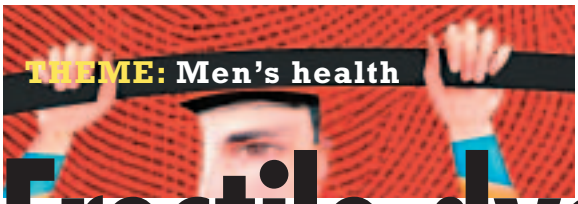

Erectile dysfunction

A guide to diagnosis and management

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BACKGROUND Erectile dysfunction (ED) is a common age related problem best managed in general practice. The incidence of ED will thus increase as men live longer. It is only in the past decade that the pathophysiology of ED has been well understood.
OBJECTIVE This article discusses the mechanisms of normal erectile function and dysfunction, and the assessment and management of ED.
DISCUSSION The success of currently available and newly emerging oral agents has revolutionised the management of ED. However, the majority of men with ED remain undiagnosed and untreated and patients are often unable to distinguish between a problem of ED, desire or libido. It is particularly important for general practitioners to enquire about ED in middle aged and older men, diabetics and patients with vascular disease. Appropriate management goes beyond management of the actual condition, and involves addressing lifestyle and psychosocial issues.

Erectile dysfunction (ED) is defined as the persistent inability to achieve or maintain an erection sufficient for satisfactory sexual performance. The prevalence of the disorder is age related and varies depending upon the degree of dysfunction.[1] Erectile dysfunction affects men of all ages, from very early adulthood (when almost 10% of men are affected), to old age (76% of men aged 80 years and over are affected).[1]

For practical clinical purposes, ED is due to:

- organic
- psychogenic, or
- a mixture of both organic and psychogenic factors (*Table 1*).

In organic ED, the man is usually over 40 years of age and the ED is more likely to be progressive in its presentation. There is usually loss of early morning erections and masturbation is not possible. As the majority of these men are usually in stable, long term relationships, the ED is not situational.

A man under the age of 40 years with anxiety related ED may have early morning erections or be able to masturbate without difficulty. The ED may have come on suddenly, be episodic, and occur in some situations and not in others. Naturally, these generalisations are simplifications, and organic and psychological causes are often both present.

Organic causes account for the vast majority of cases of ED and these are primarily vascular in origin, particularly associated with hypertension, ischaemic heart disease and diabetes mellitus.[1] Erectile dysfunction may be an early predictor of cardiovascular disease. Studies show that 64% of men hospitalised for myocardial infarction had previous ED[2] and 57% of men who had bypass surgery had previous ED.[3]

Long standing diabetes is also associated with neuropathy and this is important as oral agents are less efficacious in the treatment of ED in these patients. Saenz de Tejada et al[4] suggest that 75% of men will develop ED within 10 years of onset of diabetes and that ED may not only be a presenting symptom of diabetes mellitus, but that it is significantly predictive of neuropathic symptoms and poor glycaemic control.

Severe depression like any severe chronic illness will be associated with ED, in part because of general malaise, poor circulation and associated reduced desire exacerbated by antidepressants.

Performance anxiety and other anxiety related circumstances are also worthy of discussion, as they are not uncommon. While these may contribute to the organically based ED of a middle aged man, they are the usual cause in men under the age of 40 years.

Table 1. Common causes of erectile dysfunction

Organic
- Vascular disease
- Diabetes
- Medications
  - antidepressants
  - cholesterol lowering drugs
  - psychotropics
  - antihypertensives
- Cigarette smoking
- Alcohol

Psychogenic
- Major depression
- Generalised anxiety
- Performance anxiety

Mixed organic and psychogenic

More severe psychiatric disorders, such as entrenched body image problems may require psychiatric referral.

Identifying the problem

Erectile dysfunction is generally under diagnosed and consequently under treated, with only approximately 10% of men with ED having discussed their problem with their doctor.[5] Studies in Europe and Australia indicate that 75–88% of men with ED are not treated.[6] Many affected men visit their general practitioners for management of other morbidities and others may present for a check up, hoping to be asked about ED. Some suggestions for 'breaking the ice' in inquiring about a patient's sexual life are:

- creating a friendly, nonthreatening atmosphere (this may be difficult because of pressure of the waiting room), and
- do not assume sexual orientation or sexual preference or indeed believe the patient is, or wishes to be, sexually active.

If a patient presents for a general check up, it is essential to include a sexual history as part of assessing sexually transmitted infection risk as well as sexual dysfunction. A useful approach is:

'Do you suffer from headaches, dizziness, chest pain, reflux, shortness of breath, bowel symptoms, urinary symptoms?'

Then: 'Are you sexually active?'

If the answer is 'No': 'Is this of any concern to you?'

If the answer is 'Yes': 'Do you have any concerns about this?'

An affirmative reply is permission to discuss. If the reply is 'No' when in fact he is concerned, there remains an invitation for him to return.

A patient coming in for a repeat prescription provides an opportunity to discuss possible side effects: 'It is not uncommon that treatment may also cause difficulty with sexual activity; have you any concerns about this?'

Opportunities are endless as to how the GP may ask about sexual concerns in a nonthreatening way. Patients are often very relieved and, not infrequently, the atmosphere of trust reaches a new level. The patient may return to discuss other related and nonrelated personal concerns in his life.

Assessing ED

History taking is the mainstay of diagnosis. It is crucial to ascertain that the patient has a clear complaint of ED and not any other symptom (eg. loss of libido or premature ejaculation which may be related to ED).

When a patient's presenting complaint is one of a loss of interest in sexual activity, this may be secondary to organic or psychological ED. However, it is important to exclude hypogonadism (testosterone deficiency). Conway et al[7] give a clear guide as to what constitutes androgen deficiency. It affects approximately one in 200 men and while these men may present with ED, on careful history taking, they actually lack libido (desire) rather than having ED. Not uncommonly, it is the partner who suggests seeking medical opinion. (*See* the article on testosterone deficiency by Carolyn Allan and Robert McLachlan page 422 this issue).

Discussion of the situations in which ED occurs and the presence or absence of early morning erections can help elucidate the cause. Symptoms of vascular disease and diabetes should be sought, along with a medication history, cigarette and alcohol use.

The routine examination should exclude comorbid diseases:

- examination of genitalia is important to exclude plaques in the shaft of the penis (Peyronie disease), however, patients will usually present to complain about a curvature in the erect or semi-erect penis which may/may not be painful and may/may not interfere with satisfactory sexual intercourse

Table 2. Investigation for ED

Full blood count
Liver function test
Electrolytes, urea and creatinine
Lipid profile
Glucose
Thyroid function test
Testosterone, luteinising hormone, progesterone (hypogonadism)
Ferritin (haemochromatosis may cause hypogonadism in Anglo-Celtic patients)

- scrotal examination may reveal small testicular volume, suggesting hypogonadism.

Because the neurological supply to the corpus cavernosum travel around the outer capsule of the prostate, only significant damage to these would lead to ED. Under these circumstances, digital rectal examination (DRE) would theoretically reveal significant prostate disease such as hardness and irregularity of the prostate consistent with advanced cancer of the prostate. This is uncommon but needs to be excluded. In the absence of significant prostate abnormality upon DRE, the issue of prostate specific antigen (PSA) should be dealt with separately, ie. only after obtaining informed consent. Usual investigations are shown in *Table 2*.

Addressing psychological issues

The patient's age is important in that it reflects the individual's 'overriding concern' or 'gaze'. For example, a man in his early 20s is primarily consumed with his emerging identity. Contradictions he may be facing include:

- strong-weak
- mature-immature
- independent-dependent
- stoic-emotional
- sexual predator-sexually vulnerable.

In addition, he may also be wrestling with the issue of sexual identity, and clearly the issue of body image is central to his being.

For a man in his mid 20s onward, his 'gaze' is predominantly that of 'engagement', referring to the external environment, namely work, and internal engagement at a personal, intimate level with another person or people in general. Confusion and uncertainty about any of the above are common, and the possible resultant anxiety may present as ED.

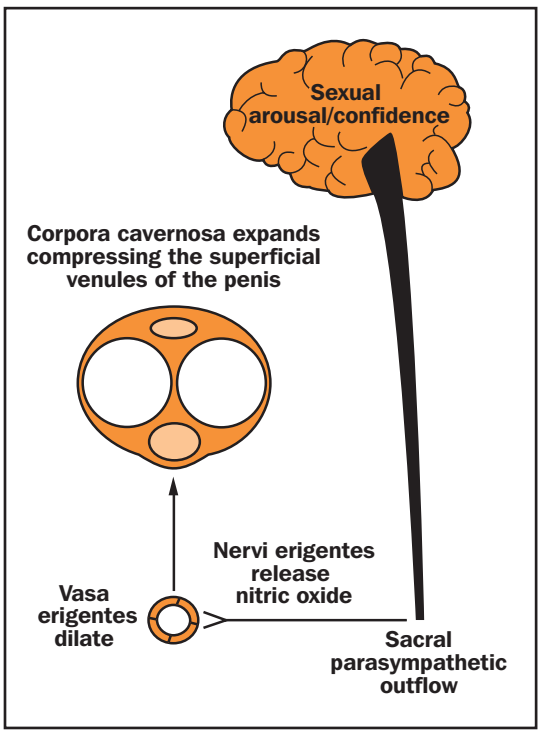

Figure 1. Physiology of erection

Similarly, middle aged men may have significant anxiety in dealing with loss of youth and emerging old age. Despair rather than acceptance may result, leading to, or at least contributing to ED. This group is also preoccupied with 'disengagement' from the workforce. While this stage may lead to a higher quality of life, it may also bring with it anxieties for him and or his partner who may not be used to having him home all day.

Consideration of these issues often leads to an appreciation by the patient that his concerns have been validated (regardless of whether or not his dysfunction is resolved).

Treatment

For an appreciation of the treatment of ED, an understanding of the physiology of erectile function is very useful (*Figure 1*). The basic requirement for normal erectile function is the ability of the smooth muscle of the corpus cavernosum to relax. During sexual arousal, this is mediated through the release of nitric oxide (NO) from the para-sympathetic nerves, endothelial cells and possibly the corporeal smooth muscle cells. The release of NO in the smooth muscle cells of the corporea leads to relax-

ation of these cells mediated through c-GMP which is then converted by the enzyme PDE5 to GMP.

In the flaccid state arterial blood flow and venous outflow are in equilibrium. The emissary veins are open and the cavernosal sinusoids and arterioles are in a contracted state. Relaxation of the corporeal smooth cells expands the sinusoids which become engorged with blood which itself becomes trapped as the emissary veins are themselves compressed against the relatively unyielding tunica albuginea. Therefore, the penis is in an erect state. For normal erectile function at the micro level, there needs to be, in order:

1. neural control (parasympathetics)
2. sinusoidal relaxation of the corpus cavernosa
3. arterial inflow to corpus cavernosa
4. venous occlusion from corpus cavernosum.

First line treatments

PDE5 inhibitors

The commonest cause of ED is insufficient sinusoidal relaxation (step 2 above). PDE5 inhibitors (sildenafil, tadalafil), cause a 'build up' of c-GMP in the presence of sexual stimulation. It is important to appreciate that PDE5 inhibitors' ability to treat ED is dependent upon the level of sexual arousal (leading ultimately to release of NO) and thus cannot function as 'aphrodisiacs'. This is a common misconception in the lay community leading to misuse or abuse of the medication. It may also lead to a man being denied treatment by his partner who may feel offended that he needs such medications to 'arouse' him into satisfactory intercourse.

Neuropathy (eg. diabetes) or other nerve damage (eg. radical prostatectomy) is less likely to respond to PDE5 depending upon the extent of nerve damage.

The first PDE5 inhibitor sildenafil (Viagra) became available in 1998. Goldstein et al[8] first demonstrated its efficacy and safety. Four years of clinical experience as first line therapy has confirmed that sildenafil is successful in treating overall 70% of patients with ED and its associated conditions.[9]

From its mode of action it becomes clear why the use of nitrate medication is absolutely contraindicated with sildenafil. The build up of exogenous NO with nitrate medication together with the indirect internal build up of NO via sildenafil may lead to a profound hypotensive event.[2]

A relative contraindication to the use of sildenafil (and, it may be argued, for any treatment for ED) is the patient's cardiovascular risk. It has been demonstrated that if a patient can, for example, walk 1 km in 15 minutes on the flat and climb two flights of stairs in 10 seconds without chest discomfort, pain or undue breathlessness, the risk for ischaemia during sexual activity is low, provided that the patient is with the usual sexual partner in a familiar setting, and without the added stress of a heavy meal and/or alcohol.[10]

Sildenafil is generally well tolerated. Adverse events such as headache, flushing, dyspepsia, and nasal congestion occurred in 4–16% of patients (compared to placebo: 1–4%). Only a small proportion of these patients ceased medication as a result of these side effects which are usually mild and transient.[9]

Tadalafil (Cialis) was launched in Australia in March 2003, and vardenafil (Levitra) in May 2003. They have similar efficacy, safety and tolerability to sildenafil. Vardenafil has a half life of 4–5 hours.[15] Pharmacokinetic differences between tadalafil and sildenafil are shown in *Table 3*.

Table 3. Comparison sildenafil and tadalafil

	Onset	Duration	Dose	Special comments
Sildenafil	60 min	3–4 hours	50 mg	25 mg in the elderly 100 mg in some patients Absorption retarded by heavy meals Efficacy reduced by alcohol Partially inhibits PDE6 causing Transient blue-green difficulty in 3% of patients
Tadalafil	30 min	36 hours	10–20 mg	10 mg dose in renal impairment Not affected by meals or alcohol Do not give nitrate within 4–5 days of dose

Apomorphine

An alternative first line medication to PDE5 inhibitors is apomorphine, soon to be available in Australia. Taken sublingually, it acts centrally via the paraventricular nucleus of the hypothalamus, an area involved in the initiation of erection during sexual stimulation. The onset of effect is within 20 minutes. With efficacy rates of 46–55%, studies suggest that apomorphine is not quite as effective as PDE5 inhibitors.[16] It can be used in the presence of other conditions such as diabetes, ischaemic

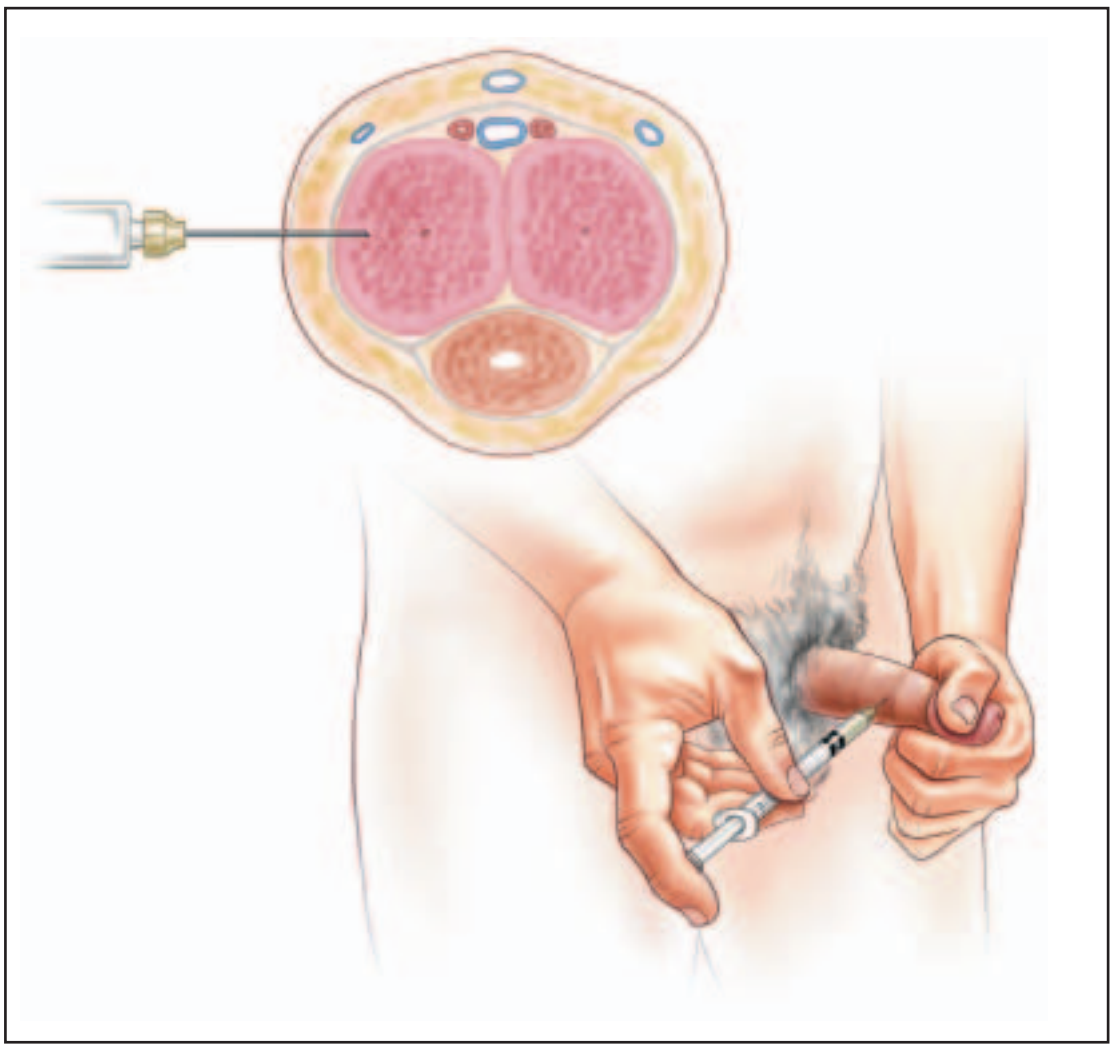

Figure 2. Intracavernosal self injection technique

heart disease and depression and concomitant medications (including nitrates) are not contraindicated, although caution in those susceptible to hypotension is required.[17] Side effects include nausea and the potential to lower blood pressure when taken with alcohol in some individuals.

Second line treatments

Intracavernosal injections

This treatment is useful where PDE5 inhibitors have failed or are contraindicated. They work by directly relaxing the smooth muscle lining the vascular spaces in the corpora cavernosum.[18] Unlike PDE5 inhibitors, no sexual stimulation is required for the injections to work. However, patients do require adequate instruction in injection technique (*Figure 2*) and dosage titration. Side effects include pain at the site of injection, priapism, and in long term use, scarring of the tunica albuginea with potential curvature and shortening of the shaft of the penis. Alprostadil (Caverject) is the commonest injection used in Australia. Intracavernosal injections containing phentolamine and papaverine with or without alprostadil are also available. Patients should be warned about priapism and advised on initial management with moderate exercise and decongestant tablets and to seek medical advice if priapism persists after 4–6 hours.

Transurethral alprostadil therapy is rarely used in Australia. Clinically it was only approximately 30% effective and not uncommonly caused urethral burning and penile and testicular pain.[9]

Vacuum erection devices

Vacuum devices can be useful for patients with chronic or occasional organic or psychogenic ED or where other treatments have failed, and may be

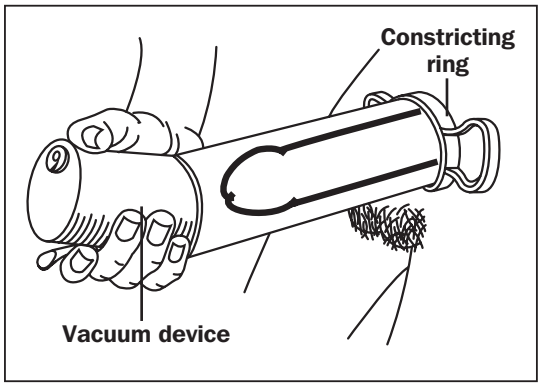

Figure 3. The vacuum device is placed over the penis, subsequent vacuum draws blood into the penis: the constructor ring is rolled onto the base of the penis and the device is removed from the engorged penis

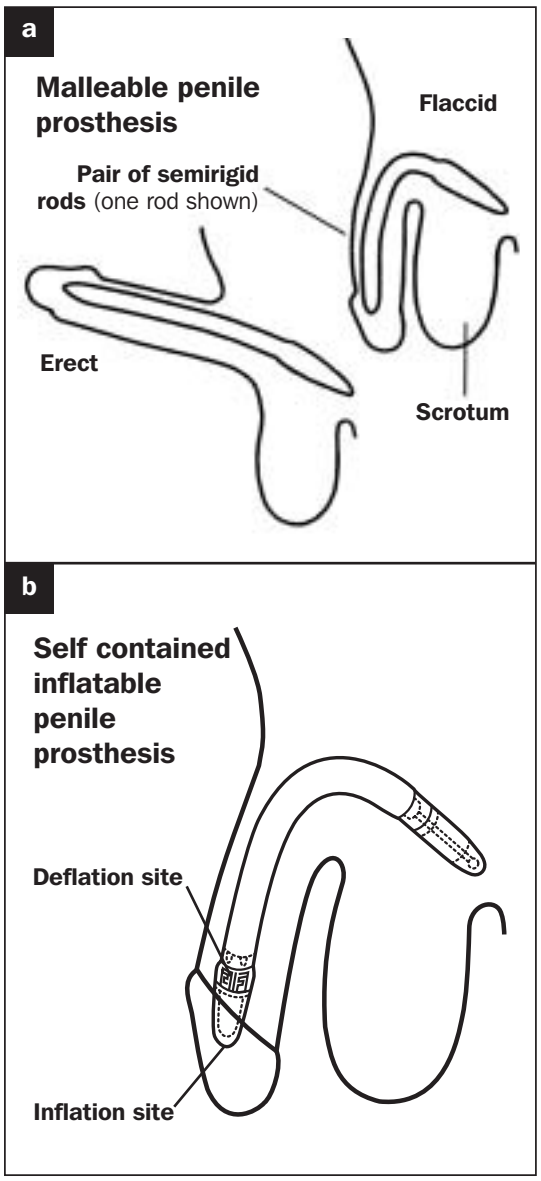

Figure 4a, b. Penile prosthetic implants a. Malleable rod b. Inflatable implant

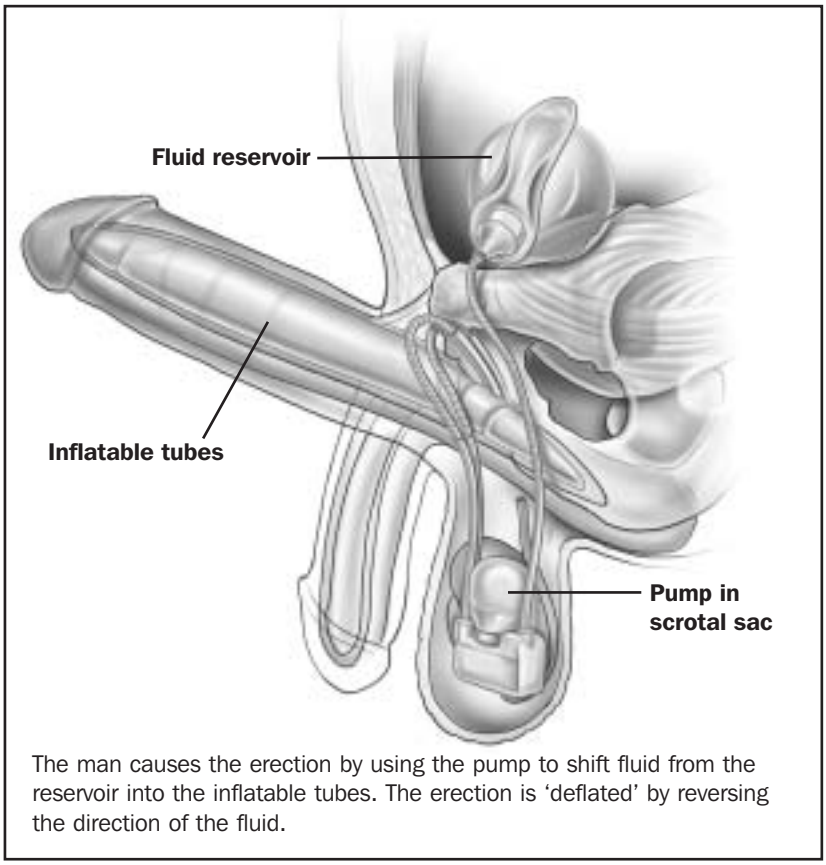

Figure 5. Penile inflatable implant

used together with other ED therapies. *Figure 3* demonstrates the use of a vacuum device. The erect penis is bluish in colour and cool to touch. Side effects include pain, numbness, bruising and a sense of altered ejaculation. Cooperation by the partner is required and drop out rates tend to be high.

Surgical implants

Men with severe ED not responding to other treatments may opt for surgical implants. Different types of prostheses are available, ranging from malleable rods (*Figure 4a, b*) to inflatable tubes that mimic the function of the corpora cavernosa (*Figure 5*) and semi-rigid devices. Surgery is quite expensive and complications such as mechanical failures and infection can occur even years later. Urologists with a particular interest in this area and in other forms of penile surgery for ED (severe Peyronies, re-establishment of penile vascular supply following pelvic trauma) should be consulted.

Conclusion

Erectile dysfunction is a common disorder in middle aged and older men. Although less

common in younger men, it is usually a more urgent condition for these individuals. Erectile dysfunction requires understanding in areas such as pharmacology, cardiology, psychology andrology, endocrinology and urology. None of these disciplines on their own are sufficient to deal with ED, and that is why the well informed GP is ideally placed in being able to synthesise from all these to manage the condition.

Conflict of interest: none declared.

SUMMARY OF IMPORTANT POINTS

- ED is a common condition that is under diagnosed.
- ED is essentially a vascular disorder associated with other comorbid conditions of middle age.
- The availability of efficacious, tolerable, and safe oral treatment allows most cases of ED to be managed in a general practice setting.
- The doctor-patient relationship will be enhanced if a sexual history and diagnosis of ED is included as part of the overall management plan of male patients.

References

1. Chew K K, Earle C M, Stuckey B G A, Jamrozik K, Keogh E J. Erectile dysfunction in general medical practice: Prevalence and clinical correlates. Int J Impot Res 2000; 12:41–45.
2. Zusman R M. Cardiovascular data on sildenafil citrate: Introduction. Am J Cardiol 1999; 83(5A):1c–2C.
3. Feldman H, Goldstein I, Hatzichristou D G, Krane R J, McKinlay J B. Impotence and its medical and psychosocial correlates: Results of the Massachusetts Male Aging Study. J Urology 1994; 151(1):54–61.
4. Saenz de Tejada I, Anglin G, Knight J R, Emmick J T. Effects of tadalafil on erectile dysfunction in men with diabetes. Diabetes Care 2002; 25:2159–2164.
5. Diagnosis and management of erectile dysfunction: A guide for practice in Australia. New South Wales: Medimedia, 1998.
6. Giuliano F, Chevret-Measson M, Tsatsaris A, Reitz C, Murino M, Thonneau P. Prevalence of erectile dysfunction in France: Results of an epidemiological survey of a representative sample of 1004 men. Eur Urol 2002; 42(4):382–389.
7. Conway A J, Handelsman D J, Lording D W, Stuckey B, Zajac J D. Use, misuse and abuse of androgens. Med J Aust 2000; 172:220–224.
8. Goldstein I, Lue T F, Padma-Nathan H, Rosen R C, Steers W D, Wicker P A. Oral sildenafil in the treatment of erectile dysfunction. N Engl J Med 1998; 338:1397–1404.
9. Lyseng-Williamson K A, Wagstaff A J. Management of erectile dysfunction. Disease Management and Health Outcomes 2002; 10 7:431–432.
10. Drory Y. Sexual activity and cardiovascular risk. Euro Heart J Suppl 2002; 4(Suppl H):H13–H18.
11. Hackett G I. What do patients expect from erectile dysfunction therapy? Eur Urol 2002; 18:4–11.
12. Brock G. Oral agents: First line therapy for erectile dysfunction. Eur Urol 2002; 18:12–16.
13. Emmick J T, Stuewe S R, Mitchell M. Overview of cardiovascular effects of tadalafil. Eur Heart J Suppl 2002; 4(Suppl H):H32–H37.
14. Padma-Nathan H, Hellstrom W J G, Kaiser F E, et al. On demand IC351 (Cialis) enhances erectile function in patients with erectile dysfunction. Int J Impot Res 2001; 13:2–9.
15. Ormrod D, Easthope S E, Figgit D P. Vardenafil. Drugs Aging 2002; 19(3):217–227.
16. Heaton J. Key issues from the clinical trials of apomorphine SL. World J Urol 2001; 19:25–31.
17. Newsletter of European Association of Urology. Debruyne F M J, ed. Report of symposium held EAU Congress, Birmingham, UK, 23–26 Feb. Eur Urol 2002; 13(2):5.
18. Fallon B. Intracavernous injection therapy for male erectile dysfunction. Urol Clin North Am 1995; 22:833–845.

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