

## Erectile dysfunction (ED)

*Synonym: impotence (no longer used, as it implies failure)*

### What is erectile dysfunction?

Erectile dysfunction (ED) used to be called impotence. Erectile dysfunction is the inability to attain and maintain an erection sufficient for satisfactory sexual performance. Although a benign disorder, it can have a significant impact on the quality of sex life of sufferers, partners and families. It is important also to consider the physical and psychosocial health of the person who has erectile dysfunction.<sup>[1]</sup> <sup>[2]</sup> Patients should be properly assessed and investigated before embarking on erectile dysfunction treatment.

### How common is erectile dysfunction?

- There is in all studies a steep age-related increase.
- Accurate estimates are difficult to obtain, as many patients fail to seek any medical help. The best available data indicate that 52% of men in the USA between 40 and 70 years of age suffer from erectile dysfunction. At least 30 to 50 million men in the USA and at least 150 million men globally have ED.<sup>[3]</sup>
- In the Cologne study of men aged 30–80 years, the prevalence of ED was 19.2%, with a steep age-related increase from 2.3% to 53.4%.<sup>[1]</sup>
- Only about 10–20% of patients with ED are believed to have a solely psychogenic cause but psychogenic factors are often present in those who are diagnosed as having a physical cause.<sup>[4]</sup>

### Risk factors for erectile dysfunction<sup>[1]</sup>

ED shares risk factors with cardiovascular disease (CVD) . Screening for CVD is a cost-effective method of secondary prevention for CVD in men presenting with ED. The following are all associated with both CVD and ED:

- Lack of exercise.
- Obesity.
- Smoking.
- Hypercholesterolaemia.
- Hypertension .
- Metabolic syndrome.
- Diabetes mellitus .

## **Erectile dysfunction causes (aetiology)**

It is important that underlying diseases and causative conditions of erectile dysfunction do not go undetected. There are many different causes of erectile dysfunction, including many drugs:

- CVD.
- Atherosclerosis (approximately 50% of cases).
- Hypertension.
- Diabetes mellitus.
- Hyperlipidaemia.
- Smoking.
- Surgery or radiotherapy to the pelvis or retroperitoneum - eg, radical prostatectomy (25-75% of these men have ED).
- Trauma.

### **Neurological Central causes**

- Parkinson's disease, stroke.
- Multiple sclerosis (MS).
- Tumours.
- Traumatic brain injury (causing hypothalamic-pituitary deficiency).

- Cerebrovascular disease.
- Intervertebral disc disease.
- Spinal cord disease or injury.

### **Peripheral causes**

- Polyneuropathy.
- Peripheral neuropathy.
- Diabetes mellitus.
- Alcoholism.
- Uraemia.
- Surgery (for example, of pelvis or retroperitoneum).

### **Hormonal**

- Hypogonadism.
- Hyperprolactinaemia.
- Thyroid disease.<sup>[5]</sup>
- Cushing's disease.

### **Anatomical**

- Peyronie's disease.
- Micropenis and other penile anomalies.

### **Drugs**

- Antihypertensives.
- Beta-blockers.
- Diuretics.
- Antidepressants: both tricyclics and selective serotonin reuptake inhibitors (SSRIs).
- Antipsychotics: phenothiazines, risperidone.

- Hormonal agents: cyproterone acetate, luteinising hormone-releasing hormone analogues - those used in the treatment of prostate cancer.
- Anticonvulsants: phenytoin, carbamazepine.
- Antihistamines.
- Recreational drugs.
- H<sub>2</sub> antagonists such as cimetidine.

## **Psychogenic causes**

### **Psychosexual factors**

- General (disorders of sexual intimacy, lack of arousability).
- Situational (partner, performance or stress).
- One study found that maintaining a regular frequency of intercourse can reduce the risk of ED for males aged 30-75 years.<sup>[6]</sup>

### **Psychiatric illness**

- Generalised anxiety states.
- Depression.<sup>[7]</sup>
- Psychosis.
- Alcoholism (the relationship with alcohol is not straightforward). A Chinese study suggested an additive association with smoking. It reported that drinking three or more standard alcoholic drinks per week might reduce sexual satisfaction and impair erectile function in current smokers and might have less effect in those who had never smoked.<sup>[8]</sup> A meta-analysis showed a protective effect of alcohol at some levels of consumption.<sup>[9]</sup>

## **Erectile dysfunction symptoms<sup>[1]</sup>**

### **History**

- Sexual history. Validated questionnaires to assess sexual function and the effects of treatment are available – for example, the International Index of Erectile Function (IIEF) . The following should be covered:
  - Current and past sexual relationships.
  - Current emotional status.
  - Erectile symptoms: onset and duration.
  - Previous advice or treatments.
  - Quality of erections (erotic and morning erections).
  - Arousal, ejaculation and orgasmic difficulties.
- Medical and past medical history:
  - This may include detail of any relevant conditions (see the causes of erectile dysfunction, above).
  - Medication should be listed.

### **History suggesting psychogenic causes** <sup>[10]</sup>

- Sudden onset.
- Early collapse of erection.
- Self-stimulated or waking erections.
- Premature ejaculation or inability to ejaculate.
- Problems or changes in a relationship.
- Major life events.
- Psychological problems.

### **History suggesting organic causes** <sup>[10]</sup>

- Gradual onset.
- Normal ejaculation.

- Normal libido (except hypogonadal men).
- Risk factor in medical history (cardiovascular, endocrine or neurological).
- Operations, radiotherapy, or trauma to the pelvis or scrotum.
- A current drug recognised as associated with ED.
- Smoking, high alcohol consumption, use of recreational or bodybuilding drugs

### **Physical examination**<sup>[1]</sup>

The examination should be focused and performed on all patients with ED:

- Genitourinary examination (it is necessary to detect, for example, Peyronie's disease, gonadal anomalies, retractile foreskin).
- Attention to any endocrine (including testicular size and secondary sexual characteristics), neurological or vascular causes as appropriate, especially if indicated by the history.
- Pulse (including peripheral pulses) and blood pressure if recent readings are not available. Because ED shares risk factors with CVD, a full cardiovascular assessment should be performed.
- Rectal examination in patients over the age of 50 years.

### **Investigations**<sup>[1]</sup> <sup>[11]</sup>

Investigations will be directed by the history and clinical findings.

- The European Association of Urology and the British Society of Sexual Medicine suggest:
  - Fasting glucose or HbA1c and lipid profile for all patients (if not assessed in the previous 12 months).
  - Morning sample of total testosterone (free testosterone if available, as it is more reliable in detection of hypogonadism).
  - Further tests (for example, PSA) only in selected patients.
  - Addition of follicle-stimulating hormone (FSH), luteinising hormone (LH), and prolactin when low testosterone is detected.
- Other specific investigations may be indicated and are appropriately arranged by urologists. Indications for referral for these further tests are given below. Further tests include:
  - Nocturnal penile tumescence and rigidity studies.
  - Vascular studies:
    - Duplex ultrasound cavernous arteries.
    - Intracavernous vasoactive drug injection.
    - Dynamic infusion cavernosography.
    - Arteriography (internal pudendal).
  - Neurological studies.
  - Endocrinology work-up.
  - Specialist psychodiagnostic evaluation.

## Indications for referral<sup>[1]</sup>

The following should be referred for further assessment or specific diagnostic tests:

- Endocrine abnormality.

- Referral for underlying organic disease as appropriate – eg, cardiovascular or neurological.
- Young patients who have had pelvic or perineal trauma.
- Penile disorders or deformities requiring possible surgical correction.
- Complex cases (whether psychiatric, cardiovascular, psychosexual or endocrine).
- If a patient or partner requests referral or special tests.

## Erectile dysfunction treatment and management<sup>[1]</sup>

- The main aim of ED management is to diagnose and treat the cause of ED when possible.
- Associated modifiable or reversible factors (lifestyle, drug-related factors) should be considered as well as specific therapies.
- Most often it cannot be cured but, where appropriate, curative therapies should be offered .
- Erectile dysfunction treatments will be selected, therefore, according to efficacy, safety, invasiveness, cost and patient preference.
- With increasing longevity, the treatment of ED in the elderly has assumed greater importance. Hypogonadism should be treated with testosterone replacement, regardless of age.<sup>[12]</sup>
- A flow chart or algorithm can be used to assist treatment plans .

### Lifestyle

Data from basic science and clinical studies have identified a link between the occurrence of ED and a number of lifestyle factors, such as smoking, obesity, alcohol consumption and lack of physical activity.<sup>[13]</sup> Cycling for more than three hours per week has been identified as an independent risk factor for ED. Large-scale trials are needed to assess the place of lifestyle modification in the management of ED.<sup>[1]</sup>

### Treating the cause

The following are regarded as curable causes for ED, which can be treated:



- Hormonal causes:
  - Testicular failure – treat with testosterone.
  - Pituitary or hypothalamic causes – treat the underlying causes; for example, pituitary tumours causing hyperprolactinaemia.
- Post-traumatic arteriogenic ED in young patients:
  - Surgery following pelvic or perineal trauma has a 60–70% success rate.<sup>[1]</sup>
  - This requires proper diagnostic work-up (including duplex ultrasound and arteriography).
- Psychosexual causes:
  - Management includes the management of any specific underlying psychological problem.
  - Psychosexual therapy:
    - See the separate [Sex Therapy and Counselling](#) article.
    - A meta-analysis confirmed the effectiveness of group psychotherapy in the treatment of ED and that psychological interventions were as effective as vacuum devices and local injections.<sup>[14]</sup>
    - Psychological therapy is most effective when appropriately targeted.<sup>[15]</sup>
  - Drug treatments (eg, the phosphodiesterase type-5 inhibitors sildenafil, tadalafil, vardenafil and avanafil) may be effective and sometimes need only be used short-term.

## First-line therapy for ED<sup>[1]</sup>

### Oral agents

Phosphodiesterase inhibitors (sildenafil, tadalafil, vardenafil and avanafil) improve the relaxation of smooth muscle. Efficacy of the drug is dependent on release of nitric oxide from the nerve terminals of the cavernosal nerve

Use of high-dose sildenafil after radical prostatectomy (RP) has been suggested to be associated with preservation of smooth muscle within the corpora cavernosa and daily use results in a greater return of spontaneous normal erectile function after RP compared to placebo in patients who were fully potent before surgery.

Sildenafil, tadalafil, vardenafil and avanafil are contra-indicated in patients receiving nitrates (because of possible severe hypotension, which may lead to acute myocardial infarction, stroke and even death).

- Phosphodiesterase inhibitors are also contra-indicated in patients in whom vasodilation or sexual activity are inadvisable, and where there is previous history of non-arteritic anterior ischaemic optic neuropathy, hypotension (avoid if systolic blood pressure is below 90 mm Hg and there is recent stroke, unstable angina or myocardial infarction).

- There are no meta-analyses to compare the four preparations, so choice will depend on personal preference of the patient and frequency of intercourse:
  - Sildenafil:
    - Improves erectile function and is generally well tolerated.
    - Efficacy is reduced after fatty meals.
    - 50 mg is the recommended starting dose (change according to response).
    - Adverse events are rare and the drop-out rate similar to placebo.
  - Tadalafil:
    - Has a longer half-life - therefore, potentially, a longer action and therefore greater spontaneity (effective after 30 minutes, with peak efficacy at two hours and lasting up to 36 hours).
    - Start at 10 mg (change according to response).
    - Adverse events and drop-outs similar to above.
    - Better results in subgroups which are difficult to treat.

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  - Vardenafil:
    - Effective after 30 minutes.
    - Useful in subgroups which are difficult to treat.
    - Its effect is reduced by a fatty meal but it has less interaction with food. A rapidly absorbed orodispersible preparation has now been made available which is more rapidly absorbed.

- Avanafil:
  - Effective after 30 minutes.
  - High selectivity for phosphodiesterase inhibition minimises the risk of side-effects.
  - Effect may be delayed when administered with food but can be taken with or without food.

Increasing numbers of products are available via the internet. They are all unlicensed and many have adverse effects. They include yohimbine, maca, horny goatweed and ginkgo biloba.<sup>[16]</sup>

### **Vacuum devices**<sup>[17]</sup>

- An external cylinder is fitted over the penis to allow air to be pumped out, resulting in engorgement of penis with blood.
- Studies suggest that whilst two thirds of patients are unable to achieve ejaculation, 74% are able to achieve orgasm.
- They work best when there is a motivated, interested and understanding partner. They may be the treatment of choice in well-informed older patients and in those with comorbidities precluding use of drugs or invasive methods.
- Adverse events include pain, petechiae, bruising and numbness.

### **Second-line therapy for ED**<sup>[1]</sup>

#### **Intraurethral alprostadil (prostaglandin E1)**<sup>[18]</sup>

- This is inserted as a medicated pellet called MUSE® into the urethral meatus and produces an erection after about 15 minutes.
- Barrier contraception must be used if the partner is pregnant.
- 30-65.9% of patients achieve erections sufficient for intercourse.
- However, it is less effective than intracavernous injections.
- The most common side-effect is mild penile pain (29-41% of patients).

#### **Topical alprostadil (prostaglandin E1)**<sup>[19]</sup>

- A cream is licensed for topical use.
- It should be applied 5–30 minutes before intercourse.
- It is administered using a plunger which delivers the cream to the tip of the penis and surrounding skin.

### **Intracavernosal alprostadil (prostaglandin E1)**

- Injections of alprostadil are given into the corpora cavernosa to produce an erection. It is licensed in the UK for a maximum dose of 40 micrograms. The duration of erection depends on the dose.
- Efficacy rates for intracavernous alprostadil of >70% in the general population have been reported and it is often effective for those men who do not respond to oral drug treatment.
- Penile pain (50% of patients) is usually mild but a significant number of men stop using this method because of this side-effect.
- **If priapism occurs** with alprostadil:
  - The patient should be referred urgently to hospital.
  - Patients are advised to seek medical advice if the erection has lasted longer than four hours.
  - Treatment should not be delayed for more than six hours. Initial treatment is by aspiration of blood from the corpus cavernosum.
  - If this is unsuccessful, cautious intracavernosal injection of a sympathomimetic (eg, phenylephrine or adrenaline (epinephrine) may be required).
  - If sympathomimetics are unsuccessful, urgent surgical referral is required (possibly including shunt procedure).

### **Third-line therapy for ED<sup>[1]</sup>**

#### **Penile prosthesis**

- Semi-rigid, malleable or inflatable devices surgically inserted to produce an erect state. Most patients prefer the three-piece inflatable penile prosthesis which includes a separate reservoir placed in the abdominal cavity.

- Prostheses should be considered in patients whose ED has an organic cause and who are unwilling to consider, fail to respond to, or are unable to continue with medical treatment or external devices.

Low-intensity shock-wave therapy has shown promising results in trials in patients resistant to other ED treatments.<sup>[20]</sup>

## NHS or private prescription?

In England, Scotland and Wales, sildenafil can be prescribed on the NHS for any man with ED. In Northern Ireland, it is on the Red List, which means that responsibility for prescribing should remain with a hospital specialist.<sup>[21]</sup>

The other phosphodiesterase inhibitors and alprostadil can only be prescribed on the NHS for men who:

- Have diabetes, MS, Parkinson's disease, poliomyelitis, prostate cancer, severe pelvic injury, single-gene neurological disease, spina bifida, or spinal cord injury.
- Are receiving dialysis for chronic kidney disease.
- Have had radical pelvic surgery, prostatectomy, or a kidney transplant.
- ED treatment should also be available from specialist services (under local agreement) when the condition is causing severe distress. The criteria for severe distress include:
  - Significant disruption to normal social and occupational activities.
  - A marked effect on mood, behaviour, social and environmental awareness.
  - A marked effect on interpersonal relationships.

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## Further reading

- [Lin CS, Xin ZC, Wang Z, et al](#); Stem cell therapy for erectile dysfunction: a critical review. *Stem Cells Dev.* 2012 Feb 10;21(3):343–51. doi: 10.1089/scd.2011.0303. Epub 2011 Sep 7.
- [Muneer A, Kalsi J, Nazareth I, et al](#); Erectile dysfunction. *BMJ.* 2014 Jan 27;348:g129. doi: 10.1136/bmj.g129.
- [Shridharani AN, Brant WO](#); The treatment of erectile dysfunction in patients with neurogenic disease. *Transl Androl Urol.* 2016 Feb;5(1):88–101. doi: 10.3978/j.issn.2223-4683.2016.01.07.

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