

Guideline for

The Investigation and Management of Erectile Dysfunction

This clinical practice guideline replaces the Alberta Laboratory Endocrine Testing Guideline for the Investigation of Impotence and Male Androgen Insufficiency.

GOAL

- ◆ To assist physicians with the investigation and management of erectile dysfunction (ED)

DEFINITION

- ◆ Inability to have or sustain an erection adequate for satisfactory sexual activity for at least 3 months¹

EXCLUSIONS

- ◆ This guideline does not apply to those patients with:
 - Other forms of sexual dysfunction (i.e., lack of sexual desire, premature ejaculation)
 - Peyronie’s Disease not associated with erectile dysfunction

RECOMMENDATIONS (See [Algorithm](#))

PRACTICE POINT

- ED is an issue that impacts relationships
- Explore the impact with both partners

TABLE 1

Commonest Causes of ED

- ◆ Diabetes
- ◆ Cardiac and peripheral vascular disease
- ◆ Medications linked to ED (see page 2)
 - Including substance abuse and cigarette smoking
- ◆ Psychogenic
 - Anxiety or depressive disorder
 - Concern about poor sexual function
 - Previous traumatic sexual experience

Diseases with a High Prevalence of ED

- ◆ Renal failure
- ◆ Liver disease
- ◆ Multiple sclerosis
- ◆ Spinal cord injuries
- ◆ Penile anomalies or disease (Peyronie’s Disease)
- ◆ Pelvic surgery
- ◆ Pelvic trauma
- ◆ Prostate cancer treatment
- ◆ Hypogonadism

PRACTICE POINT

Testosterone deficiency is an uncommon cause of ED

The above recommendations are systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances. They should be used as an adjunct to sound clinical decision making.

Initial Assessment

History

PRACTICE POINT

History is the most important component in the evaluation of ED

- ◆ Detailed medical, sexual (**see Appendix**) and social history to:
 - Rule out decreased libido, ejaculatory disorders, performance anxiety, depression, and other psychological disorders
 - Identify reversible causes (e.g., recently prescribed medications such as antidepressants or anti-hypertensives: see box below) with concurrent development of ED
- ◆ Consider evaluation for diseases associated with ED (see Table 1 - page 1)

Medications Linked to ED

- ◆ Antiandrogens
- ◆ Mood stabilizers
- ◆ Estrogens
- ◆ Cytotoxic drugs
- ◆ Antiarrhythmics
 - Digoxin
- ◆ Histamine H₂ receptor antagonists
- ◆ Antidepressants
- ◆ Narcotics
- ◆ Lipid lowering medications
- ◆ Nonsteroidal anti-inflammatory drugs
- ◆ Antihypertensives
- ◆ Barbiturates
- ◆ Diuretics
- ◆ Ketoconazole
- ◆ Beta-blockers
- ◆ Anticonvulsants
- ◆ Antipsychotics

Focused Physical Examination

- ◆ Perform focused physical examination for signs of hypogonadism:
 - Gynecomastia
 - Decreased male hair distribution
 - Small testes
- ◆ Perform focused examination for signs of vascular disease and diabetic complications (including blood pressure, ankle brachial index and peripheral pulses)

Laboratory Evaluation

- ◆ Screen for unrecognized systemic disease (e.g., diabetes, hypogonadism - see Algorithm)

Management

PRACTICE POINT

A psychogenic component is present in all cases of erectile dysfunction. Counselling of patient (+/- partner) is recommended

- ◆ Treat associated medical conditions. **Note: This alone may not reverse ED.**
and/or
 - ◆ Modify medication regimen
- ◆ If laboratory test abnormal: hormonal cause suspected:
 - If testosterone low and LH and FSH high: consider testosterone replacement therapy
 - If prolactin high: consider pituitary imaging and referral
- ◆ If psychogenic cause suspected consider:
 - Sex therapy/psychiatric referraland/or
 - Trial of therapy (education, oral medications, intraurethral medications, vacuum constriction device, etc.)

- ◆ If neurogenic cause suspected consider:
 - Trial of therapy (education, oral medications, intraurethral medications, vacuum constriction device, etc.)
- ◆ If vasculogenic cause suspected a trial of medication or referral is warranted

Referral

- ◆ Common indications for referral include:
 - Failed medical therapy
 - Significant penile anatomic disease
 - A younger patient with a history of pelvic or perineal trauma
 - Cases requiring vascular or neurological assessment
 - Complicated endocrinopathies
 - Complicated psychiatric or psychosocial problems
 - Patient or physician desire for further evaluation

Follow-up

- ◆ Patients should be seen after initiation of treatment to evaluate progress and monitor therapy (e.g., testosterone)

BACKGROUND

Epidemiology

The definition of ED is the inability to have or sustain an erection adequate for satisfactory sexual activity.¹ It is one of the most common chronic medical disorders in men over the age of 40. In an American study, 39% of men aged 40 to 70 reported moderate or complete impotence, with 52% of the whole group reporting some degree of ED.² The prevalence and severity of the disorder increases with age; men in their 50's are 3 times more likely to experience ED than men in their 20's. It is estimated that moderate to complete ED affects 45% of men in their mid sixties, with a further increasing prevalence in older age groups.^{2,3}

Pathophysiology

Two-thirds of cases of ED are organic in origin and comorbid conditions should therefore be actively evaluated. Heart and vascular diseases (especially those associated with hyperlipidemia, diabetes, and hypertension) are associated with ED.^{2,4} The combination of these conditions and aging increases ED risk in older men. Other hormonal and metabolic problems including primary and secondary hypogonadism, hypothyroidism, chronic renal failure, and hepatic failure, also negatively impact on erectile function.⁵ Substance abuse, such as excessive intake of alcohol or other recreational drugs is a major contributor to ED. Smoking, a known cause of arterio-occlusive disease, is clearly a co-factor and probably an independent etiologic factor itself. Penile anatomical defects and Peyronie's Disease may contribute to erectile problems. Psychogenic disorders, including depression, dysphoria, and anxiety states are associated with an increased incidence of multiple sexual dysfunctions including erectile difficulties.⁶ Spinal cord injuries, pelvic and prostate surgery and pelvic trauma are less common causes of dysfunction. Iatrogenic ED can be caused by nerve disrupting pelvic or prostate surgery; inadequate glycemic, blood pressure, or lipid control; and many of the medications commonly used in primary care. Antihypertensives, notably diuretics and central acting agents, can cause ED, as can digoxin, psychopharmacologic agents, including some of the newer antidepressants, and anti-testosterone hormonal agents. Testosterone levels do decline slightly with age but are only related to ED in the small minority of men who are truly hypogonadal and have low hormone levels.

Diagnosis

Medical History

The medical history should include review for risk factors and screening for psychological difficulties. A medication review, including over-the-counter drugs may reveal the source of the problem since medications have been implicated in up to 25% of cases of ED.⁷ Some medications have adverse effects on all phases of sexual functioning, making

clarification of the patient's complaint a priority before ascribing symptoms to specific medication side-effects.⁸

In evaluating for the presence of psychological problems, brief screening for depression may elicit responses. Other psychiatric conditions, such as anxiety, may also be responsible for ED. It is critical that the social history looks for stress surrounding a relationship or substance abuse including alcohol and cigarettes. Specific questions regarding the presence of claudication during activity (e.g., walking up stairs), or decreased thigh muscle strength or size increases suspicion for pelvic inflow vascular occlusive disease. Finally a review of daily activities and a review of cardiovascular status is important to determine the potential risk for enhancing ED in patients who may have a sedentary lifestyle and who may be at risk for an adverse cardiac event when sexual activity potential is increased.⁹

Sexual History

A sexual history is the most important component of diagnosis. Some physicians may find it useful to use a sexual health questionnaire (see Appendix) and to involve the partner as this will not only confirm the problem but also may reveal other causes of sexual dysfunction.

Focused Physical Examination

The physical examination should be comprehensive, with emphasis on several areas.¹⁰⁻¹¹

Evaluation of blood pressure, cardiac size and heart sounds, and a complete peripheral vascular examination looking specifically for abdominal or femoral bruits, diminished femoral pulses, or thigh muscle wasting (signs of decreased pelvic inflow), may contribute to the diagnosis of vascular disease as an associated cause. A neurologic examination that includes the evaluation of pelvic sensory function and anal sphincter tone is needed to confirm both sympathetic and parasympathetic function. A digital rectal examination of the prostate should be conducted and a visual and manual exam of the penis to discover any anatomical defects and help to identify Peyronie's Disease.

Immature secondary sex characteristics, including lack of male hair distribution, poor penile and testicular development, gynecomastia, and fine wrinkling at the corners of the eyes and mouth, indicate the possibility of hypogonadism.

Laboratory Evaluation

Laboratory testing in the evaluation of ED looks for the risk factors/entities previously identified. A urine analysis to rule out renal disease or infection, a complete blood count to note any potential hematologic disorder, a chemistry profile to check for glucose and renal function, a lipid profile to rule out hyperlipidemia, and TSH to evaluate thyroid function. Prostate specific antigen (PSA) should be considered in men with risk factors for prostate cancer especially if testosterone treatment is a possibility. Some experts recommend a morning serum free testosterone and prolactin level, but the value of routine endocrinologic testing is controversial.¹² If the patient is well known to the physician and the problem is clearly not related to libido or ejaculatory disorders, and there are other contributing factors that can account for the ED, these tests can be ordered on an individual basis. If there is any evidence of hypogonadism or the dysfunction is particularly consistent at a young age, this further hormone evaluation is obligatory.

Advanced testing with nocturnal penile tumescence studies and vascular evaluation with sonography, and other tests are somewhat subjective and rarely provide useful information except in cases of trauma or other vascular injury, or if there is a need for legal documentation. Referral may be indicated for these studies.

Treatment

Counselling

Because ED always has a psychological component, patient or couple counselling may help reduce anxiety and overcome the condition. This therapy is sometimes used in combination with other treatments as directed by the doctor.

Lifestyle Modification

Making healthy lifestyle changes can reduce the symptoms of ED and improve general physical health (see Table 2). Patients need to understand that what is bad for the heart and the peripheral vascular system or the nervous system is bad for the penis. Elimination of smoking is critical as may be elimination of all other recreational drug use. The occurrence of ED in the smoking patient provides an opportunity to discuss smoking cessation. Dietary issues including reduction of cholesterol and fats, eliminating hyperglycemia when present, and decreasing salt intake when salt sensitive hypertension is noted, all help to reduce the progression of vascular insufficiency. Exercise can increase cardiac output and improve peripheral circulation. Moderate exercise for sedentary men may minimize the small increase in relative risk of a myocardial infarction.¹³⁻¹⁴ Prevention of obesity is associated with a decreased risk of ED.¹⁵

TABLE 2

Recommended Lifestyle Changes

- ◆ Smoking cessation
- ◆ Reduction of fat and cholesterol in diet
- ◆ Increased exercise
- ◆ Weight loss
- ◆ Improved compliance with diabetes and cardiovascular medications
- ◆ Reduction of stress

Changing medication regimens to remove causative agents can be tried when good alternatives are available and the clinical situation permits pharmacologic adjustments. Medication changes must be individualized depending upon the specific clinical circumstances.

Specific treatment regimens for ED are varied; they include oral medications, transurethral suppositories, intracavernosal injection, vacuum devices, and surgery.

Oral Medications

The most effective and useful drugs available are inhibitors of **phosphodiesterase type V**, an enzyme present predominantly in the penile smooth muscles and responsible for vasoconstriction. Currently, sildenafil (VIAGRA[®]) is the only marketed such drug but newer, more selective phosphodiesterase V inhibitors are in clinical trials. Randomized trials demonstrate that sildenafil is effective in most etiologies of ED with efficacies of up to 80%. In some groups, i.e., post radical prostatectomy, sildenafil may have lower efficacy ranging from 40 to 57%.¹⁶⁻¹⁹

Lower doses (25mg) of sildenafil may be given to patients who are elderly, have renal or hepatic insufficiency, have spinal cord injury (where there is an increased sensitivity to sildenafil), have moderate to severe coronary vascular insufficiency not using nitrates (see note below), or are taking another drug that is a cytochrome P450 inhibitor).

Note: When used in conjunction with nitrate containing medications, sildenafil can cause excessive vasodilation and hypotension, which can result in death. The use of nitrate containing medication is a definite contraindication to prescribing sildenafil. Recent data suggest severe coronary disease may not be a contraindication to sildenafil. However, data is limited and caution is urged in these situations.

The efficacy of **Yohimbine** (another oral medication) in improving ED has never been clearly proven, especially when the strong placebo effect of any oral medication for this problem is considered.¹⁴

Non-oral Medications

PRACTICE POINT

- Testosterone therapy requires thorough evaluation to exclude prostate cancer (in men over age 45 conduct DRE + PSA) prior to starting therapy
- Monitoring of therapy is mandatory

Testosterone therapy, available in intramuscular injection (testosterone enanthate or cypionate), oral (testosterone undecanoate), or by dermal patch should be used only for patients with documented hypogonadism. Generally, testosterone augmentation is associated with enhanced libido. This may improve erectile status by restoring interest and perhaps through other neurohormonal mechanisms, however, relying solely on testosterone to restore ED is inappropriate.²⁰ Monitoring includes surveillance for prostate cancer (yearly rectal examinations +/- PSA) and detection of polycythemia (measure hematocrit every 6 to 12 months; decrease testosterone dose if hematocrit rises above normal range).

Alprostadil (MUSE[®]) is a prostaglandin E preparation in a pellet form that is inserted with a plunger-like device into the urethral opening.²¹

Intracavernosal injection therapy can be considered when oral medications appear to be ineffective. This injection is given directly into the corpus cavernosum through the side of the penis. The success rate is high, but problems include pain, prolonged erections or priapism, and penile fibrosis and plaques.²² It is recommended to start with the minimal effective dose and titrate upwards. Spinal cord injury patients often have an exaggerated response and require lower doses. The recommended maximal frequency of usage is 3 times weekly with 24 hours between dosages.

Note: Caution should be exercised in patients on anticoagulation medications.

Vacuum devices are a reasonable choice for many men who are in a stable relationship if their partners are willing to accept the inconvenience.²³ Sickle Cell Disease is a contraindication and anticoagulation is a caution.

Penile implant surgery is a very successful therapy, although it should be reserved for patients who have considered or tried several other treatments. The surgery is irreversible and the normal function of the corpus cavernosa is obliterated. The surgery carries low morbidity and mortality and the satisfaction rate is high. It is a well established urological procedure.

Indications for Referral

Common indications for referral to a specialist include: significant penile anatomic disease; a younger patient with a history of pelvic or perineal trauma; cases requiring vascular or neurosurgical intervention; complicated endocrinopathies; complicated psychiatric or psychosocial problems; and patient or physician desire for further evaluation.

REFERENCES

1. NIH Consensus Development Panel on Impotence. JAMA, 1993; 270: 83-90
2. Feldman H, Goldstein I, Hatzichristou D, et al. Impotence and its medical and psychological correlates: results of the Massachusetts male aging study. Journal of Urology, 1994;151: 54-61.
3. Morley J. Impotence. American Journal Medicine, 1986; 80: 897
4. Benet A, Melman A. The epidemiology of erectile dysfunction. Urology Clinics of North America, 1995; 22: 699-709.
5. Wierman M, Casel C. Erectile dysfunction: a multifaceted disorder. Hospital Practice, October 1998:65-90.
6. Bartlik B, Kocsis J, Legere R et al. Sexual dysfunction secondary to depressive disorders. Journal Sexual Marital Therapy, 1999; 2(2): 52-60.
7. Slag M, Morley J, Elson M, et al. Impotence in medical clinic outpatients. JAMA, 1983; 249: 1736-1740.
8. Finger W, Lung M, Stagle M. Medications that may contribute to sexual disorders. Journal Family Practice, 1996; 44: 33-43.
9. Muller J, Mittelman M, Maclure M. et al. Triggering myocardial infarction by sexual activity. JAMA, 1996; 275: 1405-1409.
10. Lue T. Impotence: a patients goal directed approach to treatment. World J. Urology, 1990;8: 67-74.
11. Althof S, Seftel A. The evaluation and management of erectile dysfunction. Psychiatric Clinics of North America, 1995; 18: 171-192.
12. Burnett A. Erectile dysfunction : a practical approach for primary care. Geriatrics, 1998; 53L 34-48.

13. Gunnarsson O, Judge J. Exercise at midlife: how and why to prescribe it for sedentary patients. *Geriatrics*, 1997; 52: 71-80.
14. Kurnelius P, Hakkinen J, Lukkarinen O. Is high dose yohimbine hydrochloride effective in the treatment of mixed type impotence? *Urology*, 1997; 49: 441-444.
15. Derby C, Mohr B, Goldstein I, et al. Modifiable risk factors and erectile dysfunction: can lifestyle changes modify risk? *Urology*, August 2000; 56(2): 302-306.
16. Pfizer Inc. File data.
17. Giuliano F, Hultling C, ElMasry W, et al. Randomized trial of sildenafil for the treatment of erectile dysfunction in spinal cord injury. *Annals of Neurology*, Jul 1999; 46(1):15-21.
18. Feldman R: The Sildenafil Study Group. Sildenafil in the treatment of erectile dysfunction: efficacy in patients taking concomitant antihypertensive therapy [abstract]. 13th Scientific meeting of the American Society of Hypertension, May 1998. *American Journal Hypertension*, April 1998; 11(4 Pt 2): 10A.
19. Hargreave TB. *CINP Journal*, 1998
20. Greiner K, Weigel J. Erectile dysfunction *American Family Physician*, 1996; 54: 1675-1682.
21. Padma-Nathan H, Hellstrom W, Kaiser F, et al. Treatment of men with erectile dysfunction with transurethral alprostadil. *NEJM*, 1997; 336: 1-7.
22. Linet O, Prince F. Efficacy and safety of intracavernosal alprostadil in men with erectile dysfunction. *NEJM*, 1996; 334: 873-877.
23. Bosshardt R. Objective measurement of the effectiveness, therapeutic success, and dynamic mechanisms of the vacuum device. *British Journal of Urology*, 1995; 75: 786.
24. Cappelleri J, et al. Diagnostic evaluation of the erectile function domain of the International Index of Erectile Function. *Urology*, 1999 August; 54(2): 346-351.

THE ALBERTA CLINICAL PRACTICE GUIDELINES PROGRAM

The Alberta Clinical Practice Guidelines Program promotes appropriate, effective and quality medical care in Alberta by supporting the use of clinical practice guidelines. The program is administered by the Alberta Medical Association under the direction of a multi-stakeholder steering committee.

Alberta CPG Steering Committee

Alberta Health and Wellness
 Alberta Medical Association
 College of Family Physicians of Canada,
 Alberta Chapter
 College of Physicians and Surgeons of Alberta
 Physicians at Large
 Public Representative
 Regional Health Authorities
 University of Alberta
 University of Calgary
 Alberta Association of Registered Nurses
 Alberta College of Pharmacists

TO PROVIDE FEEDBACK

The Alberta CPG Working Group for Erectile Dysfunction is a multi-disciplinary team composed of family physicians, urologists, a psychiatrist and an endocrinologist. The team encourages your feedback. If you have difficulty applying this guideline, if you find the recommendations problematic, or if you need more information on this guideline, please contact:

The Alberta Clinical Practice Guidelines Program:
 12230 - 106 Avenue NW
 Edmonton AB T5N 3Z1
 Phone: (780) 482-2626
 or toll free 1-800-272-9680
 Fax: (780) 482-5445
 Email: ama_cpg@albertadoctors.org
 AMA website: www.albertadoctors.org

*Erectile Dysfunction, June 2001
 Publication Mail Agreement #1630008*

APPENDIX: SEXUAL HEALTH INVENTORY FOR MEN (SHIM)²⁴

To administer the Sexual Health Inventory for Men (SHIM), patients answer each of the questions in the SHIM scale from 0 to 5, where “0” indicates no activity, “1” is the most negative response, and “5” is the most positive response. Overall, scores on the SHIM range from 1 to 25. Higher scores indicate better erectile function, with a score of 20 or higher indicating a normal degree of erectile functioning. Low scores (10 or less) indicate moderate to severe erectile dysfunction. The scale can be given at the initial visit or follow-up visits as a means to facilitate patient-physician communication about erectile function or sexual satisfaction.

1.	How do you rate your confidence that you could get an erection?	Very Low 1	Low 2	Moderate 3	High 4	Very High 5	
2.	When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	No sexual activity 0	Almost never/ Never 1	A few times 2	Sometimes 3	Most times 4	Almost always/ Always 5
3.	During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	Did not attempt 0	Almost never/ Never 1	A few times 2	Sometimes 3	Most times 4	Almost always/ Always 5
4.	During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	Did not attempt 0	Extremely difficult 1	Very difficult 2	Difficult 3	Slightly difficult 4	Not difficult 5
5.	When you attempted sexual intercourse, how often was it satisfactory to you?	Did not attempt 0	Almost never/ Never 1	A few times 2	Sometimes 3	Most times 4	Almost always/ Always 5

ED is an issue that impacts relationships:

- Have you discussed your ED issues and concerns with your partner?
- Is your partner willing to attend appointments with health care professionals with you to learn more about this problem?

Algorithm: Investigation and Management of Erectile Dysfunction

