Urological and Medical Evaluation of Men with Erectile Dysfunction

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As the medical understanding of erectile dysfunction has evolved, the approach to its evaluation must also change. A good doctor/patient rapport is crucial to making patients more comfortable talking about their sexual function. Questionnaires help elicit specific information on which to base the diagnosis and find the etiology, along with examination of the genitals and hormone and other assays. If oral therapy is unsuccessful, other studies may find underlying conditions, leading to appropriate treatment. [Rev Urol. *2002;4(suppl 3):S2–S8*]

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Over the past two decades, the concept of erectile dysfunction has evolved from that of a disorder referred to as *impotence* and considered predominantly psychogenic to that of *erectile dysfunction* (ED), a well-understood physiologic result of multiple risk factors, both organic and psychological, which result in inadequate erectile function for coitus. Masters and Johnson suggested in 1970 that the majority of ED cases were psychogenic in nature, with less than 10% involving organic abnormalities.[1] In 1972, Finkle and Thompson wrote that "pragmatic counseling" rather than psychotherapy renewed sexual function.[2] These clinicians suggested that "congestive prostatitis" was associated with a psychological burden, a "problem in the head." The first extensive epidemiologic study of male sexual behavior in the United States was reported in 1948 by Kinsey and colleagues.[3] They concluded that the prevalence of ED was less than 1% in men

younger than 30 years, less than 3% in those 30–45, 6.7% in those 45–55, 13.5% in those 55–65, 25% in those 65 and up, and up to 80% in those 80 years of age or more.

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Unfortunately, however, their sample of patients older than 55 was small, and the results for older ages not significant. It was not until the Massachusetts Male Aging Study in 1987 to 1989 and the National Health and Social Life Survey in 1992 that prevalence of ED in men in the United States was accurately measured as more than 50% in those above 40 and 31% in men overall.[4,5]

Similarly, the term *impotence* has been supplanted by the term *erectile dysfunction*, defined by the 1992 National Institutes of Health Consensus Panel as "the inability to achieve and maintain an erection sufficient for satisfactory sexual function."[6] With the introduction of new, effective, oral, noninvasive medications, such as sildenafil, to treat ED in 1998, the field of ED has been revolutionized. Indeed, the evaluation of men with ED has changed from an extensive, invasive series of procedures necessary to identify those patients who could be treated by injection therapy or surgery to an evaluation scheme to identify those patients at risk for ED, modify the risk factors, and provide a trial of oral therapy as the first line of treatment.

Despite the emphasis on organic ED, pure psychogenic ED occurs, and in those patients with organic ED an emotional aspect of sexual function is virtually always present. The problems of sexuality overlap into relationship issues; self-esteem; moral and cultural values; and patient fears about their bodies, aging, and psychological health. Clearly, appropriate management and understanding of psychological issues are essential for appropriately evaluating and treating patients, gaining their trust, and providing state-of-the-art therapy for patients with sexual concerns and dysfunction.

Setting and Approach

As a first step, a physician/patient dialogue must be initiated to fully evaluate the clinical abnormalities associated with ED. This begins with a face-to-face interview, a sympathetic history taking with privacy and physician concern to maintain patient trust, comfort, and openness. A knowledgeable professional medical staff must be available to answer questions that patients may be initially embarrassed to ask physicians. Facilitating this interaction using a standardized questionnaire may open discussion, provide comfort for the patient in initiating conversation, and allow physicians to evaluate the severity of ED.

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Standardized questionnaires available include the Brief Male Sexual Function Inventory for Urology (BSFI); the more frequently used International Index of Erectile Function (IIEF); and its short form, the five-question Sexual Health Inventory for Men (SHIM).[7,8] After initiating treatment, such outcomes questionnaires as the Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS) may be useful.[9] The BSFI is composed of 11 questions developed to measure sexual drive, erectile function, problem assessment, and overall sexual satisfaction. It is a brief, clinically validated, and standardized self-administered questionnaire that works well in the office setting. The IIEF, a cross-culturally and psychometrically validated questionnaire, is widely used in clinical trials for medications and other interventions for ED. This 15-item questionnaire is evaluated for multiple domains, including erectile function, ejaculatory function, and desire. Erectile function is graded by severity, based on a scale from 6 to 30. The shorter 5-question SHIM is, perhaps, the easiest for patients to take and for physicians to evaluate as a screening instrument. The EDITS questionnaire, not designed for initial evaluation, is useful for quantifying patient and partner satisfaction with treatment modalities initiated for ED.

In addition to a comfortable, safe environment for the patient to discuss the issue with the physician, an interview with the patient's partner may be helpful in evaluating ED. The partner may provide insight into sexual difficulties, relationship problems, and underlying health concerns that the patient may be uneasy about discussing. This may also identify the partner's approach to and valuing of intimacy and sexual function in their relationship.[10]

The physician/patient interaction, relationship, and interview have been discussed widely, and Marwick has documented that patients are clearly uneasy about bringing up the

subject of ED or sexual problems with their physicians.[11] Marwick demonstrated that more than 70% of patients felt that it would be embarrassing to discuss sexual problems and that the physician would be also be embarrassed and find the problems of ED trivial or insignificant. The burden is, therefore, on the physician to initiate questioning and begin the discussion of erectile function in patients seen either for routine visits or for treatment of diagnoses associated with risk factors for ED. The use of the SHIM in the office prior to the visit may facilitate this interaction and help the physician initiate a conversation regarding ED.

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Clinical Evaluation

The concept of what constitutes an adequate evaluation for ED continues to evolve. Prior to the introduction of sildenafil, there was an emphasis on a "goal-directed" approach to male sexual dysfunction, which included careful identification of the etiology of ED. The goal of this approach was to identify a specific etiology, after which more invasive, costly, uncomfortable treatments could be used based on the patient's treatment goals. In the era of managed care, cost consciousness, and minimally invasive safe and effective oral medications, extensive evaluation of patients is no longer the first-line approach for patients presenting with ED. It is critically important, however, to review the patient's history carefully to identify underlying physiologic risk factors, medications, and lifestyle factors that may contribute to ED, with the hope that modifying these risk factors will facilitate further treatment with oral agents.

History

A full medical history is critical, with special attention to risk factors and medications. This should be followed by a thorough physical examination, laboratory studies, and appropriate clinical diagnostic studies. ED may have any of a variety of etiologies or combinations of causative factors. History taking should include a careful sexual history to elicit these possible causes.[6] Patients should be queried regarding morning erections, nocturnal erections, erectile quality, erections during masturbation, and ejaculatory function. Open-ended questions are best for this purpose, as they provide the most spontaneous, accurate, and detailed information regarding the current status of erectile function, onset of ED, and surrounding precipitating factors.

For patients who complain of loss of libido or sexual desire, hypogonadism may be considered as a possible cause. Low libido, however, may also be caused by medications, hypochondriasis, stress, anxiety, or depression. Low libido clearly requires evaluation in order to identify patients with androgen deficiency of the aging male or other causes of hypogonadism. Those with chronic renal failure, especially if they are on chronic dialysis, may have low libido caused by low testosterone and high prolactin levels.[12] These abnormalities can be addressed by medical treatment to decrease prolactin and increase testosterone levels.

A history of ejaculatory dysfunction must also be elicited to identify patients with premature or delayed ejaculation. Younger men more often complain of premature ejaculation, whereas those in the older age group more often have difficulties with retarded or even absent ejaculation. This may be caused by natural aging, lack of androgen, neurological abnormalities, medications, or pelvic surgery. Patients with retrograde ejaculation must be suspected to have diabetes mellitus; they also may be using α adrenergic receptor agonist medication or may have had previous urological or neurological surgery.

Medical problems associated with ED may include those listed in Table 1. Each of these should be discussed with the patient during history taking. Any condition associated with cardiac disease, hypertension, diabetes, or lipid abnormalities can be associated with ED. Atherosclerosis is, indeed, a risk factor for ED in 70% of men more than 60 years of age, and ED occurs in diabetic men at 10–15 years after onset in 50% of diabetic men.[6] ED in type 1 diabetes often has a neurogenic etiology, whereas type 2 diabetics more often have vascular problems or combinations of etiologies.

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Medications are also frequently causes of ED. Some of the medications associated with ED are listed in Table 2. Most often, antihypertensive and antidepressive medications are culprits. Recreational drugs, such as cocaine, marijuana, and cigarettes

Table 1
Risk Factors for ED

Diabetes mellitus
Cardiovascular disease
Hyperlipidemia
Spinal cord injury
Cigarette smoking
Depression
Atherosclerosis
Hypertension
Pelvic surgery/trauma
Medications
Arthritis
Peripheral vascular disease
Renal failure
Substance abuse
Endocrine abnormalities
Peptic ulcer disease

also have the potential to cause ED.

Additional history should include history of penile trauma, priapism, curvature of the penis from Peyronie's disease or congenital corporal disproportion. Depression and anxiety can often be identified in this initial phase of the examination.

Physical Examination

Physical examination of patients with ED should be focused on the genitalia. A general inspection of body habitus to identify hair distribution, overweight, and secondary sex characteristics should be carried out. Patients with severe obesity should be suspected to have sleep apnea or high estrogen levels, either of which may be associated with ED. Testicular size and consistency, as well as penile anatomy, should be examined carefully. In patients with small or soft testes, hypogonadism should be suspected, and lesions of the shaft of the penis can be identified in patients with Peyronie's disease. A brief neurological examination should be carried out, with evaluation of sensation in the lower extremities, deep tendon reflexes, and perineal sensation. A bulbocavernosus or cremasteric reflex and sphincter tone on rectal examination can be quantified. Digital rectal examination for prostate size, consistency, nodularity, pain, or prostatitis should be carried out. If questions arise regarding penile sensation, vibratory sensation of the glans penis and penile shaft can be carried out in the office with a biothesiometer.[13] Results should be compared with an age-adjusted nomogram to identify patients with decreased glans penis sensation.

Laboratory Tests

Once a careful physical examination is completed, laboratory investigation should be tailored to the individual patient and goals of therapy. In patients who have not had a recent health evaluation, fasting blood glucose should be measured to identify patients at risk for diabetes mellitus. This is especially important in patients with a family history of diabetes or those with personal histories of polyuria or polydipsia. In known diabetics, a hemoglobin A_{1c} assay can evaluate control and medical compliance with diabetic therapy. Similarly, laboratory studies can include a lipid profile to identify hypercholesterolemia. In those patients with a suggestive history, a thyroid profile can be obtained as well.

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Table 2
Medications Associated with ED

β-adrenergic-receptor antagonists
Thiazide
Verapamil
Naproxen
Amitriptyline
Digoxin
Phenytoin
Hydralazine
Clofibrate
Indomethacin
Cimetidine
Omeprazole
Metoclopramide
Famotidine
Lithium
Selective serotonin reuptake inhibitor antidepressants
Antiandrogen hormones
Recreational drugs (marijuana, cocaine, and heroin)

Most important, however, is an evaluation of hormone status. Hypogonadism, though found in only a small number of patients, should be tested for in all patients with ED.[14] An initial screening of morning total testosterone should be performed to quantify testosterone level. It is important to perform this as a morning evaluation, because the daily testosterone concentration peak occurs between 8 and 10 AM. Repeat testosterone levels with free testosterone, luteinizing hormone, and prolactin levels should be performed if the initial testosterone level is suspicious. Buvat and Lemaire reviewed endocrine screening results in 1022

Table 3
Diagnostic Tests for ED

Body System	Example
Neurological	
Somatic nerves	Biothesiometry
	Nerve conduction velocities
	Evoked potentials
Autonomic nerves	Cardiovascular reflex tests
	Sympathetic skin response
	Corpus cavernosum electromyography
	Thermal threshold testing
	Urethroanal reflex latency
Vascular	
Arteriogenic	Penile brachial index
	Pharmacopenile duplex ultrasonography
	Selective pudendal arteriography
Venoocclusive	Intracavernous injections
	Pharmacopenile duplex ultrasonography
	Dynamic infusion cavernosometry and cavernosography
Psychogenic	Nocturnal penile tumescence

patients with ED and found that limiting testosterone evaluation to patients with abnormal physical examinations or decreased libido would miss 40% of patients with low testosterone.[15] They recommend testosterone determinations for all men over 50 years of age. Other hormonal studies appropriate for men with decreased libido and decreased sexual function include dehydroepiandrosterone (DHEA) and DHEA sulfate (DHEAS). Reiter and colleagues have demonstrated that replacement of DHEA in patients with low DHEA and normal testosterone levels may improve sexual desire and libido substantially in addition to improving sexual performance and erectile function.[16]

With this basic group of studies, in addition to the history, physical examination, and questionnaires, the majority of patients having ED can be identified and started on appropriate oral medications.

Other Tests

If oral medications are unsuccessful, if patients are interested in their underlying ED etiology, or if surgical intervention is contemplated, further evaluation may be required (Table 3). This evaluation may include the standard studies of nocturnal penile tumescence (NPT) monitoring and arterial and venous studies, including color Doppler arterial studies and ultimately cavernosography and selective pudendal arteriography.

NPT monitoring was first described in the 1970s by Fisher[13] for distinguishing organic and psychogenic ED patients. It is well known that normal men have significant erectile activity during rapid eye movement sleep. A total of four to six erections occur during the usual night's sleep, with base and tip rigidity greater than 55% sustained for at least 10 minutes. The RigiScan recording device (Timm Medical, Augusta, GA) is an economical, safe, noninvasive home monitoring device for evaluating NPT.[13] Although controversy remains regarding the diagnostic accuracy of NPT evaluation, it may be useful in differentiating patients with organic and psychogenic ED and for use in medical legal situations. False-negative results may occur in patients having depression, sleep disorders, or sleep apnea or using sleep-altering medications, tobacco, or caffeine. The overall accuracy of NPT monitoring is approximately 80%.[17] An abnormal NPT test should be confirmed with at least two nights' study and subsequent independent validation studies, such as duplex Doppler ultrasound after intracavernosal injection of alprostadil studies.

Although specific widely available clinical studies for neurogenic testing (except for tactile testing) have limited availability, such studies as dorsal nerve conduction velocities and sacral nerve evoked potentials may be useful in some patients and are available at research institutes and ED centers. Vascular studies of the arterial and venous systems can be used to obtain accurate determination of vascular function and anatomy.

Older studies using hand-held Doppler with penile brachial index identification appear to be inaccurate and poorly reproducible. The use of duplex ultrasound color Doppler flow studies with intracavernosal injection of vasoactive agents, however, can facilitate careful evaluation of both the arterial and the venous systems that produce erections in a functional fashion. In 1985, Lue and colleagues reported that the combination of intracavernous injections of vasoactive agents with duplex ultrasonography provided high-resolution sonography and pulsed Doppler blood flow analysis to evaluate the penile arteries and provide information regarding venous outflow

incompetence.[18] This noninvasive technique measures cavernous arterial diameter, detects abnormalities in cavernous bodies, such as fibrosis and calcifications, and evaluates venous outflow. In 1990, Mueller and associates compared selective internal iliac arteriography with duplex Doppler ultrasonography for the diagnosis of arteriogenic ED.[19] In the 43 men evaluated, selective arteriography and duplex sonography correlated with duplex ultrasound in 91% of cases, providing higher diagnostic accuracy than selective arteriography alone. Duplex ultrasonography can also indirectly identify venous leak or venoocclusive ED. If venoocclusive dysfunction is suspected from initial studies, dynamic infusion cavernosography and cavernosometry can be performed to identify areas of venoocclusive dysfunction and indicate whether surgical or nonsurgical intervention is appropriate.

In patients with suspected traumatic injuries to the arteries supplying the penis, selective pudendal arteriography in combination with intracavernous injection can provide an accurate review of the penile arterial anatomy and identify those who are candidates for arterial revascularization. Duplex Doppler studies can identify those in whom arteriography may be helpful. Ideal candidates for this procedure include those with a solitary obstructive lesion of the pudendal arterial system who are less than 40 years of age and nonsmokers who have no other significant vascular disease risk factors, such as diabetes or hypercholesterolemia.

Conclusions

ED is currently treatable with safe, effective oral medication that can restore not only erectile function but quality of life for men with sexual problems. The most important part of evaluation of patients with ED is asking them about their erectile status. Although clinical diagnostic studies, laboratory studies, and physical examination may provide many possible findings, the most important part of evaluation and treatment is taking an adequate history and eliciting information on an erectile problem from patients. An adequate physician/patient rapport is the most important starting point for successful treatment of ED. ■

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Main Points

- Erectile dysfunction (ED) has a variety of possible etiologies, including combinations of factors.
- Having the physician bring up the subject and the use of a standardized questionnaire may help elicit information from patients who are uncomfortable discussing ED.
- Medical conditions associated with ED include cardiac disease, hypertension, diabetes, and lipid abnormalities; medications, especially antihypertensives and antidepressants, can also increase the risk.
- Physical examination should focus on the genitals and may include a neurological evaluation in addition to the routine overall exam.
- Evaluation of hormone status is the most important part of laboratory studies for ED, but blood glucose and cholesterol tests should also be performed to identify underlying conditions.
- Nocturnal penile tumescence monitoring, further neurological testing, and vascular studies may be appropriate if initial oral treatment fails.

Summary of Discussion Following Dr. Carson's Presentation

Dr. Carson summarized the main points of his presentation as: 1) Ask the question. The most important thing is to ask patients if they have erectile dysfunction and to begin the history; 2) Do the appropriate physical examination and appropriate laboratory studies.

Dr. McCullough asked Dr. Carson if he felt that the working paradigm for the urologist had changed, given that 86% of men with ED are being diagnosed primarily by non-urologists, and that urologists are now seeing more complicated patients, many who have failed oral therapy. What, he asked, should the urologist to do at this point?

Carson replied that at that point it depends on the individual patient and the needs of the referring physicians. The first thing to do is to make sure that the patient is taking the oral agents appropriately. Also, often patients do not have a hormone profile when the urologist sees them. Carson asserted that a hormone profile is extremely important in these patients, because he thinks androgen deficiency is underdiagnosed in many patients. If the androgen profile is normal and the patient still is not responding to sildenafil, at that stage a vascular diagnostic schema can begin if the patient or his primary physician want to investigate the underlying cause of the ED.

"I think," Carson said, "at that stage we go back to what was described by Tom Lue in the early 1990s as the goal-oriented approach to erectile dysfunction." The patient should be asked what they are interested in, where do they want to go with treatment? If they are interested in proceeding and trying injection therapy, then an in-office injection will identify the patient who will respond to that particular treatment. If the patient responds to injection and that is as far as he wants to go, then he has a treatment that works for him.

McCullough countered, "The primary care clinician sent him to you to find out why he failed sildenafil. Have you answered that question?"

Carson responded, that if that is the question that the patient, the partner, and the physician want to know the answer to, then at that stage a Doppler study or NPT is appropriate. Those are good tests, either taken together or done separately. But the point is that the majority of patients really are not interested, and the majority of referring physicians are more interested in a successful treatment outcome. If the urologist is convinced that the patient took the oral medication correctly, that the patient doesn't have a relationship problem and is not depressed, and it therefore seems that the ED is organic in etiology, there is no need for diagnostics. Testing is not necessary in any of those patients unless the patient says, "I want to know if I have vascular disease."

Dr. Steers agreed, stating his opinion that testing does not tell much, in terms of ruling out vascular disease. The role of testing would be great, he said, if there were tests that had very high specificity and sensitivity, but there are not. In the absence of those tests, the only reason to do injections in the office is to teach patients how to do them and as a predictor of response to injection therapy.

Carson returned to the theme of the goal-oriented approach. The patient that walks in the door may not really want to know what the etiology of his ED is. He wants something that will work; he wants treatment. Is it worthwhile for the physician to go through a very complicated diagnostic algorithm, costing several of thousands of dollars, only at the end to say, "Well, we're not really sure what's going on?" Then the patient is back to starting injection therapy, despite the workup. The specificity and sensitivity of the tests available now are not adequate to warrant putting every patient through them, and the tests do not tell which therapy is going to work.

Dr. Montague echoed the need for a good history and the lack of utility of diagnostic tests in men undergoing implant surgery unless there are medico-legal issues.