CLINICAL PERSPECTIVES

Erectile dysfunction
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Key words
erectile dysfunction, phosphodiesterase type 5 inhibitor, alprostadil, intrapenile prosthesis, vacuum constriction device.

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Abstract
In the past 30 years, advances in basic science have been instrumental in the evolution of the male sexual health treatment paradigm from a psychosexual model to a new model, which includes oral and intracavernosal injection pharmacotherapy, vacuum constriction devices and penile prostheses for the treatment of erectile dysfunction. This progress has coincided with an increased understanding of the nature of male sexual health problems, and epidemiological data that confirm that these problems are widely prevalent and the source of considerable morbidity, both for individuals and within relationships.

Introduction
Community-based epidemiological studies suggest that erectile dysfunction (ED), the persistent inability to achieve or maintain penile erection sufficient for satisfactory sexual performance, is a common disorder in men, affecting up to 52% of men between the ages of 40 and 70 years and is associated with reduced quality of life.1 It is now recognised that vascular disease of the penile arteries is the most common cause of ED, accounting for up to 80% of cases.2 The nitric oxide–cyclic guanosine-3’5’-monophosphate (NO-cGMP) system is important in producing the arterial dilation and venous occlusion necessary to attain and sustain an erection. Abnormalities of this vasodilator system due to endothelial dysfunction are present in atherosclerosis and play an important role in the pathophysiology of ED.3 Phosphodiesterase type 5 (PDE5) inhibitor drugs, which inhibit the breakdown of cGMP producing vasodilation and improve endothelial cell function, are very effective in treating ED.4

Epidemiology
Data from Australian, US and UK studies are similar, estimating the prevalence of complete ED as approximately 5% among 40-year-olds, 10% among men in their 60s, 15% among men in their 70s and 30–40% among men in their 80s. It is projected that, by 2025, 322 million men worldwide will have ED.5 Prevalence studies show that, when controlling for other factors, increasing age obesity, diabetes, hypertension, hyperlipidaemia and vascular disease are causative factors.1 Although the incidence of ED rises significantly with increasing age, recent studies indicate that 55–70% of men aged 77–79 years are sexually active. However, only half of the men who self-report ED are concerned about it.

Pathophysiology
Penile erection is a neurovascular phenomenon that requires dilation of penile vasculature, relaxation of smooth muscle, increased intracavernosal blood flow and normal veno-occlusive function. Penile vascular disease is the most common cause of organic ED and may involve several pathophysiological mechanisms, including impaired arterial inflow, impaired smooth-muscle cavernosal relaxation, chronic ischaemia-induced increased cavernosal smooth-muscle contraction, cavernosal fibrosis, veno-occlusive dysfunction and chronic or episodic hypoxaemia. Endothelial dysfunction appears to be the final common pathway for many cases of ED.1 ED may be an early manifestation of generalised endothelial dysfunction, and a predictor of a precursor of other
forms of cardiovascular disease. More than half of men with ED who have no cardiac symptoms have an abnormal stress test, and 40% have been found to have significant coronary artery disease when studied.

Apart from age, the main risk factors are those for vascular disease (smoking, diabetes mellitus, hypertension, abnormal lipid profile, obesity and lack of exercise). Essentially, any condition that damages endothelial function can result in ED. Other factors include depression and endocrine disorders (Table 1).

### Diabetes mellitus

ED occurs at an earlier age in men with diabetes mellitus (DM) compared with men without DM, and the age-adjusted probability of complete ED is nearly three times higher. More than 50% of men develop ED within 10 years of being diagnosed with DM. The prevalence of ED increases with duration, poor glycaemic control and complications of DM, such as vascular and microvascular disease and neuropathies. Studies have revealed ED prevalence rates of 49% in patients with type 1 diabetes, and 34% and 24% of severe and mild to moderate ED, respectively, in patients with type 2 diabetes.

### Neurological disease

Many neurological disorders including spinal cord injury, multiple sclerosis and cavernous nerve damage following major pelvic cancer surgery, such as radical prostatectomy or anterior resection, commonly lead to ED.

### Endocrine disorders

Endocrine disorders, such as hypogonadism, hyperprolactinaemia and thyroid disease play a significant role in ED physiology. Testosterone regulates cavernosal nerve structure and function, nitric oxide synthase expression and activity, PED5 and corporal smooth-muscle cell growth and differentiation.

### Benign prostatic hyperplasia (BPH)

Men with BPH have a high prevalence of ED. The explanation for this association remains unclear, and the quality of life of men with BPH is reduced by its effects on sexual function.

Although most men with ED have an underlying vascular cause, usually related to endothelial dysfunction, there is always a contributing, sometimes substantial, psychogenic component related to performance anxiety. Treatment of this component alone may be sufficient to restore normal erections.

### Diagnosis

A full history and thorough clinical examination of the patient are needed to:
- Confirm that the patient is suffering from ED and/or another sexual dysfunction, such as hypoactive desire or premature ejaculation
- Assess the severity of the condition
- Determine whether ED is psychogenic or organic in origin
- Identify risk factors or comorbid disease.
- Assess the fitness of the patient for resuming sexual activity.

Several questionnaires have been developed to score the erectile problem objectively. The short five-question form of the International Index of Erectile Function
The examination of a man with ED will be directed, to a certain extent, by his history and should include assessment of the external genitalia, the endocrine and vascular systems, and the prostate gland in most patients. The penis should be carefully palpated to exclude the presence of fibrous Peyronie plaques and to check for phimosis. Prostatic induration or a palpable nodule should raise the suspicion of prostate cancer.

Physical examination

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Clinical investigations

The degree to which men should undergo clinical investigation depends on the patient’s history and examination findings. General investigations include serum concentrations of total testosterone (before 11am), fasting glucose, fasting lipids and, in men over 50 years of age, prostate-specific antigen. Further investigations may be required based on the results of these initial investigations, including serum concentrations of luteinising hormone, prolactin and high-density lipoprotein/low-density lipoprotein fractions of cholesterol. Special investigations are not always required, but if patients fail to respond to minimally invasive treatments, such investigations may be necessary before other options can be explored. Colour Doppler imaging provides information about penile haemodynamics after maximal smooth-muscle relaxation has been induced with a vasoactive agent. Its aim is to distinguish arterial insufficiency and veno-occlusive dysfunction from other causes of erectile failure. Nocturnal penile tumescence and rigidity testing to evaluate the frequency, duration and rigidity of nocturnal erections is more of historical interest, and its contemporary use is largely limited to medicolegal assessment of erectile function.

Impact of a diagnosis of ED

It is increasingly recognised that a diagnosis of ED can have a profound impact on the patient’s and partner’s quality of life. ED can lead to withdrawal from intimacy, avoidance of all physical contact with a partner and an increase in emotional stress, which itself can perpetuate any psychogenic component to the ED. The condition can affect a man’s self-esteem and self-image, and lead to anxiety and hence depression. Treatment of ED has been shown to lead to resolution of depression and restoration of self-esteem, and thus improvement in quality of life.

Treatment options

The treatment options for men with ED are now varied and effective when compared with those of 20 years ago. The selection from these various treatment options depends on several factors, such as severity of ED, underlying cause and patient and partner choice. The results of the few studies that have been performed indicate that the only lifestyle modification that may make a difference in ED incidence is continuation or initiation of physical activity. Midlife changes in lifestyle other than physical activity may not have a beneficial effect on ED because it is simply too late. Some studies have suggested that smoking cessation may improve erectile function, which other studies have refuted. In addition, use of some antihypertensive and lipid-lowering drugs may actually exacerbate ED.
It is well known that ED is associated with numerous risk factors for coronary artery disease (CAD), including lipid abnormalities, hypertension, smoking, diabetes, obesity and lack of physical activity. However, most physicians do not routinely ask cardiac patients about ED, and these patients often are reluctant or embarrassed to discuss it. In addition, there is a paucity of studies examining the effect of control of risk factors on ED once the ED has been diagnosed.

Accumulating evidence indicates that ED is a predictor of cardiovascular health. Men with proven vasculogenic ED or multiple vascular risk factors and suspected vasculogenic ED should be screened for silent myocardial ischaemia by treadmill stress electrocardiogram or computed tomography coronary angiography.

In men with CAD, fitness for renewed sexual activity should be assessed with an exercise stress test before initiating or resuming sexual activity. Ability to exercise up to 3–6 METs without evidence of myocardial ischaemia should be screened for silent myocardial ischaemia by treadmill stress electrocardiogram or computed tomography coronary angiography.

In men with CAD, fitness for renewed sexual activity can be confirmed by tolerance of a simple exercise challenge of walking 1.5 km briskly on the level in 20 min (3–4 METs) or climbing two flights of stairs without limiting symptoms (6 METs) (Table 3).14

### Psychosexual therapy

Psychosexual therapy for ED cannot be standardised because the source of anxiety varies between patients. Relationship difficulties, depression, guilt, problems with intimacy and lack of sexual experience may all increase anxiety and/or conflict, which may then manifest as ED. Psychosexual treatments range from simple sex education through improved partner communication to cognitive and behavioural therapy and are often combined with ED pharmacotherapy. Results of psychosexual therapy are relatively good in the short term, but long-term results are disappointing.15,16

### Pharmacotherapy

Most patients suffering from ED will respond to the safe, effective oral pharmacological agents now available. These include the PDE5 inhibitors sildenafil, tadalafil and vardenafil. Other physical treatments, such as vacuum devices and intracavernosal drugs, are used 'on demand'; however, the rates of discontinuation with these treatment alternatives are high owing to side-effects, dislike of needles and unwillingness of the partner to participate.

A large proportion of patients has a combination of psychogenic and organic ED. Organic ED may be associated with progressively worsening performance anxiety, which further worsens erectile function. To treat these men holistically, the physician and psychotherapist may need to collaborate and combine counselling with a physical therapy, such as oral pharmacological agent.

### Pharmacological treatment

#### Oral pharmacological agents

PDE5 inhibitors are a breakthrough therapy in the treatment of ED (Table 4). The PDE5 inhibitors selectively inhibit PDE5 and increase the amount of cGMP available for smooth-muscle relaxation, inducing vasodilatation, increased corporal blood flow and erection.

Numerous studies have documented the efficacy, safety and tolerability of the potent, competitive on-demand PDE5 inhibitor drugs sildenafil (Viagra, Pfizer, Inc., New York, NY, USA), tadalafil (Cialis, Eli Lilly and Company, Indianapolis, IN, USA) and vardenafil (Levitra, Bayer Schering, Pharma AG, Leverkusen, Germany), and daily dosing of tadalafil in the treatment of ED in a wide range of patients, including those with hypertension, diabetes, spinal cord injury, other concomitant medical conditions and in those patients taking a wide variety of concomitant medications.14,17,18 The overall efficacy for the different PDE5 inhibitors appears similar with 65–70% of men achieving completion of sexual intercourse. Efficacy is related to the extent and severity of ED, with significantly reduced efficacy demonstrated in patients with severe coronary disease and risk

<table>
<thead>
<tr>
<th>Risk</th>
<th>Cardiac status</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>• Controlled hypertension</td>
<td>Manage in primary care</td>
</tr>
<tr>
<td></td>
<td>• Mild valvular disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Mild stable angina</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Post-revascularisation</td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>• Recent MI or cerebrovascular accident (6 weeks)</td>
<td>Specialised evaluation recommended</td>
</tr>
<tr>
<td></td>
<td>• Congestive heart failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Murmur of unknown cause</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Moderate stable angina</td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>• Uncontrolled angina</td>
<td>Refer for cardiac opinion</td>
</tr>
<tr>
<td></td>
<td>• Uncontrolled hypertension</td>
<td></td>
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<tr>
<td></td>
<td>• Severe heart failure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Recent MI or cerebrovascular accident (2 weeks)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• High-risk arrhythmia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Hypertrophic cardiomyopathy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Moderate/severe valve disease</td>
<td></td>
</tr>
</tbody>
</table>

ED, erectile dysfunction; MI, myocardial infarction.

**Table 3 Guidelines for prescribing ED treatment in patients with cardiac disease**

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vasculogenic ED, diabetic ED and post-radical prostatectomy ED. Data indicate that there are differences among sildenafil, tadalafil and vardenafil in pharmacokinetic properties, efficacy, potency, half-life and adverse effect profiles (Table 4). Food high in fat delays and reduces the absorption of sildenafil and vardenafil, but does not affect the rate or extent of absorption of tadalafil. The mean time to maximum plasma concentration of sildenafil and vardenafil is 1 h and for tadalafil is 2 h, while the half-lives of sildenafil and vardenafil are 4–5 h and that of tadalafil is 17.5 h.

Daily dosing with tadalafil (Cialis 2.5, 5 and 10 mg) results in efficacy and side-effect rates comparable with those of on-demand application of the highest doses of either tadalafil or other PDE 5 inhibitors, and can be considered first-line therapy, especially in men who engage in frequent intercourse or regard spontaneity of sexual intercourse as a key treatment goal.19 Daily dosing

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Table 4 On-demand/daily phosphodiesterase type 5 (PDE5) inhibitors

<table>
<thead>
<tr>
<th>Drugs</th>
<th>Onset</th>
<th>Duration of response following on-demand dosing</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sildenafil</td>
<td>Sexual arousal is essential for a response; May occur as early as 20 min after on-demand administration</td>
<td>Sildenafil 4–6 h</td>
<td>On-demand sildenafil, tadalafil and vardenafil or daily dosing of tadalafil</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>High fat meal limits speed and extent of absorption of sildenafil and vardenafil, but not tadalafil</td>
<td>Vardenafil 6–8 h</td>
<td>Assess patient fitness for renewed sexual activity prior to initiating treatment</td>
</tr>
<tr>
<td>Vardenafil</td>
<td>Detumescence occurs immediately following ejaculation or cessation of sexual arousal</td>
<td>Tadalafil up to 36 h</td>
<td>Dosage</td>
</tr>
<tr>
<td>Sildenafil</td>
<td>Tablets and Starting dose</td>
<td>Timing of dose</td>
<td>Maximum dose</td>
</tr>
<tr>
<td>(Viagra, Pfizer Inc., New York, NY, USA)</td>
<td>25, 50, 100 mg and 50 mg</td>
<td>On-demand-30–60 min</td>
<td>100 mg</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>10, 20 mg</td>
<td>20 mg</td>
<td>On-demand-60–120+ min</td>
</tr>
<tr>
<td>Vardenafil</td>
<td>10, 20 mg</td>
<td>10 mg</td>
<td>On-demand-20–60 min</td>
</tr>
<tr>
<td>Tadalafil</td>
<td>2.5, 5 mg</td>
<td>5 mg</td>
<td>Daily (nightime)</td>
</tr>
</tbody>
</table>

Drug selection
- Choice of drug should be individualised to patient’s needs
- No ‘head-to-head’ comparative studies are available
- The extended period of response to tadalafil may suit some patients
- Daily dosing of tadalafil may offer some patients additional sexual spontaneity

Metabolism
- Rapidly absorbed after oral administration
- Maximum plasma concentrations are reached within 30–120 min in the fasted state
- Pharmacokinetics are dose-proportional over the recommended dose range
- Extensively metabolised by CYP3A4 (major route) and CYP2C9 (minor route) hepatic microsomal isoenzymes

Adverse effects
- Adverse effects are dose related and are usually of mild to moderate severity
- Most common are headache, facial and upper trunk flushing, dyspepsia, muscle/back ache and nasal congestion.
- Transient alteration in colour vision may occur with sildenafil and vardenafil
- No cases of priapism have been reported in routine clinical use

Drug interactions
- Concomitant use of potent cytochrome P450 3A4 inhibitors (e.g. erythromycin, ketoconazole, itraconazole and protease inhibitors) as well as the non-specific CYP inhibitor, cimetidine, is associated with increased plasma levels
- Concomitant administration of CYP3A4 inducers, such as rifampin, will decrease plasma levels
- Potentiation of the hypotensive effects of nitrates and administration in patients who use nitric oxide donors or nitrates in any form is therefore contraindicated

cGMP, cyclic guanosine-3’5’-monophosphate; CYP, cytochrome P450.
may improve endothelial function and improve or restore erectile function. Salvage of on-demand tadalafil failures with daily or alternate day administered high-dose tadalafil (10–20 mg) has been reported but is limited by the relatively high cost of treatment.20

Treatment with PDE5 inhibitor drugs is generally well tolerated and the adverse effects reported are usually transient, mild to moderate in nature, dose dependent and often attenuate or disappear with continued use. The most commonly reported adverse effects are headache (11–16%), flushing (2–11%), dyspepsia (4–10%), muscle/back ache (0–4%) and nasal congestion (2–9%). In most instances, adverse effects are mild, are best managed symptomatically and will resolve with 4–6 weeks, but on occasions, cessation and/or a trial to a second PDE5 inhibitor drugs and another treatment may be indicated. Blindness due to non-arteritic anterior ischaemic optic neuropathy has been linked to the use of PDE5 inhibitors. Although a causal relationship has not been established, loss of vision or reduced vision, whether painful or painless, demands urgent patient assessment and immediate cessation of PDE5 inhibitor use.

PDE5 inhibitor drugs are contraindicated in patients taking aerosol, tablet or topical short- or long-acting organic nitrates, such as nitroglycerin or isosorbide dinitrate. PDE5 inhibitors have been shown to cause greater decreases in blood pressure in some patients on organic nitrates. There is currently no evidence of any direct deleterious effect on myocardium, and there is an increasing body of evidence to support the concept that PDE5 inhibitors improve endothelial function and, therefore, are likely to be cardioprotective.

**Intracavernosal injection (ICI) therapy**

Treatment with patient-administered ICI therapy using vasodilator drugs, such as alprostadil (Caverject Impulse, Pfizer) alone, or in combination with papaverine and phentolamine, which relax the arterial and trabecular smooth muscle, is an effective treatment for ED.21 ICI therapy can be used in most men with ED but is especially useful in men who fail to respond to oral pharmacological agents (Table 5).22

Alprostadil resulted in an erection of sufficient rigidity for sexual intercourse in 72.6% of men with ED.21 The principal side-effects of ICI of alprostadil are pain at the site of injection, which occurs in up to 30% of patients, and corporal fibrosis resulting in the development of penile nodules and curvature in 9–23.3% of mid- and long-term users. Priapism is a rare complication that can cause irreversible ischaemic damage to the corpora cavernosa with subsequent fibrotic damage and permanent loss of erectile function. Systemic side-effects are

### Table 5 Alprostadil

<table>
<thead>
<tr>
<th>Action</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relaxation of trabecular smooth muscle and dilatation of cavernosal arteries, expansion of lacunae and entrapment of blood by compression of the drainage venules against the tunica albuginea</td>
<td></td>
</tr>
<tr>
<td>Administered by direct intracorporal injection (Caverject, Pfizer Inc., New York, NY, USA)</td>
<td></td>
</tr>
</tbody>
</table>

**Onset**

- 5–15 min of intracavernosal injection (ICI)
- Arousal is usually required to produce a maximal response.
- With correct dosing, detumescence should commence within 10–20 min of ejaculation, but a fully flaccid penis may not occur for a further 1–2 h.

**Dosage**

- Assess patient fitness for renewed sexual activity
- Administered 5–15 min before planned sexual activity
- Individualise dose by initial in-office physician supervised dosage titration using the lowest possible effective dose

**Caverject Impulse**

- 1 mL ampoules as Caverject Impulse 10 (10 mcg), Caverject Impulse 20 (20 mcg)
- Instruct patient in sterile injection technique, used needle disposal, management of prolonged erections
- Maximum frequency of use is no more than three times a week, with at least 24 h between each dose.
- Start with 5 mcg and titrate in 5 mcg increments to a maximum of 20 mcg
- Start with 1.25 mcg and titrate in 1.25 mcg increments in spinal cord injured (SCI) patients

**Management of prolonged erection**

- Use lowest possible effective dose
- If still rigid
- 2 h after administration – 120 mg pseudoephedrine
- 4 h after administration – 120 mg pseudoephedrine/walk briskly for 10–15 min
- 6 h after administration – contact treating doctor or hospital A&E
- Some patients may require aspiration of corpora/irrigation with dilute vasoconstrictors/surgical drainage

**Metabolism**

- Short duration of action and a brief plasma half-life
- 30% of the drug is metabolised within the corpora cavernosa and/or urethral mucosa and up to 80% after the first pass through the lung to inactive metabolites.

**Adverse effects**

- Mild penile pain (15–20%), priapism (0.25%) AND corporal fibrosis (5–10%) with long-term use
- Approximately 30% of users discontinue ICI each year

**Drug interactions**

- Systemic drug–drug interactions are unlikely due to low or undetectable levels of alprostadil in the peripheral venous circulation
uncommon (∼1%), include dizziness, tachycardia and hypotension, and result from leakage of the drug into the circulation. Alprostadil has superior efficacy and reduced risk of priapism and intracorporal fibrosis compared with papaverine alone or in combination with phentolamine. As such, papaverine should be restricted to informed patients refractory to alprostadil.

Combination pharmacotherapy of alprostadil combined with other agents, such as papaverine and phentolamine, is effective in 91.6% of patients and appears effective as ‘salvage therapy’ in treating patients with severe vasculogenic ED.21

The self-injection technique should be taught by either the physician or the practice nurse. Relative contraindications to ICI therapy include anticoagulation, previous poor compliance and a history of priapism.

Vacuum constriction devices
The vacuum constriction device involves application of a vacuum to the penis in a vacuum cylinder causing tumescence and rigidity, which is sustained using a constricting ring at the base of the penis. The penile physiological changes differ from a normal erection in that trabecular smooth-muscle relaxation does not occur, and blood is simply trapped in both the intracorporal and extracorporal compartments of the penis distal to the constricting ring.

Vacuum constriction devices require a motivated patient and a cooperative partner. They are more popular in middle and old age group couples and are uncommon treatment choices in single younger men. Approximately 60–70% of men find the device straightforward. Satisfaction rates, both short and long term, vary considerably from as low as 27% to 68% short term, to as high as 69% with 2 years follow-up. Complications include petechiae, pain occurs at the site of the ring and ejaculatory changes, including pain on ejaculation and blocked ejaculation, numbness and pivoting of the penis at the base. Vacuum constriction devices are relatively contraindicated in men taking warfarin and in men with an increased risk of intravascular thrombosis due to myeloproliferative diseases and sickle-cell anaemia.

Surgical treatment
Surgical treatment of ED is usually reserved for patients in whom more conservative therapy has failed or for whom conservative therapy is contraindicated. Most of these patients will have significant arterial or venous disease, penile corpus cavernosum fibrosis or Peyronie disease, or will, by choice, prefer the prospect of a ‘one-off’ solution. While the outcome of surgical intervention may be more reliable in certain selected patients, the incidence of morbidity and complications is significantly greater than with medical treatment.

Penile prosthetic implants
Malleable or multicomponent inflatable penile implants are usually reserved for patients in whom more conservative therapy has failed and are associated with high satisfaction rates. Device failure and prosthetic infection are uncommon. Infection is the most problematic complication following surgery and often requires removal of the prosthesis, and either immediate replacement or staged reimplantation at a later stage.

ED in special populations
Peyronie’s disease
Peyronie’s disease is curvature of the penis due to fibrosis within the tunica albuginea. The affected corpora cavernosa cannot lengthen on erection, leading to curvature. The condition is most common in middle-aged men who are sexually active. Its exact aetiology remains unknown, but it may result from trauma and bleeding into the tunica, followed by activation of the inflammatory process and fibrosis. It is regarded as a disorder of wound healing, is associated with similar conditions such as Dupuytren’s contracture and Ledderhose disease, and may have an inherited basis.23

ED occurs in 30–40% of men with Peyronie disease. Although the mechanism of their ED is not clearly understood, most appear to have a vascular problem, such as arterial insufficiency where the fibrosis actually distorts the vessels or failure of the veno-occlusive mechanism. To a certain extent, treatment is determined by whether the patient has ED and Peyronie disease. If the patient has this combination, he may be best advised to undergo insertion of a penile implant, as surgical straightening of the penis alone is unlikely to overcome the ED. If penile curvature alone is the factor that precludes intercourse, medical or surgical treatment may be indicated. Medical treatment is limited to non-calcified plaques, curvatures less than 70 degrees, and is usually multimodal and may include antifibrotic agents, such as pentoxifylline (Trental, Paris, France) and intraplaque infiltrations with verapamil. Curvature can be surgically corrected by plaque excision and grafting or a Nesbit operation. This procedure involves shortening of the contralateral corpus cavernosum. Patients should be warned of the risks of penile shortening and onset of ED after surgery.
Renal failure
Chronic renal impairment is associated with a high incidence of ED, with the incidence increasing with the level of creatinine. ED is present in about 50% of patients by the time they require dialysis and is associated with anaemia, autonomic neuropathy, reduced testosterone levels with elevated prolactin, accelerated arterial disease, other drug therapies and psychological stress. Erythropoietin treatment and transplantation with normalisation of renal function often restore or improve the patient’s overall quality of life and erectile function.

Pelvic surgery
Damage to cavernous and other pelvic nerves following surgery to the rectum, bladder or prostate is often associated with erectile and/or ejaculatory dysfunction. Anatomic nerve-sparing surgical techniques minimise damage and reduce the risk of ED. Patients who undergo gastrointestinal surgery that results in an ileostomy or colostomy may suffer depression or loss of self-esteem, which may cause ED. Preliminary evidence suggests that the sooner pharmacological treatment is started after an operation, the more likely the patient is to regain normal erectile function.

Penile injuries
Blunt or penetrating injuries can cause a penile fracture, rupture of the tunica albuginea or neurovascular bundle damage, with resultant ED. Complete urethral disruption injuries from a pelvic fracture are almost universally associated with ED, often due to a combination of neurological and vascular impairment, which may be difficult to treat.

Radiation therapy
Pelvic radiation therapy, whether by external beam or brachytherapy with radioactive seeds inserted into the prostate, can produce ED. While ED rates immediately after external radiotherapy are low – less than 10% at 1 month and 12 months – they increase over time, with 33% of patients reporting ED at 36 months and a mean time to ED of 14.5 months.

BPH with lower urinary tract symptoms (LUTS)
Recent studies have shown a clear association between ED and BPH with LUTS. The association is independent of age, but the more severe the LUTS, the more severe the ED. Recent data have not only confirmed this association but also demonstrated a moderate effect of tadalafil on patients with LUTS.

Conclusion
ED is a common compliant and is often associated with a reduced quality of life for sufferer and partner. ED is associated with a variety of risk factors, including diabetes mellitus, hypertension, hyperlipidaemia and cigarette smoking. ED may be the first manifestation of generalised endothelial dysfunction and is a predictor of overall cardiovascular health and silent myocardial ischaemia. Treatment with ED pharmacotherapy alone or in combination with graded psychosexual therapy is effective in improving and/or restoring sexual function in most men.

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