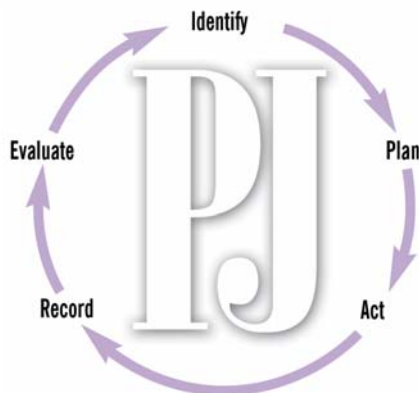


Erectile dysfunction and other problems

In the second article in a series of three on men's health, **Christine Clark** discusses erectile dysfunction, sexually transmitted diseases and testicular cancer



Identify knowledge gaps

1. List four drugs that are licensed for the treatment of erectile dysfunction.
2. What counselling points would you raise when dispensing a treatment for erectile dysfunction?
3. How is genital herpes treated?

Before reading on, think about how this article may help you to do your job better. The Royal Pharmaceutical Society's areas of competence for pharmacists are listed in "Plan and record", (available at: www.rpsgb.org/education). This article relates to "common disease states and their drug therapies" (see appendix 4 of "Plan and record").

Conditions for which pharmacists dispense medicines include erectile dysfunction and sexually transmitted infections (STIs). The provision of advice in these situations, however, is not so straightforward — both parties can feel embarrassed. Perhaps a sound knowledge of these conditions would help alleviate embarrassment on the part of the pharmacist. The availability of an area in the pharmacy for a confidential conversation will not only help with embarrassment, but may also make it easier for men to approach the pharmacist initially.

Erectile dysfunction

Erectile dysfunction (ED, impotence) is defined as "the persistent or recurrent inability to achieve or maintain an erection good enough to complete the chosen sexual activity satisfactorily".¹ Persistent ED is estimated to affect about 10 per cent of men at any time. ED can have physical and psychological causes — stress, anxiety and depression have all been implicated. Physical causes of ED are shown in Panel 1. The occasional inability to

achieve a satisfactory erection is not normally regarded as a problem, but it is important to note that ED may be a symptom of cardiovascular disease or diabetes.

Treatments Until recently, the only licensed treatment for ED was alprostadil, which has to be either injected into the penis (Caverject) or inserted into the urethra (MUSE). This changed when sildenafil (Viagra) the first oral treatment for ED became available in 1998. At the time there was concern as to whether this medicine would be allowed on NHS prescriptions. Since then, a number of oral treatments — tadalafil (Cialis), vardenafil (Levitra) and apomorphine (Uprima) — have become available.

Sexual stimulation activates the nitric oxide/cyclic guanosine monophosphate (cGMP) pathway. Nitric oxide is released in the corpora cavernosa and activates guanylate cyclase, which increases cGMP levels. This causes the smooth muscle in the corpora cavernosa to relax, allowing the inflow of blood needed for an erection. ED drugs work on parts of this mechanism. For example, alprostadil is prostaglandin E1. It can, therefore, act directly to produce artificial erection by inhibiting α_1 adrenergic activity (relaxing smooth muscle) and causing vasodilation.

Sildenafil, tadalafil and vardenafil are all phosphodiesterase type 5 (PDE5) inhibitors. There are many families of phosphodiesterases in the body but PDE5 is the most important in relation to penile function. Inhibition of phosphodiesterase prevents the breakdown of cGMP and thereby maintains the smooth muscle response to sexual stimulation and increases blood flow to the penis. PDE5 inhibitors do not, therefore, provoke erections but they make erection possible. According to the manufacturers, the effects of tadalafil can last for up to 36 hours (mean half-life is 17.5 hours).

Apomorphine is believed to act through stimulation of central dopamine receptors. Apomorphine selects D_2 , D_3 and D_4 receptors, particularly in the hypothalamic region of the brain, which is involved in the mediation of erections. Stimulation of these receptors mediates local actions of nitric oxide, the conversion of guanosine triphosphate to cGMP and subsequent smooth muscle relaxation in the corpora cavernosa. There is also evidence for effectiveness of yohimbine, an α_2 -adrenoceptor antagonist, derived from the bark of the yohimbe tree, for ED. Table 1 (p609) summarises some of the features of ED drugs.

The most commonly reported side effects with ED tablets are headache and facial flushing. Dizziness and disturbed vision have also been reported, so men should be advised to monitor themselves and be aware of their

own responses if they wish to drive after taking a drug. Priapism (persistent, painful erection lasting for more than four to six hours) is a rare side effect with ED tablets, but more common in men using alprostadil (0.4 per cent in clinical trials). Priapism is potentially dangerous because it can result in blood clotting and penile tissue damage; any patient with an erection that lasts over four hours must seek immediate medical treatment.

ED drugs are contraindicated in men with conditions that make sexual intercourse dangerous (eg, severe unstable angina or severe heart failure). Sildenafil, tadalafil and vardenafil are also contraindicated in patients receiving nitrates, because of the risk of hypotensive crisis. Alprostadil and apomorphine are not contraindicated in such patients, but must be used with caution. The summary of product characteristics for MUSE states "systemic interactions are un-

Panel 1: Physical causes of erectile dysfunction

Diabetes 75 per cent of men with diabetes aged 60–64 years are affected by erectile dysfunction but younger men are also affected.

Atheroma Atheroma affecting arteries that supply blood to the penis accounts for about 40 per cent of ED cases in men aged over 50. Cigarette smoking (and consequent vascular disease) is implicated in up to 80 per cent of ED cases.

Cycling Cycling has recently been recognised as a cause of ED. When cyclists sit on a thin saddle, there is a 66 per cent average reduction in blood flow through the artery running to the penis. A 25 per cent reduction occurs with a wide saddle. Over time, there can be permanent changes to the shape and performance of the artery. Regular cyclists should protect themselves by padding their bicycle crossbar, fitting a wider saddle and standing up on the pedals every 10 minutes to help keep the blood flowing.

Alcohol Regular heavy drinking can damage the nerves serving the penis and reduce testosterone levels.

Drugs Side effects of prescribed drugs, particularly those used to treat high blood pressure, heart disease, depression, peptic ulcers and cancer, can cause ED. Up to 25 per cent of ED cases may be caused by drugs taken to treat other conditions.

Neurological problems Diseases that affect nerve function (eg, multiple sclerosis), spinal injury or radical prostatectomy can cause ED.

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Table 1: Features of drugs used for erectile dysfunction, according to patient information leaflets and SPCs

Product	Recommended timing for administration	Mode of action	Dosage forms and recommended dose	Maximum recommended dose and dosage frequency	Additional information	Cost of one dose
Viagra (sildenafil)	One hour before intercourse	Phosphodiesterase type-5 inhibitor	25, 50 and 100mg tablets (50mg recommended, 25mg for elderly or those on protease inhibitors or alpha blockers)	100mg, not more than once a day	<ul style="list-style-type: none"> ■ Inhibitors of cytochrome p450 (eg, grapefruit juice) reduce clearance ■ Taking the tablet with food (especially a high fat meal) can delay the onset of action 	£4.84 (50mg tablet)
Cialis▼ (tadalafil)	At least 30 minutes before intercourse	Phosphodiesterase type-5 inhibitor	10 and 20mg tablets (10mg recommended)	20mg, not more than once a day, but continuous daily use is discouraged		£4.84 (10mg tablet)
Levitra▼ (vardenafil)	25–60 minutes before intercourse	Phosphodiesterase type-5 inhibitor	5, 10 and 20mg tablets (10mg recommended)	20mg, not more than once a day		£4.84 (10mg tablet)
Upriam▼ (apomorphine)	20 minutes before intercourse	Dopamine receptor agonist	2 and 3mg sublingual tablets (2mg recommended)	Not more than 3mg at eight-hourly intervals	<ul style="list-style-type: none"> ■ Drinking a small amount of water before taking the tablet can help it dissolve under the tongue 	£5.34 (2mg tablet)
Caverject (alprostadil)	Erection occurs 5–15 minutes after injection	Prostaglandin E1	5, 10, 20 and 40µg injections	Not more than one injection in 24 hours and not more than three times a week	<ul style="list-style-type: none"> ■ The dual chamber device can be prepared 24 hours before use but once made up, the powder for injections must be used straight away 	£7.33 (10µg cartridge)
MUSE (alprostadil)	Erection occurs 5–10 minutes after insertion	Prostaglandin E1	125, 250, 500 and 1,000µg intraurethral pellets	Two pellets in 24 hours and up to seven times in seven days	<ul style="list-style-type: none"> ■ A condom must be used with a pregnant woman ■ Must be stored between 2 and 8°C but can be kept below 30°C for 14 days 	£10.76 (250µg pellet)

Adapted from patient information leaflets and summary of product characteristics

likely because of the low levels of alprostadil in the peripheral venous circulation” but “insufficient data exists concerning the concomitant use of MUSE with vasoactive medicines”.

Sexually transmitted infections

STIs include: *Chlamydia trachomatis*, genital herpes, genital warts, gonorrhoea, hepatitis A, B or C, HIV, non-specific urethritis, pubic lice, scabies, syphilis, *Trichomonas vaginalis* and thrush. It is beyond the scope of this article to cover all of these in detail. Overall, the incidence of STIs is increasing. Many symptoms of STIs are non-specific and a full history and examination will be required to establish a differential diagnosis. Men who have any of the following symptoms should be encouraged to visit a genitourinary medicine (GUM) clinic as soon as possible:

- Discharge from the penis
- Sores or blisters on or near the penis or anus
- Rash or irritation around the penis or anus
- A burning feeling when urinating
- Pain during intercourse

Chlamydial infection Genital chlamydial infection is the most commonly diagnosed STI seen in GUM clinics in the UK. Symptoms can include discharge from the tip of the penis, pain when passing urine and burning and itching in the genital area. Infection of the rectum with chlamydia can

produce a discharge from the anus and inflammation (proctitis). However, up to half of all men infected with chlamydia will have no symptoms or mild, transient symptoms. Diagnosis is currently made by culture of a urethral swab. A urine test is under development. If *Chlamydia trachomatis* is identified it can be treated with a seven-day course of doxycycline or a single dose of azithromycin.

Herpes Genital herpes is an infection caused by herpes simplex virus (HSV) and is associated with a painful rash on the genitals. There are two types of HSV: type 1 and type 2. HSV1 usually causes oral herpes (cold sores), but can also cause genital disease. Infection is acquired by direct contact with a blister or sore. It can also be acquired from a partner shedding virus asymptotically.

More than 20,000 cases of genital herpes are reported annually in the UK, of which over 60 per cent are first episodes. Like any other viral illness, an attack of genital herpes may start with prodromal symptoms. Influenza-like symptoms and tingling or irritation in the genital area are followed by patches of genital erythema that develop into clusters of small vesicles. The vesicles rupture to form shallow, painful ulcers that then crust and heal. Most will heal by the third week. During the acute episode, inguinal lymph nodes become swollen and tender. Dysuria is also common and there may be a urethral discharge.

After primary infection the virus lies dormant in the dorsal root ganglia. Recurrence is

due to reactivation of the virus, causing either symptomatic lesions or asymptomatic viral shedding. Recurrences are usually of shorter duration and are less severe. Lesions are usually unilateral and often recur at the same site as the original lesions.

Education and counselling are important because people with genital herpes are often upset and distressed. Guilt, depression, lowered self-esteem and fear of rejection are common reactions.² People in long-term relationships often assume that their partner has been unfaithful. An explanation that genital herpes can be acquired but not clinically evident for some time (eg, months or years) may be helpful. Further, the genital herpes episode may be due to herpes simplex virus 1 (HSV-1, the main cause of cold sores) from their partner. Patient support groups such as the Herpes Viruses Association can be helpful in providing additional information and support.

Sexual contact should be avoided if prodromal symptoms or lesions are present. Men can reduce the risk of transmission to a woman by wearing a condom (if lesions are confined to the penis). Condoms may not reduce the risk of transmission from women to men, because lesions on the vulval area cannot be totally covered. However, it is important to note that infections can be acquired from people who are unaware that they are infected and are shedding the virus asymptotically. Asymptomatic viral shedding particularly occurs in the first six to 12 months

Chlamydia can cause infertility in women

after a primary infection, with HSV2 infection, and immediately before and after symptomatic recurrences.

Treatment Oral antiviral agents are effective in both first and recurrent episodes of herpes. Aciclovir, valaciclovir (a prodrug of aciclovir) and famciclovir are the currently licensed products. Oral antiviral agents reduce the duration and severity of symptoms and shorten the duration of viral shedding and time to healing. For a first episode, a five-day course of treatment should be started within five days of the onset of symptoms.

The same treatment can be given for a recurrent episode, but antiviral treatment may not always be necessary because symptoms tend to be milder and of shorter duration. Topical agents are less effective than oral agents and are not recommended.

Intermittent or continuous suppressive antiviral treatment may be necessary for some patients in whom recurrences are frequent and severe. With treatment and care, recurrent attacks can be short-lived and less severe. Up to 20 per cent of those affected never have a second attack.

Oral analgesics and bathing in salt water (half a cup of household salt in the bath) can help to relieve pain.

Testicular cancer

Testicular cancer accounts for 1 per cent of all cancers in men but it is the single largest cause of cancer-related death in men aged 18 to 35 years. The lifetime risk of developing testicular cancer is one in 400 and about

1,600 men in the UK develop testicular cancer each year. The incidence of this condition has risen by 70 per cent over the past 20 years but the reasons for this are not understood.³

In the early stages, testicular cancer may not cause any discomfort or pain and minor changes may not be immediately obvious. For this reason, self-examination of the testicles is advocated. Several organisations provide leaflets that show how to do this correctly (eg, www.icr.ac.uk/everyman contains a guide with pictures). Most testicular cancers are diagnosed because of the appearance of a painless lump in one testicle. Symptoms can also include:

- Pain and tenderness in either testicle
- Enlargement of the testicle
- A feeling of heaviness in the scrotum
- A dragging sensation in the abdomen or groin
- A sudden collection of fluid in the scrotum
- Enlargement or tenderness of the breasts

Although these symptoms can have benign causes, they should always be checked by a doctor. The cause of testicular cancer is unknown, but a number of risk factors have been identified. About 10 per cent of men with testicular cancer give a history of undescended testicles. Having a father or brother with the disease also increases an individual's risk.

No link between injury or sporting strains and testicular cancer has been found. Nor is there any evidence that hot baths can cause testicular cancer. Vasectomy does not increase the risk of developing testicular cancer.

Diagnosis and treatment About 95 per cent of testicular cancers are made up of germ cell tumours — seminomas and teratomas. Teratomas are more common in younger men (under 50 years) and account for about 70 per cent of testicular tumours. Diagnosis is established by histological examination of biopsy samples. High serum levels of the tumour markers (alpha-fetoprotein, human chorionic gonadotrophin and lactate dehydrogenase) are associated with both types of tumour. Ultrasound examination may help to distinguish between malignant and benign lesions.

Even if cancer is only suspected, the testicle will have to be surgically removed, unless it is possible to perform a biopsy during the operation, before the testicle is removed. All patients should be given the option to receive a testicular prosthesis straight after an orchidectomy, to avoid the need for an additional surgical procedure. If chemotherapy, radiation or removal of both testes is likely, then the possibility of sperm banking should also be discussed.

As with all cancers, staging of the disease is an important step in determining the most appropriate treatment. The stages of testicular cancer are described in Panel 2. The exact treatment regimen depends on the stage of the cancer. For example, for a stage 1 seminoma, radiotherapy is recommended after orchidectomy. Metastatic seminoma is treated with radiotherapy and chemotherapy using cisplatin and etoposide. Metastatic teratoma is treated with chemotherapy using the "BEP" (bleomycin, etoposide and cisplatin) regimen.

The results of treatment are good. If diagnosed early, 96 per cent of patients can be cured completely. Even when the cancer has spread, up to 80 per cent of men can be cured.

References

1. Erectile dysfunction. Available at: www.malehealth.co.uk (accessed 25 April 2004).
2. Prodigy guidance on genital herpes. Available at: www.prodigy.nhs.uk (accessed 25 April 2004).
3. Institute for Cancer Research www.icr.ac.uk (accessed 25 April 2004).

Resources

- COIN guidelines. The testis. *Clinical Oncology* 2000;12:S173.
- Health Protection Agency (www.hpa.org.uk)
- Playing Safely (www.playingsafely.co.uk).
- Herpes Viruses Association (www.herpes.org.uk).

Action: practice points

Reading is only one way to undertake CPD and the Society will expect to see various approaches in a pharmacist's CPD portfolio.

1. Obtain leaflets on testicular cancer for your pharmacy.
2. Find out how the side effect priapism is treated (read the British National Formulary, section 7.4.5, under side effects for the alprostadil monograph) and which men can be prescribed drugs for erectile dysfunction on the NHS (BNF p404).
3. Enter the window display competition being held by Developing Patient Partnerships as part of the "Pop down your local" campaign. Details available at: www.npa.co.uk

Evaluate

For your work to be presented as CPD, you need to evaluate your reading and any other activities. Answer the following questions: What have you learnt? How has it added value to your practice? (Have you applied this learning or had any feedback?) What will you do now and how will this be achieved?

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Panel 2: Stages of testicular tumours

- Stage 1 tumours are completely contained within the testicle
- In stage 2 tumours, the cancer cells have spread to the lymph nodes in the pelvic area or the back of the abdomen
- In stage 3 tumours, there are cancer cells present in the lymph nodes in the chest or above the collarbones
- By stage 4, cancer cells have spread into other organs, such as the lungs