

# Erectile Dysfunction

**Key Advisor:** Associate Professor John V Conaglen, Waikato Clinical School, Faculty of Medical and Health Science, University of Auckland

Erectile dysfunction (ED) is defined as the inability to achieve or maintain an erection sufficient for satisfactory sexual activity. Persistent ED is common, particularly in older men, and can significantly impair quality of life both for the man and his partner.



## Erectile dysfunction: organic or psychogenic

ED has organic and psychogenic causes. It is increasingly recognised that even for men with an obvious organic cause there are psychological factors that may play a role in either exacerbating or maintaining the difficulty. Men suffering from ED differ in the way they present, the severity of the disorder, and associated co-morbidities.<sup>1</sup> (Table 1)

Distinguishing whether the cause of ED is predominantly organic or psychological may be useful in directing management.

Men with an organic cause for their ED usually present with a gradual onset and the difficulty becomes progressively worse with time. Early morning erections are usually decreased or absent.<sup>2</sup>

When the cause is psychological, the ED may present suddenly with a complete and immediate loss of sexual function which may vary with the partner or situation, or may be indistinguishable from ED caused by organic disease. A useful clinical indicator is that men with psychogenic ED usually have maintained their early morning erections.<sup>1,2</sup>

Organic and psychogenic causes are not mutually exclusive; many men have components of the two.

## Initial diagnosis and management of erectile dysfunction<sup>3</sup>

A detailed history is essential:

- To understand the nature of the patient’s complaint, the impact on himself, his partner and their relationship. It is also important to understand how the man and his partner have adapted to the condition which is often present for many years before a man presents to his GP.
- To try and determine the likely cause of ED, i.e. the impact of organic or psychological factors involved.
- To identify co-morbidities (e.g. vascular factors, diabetes mellitus, depression or anxiety) or drugs that may be contributing to ED.
- To ask about other sexual difficulties that may be associated with the ED, i.e. low sexual desire, rapid ejaculation and associated sexual difficulties for the partner (e.g. low desire, vaginal dryness and discomfort).

**Table 1:** Common causes of erectile dysfunction<sup>2</sup>

Organic	Psychogenic
<ul style="list-style-type: none"> <li>▪ Vascular disease</li> <li>▪ Diabetes mellitus</li> <li>▪ Medications:                             <ul style="list-style-type: none"> <li>▫ Antidepressants</li> <li>▫ Psychotropics</li> <li>▫ Antihypertensives</li> </ul> </li> <li>▪ Cigarette smoking</li> <li>▪ Alcohol</li> <li>▪ Neurological disorders</li> <li>▪ Hypogonadism</li> </ul>	<ul style="list-style-type: none"> <li>▪ Performance anxiety</li> <li>▪ Generalised anxiety</li> <li>▪ Major depression</li> </ul>

## Physiology of erection

Sexual stimulation, both physical and mental, directs the release of nitric oxide from the penile nerves. This nitric oxide stimulates the production of cyclic guanosine monophosphate (cGMP) within the vascular smooth muscle of the corpora cavernosae necessary for an erection. In addition, nitric oxide is also released from endothelial cells of the corpora cavernosae to maintain the cGMP levels within the corpora cavernosae smooth muscle. cGMP induces corpora cavernosae smooth muscle relaxation and the vascular lakes of the penis fill with blood. As

the penis engorges, the penile veins are passively compressed by increased intracavernosal pressure and this restricts venous return from the penis. A full erection results from the combination of increased blood flow to the penis and decreased venous return. cGMP is degraded to 5’GMP by the action of type 5 cGMP phosphodiesterase (PDE5), returning the penis to the flaccid state.<sup>4</sup> Drugs such as sildenafil, tadalafil and vardenafil (PDE5 inhibitors) act by inhibiting this enzyme.

Physical examination should be tailored to the individual clinical presentation:

- Given the association of ED with cardiovascular disease, cardiovascular risk assessment may be appropriate.
- Genital examination can occasionally identify anatomical abnormalities and signs of hypogonadism, but more importantly may reassure the patient that the doctor is taking the condition seriously.
- As diabetes is a risk factor for ED and undiagnosed diabetes may be present in men with ED, assessment for complications of diabetes may be useful.
- Digital rectal examination can be used to identify suspected prostate disease.

Physical examination may guide further investigations:

- If unexplained low libido or suspected hypogonadism, measure testosterone and prolactin at 0800hrs.
- Laboratory tests useful as part of a cardiovascular risk assessment may include blood glucose and fasting lipids.

- Other investigations, such as thyroid function tests, renal and liver function tests, and a complete blood count, may be done on a case by case basis.

Treat the cause of erectile dysfunction wherever possible:

- It is desirable to obtain the views of the partner as to both the cause and what she or he would like to do about the difficulty.
- Consider psychological intervention for psychogenic erectile dysfunction.
- Although predominantly organic ED rarely benefits from modification of risk factors (Table 2) or a change from any possible drug causes (Table 3), the general health of the patient may be improved by attention to these issues.

### Specific treatment options for erectile dysfunction

Treatments for erectile dysfunction include oral therapy with phosphodiesterase type 5 inhibitors (PDE5 inhibitors), injection therapy, and penile devices. Testosterone therapy should only be used in men with established hypogonadism. Psychotherapy should be considered in all men who have a psychogenic component to their erectile dysfunction.<sup>5</sup>

**Table 2:** Risk factors for erectile dysfunction<sup>5</sup>

Risk Factor	Treatment
Metabolic syndrome	Diet, exercise and weight loss
Cardiovascular disease	May use PDE5 inhibitor with caution. For some patients, specialist review is recommended (Box 1). Use of PDE5 inhibitors is contraindicated with concomitant nitrates.
Tobacco smoking	Smoking cessation
Social or relationship stress, depression	Counselling, lifestyle change, medical treatment
Endocrine disorders such as hypogonadism, hypo- or hyperthyroidism	Correction of underlying endocrine disorder; and if needed, possible use of a PDE5 inhibitor
Diabetes	Appropriate glycaemic management

### Box 1: ED and coronary heart disease

PDE5 inhibitors are contraindicated until cardiac status is stabilised in the following conditions:<sup>5, 6</sup>

- Unstable angina
- Uncontrolled hypertension
- Congestive heart failure (NYHA III, IV)
- Very recent myocardial infarction (less than two weeks ago)
- High risk arrhythmias
- Obstructive hypertrophic cardiomyopathies
- Moderate to severe valve disease

### Best practice tip

A Nelson GP offers a best practice tip for questions that can be asked to establish a patient's suitability for PDE5 treatment:

- Does exertion, stress or sexual activity cause any symptoms?
- What is the most strenuous physical activity that you currently do?
- Do you accept the risk of taking this medication?

**Table 3:** Drugs associated with erectile dysfunction<sup>4, 5</sup>

Drug class	Examples	Possible alternative with lower risk of erectile dysfunction
Antihypertensives	Beta blockers, calcium channel blockers	ACE inhibitors
Diuretics	Thiazides, spironolactone	Loop diuretics
Antidepressants	Selective serotonin reuptake inhibitors, tricyclic antidepressants, monoamine oxidase inhibitors	Limited evidence to guide alternative; specialist review required for any change
Antipsychotics	Phenothiazines, carbamazepine, risperidone	Limited evidence to guide alternative; specialist review required for any change
Hormones	Cyproterone acetate, oestrogen, 5 $\alpha$ -reductase inhibitors (e.g. finasteride)	Limited evidence to guide alternative; specialist review required for any change
Dyspepsia and ulcer healing drugs	H <sub>2</sub> antagonists	Proton pump inhibitors
Recreational drugs	Alcohol, marijuana, cocaine	Discontinue use

### **PDE5 inhibitors are recommended first line therapy**

The PDE5 inhibitors currently available are; sildenafil (Viagra), tadalafil (Cialis), and vardenafil (Levitra). They improve erectile function by inhibiting type 5 cGMP phosphodiesterase, thereby increasing penile cyclic guanosine monophosphate (cGMP) which mediates relaxation of cavernosal smooth-muscle cells.<sup>7</sup>

The main difference between the PDE5 inhibitors is the longer half-life of tadalafil at approximately 18 hours compared with approximately four hours for sildenafil and vardenafil.<sup>8</sup>

There is insufficient evidence to support the superiority of one agent over the others and patient preference will usually guide selection.

The PDE5 inhibitors are not funded and vary in price from approximately \$80 to \$115 for a pack of four tablets.

### **PDE5 inhibitors are contraindicated in patients taking organic nitrates**

PDE5 inhibitors potentiate the hypotensive effects of organic nitrates and therefore the concomitant use of nitrates is contraindicated.<sup>8</sup> The safe time interval, if nitrates need to be used in a medical emergency, has not been determined. Most recommendations suggest withholding nitrate therapy for 24 hours after sildenafil and vardenafil, and 48 hours after tadalafil have been taken.<sup>7</sup>

If the patient requires nitrates after taking a PDE5 inhibitor a cardiologist should be consulted immediately.

### **PDE5 inhibitors require sexual stimulation to have an effect**

PDE5 inhibitors do not cause erections in the absence of sexual stimulation. It is essential for the doctor prescribing PDE5 inhibitors to educate men in the need for sexual stimulation to ensure the drug is effective. Some men who initially fail to respond to a PDE5 inhibitor can be successful with these medications after being correctly educated about their use.<sup>7</sup> As anxiety can over-ride the effect of a PDE5 inhibitor, a patient should not be considered to have failed in the use of a particular PDE5 inhibitor until they have tried them on five to six occasions.

PDE5 inhibitors need to be taken at least 30 minutes to one hour before sexual activity and taking sildenafil with fatty food and/or alcohol may delay its onset of action.

### **Monitor for adverse effects and therapeutic response**

Common adverse effects such as headache, flushing, gastric upset, diarrhoea, nasal congestion, and light-headedness are similar for all three PDE5 inhibitors and are often the result of PDE inhibition in other parts of the body.<sup>7</sup>

Sildenafil and vardenafil have some cross-reactivity with PDE6 and produce visual side effects on rare occasions.

### **Testosterone therapy is not usually indicated for ED in men with normal testosterone levels.<sup>8</sup>**

Testosterone replacement is appropriate when a man with ED is established to have hypogonadism.<sup>1</sup> Gynaecomastia, increased haematocrit, alterations in lipid profile, hypertension, and infertility are some side effects associated with exogenous testosterone therapy.

It also is possible that testosterone may increase the risk of prostate cancer and the risk of treatment versus benefit should be considered and discussed with the patient.

N.B. Hyperprolactinaemia of any cause may result in ED and appropriate management of the raised prolactin may restore normal erections.



PDE5 inhibitors tend to be less effective in the presence of reduced neural nitric oxide release as is the case in men with diabetes.<sup>9</sup>

### **Injection therapies are usually second line treatments**

If oral therapy with PDE5 inhibitors fails or if they are contraindicated or not tolerated, injection therapy may be required.

#### **Intracavernosal injections**

These agents act by directly relaxing smooth muscle in the corpora cavernosum and result in an erection.<sup>10</sup> Unlike PDE5 inhibitors, they do not require sexual stimulation to work.

Side effects include pain at the injection site and priapism, and long term use can result in scarring of the tunica albuginea with potential curvature and shortening of the penis.<sup>2</sup>

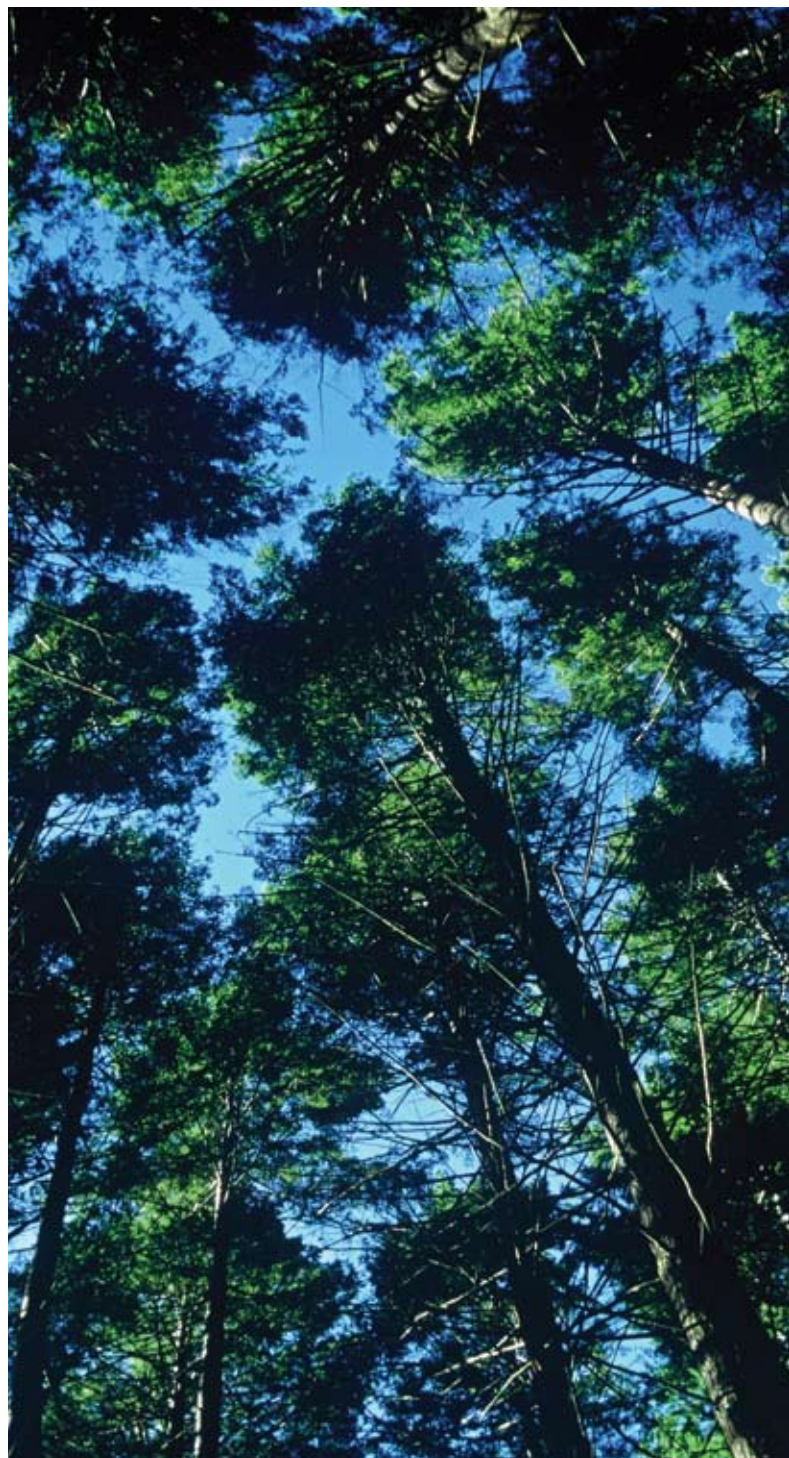
It is generally recommended that the first dose be administered under medical supervision because of the small risk of priapism and the importance of detailed education in the technique of self-injection.<sup>5</sup>

Alprostadil (Caverject) is the most commonly used agent in New Zealand. Other injectable agents include; an aviptadil and phentolamine combination (Invicorp) and papaverine. Caverject and Invicorp are not funded, however the papaverine injection is. Papaverine is associated with a higher incidence of priapism and scarring of the tunica albuginea and should only be used as a second-line therapy by experienced practitioners.

### **Penile devices may be suitable for men who fail to respond to other therapies**

Vacuum constriction devices and penile prosthetic devices are options for men who fail to respond to other therapies.

Vacuum devices draw blood into the penis by means of a vacuum and a constriction band is applied to retain the blood. Adverse effects include pain, numbness, bruising, a cold blue penis and difficulty with ejaculation. These devices require significant education in their use and the constriction band should not be applied for any longer than 30 minutes.



Penile prostheses are usually malleable or inflatable devices which are surgically implanted into the penis. They are expensive and should only be implanted by an experienced surgeon who is regularly performing the procedure. Due to their permanence they must not be considered until all less invasive options have been tried and failed.<sup>2</sup>

## Summary

Erectile dysfunction is common, with increasing prevalence as men age.

A detailed history is essential to identify the possible cause and reveal any factors contributing to the ED such

as underlying medical conditions or medication use. As sexual dysfunction usually impacts on the relationship with the partner it is best to try and obtain the views of the partner on both the impact of the ED and its management.

PDE5 inhibitors are first-line therapy for most men with ED. Testosterone should be reserved for those men with hypogonadism. Injection therapy may be appropriate in men who fail to respond to PDE5 inhibitors, are intolerant to them or have contraindications to their use.

Penile devices are usually reserved for men who fail to respond to all other therapies.

## References:

1. Burnett AL. Erectile dysfunction. *J Urol* 2006; 175: S25-31.
2. Arduca P. Erectile dysfunction: A guide to diagnosis and management. *Aust Fam Physician* 2003; 32(6): 414-420.
3. Rees J, Patel B. 10 minute consultation: Erectile dysfunction. *BMJ* 2006; 332: 593.
4. Ralph D, McNicholas T. UK management guidelines for erectile dysfunction. *BMJ* 2000; 321: 499-503.
5. McVary K. Erectile dysfunction. *N Engl J Med* 2007; 357: 2472-81.
6. Jackson G, Rosen RC, Kloner RA, Kostis JB. The second Princeton Consensus on sexual dysfunction and cardiac risk: new guidelines for sexual medicine. *J Sex Med* 2006; 3: 28-36.
7. Beckman TJ, Abu-Lebdeh HS, Mynderse LA. Evaluation and medical management of erectile dysfunction. *Mayo Clin Proc* 2006; 81(3): 385-390.
8. Montague DK, Jarrow JP, Broderick GA, et al. Chapter 1: the management of erectile dysfunction: an update. American Urological Association. Available from: <http://www.auanet.org/guidelines/edmgmt.cfm> Accessed Feb 08.
9. Burnett AL. Phosphodiesterase 5 mechanisms and therapeutic applications. *Am J Cardiol* 2006; 96(12B): 42M-46M.
10. McMahon CH, Smith CJ, Shabsigh R. Treating erectile dysfunction when PDE5 inhibitors fail. *BMJ* 2006; 332: 589-592.