Erectile dysfunction (ED) is the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance.¹ The overall prevalence of ED in Australia is estimated at 40%.²,³ The risk of developing ED is age related, occurring in approximately 26% of men aged 50–59 years, and approximately 40% of men aged 60–69 years.²,⁴ With the advent of phosphodiesterase-5 (PDE-5) inhibitors, the management of ED occurs predominantly in the primary care setting. Risk factors for ED are shown in Table 1. Guidelines for assessment and management of ED are available from Andrology Australia⁵ (see Resources).

Erectile dysfunction is primarily an organic condition, sharing common risk factors with cardiovascular disease including lack of exercise, obesity, smoking, hypercholesterolaemia and the metabolic syndrome.⁶,⁷ This is an important consideration as ED may be an early marker of subclinical metabolic and vascular disease.⁹ Many medications can potentiate ED including commonly used antihypertensives such as calcium channel blockers, angiotensin II receptor antagonists, angiotensin converting enzyme receptor antagonists, beta blockers and thiazides.

The physical symptoms of ED are often associated with depression, a loss of self confidence, loss of intimacy in a relationship, and a reduced quality of life.⁹ Although public awareness of ED has improved in the past decade, less than half the men with the disorder seek treatment.¹⁰ A delay often occurs between the onset of symptoms and attendance in the primary care setting, with a mean time of 1.0–3.5 years.¹⁰ The goals of ED treatment are to restore quality of life and allow the patient and his partner to enjoy a satisfying sex life.

Assessment

Consultations around the issue of erectile dysfunction should be conducted in a relaxed, reassuring and nonjudgmental manner. The first step is to take a full medical, sexual, surgical and psychosocial history (Table 2). A focused physical examination includes:

- a genital examination
- assessment of secondary sexual characteristics
- a digital rectal examination to assess the prostate gland.

A cardiovascular risk assessment should be performed before commencing a patient on a PDE-5 inhibitor and advising the resumption of sexual activity.¹¹,¹² Kostis et al, have developed...
Management
The management of ED should follow a stepwise approach as outlined in Table 3. Importantly, partners play a key role in supporting the patient, allaying anxiety and achieving treatment compliance; a couples based approach should be encouraged.

First line: PDE-5 inhibitors
There are currently three PDE-5 inhibitors on the market: sildenafil (Viagra™), vardenafil (Levitra™) and tadalafil (Cialis™), which is available as a daily dose. Features of these medications are described in Table 4. The efficacy of this class of medication is well established for the general population, as well as in men following radical prostatectomy and radiotherapy for prostate cancer and those with diabetes mellitus, spinal cord injury, multiple sclerosis, and depression.11,17,18 PDE-5s are contraindicated following a recent myocardial infarction, concurrent nitrate therapy, and high risk cardiovascular disease.

The success rate of PDE-5 inhibitors is dependent upon the aetiology of the ED and can range from approximately 43–89%.19 A poorer response to PDE-5 inhibitors is seen in the context of adverse factors such as following prostate surgery (43%), diabetes with neuropathy (50%) and peripheral vascular disease (63%).19 A better response is seen in an otherwise healthy male whose ED is secondary to depression (89%), neurological disease (85%) and smoking (80%).19

Other factors contributing to the failure of PDE-5s include incorrect usage, worsening corporal endothelial dysfunction, poor tolerance to side effects, and hypoandrogenism.19 For initial nonresponders, education alone can improve the response by 40–55%.19 The probability of successful intercourse increases with each treatment attempt, therefore patients should be encouraged to persevere with a trial of at least two PDE-5 inhibitors for up to four attempts of each, and at the maximum dosage.19 Information regarding the need for sexual stimulation and the onset and duration of action of PDE-5 inhibitors can also increase success rates.

Second line: vacuum devices, intercavernosal injections and testosterone therapy
Following a complete trial with PDE-5 inhibitors, second line therapies can be used in combination with PDE-5 inhibitors to improve response, or as a single therapy when PDE-5s are contraindicated. The advantages and disadvantages of vacuum erection devices (VEDs) and intercavernosal injections are shown in Table 5.

Vacuum erection devices
Vacuum erection devices provide a safe, cost effective, and noninvasive alternative for men who have failed oral pharmacotherapy. Negative pressure is applied to the penis, producing passive engorgement of the corpora cavernosa, resulting in an erection that can be maintained by an elastic band at the base of the penis for 30 minutes (Figure 1). Successful vaginal penetration is as high as 90%, however device satisfaction

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### Table 1. Risk factors associated with erectile dysfunction

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Increased pressure in the arteries</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>Problems with the heart and blood vessels</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>High blood sugar levels</td>
</tr>
<tr>
<td>Smoking</td>
<td>Cigarette smoke</td>
</tr>
<tr>
<td>Alcohol</td>
<td>Drinking alcohol</td>
</tr>
<tr>
<td>Prostate surgery</td>
<td>Treatment for prostate problems</td>
</tr>
<tr>
<td>Pelvic trauma</td>
<td>Injury to the pelvic area</td>
</tr>
<tr>
<td>Pelvic radiotherapy</td>
<td>Treatment for pelvic problems</td>
</tr>
<tr>
<td>Medications</td>
<td>Prescription medications</td>
</tr>
<tr>
<td>Depression</td>
<td>Mental health condition</td>
</tr>
<tr>
<td>Penile abnormalities</td>
<td>Conditions affecting the penis</td>
</tr>
<tr>
<td>Obesity</td>
<td>Excess body weight</td>
</tr>
<tr>
<td>Sleep apnoea</td>
<td>Obstructive sleep apnea</td>
</tr>
<tr>
<td>Hyperlipidaemia</td>
<td>High levels of lipids in the blood</td>
</tr>
<tr>
<td>Spinal cord trauma</td>
<td>Injury to the spinal cord</td>
</tr>
<tr>
<td>Medical conditions</td>
<td>Conditions affecting the health</td>
</tr>
<tr>
<td>Multiple sclerosis</td>
<td>Nerve disorder</td>
</tr>
</tbody>
</table>

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### Table 2. History taking in patients with erectile dysfunction

<table>
<thead>
<tr>
<th>Category</th>
<th>Information Collected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexual</td>
<td>Nature of problem, mode of onset, degree of disability, precipitating factors</td>
</tr>
<tr>
<td>Medical</td>
<td>Medical history, psychological history, surgical history, medications, recreational drug use, alcohol use, smoking history</td>
</tr>
<tr>
<td>Urological</td>
<td>History of lower urinary tract symptoms, penile complaints (e.g. pain, curvature)</td>
</tr>
</tbody>
</table>

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### Table 3. Stepwise approach to management of erectile dysfunction

#### First line
- Lifestyle modifications (e.g. quitting smoking, exercise, weight loss)
- Management of cardiovascular risk factors
- Trial of PDE-5 inhibitors (at least four attempts with two different PDE-5 inhibitors) in the absence of contraindications

#### Second line
- Self intercavernosal injections
- Vacuum erection devices
- Hormonal therapies (e.g. testosterone replacement)
- Combination therapy

#### Third line
- Penile prostheses

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trials comparing PGE1 to placebo demonstrated a 63.6% success rate of alprostadil, with a relatively low incidence of priapism (0.35–4.0%) and tunica albuginea fibrosis (1–23%).21,23

Combination therapy

Combination intracavernosal injections such as Trimix (phentolamine, papaverine, and PGE1) and Quadmix (phentolamine, papaverine, prostaglandin E1 and atropine) can be initiated after an unsuccessful trial of alprostadil. Although data is limited, the reported rate of full erection is more than 90%.22,24 There is, however, a higher incidence of priapism with combination therapy, and these need to be prepared by a compound chemist and generally warrant urologist referral for monitoring.

Testosterone therapy

Testosterone supplementation can be considered for all men who have signs and symptoms of

**Table 4. PDE-5 inhibitors**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Onset of action</th>
<th>Half life</th>
<th>Adverse effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sildenafil</td>
<td>Tmax* 30–120 minutes Median 60 minutes</td>
<td>2–5 hours</td>
<td>• Headache • Flushing • Dyspepsia</td>
</tr>
<tr>
<td>Vardenafil</td>
<td>Tmax 30–120 minutes Median 60 minutes</td>
<td>4.5 hours</td>
<td>• Headache • Flushing • Dyspepsia</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>Tmax 30–120 minutes Median 120 minutes</td>
<td>15.5 hours</td>
<td>• Headache • Flushing • Dyspepsia</td>
</tr>
</tbody>
</table>

* Tmax = median time to peak plasma concentration of drug

**Table 5. Advantages and disadvantages of VEDs and intracavernosal injections**

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Advantage</th>
<th>Disadvantage</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vacuum erection devices</td>
<td>• Effective in all aetiological groups • Do not require erectile reserve • Noninvasive • Low complication rates • No restriction on frequency of use</td>
<td>• Bruising • Interference of ejaculation due to constriction ring • Loss of acute angle of erection • Pain • ‘Nonphysiological’ erection • Requires the use of bulky equipment</td>
<td>• Bleeding disorders • Anticoagulation therapy</td>
</tr>
<tr>
<td>Intracavernosal injections</td>
<td>• Suitable for all causes of ED</td>
<td>• Risk of priapism • Fibrosis of tunica albuginea • Painful erections • Tolerance • Urethral bleeding • Hypotension • Low compliance rates</td>
<td>• Conditions that predispose to priapism • Sickle cell anaemia • Leukaemia</td>
</tr>
</tbody>
</table>

ranges from 26–94%, and long term use reduces satisfaction to 50–64% after 2 years.11,20 Proper instruction and manual dexterity are crucial to the success of, and compliance with, VEDs. Quality devices with an instructional DVD and technical support can be obtained from medical aid sources.

**Self intracavernosal injections**

Injectable agents effective in treating ED where PDE-5 inhibitors have failed include papaverine, phentolamine and alprostadil (PGE1).20,21 Men must receive education on the risk of priapism, injection technique, and dosing, before beginning home injections (Figure 2). Discontinuation rates with intracavernosal therapy range from 40.7–68.0%.11 A return of spontaneous erections has been reported in men undergoing intracavernosal injections.22

Alprostadil (Caverject Impulse®) is a vasoactive mediator that acts primarily on cavernosal smooth muscle receptors.20 Erection usually occurs within 5–20 minutes of injection and can last up to 2–3 hours after ejaculation.20 A meta-analysis of four randomised controlled trials comparing PGE1 to placebo demonstrated a 63.6% success rate of alprostadil, with a relatively low incidence of priapism (0.35–4.0%) and tunica albuginea fibrosis (1–23%).21,23

**Combination therapy**

Combination intracavernosal injections such as Trimix (phentolamine, papaverine, and PGE1) and Quadmix (phentolamine, papaverine, prostaglandin E1 and atropine) can be initiated after an unsuccessful trial of alprostadil. Although data is limited, the reported rate of full erection is more than 90%.22,24 There is, however, a higher incidence of priapism with combination therapy, and these need to be prepared by a compound chemist and generally warrant urologist referral for monitoring.

**Testosterone therapy**

Testosterone supplementation can be considered for all men who have signs and symptoms of
Erectile dysfunction – when tablets don’t work

Summary of important points

- Erectile dysfunction is a significant clinical problem largely undertreated in the community; the issue should be explored in any man who is over 40 years of age or has cardiovascular disease.
- Erectile dysfunction may be an early marker of subclinical metabolic and vascular disease.
- The physical symptoms of ED are often associated with depression, a loss of self confidence, loss of intimacy in a relationship, and a reduced quality of life.
- The severity of ED should be evaluated with a self assessment questionnaire.
- Partner inclusion will improve success of treatment and increase treatment compliance.
- Treatment of ED should follow a stepwise approach, including ongoing education and support.
- PDE-5s are first line treatment. They are contraindicated in the context of recent myocardial infarction, concurrent nitrate therapy, and high risk cardiovascular disease.
- Second line treatments for ED can be offered in conjunction with PDE-5 inhibitors to increase success rates.
- Penile implants are well tolerated and have high success rates in well selected patients.

Resources

- Andrology Australia. Erectile dysfunction: diagnosis and management. GP summary guide: www.andrologyaustralia.org
- The Sexual Health Inventory for Men (SHIM): www.rohbaltimore.com/shim.pdf
- The International Prostate Symptom Score Sheet (IPSS): www.gp-training.net/protocol/docs/ipss.doc

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Conflict of interest: Prem Rashid has been a visitor to the American Medical Systems (AMS) USA manufacturing facility undertaking a cadaveric dissection clinic and observing operative procedures by high volume implant urologists affiliated with AMS during that time. He also has acted as a consultant for Coloplast, AstraZeneca, Hospira & Abbott Pharmaceuticals. No commercial organisation initiated or contributed to the writing of this article apart from granting permission to use diagrams of their respective devices.

References

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