyroid-stimulating hormone or free thyroxine (or both) if hypothyroidism suspected
   F. Other tests, depending on history and physical examination

Step 4: Treatments
   A. Related to risk factors
      Action: Diagnose diabetes
            Stop any substance abuse
            Change medications
            Treat abnormal hormones (testosterone or prolactin)
            A 3-month testosterone trial, if indicated
            Nocturnal penile tumescence and rigidity testing if risk factors changed and nonresponse may be
               due to psychologic factors
   B. If good erections but early detumescence—venous constriction rings
   C. Nonspecific treatments
      Trial sildenafil
      Trial yohimbine
      Other orally administered drugs, phentolamine, apomorphine (when approved)
      Apomorphine (sublingually)
      Vacuum pump
      Medicated urethral system for erection (intraurethral prostaglandin pellet)
      Penile injections
         Papaverine and phentolamine
         Papaverine, phentolamine, alprostadil
         Alprostadil alone
      Penile implants (as last resort)
   D. Surgical referrals (urologist)
      Severe Peyronie's disease
      Penile injections (if not done by endocrinologist)
      Penile implant
      Selected cases of arterial damage or venous ligation