

# Laboratory Evaluation of the Patient with Erectile Dysfunction

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**Erectile dysfunction (ED) as a clinical entity is a problem that more than 50% of men will face as they age, and it can adversely affect overall quality of life and impact sexual partners. Our understanding of the pathophysiology and the multiple risk factors that contribute to ED has led to successful treatments, both non-surgical and surgical, over the past two decades. Now, more nonurologists and primary care providers are seeing patients for their initial evaluation. It is imperative that they approach the workup and evaluation in a logical and efficient manner. After a thorough history and physical examination, followed by a relevant and systematic laboratory evaluation, most cases can be effectively identified and medical treatment can be initiated. However, patients who continue to have erectile difficulties or fail initial oral treatment are candidates for specialized evaluation of vascular, neurogenic, and hormonal dysfunction, which can lead to more specific treatment or possible surgical management.**

**Key Words:** Erectile dysfunction; hypogonadism; laboratory evaluation; nocturnal penile tumescence.

## Introduction

Erectile dysfunction (ED) is defined as the inability to achieve or maintain an erection suitable for sexual intercourse. The concept of ED has evolved over the past two decades from mere “impotence,” in which the etiology was often attributed to a psychogenic cause, to the better understood disorder that is the result of multiple risk factors, both organic and psychological, as well as concomitant medical disease (1). Many clinicians now recognize that ED can often be a sentinel symptom in a patient with an occult vascular or endocrinologic disease. Early epidemiologic studies in the United States underreported the prevalence of ED, and it was not until the publication of the Massachusetts Male Aging Study in 1989 as well as the Social Life Survey in 1992 that the wide scope of ED was placed into an appro-

priate context. These studies estimated overall prevalence at 31% and more than 50% in men over the age of 40 (1–3). In addition to medical disease, patient age and lifestyle are contributing factors to overall potency. Since the introduction of viable oral treatment, public awareness of ED has gained a firm foothold within popular culture, and patients are more apt to seek treatment. Therefore, more nonurologists—general internists, endocrinologists, family practitioners—are seeing patients during their initial presentation of ED. A thorough evaluation of a patient with ED should include a detailed history, sexual inventory, physical examination, and laboratory investigation.

## History and Physical Examination

A complete history is a critical first step in the evaluation of ED. The clinician in a face-to-face patient interview should scrutinize the patient’s medical and surgical history. Diseases such as diabetes, hypertension, hyperlipidemia, depression, renal insufficiency, hypogonadism, and cardiovascular disease, as well as prior pelvic surgery or penile trauma, can be the root cause of or contribute to the development of ED (4). Equally important is a review of the patient’s medications (Table 1) because those used to treat hypertension and depression are often implicated as culprits (1,2). Clinicians must direct questions to assess libido, quality of erections during masturbation and intercourse, presence of nocturnal erections, and overall ejaculatory function (5). A complete sexual history also should include validated questionnaires such as the Sexual Health Inventory for Men and International Index of Erectile Function to assess erectile quality, or the Androgen Deficiency in the Aging Male survey to assess possible androgen deficiency (1,2). These questionnaires can guide the subsequent workup and are convenient and easy for patients to complete during their clinical visit. Most urologists also advocate partner interview because she or he can provide insight into relationship problems, sexual difficulties, and her or his overall value of sexual function and intimacy (1). Obese patients, especially those with possible upper airway obstruction, should be queried about sleep habits and loud snoring because there appears to be a link between obstructive sleep apnea and ED (6). These patients may require referral and further workup with a sleep study with continuous pulse oximetry. Clinicians should also be aware that ED can be the presenting complaint of patients with “metabolic syndrome”

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**Table 1**  
Medications Linked to ED

Antihypertensives and miscellaneous cardiac	Antidepressants, antiepileptics, neuroleptics	Antiulcer and miscellaneous gastrointestinal	Nonsteroidal antiinflammatories	Other (recreational drugs)
$\beta$ -Adrenergic blockers	Tricyclics	Cimetidine	Indomethacin	Tobacco abuse
Calcium-channel blockers	Monamine oxidase inhibitors	Omeprazole	Naproxen	Alcohol abuse
Thiazides	Serotonin reuptake inhibitors	Ranitidine		Marijuana
Hydralazine	Phenytoin	Metoclopramide		Cocaine
Digoxin	Lithium, phenytoin, chlorpromazine			Heroin

**Table 2**  
Laboratory Testing for ED

Recommended	Optional	Specialized
<ul style="list-style-type: none"> <li>• Fasting glucose</li> <li>• Glycosylated hemoglobin<sup>a</sup></li> <li>• Fasting lipid profile</li> <li>• Testosterone</li> </ul>	<ul style="list-style-type: none"> <li>• AM Free, total testosterone<sup>b</sup></li> <li>• LH</li> <li>• PRL</li> <li>• FSH</li> <li>• SHBG</li> <li>• Estradiol</li> <li>• Thyroid-stimulating hormone</li> <li>• Complete blood count</li> <li>• Urinalysis</li> <li>• PSA<sup>c</sup></li> <li>• Psychologic testing</li> </ul>	<p><i>Vascular</i></p> <ul style="list-style-type: none"> <li>• Pharmacopenile duplex ultrasonography</li> <li>• Selective pudendal arteriography</li> <li>• Penile Brachial Index</li> <li>• Infusion cavernosometry</li> </ul> <p><i>Neurologic</i></p> <ul style="list-style-type: none"> <li>• Biothesiometry</li> <li>• Pelvic evoked potentials</li> <li>• Dorsal nerve conduction velocities</li> <li>• Corpus cavernosum electromyography</li> </ul> <p><i>Psychogenic</i></p> <ul style="list-style-type: none"> <li>• Nocturnal penile tumescence</li> </ul> <p><i>Hormonal</i></p> <ul style="list-style-type: none"> <li>• Magnetic resonance imaging of the head (in secondary hypogonadism)</li> </ul> <p><i>Hypoxia/sleep apnea</i></p> <ul style="list-style-type: none"> <li>• Sleep study</li> </ul>

<sup>a</sup>Hemoglobin A<sub>1C</sub> in known diabetics to determine glycemic control.

<sup>b</sup>Measure free testosterone by equilibrium dialysis, or calculate from total testosterone and SHBG, or measure bioavailable testosterone by ammonium sulfate precipitation.

<sup>c</sup>If the patient is over 50, PSA testing is recommended.

—a constellation of findings exhibited in patients as abdominal obesity, insulin resistance, hyperlipidemia, and hypertension (7).

On physical examination, secondary sexual characteristics and appropriate virilization should be assessed. The penis should be examined for fibrotic lesions or curvature that could identify Peyronie disease (1,2,5). Small or atrophic testicles, alteration or lack of body hair, and presence of gynecomastia should raise suspicion of hormonal dysfunction and warrant further evaluation (8). Digital rectal examination should evaluate for prostatic disease by assessing size, consistency, nodularity, or pain. Sensory examination of peripheral extremities and genitals, deep tendon reflexes, and evaluation of the bulbocavernosus reflex can assess for neurologic impairment. Vascular assessment includes measurement of blood pressure, carotid auscultation,

palpation for abdominal aneurysms, and qualification of distal pulses (5).

## Recommended Studies

In the era of managed care and escalating costs, it is not feasible to embark on a lengthy and costly diagnostic workup for every patient. The information gleaned from the history and physical should serve as an effective guide for the ensuing clinical and laboratory evaluation. It is also important to tailor the laboratory workup to the individual patient and the goals of therapy. The First International Consultation on Erectile Dysfunction established three levels of clinical testing: recommended, optional, and specialized (9). The recommended studies (see Table 2) are generally those used to identify or rule out a particular pathologic process

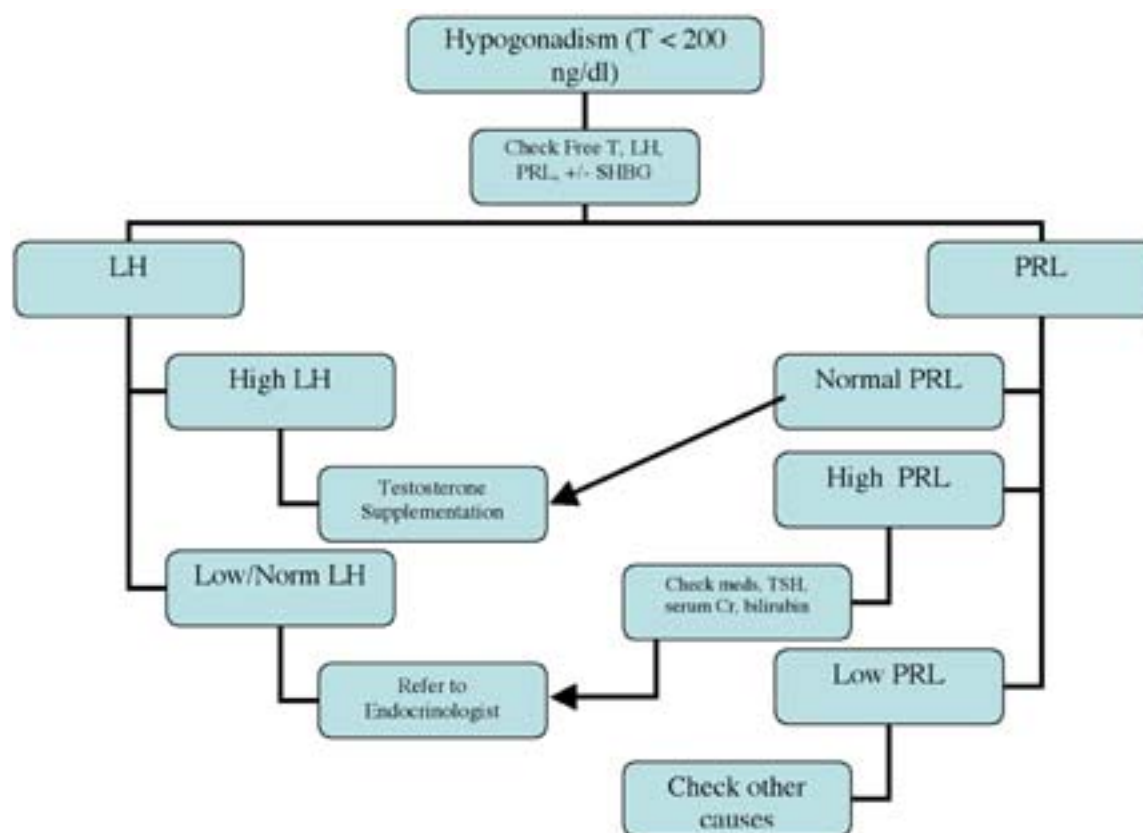


Fig. 1. Simplified endocrinologic evaluation of hypogonadism. TSH, thyroid-stimulating hormone.

or disease entity such as diabetes, hyperlipidemia, or dysfunction of the hypothalamic-pituitary axis. The remaining studies listed in Table 2 are utilized at the discretion of the clinician and often require referral to a specialist.

First, a fasting blood glucose is a simple test that can identify patients at high risk of diabetes mellitus (impaired fasting glucose [110–125 mg/dL]) because ED may be an early symptom of the disease. Second, known diabetic patients, hemoglobin A<sub>1C</sub> or glycosylated hemoglobin assay serves to establish the patient's level of control or compliance with medical management (8). Third, a fasting lipid profile is important to identify hyperlipidemia, especially in patients with a strong family or medical history of cardiac or peripheral vascular disease. Atherosclerosis, a risk factor for ED in 70% of men and patients with excessive cholesterol or triglyceride levels, should be managed appropriately with lifestyle modifications and medical therapy by a primary care physician (1,5).

Complete hormonal profiles have been shown to be cost-ineffective when the testosterone level is within normal limits. Therefore, the final and perhaps most important of the recommended studies is a total testosterone level. Routine testing of testosterone level has sparked debate among clinicians because the incidence of hypogonadism in men with ED has been estimated as low as 2% (2,8). Complicating the discussion further is the notion that the absence of tes-

tosterone is more closely linked with decreased libido than ED since up to 20% of elderly men with castrate levels of testosterone or who have undergone estrogen supplementation can still maintain erections (10). Most studies show that dehydroepiandrosterone (DHEA) and DHEA sulfate levels also fall with aging and can be implicated in the decline of sexual function and libido (2,11). Reiter et al. (12) showed that replacement of DHEA in patients with low levels but normal testosterone can improve sexual desire and libido. Despite the low probability of finding hypogonadism in patients with ED, when it is present, it may herald a more serious underlying endocrinopathy (8). Some urologists favor obtaining a testosterone level only if the patient has symptoms of low libido or evidence of testicular atrophy. However, Buvat and Lemaire (13) concluded that more than 40% of hypogonadal men would be missed if testing parameters were limited to low libido or atrophy. When measuring testosterone, given the diurnal variation, the collection should occur in the morning because concentrations tend to peak between 8 and 10 AM. If the testosterone level is subnormal, additional studies (Fig. 1) should follow, including free and total AM testosterone levels and prolactin (PRL) (13). Free testosterone can be measured directly or calculated from total testosterone and the measured sex hormone-binding globulin (SHBG). Bioavailable testosterone, which includes the free and the albumin-bound

testosterone, also provides a valid measure when SHBG levels are altered or when total testosterone levels are between 200 and 400 ng/dL. Hyperprolactinemia (>50 ng/mL) is most commonly caused by drugs, hypothyroidism, and renal or liver disease. In the absence of these conditions, it can signify the presence of a pituitary tumor (8). Patients for whom this is a possibility should be referred to an endocrinologist. Luteinizing hormone (LH) should also be measured to differentiate between primary and secondary hypogonadism. Treatment with testosterone supplementation can be initiated in patients with primary testicular failure. Patients with low or inappropriately normal LH levels and an early morning serum total testosterone <200 ng/dL should be referred to an endocrinologist (8). Additional studies that may be helpful include follicle-stimulating hormone (FSH) and estradiol.

### Optional Studies

After completion of the aforementioned laboratory work-up, in addition to the thorough history, sexual history, and physical examination, ED can be appropriately identified in most patients and medical treatment can be initiated. However, for those patients who continue to have ED without a clear etiology or who fail initial therapies, there are additional optional and specialized tests. It should be stated that these optional laboratory studies should most certainly be included in the initial workup if there is a suspicion of additional disease processes or if they are clinically warranted. For example, if there are historical or physical findings suggestive of thyroid dysfunction or liver disease, then thyroid and liver function panels should be assessed. Most urologists will evaluate a prostate-specific antigen (PSA) level if the patient presenting with ED is over the age of 50 as a screening modality for prostate cancer (1,5). Establishing the PSA level early in the laboratory workup is critical if androgen supplementation will later become part of the therapeutic regimen. A complete blood count can evaluate for anemia and can suggest underlying disease. Urinalysis obtained as a clean-catch specimen can reveal proteinuria in renal dysfunction, hematuria in patients with urothelial malignancies or prostate disease, and glucosuria and ketonuria in patients with poor glycemic control (1). Finally, psychiatric or psychosocial investigation and testing may be warranted in patients who have no organic basis for their inability to achieve erections or who demonstrate neurovegetative findings of depression. Psychogenic ED is usually found in patients who are able to obtain adequate erections with masturbation or with a person who differs from their regular partner (8).

### Specialized Studies

For the remainder of patients who continue to respond poorly to conservative treatment, specialized testing exists

to evaluate vascular and neurogenic causes of ED or assist in the differentiation between organic and psychogenic ED. Specialized studies usually involve referral to a urologist or medical specialist and are generally pursued to elucidate further the cause of a patient's ED or are obtained prior to pursuing surgical intervention. Nocturnal penile tumescence (NPT) testing was developed to help differentiate organic vs psychogenic ED (1,5). Most men have approximately three to five erections during sleep, the majority of which occur during rapid-eye-movement phase. The test involves the use of a Rigiscan (Timm Medical, Augusta, GA), a convenient home device that allows the patient to administer the test over several nights to evaluate NPT (1). Disposable strain-gage loops are attached to the base and tip of the penis and connected to a monitor; during tumescence, the circumference is measured and rigidity is calculated (1,5). More advanced forms of NPT testing involve measurement of axial strain or buckling pressure of the tumescent penis to assess for suitability for penetration (8). This advanced testing method requires patient participation in a sleep center. If the NPT test is positive, there is more likely to be a psychogenic component to the patient's ED. Studies estimate NPT accuracy to be about 80%; however, false negative results arise in patients with severe psychosis, depression, or sleep disorders, or in those who use sedative medication (1). Patients with neurologic impairment from trauma or autonomic neuropathy can have significant ED (14). Neurologic testing can play a role in the evaluation of ED by assessing dorsal nerve conduction velocities or sacral nerve potentials. Most information can be obtained from tactile testing or with the use of biothesiometry and obviates the need for sophisticated nerve studies, which may only be offered in research centers. Vascular insufficiency is first assessed by noninvasive studies such as Doppler ultrasound (1). This technology has improved markedly over the past two decades with the advent of color-flow duplex ultrasonography. Lue et al. (15) demonstrated the efficacy of color-flow duplex ultrasonography after intracavernosal injection of a vasoactive agent (i.e., alprostadil) to assess for arterial insufficiency. This minimally invasive study compares favorably with arteriography and also provides evidence for venoocclusive insufficiency or venous leak. It should be performed prior to cavernosometry. If the patient's ED was the result of trauma, then selective pudendal arteriography can provide a road map for possible revascularization surgery. This type of ED comprises a rare subset, and ideal patients for bypass surgery are typically less than 40 yr-old, and nonsmokers, and have evidence of a solitary lesion and no comorbid vascular disease or diabetes (1,5).

### Conclusion

ED is a highly prevalent disease complex made up of multiple risk factors and comorbid medical diseases. After a thorough history taking and physical examination, an

appropriate and selective laboratory evaluation is warranted prior to initiation of treatment. Although it is important to focus on the appropriate studies for each patient, the minimum laboratory workup should include a fasting blood glucose or glycosylated hemoglobin, lipid profile, and total testosterone level. If a clear etiology remains elusive or if patients fail initial medical therapies, additional studies may be warranted. Specialized assessment of neurologic, vascular, and hormonal profiles often requires referral to a specialist, especially if surgery becomes the definitive treatment.

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