Blackwell Publishing

*Asian J Androl 2007; 9 (1): 3–7*
DOI: 10.1111/j.1745-7262.2007.00232.x

AJA
www.asiaandro.com

·*Review*·

# Evaluation and diagnostic testing of erectile dysfunction in the era of phosphodiesterase type 5 inhibitors

Kenneth Jacobsohn, Run Wang

*Department of Urology, University of Texas Health Science Center and MD Anderson Cancer Center, Houston, Texas 77030, USA*

**Abstract**

The diagnosis and treatment of erectile dysfunction has changed dramatically since the availability of safe and effective oral therapies. Unfortunately, not all men can be adequately treated in this way, and might require more invasive testing to diagnose and treat the specific cause of their dysfunction. This review looks at the tests and strategies available for men who cannot be treated by oral therapy alone. *(Asian J Androl 2007 Jan; 9: 3–7 )*

**Keywords:** erectile dysfunction; testing; treatment; diagnosis; phosphodiesterase type 5 inhibitors

## 1 Introduction

Erectile dysfunction (ED) is a common problem in 40–70 years old men [1]. The Massachusetts Male Aging Study found a combined prevalence of 52% for minimal, moderate and complete ED. The International Society of Sexual Medicine groups ED into three broad categories: psychogenic, organic and mixed [2]. Organic ED can be further broken down into vascular, neurogenic, anatomic or a combination of any of the three. Organic ED is constant, present in all situations, and its onset might be gradual, as in the case of chronic vascular insufficiency, or sudden, as in the case of trauma. Psychogenic ED is not present at every encounter, and classically patients will often be able to relate differences in the quality or duration of their erections to different partners. Historically, most ED was considered to be psychogenic in origin. In the 1960s most men presenting with ED were treated with psychotherapy and counseling. Over time, we have come to understand that ED is often organic in nature, and might be a sign of other systemic diseases [3].

Following the development of phosphodiesterase type 5 (PDE5) inhibitors the need to elucidate the cause of ED has greatly diminished. In fact, following a history, and focused physical exam, a trial of a PDE5 inhibitor is often all that is ever needed to treat ED. In addition to successfully treating ED from a variety of organic causes, PDE5 inhibitors have also decreased the need for invasive testing. Oral therapy is not successful for all patients desiring treatment, and many of these patients might benefit from a more complete evaluation into the cause of their ED. Currently, there are no consensus guidelines or standardized treatment algorithms to help guide clinicians.

## 2 Basic evaluation

Correspondence to: Run Wang, MD, FACS, Department of Urology, University of Texas Health Science Center and MD Anderson Cancer Center, Houston, Texas 77030, USA.
Tel: +1-713-500-7337 Fax: +1-713-500-7319
E-mail: Run.Wang@uth.tmc.edu
Received 2006-04-24 Accepted 2006-07-30

The evaluation of any patient with ED should proceed in a stepwise manner. As in all disease states, the history of illness is important in ED. The latest American Urological Association (AUA) Guidelines on ED state that, "The typical initial evaluation of a man complaining of ED is conducted in person and includes sexual, medical, and psychosocial histories as well as laboratory tests thorough enough to identify co-morbid conditions that may predispose the patient to ED and that may contraindicate certain therapies" [4]. A detailed medical history is essential as many common disorders are associated with ED, including hypertension, diabetes mellitus, coronary artery disease, dyslipidemia, renal insufficiency and hypogonadism [5]. Prior genitourinary, retroperitoneal, pelvic surgery or radiation can result in ED. It is critical to conduct a complete medication review because many drugs, particularly anti-hypertensive and psychotropic drugs are well known to affect erectile function, and other medications, such as nitrates, might be contraindications to oral therapy. Using a validated questionnaire such as the International Index of Erectile Function can help in determining the severity of the patient's ED.

It is also essential to perform a focused physical exam on any new patient undergoing an evaluation of ED, paying particular attention to the abdomen, genitalia, digital rectal exam and secondary sexual characteristics [4]. The latest AUA consensus guidelines now state that no specific laboratory evaluations are mandatory in the evaluation and diagnosis of ED. However, the Second International Consultation on Sexual Dysfunction (2004) Committee on Sexual Dysfunction Assessment in Men recommended that serum testosterone, fasting blood glucose, fasting serum cholesterol and a serum lipid panel should all be a part of a routine basic ED evaluation [5]. Optional tests based on findings in the initial exam include tests for levels of leutinizing hormone (LH), follicle stimulating hormone (FSH), prolactin, prostate specific antigen (PSA), complete blood count, and a thyroid function panel. Once the diagnosis of ED has been established most clinicians will initially proceed with a trial of a PDE5 inhibitor. For patients who did not have an adequate initial trial of PDE5 inhibitors a second trial of PDE5 inhibitors might be necessary to make sure that patients have enough time to use the medication, with detailed instructions. In general, no further testing is needed to determine the exact etiology of ED prior to initiating therapy, because the initial treatment options will be the same regardless. In the setting of hypogonadal ED, it might be prudent to replace testosterone or treat the rare prolactinoma prior to initiating a PDE5 inhibitor trial. Patients in whom a more thorough evaluation for the cause of ED prior to, or in place of a trial of a PDE5 inhibitor might be required would include: (i) those with primary ED; and (ii) ED secondary to pelvic trauma in a young patient. Patients with concomitant severe Peyronie's disease and ED in whom a penile implant will provide the best treatment might similarly skip a PDE5 inibitor trial and proceed directly to surgery.

In the era of PDE5 inhibitors the most common indication for an invasive evaluation of ED is an inadequate response to oral therapy. Prior to commencing with any invasive testing the physician and patient should have a thorough discussion about possible treatment options. Many patients are not interested in injection therapy or any surgical intervention, and these patients should not be subjected to needless invasive tests. If, however, the patient is motivated and an appropriate candidate for the available treatment options, then further testing can proceed in a goal-directed manner.

Available diagnostic tests include nocturnal penile tumescence (NPT) and rigidity recording, intracavernosal vasoactive drug injection, color Doppler penile ultrasonography, dynamic infusion pharmacocavernosometry and cavernosography, and selective angiography of the internal pudendal cavernous arterial bed. For the general urologist and andrologist, NPT should be considered of academic interest only. In general, it is not sensitive or specific enough to diagnose ED because of the high incidence of false-negative and false-positive results. It provides little information with regards to treatment options. The only current indications for NPT include clinical pharmaceutical trials and certain medico-legal cases when the non-invasive measurement of penile activities is necessary. Even in these situations the NPT results can be challenged because of its poor sensitivity and specificity.

## 3 Intracavernosal injection (ICI) pharmacotesting

ICI testing is a simple, minimally invasive test that is useful in the initial evaluation and treatment of ED. Principally, it involves a single intracavernosal injection of either 10 or 20 mg of a vasoactive substance like prostaglandin E1, and then an assessment of the response [6]. A lasting quality erection confirms the presence of adequate arterial inflow and veno-oclusive function. Additional testing to assess the vascular system is not

necessary when an ICI test produces an adequate erection. Patients with good response to ICI can then be managed with self ICI or intraurethral use of vasoactive agents. A poor quality erection or no erection at all in response to intracavernosal prostaglandin might indicate vascular dysfunction, might be a result of insufficient pharmacologic stimulation, or might be reflective of the stress of performing the test in an office setting. Despite the simplicity of the test, not all authors agree on its use as an initial test, and some have suggested that in the setting of a failed PDE5 inhibitor trial, color duplex Doppler ultrasonography (CDDS) should be next in the evaluation of penile vasculature [6].

## 4 CDDS

CDDS has emerged as a popular, minimally invasive means of assessing penile blood flow. It can provide both anatomic detail as well as a quantitative analysis of the penile vascular system. CDDS has been found to be specific, accurate and to correlate well with dynamic infusion cavernosometry and cavernosography results, and to allow a diagnostic categorization of impotent patients [3, 7]. Although adequately sensitive detection of arterial insufficiency has been described using CDDS on a flaccid penis [8, 9], this has failed to gain acceptance [10]. This is primarily because of a lack of standardization and difficulty in inspecting the small diameters of vessels. Performing CDDS on an erect penis is more widely accepted in the published literature. The most common practice is to use an injectable, intracavernosal stimulant such as prostaglandin E1 (PGE-1) at a dose of 10–20 mg [10]. There is no standardized dose, however, and some authors argue that repeat dosing up to two injections decreases the number of false negative findings of veno-occlusive dysfunction [11]. Shah *et al.* [11] looked at 477 patients undergoing CDDS and found that 57 (20.6%) of patients who underwent a second injection had a change in their diagnosis as a result of the additional pharmacologic stimulation. Other authors prefer the addition of genital plus audio-visual sexual stimulation in place of, or in addition to repeat dosing [12, 13]. Either way, it is important to be sure that whatever type of stimulant is used, it is sufficient to overcome the anxiety and sympathetic stimulation brought on by the test itself. Men with psychogenic impotence will frequently fail to achieve a full erectile response to a pharmacologically-enhanced erection in the clinical setting because the test itself is a stressful event [14]. Basar *et al.* [15] showed that sildenafil citrate can be used in place of PGE-1 to perform an even less invasive, and equally effective penile blood flow study with CDDS; however, this method has not gained widespread acceptance.

CDDS should be performed in a quiet room, and the clinician performing the test should assess the penis in both the flaccid and erect state [3, 16]. A linear ultrasound probe should be placed longitudinally at the base of the penis using a high frequency (12.5 MHz) [10]. Arterial inflow during tumescence may vary over time. In a normal patient, systolic arterial velocity might be less than maximum after only 5 or 10 min. For this reason, assessment of vascular flow should begin 2–3 min after injection of the vasocative medication. Waiting longer might result in detection of lower than peak systolic arterial velocities, as a result of a less than peak velocity required to maintain an erection.

CDDS can be used to demonstrate vascular anatomy, identify both cavernosal arteries, communicating arteries, abnormalities in anatomy or flow, and possible penile fibrosis or plaque [13]. Commonly assessed vascular parameters include penile systolic arterial velocity (PSV), end diastolic velocity (EDV) and resistance index (RI) (RI = PSV – EDV/PSV). A PSV > 30 mL/sec is considered normal, and < 25 mL/sec is considered abnormal. PSV < 25 mL/sec has a 100 % sensitivity and 95% specificity in detecting patients with abnormal penile angiography [3]. Following pharmacostimulation EDV should fall to 0, or even be reversed in a normal patient. Patients with veno-occlusive dysfunction, but normal arterial inflow will have an RI < 0.8 [4].

In a patient with a normal PSV and adequate erectile response to pharmacostimulation, the vascular evaluation is considered normal and complete. If the maximal PSV is normal but the erectile response is inadequate, venous dysfunction should be suspected. When the maximum PSV is < 25 mL/sec, and the erection is inadequate, the arterial supply is certainly insufficient, but it is difficult to make an assessment of the quality of the veno-occlusive function [10]. Without adequate arterial inflow, the corporal bodies will not adequately compress small venous channels even in the presence of normal venous compressive function. When the results of the vascular investigation with CDDS are abnormal, it is appropriate to consider further invasive testing with DICC when patients are considered appropriate candidates for penile vascular surgery.

CDDS has been used as an evaluation tool before penile prosthesis implantation. Our recent study showed that CDDS can change the decision for penile prosthesis implantation in one-fifth of patients who have failed previous non-surgical treatment or were unwilling to try ICI for their ED [17]. Patients with full erection induced by ICI at the CDDS should be warned that decrease in erect penile length can be significant if penile implantation is used as the ultimate treatment for ED [18].

## 5 Dynamic infusion cavernosometry and cavernosography (DICC)

In the era of PDE5 inhibitors and CDDS, DICC has a limited role. Prior to the popularity of penile ultrasonography its usage played a larger part in implicating veno-occlusive dysfunction in organic ED. Veno-occlusive dysfunction, however, is often a multifocal problem and a result of degeneration of vascular smooth muscle rather than a site specific venous leakage. Not surprisingly, the results of surgeries aimed at correcting venous leaks have been disappointing. In fact, the AUA Consensus Guidelines state that, "surgeries performed with the intent to limit the venous outflow of the penis are not recommended" [16]. Currently, the use of DICC should be limited to young patients in whom surgical ligation of an indentifiable venous leak is a possibility or in medico-legal cases.

DICC is a more invasive test than CDDS. Cavernosometry involves infusion of saline into the corporal bodies while measuring cavernosal pressure. This test can be made more physiologic with injection of a vasoactive substance such as PGE-1. The key parameter is the flow to maintain a supraphysiologic cavernosal pressure of 90 mmHg. An inability to maintain this pressure with a flow of 3 mL/min or more is indicative of venous leakage [19].

Cavernosometry can be combined with cavernosography to try to identify a specific site of leakage. Typically this is performed by infusing a low osmolarity contrast agent in place of saline into the cavernosal bodies. Fluoroscopy is then used to identify specific sites of leakage. The results of crural ligation, however, have not been good enough to support continued routine use of this procedure.

## 6 Penile angiography

Penile angiography is another invasive test with a strictly limited role in the evaluation of patients with ED. It should be reserved exclusively for patients who are candidates for penile revascularization. These are typically young men who have had a trauma-induced reduction of penile arterial flow, or a perineal crushing injury. After documentation of a low maximal PSV by CDDS, angiography can serve as a guide in helping plan surgical repair. Penile angiography is a technically challenging and invasive procedure. It requires an interventional radiologist skilled at cannulating the small internal pudendal arteries as well as the inferior epigastric arteries, which are often used for revascularization.

## 7 Corpus cavernosum electromyography (CC-EMG)

Recently, several studies have investigated CC-EMG for evaluating the functional state of cavernosal smooth muscle. Jiang *et al.* [20, 21] found it a reproducible test in healthy men, and diagnostic of smooth muscle degeneration in men with ED following pelvic surgery. In a separate study, these same authors find that EMG potentials are significantly lower in patients with vasculogenic ED compared to those with non-vasculogenic ED [22]. Currently, CC-EMG is investigational only, and its future role in clinical practice is unclear.

## 8 Conclusion

The advent of PDE5 inhibitors has streamlined the

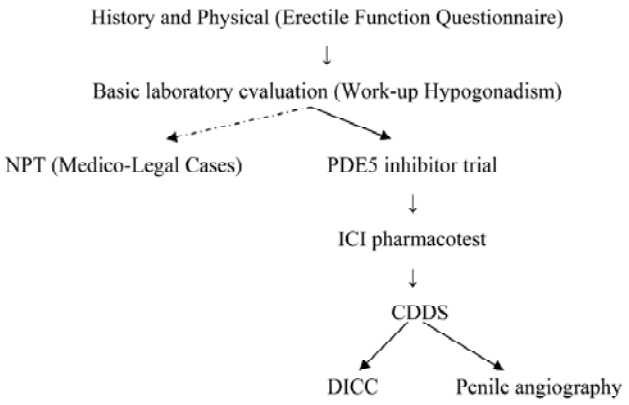


Figure 1. Algorithm for ED evaluation and testing. CDDS, color duplex Doppler ultrasonography; DICC, dynamic infusion cavernosometry and cavernosography; ED, erectile dysfunction; ICI, intracavernosal injection; NPT, nocturnal penile tumescence; PDE5, phosphodiesterase type 5.

approach to the evaluation and treatment of ED. Healthcare providers in a wide variety of disciplines are now offering the basic screening evaluation and treatment options. When oral therapy fails specialists need to be familiar with the indications for and interpretation of invasive tests. An ICI pharmacotest is a simple first line option to evaluate penile vascular function. In the setting of an abnormal ICI test a penile blood flow study with CDDS should be the mainstay of ED testing. Additional testing with DICC or penile angiography is only rarely needed and should proceed only when surgery is being planned (Figure 1).

## References


1 Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. J Urol 1994; 151: 54–61.

2 Lizza EF, Rosen RC. Definition and classification of erectile dysfunction: report of the nomenclature committee of the International Society of Impotence Research. Int J Imp Res 1999; 11: 141–3.

3 Aversa A, Bruzziches R, Spera G. Diagnosing erectile dysfunction: the penile dynamic colour duplex ultrasound revisited. Int J Androl 2005; 28 (Suppl 2): 61–3.

4 Monatgue DK, Jarow JP, Roderick A, Dmochowski RR, Heaton JP, Lue TF, *et al*. Chapter 1: the management of erectile dysfunction: an AUA update. J Urol 2005; 174: 130–9.

5 Lobo JR, Nehra A. Clinical evaluation of erectile dysfunction in the era of PDE-5 inhibitors. Urol Clin N A 2005; 32: 447–55.

6 Aversa A, Isidori AM, Caprio M, Cerilli M, Frajese V, Fabri A. Penile pharmacotesting in diagnosing male erectile dysfunction: evidence for lack of accuaracy and specificity. Int J Androl 2002; 25: 6–10.

7 McMahon CG. Correlation of penile Duplex ultrasonography, PBI, DICC and angiography in the diagnosis of impotence. Int J Imp Res 1998; 10: 153–8.

8 Mancini M, Barolini M, Maggi M, Innocenti P, Villari N, Forti G. Duplex ultrasound evaluation of cavernosal peak systolic velocity and waveform acceleration in the penile flaccid state: clinical significance in the assessment of the arterial supply in patients with erectile dysfunction. Int J Androl 2000; 23: 199–204.

9 Roy C, Saussine C, Tuchmann C, Castel E, Lang J, Jacqmin D. Duplex Doppler sonography of the flaccid penis: potential role in the evaluation of impotence. J Clin Ultrasound 2000; 28: 290–4.

10 Altinkilic B, Hauck EW, Weidner W. Evaluation of penile perfusion by color-coded duplex sonography in the management of erectile dysfunction. World J Urol 2004; 23: 361–4.

11 Shah SR, Lee U, Bruce J, Lewis RW. Repeat dosing when performing color duplex Doppler ultrasonography: The MCG experience. J Sex Med 2004; 1 (Suppl 1): 71 abstract MP35.

12 Montorsi F, Guazzoni G, Barbeiri L, Ferini-Strambi L, Iannaccone S, Calori G, *et al*. Genital plus audiovisual sexual stimulation following intracavernous vasoactive injection versus re-dosing for erectile dysfunction–results of a prospective study. J Urol 1998; 159: 113–5.

13 Wilkins CJ, Sriprasad S, Sidhu PS. Colour Doppler ultrasound of the penis. Clin Radiol 2004; 58: 514–23.

14 Granata A, Bancroft J, Del Rio G. Stress and the erectile resonse to intracavernosal prostaglandin $E_1$ in men with erectile dysfunction. Psychosom Med 1995; 57: 336–44.

15 Basar MM, Batislam E, Altinok D, Yilmaz E, Basar H. Sildeafil citrate for penile hemodynamic determination: an alternative to intracavernosal agents in doppler ultrasound evaluation of erectile dysfunction. Urology 2001; 57: 623–6.

16 Aversa A. Bertucci B, Bonifaio V, Isidori A, Fabbri A. The use of dynamic Doppler color ultrasonography of the penis in the study of erectile dysfunction. Rodiologi Medica 1999; 97: 499–505.

17 Wang R, Dang M, Stage AC, Chen PC. Does penile color duplex doppler ultrasound influence the decision for penile prosthesis implantation? J Sex Med 2006; 3 (Suppl 2): 153.

18 Wang R, Chaves JM, Jacobsohn KM. Erect penile length induced by intracavernosal injection versus that obtained with penile prosthesis. J Sex Med 2006; 3 (Suppl 2): 154.

19 Mulhall JP, Anderson M, Parker M. Congruence between venoocclusive parameters during dynamic infusion cavernosometry: assessing the need for cavernosography. Int J Imp Res 2004; 16: 146–9.

20 Jiang X, Frantzen J, Holsheimer J, Wagner G, Wijkstra H, Meuleman E. Reproducibility of corpus cavernosum electromyography. J Sex Med 2006; 3 (Suppl 1): 33 abstract 63.

21 Jiang X, Frantzen J, Holsheimer J, Wagner G, Wijkstra H, Meuleman E. Corpus cavernosum electromyography in patients with penile fibrosis and patients who underwent pelvic surgery. J Sex Med 2006; 3 (Suppl 1): 34 abstract 64.

22 Jiang X, Frantzen J, Holsheimer J, Wagner G, Wijkstra H, Meuleman E. Corpus cavernosum electromyography in patients with vasculogenic erectile dysfunction. J Sex Med 2006; 3 (Suppl 1): 34 abstract 65.


Edited by Profs Steven M. Schrader and Guang-Huan Sun