Erectile dysfunction

A man may consult and ask for "a bit of Viagra…", or he may bypass primary care altogether and buy this over the counter. But WHY does he have erectile dysfunction? Erectile dysfunction can be a symptom of underlying cardiovascular disease, diabetes, testosterone deficiency or a prolactinoma…

The British Society for Sexual Medicine published its guidelines on erectile dysfunction in 2018 (J Sex Med 2018;15:430). Below, I have summarised the bits useful for primary care.

This article was last reviewed in November 2023.

Headlines

- Erectile dysfunction is "the persistent inability to attain/maintain an erection sufficient for sexual performance".
- Prevalence is 19% of 30–80-year-old men in Europe, and increases markedly with increasing age.

In primary care, the British Society for Sexual Medicines suggests we should:

- Enquire about symptoms of erectile dysfunction in ALL men with the following:
  - Cardiovascular disease.
  - Hypertension (new diagnosis and at review).

In its guidance on both type 1 and type 2 diabetes (NICE NG17 (T1) and NG28 (T2), both updated 2022), NICE recommends asking about erectile dysfunction at the annual diabetic review.

ALL men presenting with erectile dysfunction should have bloods for:

- Diabetes screen.
- Lipid profile (CVD risk assessment).
- Testosterone level (erectile dysfunction may be due to hypogonadism).
- PSA (offer after shared decision-making conversation).

Consider checking prolactin/thyroid function if compatible symptoms (see below for more information).

For more information on hypogonadism, see separate article Testosterone deficiency *in the online handbook.*

Erectile dysfunction: questions to ask in the history

Erectile dysfunction can be caused by different underlying conditions; there may be clues in the history. It can be useful to enquire about:

- Erections: strength, when do they occur/who with/alone, are these new symptoms or long term?
- Sex: desire, orgasm, any pain?
- Relationships: sexual preference, current relationship, any history of negative sexual experiences/abuse?
- Partner factors: desire, pain, how is the relationship? If female partner, past history of pregnancy/childbirth/menopause.
- Social/cultural factors: family/social pressures, religious or cultural beliefs.
- Physical health, e.g. cardiovascular disease, diabetes, genitourinary conditions, hypogonadism and hyperthyroidism.
- Symptoms of a prolactinoma: headache, visual disturbance, decreased libido, gynaecomastia, rarely galactorrhoea (NEJM 2010;362:1219).
- Mental health, e.g. anxiety or depression.
- Drugs (it is not always clear if erectile dysfunction is caused by the disease or the drug!):
  - Cardiovascular drugs: beta-blockers, diuretics, methyldopa, clonidine, verapamil, digoxin, gemfibrozil.
  - Sedating drugs/antidepressants: SSRIs, tricyclic antidepressants, MAOIs, lithium, anticholinergics.
  - Endocrine: oestrogens/progestogens, steroids, cyproterone acetate, 5-alpha reductase inhibitors, LHRH agonists.
  - Raise prolactin levels: phenothiazines.

- Others: ranitidine, cimetidine, cyclophosphamide, methotrexate.
- Alcohol, smoking, recreational drug use.

- Other associations:
  - Increasing age, sedentary lifestyle, cycling for >3h/w.

Erectile dysfunction: after cancer

- One of the most distressing consequences of cancer for some men.
- May result from:
  - Psychological impact.
  - Surgery.
  - Chemotherapy.
  - Radiotherapy.
  - Hormonal manipulation.
- Chemotherapy and radiotherapy may cause ED secondary to hypogonadism or pelvic nerve damage, *even in non-pelvic cancers.*
- Pelvic surgery is particularly risky:
  - In males with 'excellent' baseline erections, <25% retained or recovered preoperative erection quality.
  - Highest risk was with radical prostatectomy, radical cystectomy and low anterior or AP resections.
  - Around 80% of men reported ED after radial prostatectomy compared with around 40% in matched control groups during 12-year cancer follow-up studies.
- A meta-analysis looking at over 13 000 participants pooled estimates for ED in survivors of cancer across ALL cancer sites. ED prevalence was 40% in those with cancer compared with 29% at point of diagnosis and 43% after treatment (BJGP 2021;71:e372).

Erectile dysfunction: examination and investigation

Below, I have summarised the conditions most commonly associated with erectile dysfunction, and linked these to the clinical examination and bloods. <u>All</u> the examination/investigations should be carried out in <u>any</u> man presenting with erectile dysfunction; the table below provides a framework:

Examination	
What to examine…	**…and why (underlying causes)**
• Blood pressure and heart rate. • Weight and waist circumference.	**Cardiovascular disease: erectile dysfunction can precede a cardiovascular event by 3–5y and is associated with a 1.5× increased risk of cardiovascular disease.**
	Metabolic disease: obesity, metabolic disease, diabetes.

• Examine for symptoms/signs of:
  o Hypogonadism (many symptoms, see *Testosterone deficiency* article).
  o Hyperthyroidism.
  o Prolactinoma: any visual deficit or red flags of raised intracranial pressure, e.g. headache/visual symptoms. Examine for gynaecomastia. Rarely, galactorrhoea may also be seen.
	Endocrine disease (some causes reversible):
	• Hypogonadism: causes include:
	  o Primary testicular disease: undescended testes, mumps orchitis or cancer treatment.
	  o Secondary causes: Cushing's, prolactinoma: high prolactin levels suppress LH and, in turn, testosterone levels.
	  o Functional/late-onset hypogonadism.
	• Hyperthyroidism: appropriate treatment of hyperthyroidism may resolve the erectile dysfunction.

• Examine external genitalia. • Consider a DRE (NICE 2015, NG12).	Genitourinary tract problems: lower urinary tract symptoms, benign prostatic hypertrophy.
• Mental health: ask about depression and any relationship difficulties.	Depression, anxiety and relationship difficulties can cause/impact on erectile dysfunction.
Investigations	
• Lipids. • HbA1c/fasting glucose. • Testosterone (fasted early-morning sample): if abnormal, also check LH, FSH, prolactin. • Prolactin if symptoms/signs compatible with hyperprolactinaemia. • Thyroid function if symptoms/signs compatible with hyperthyroidism. • Consider PSA with shared decision-making (NICE 2015, NG12). **If testosterone deficiency or raised prolactin, refer endocrine.**	

Referral to secondary care

The majority of patients can be managed in primary care. Urology referral is suggested if:

- Young patient with primary erectile dysfunction (all their life).
- History of trauma.
- Abnormal genitourinary examination.
- Unresponsive to medical therapies:
  - Drugs used on ≥8 occasions (with adequate sexual stimulation) before referral.
  - Should try at the highest tolerated dose of at least 2 drugs (sequentially not concurrently).

We would also suggest referral if pharmacological treatment is contraindicated, e.g. on nicorandil/nitrates.

Treatment for erectile dysfunction

The aim of treatment is to enable the individual/couple to enjoy a satisfactory sexual experience.

Treatment includes:

- Identifying and treating reversible/modifiable causes of erectile dysfunction, e.g. some endocrine causes.
- Lifestyle: e.g. stopping smoking, pelvic floor exercises, address diet, exercise, alcohol consumption if appropriate.
- Modify cardiovascular and metabolic risk factors if appropriate (lifestyle/drug treatment).
- Psychological intervention: e.g. psychosexual counselling as an individual or couple if required.
- Drugs:
  - Phosphodiesterase type 5 inhibitors (PDE5is), e.g. sildenafil.
  - Testosterone replacement if testosterone deficiency (see *Testosterone deficiency* article).

Phosphodiesterase type 5 inhibitors

Study data suggests that the use of these medications results in successful sex 75% of the time. Efficacy is lower if:

- Diabetic (50–55%).
- Nerve-sparing radical prostatectomy (37–41%).
- Testosterone deficiency (replacing testosterone often restores the response to the PDE5i).

They work by increasing arterial blood flow, leading to smooth muscle relaxation, vasodilation and penile erection.

Sildenafil over the counter

Sildenafil is now available over the counter. Prior to sildenafil becoming reclassified as an over-the-counter product, there was a national consultation by the MHRA. There were concerns about (DOI:10.1136/dtb.2018.10.000024):

- Concomitant use of nitrates, including amyl nitrate poppers.
- Missing pathology: erectile dysfunction as a *symptom* of an underlying disease.

Before selling sildenafil over the counter, a pharmacist must assess if there are any contraindications to sildenafil/significant drug interactions. The manufacturer advises that all men see their GP within 6m of starting sildenafil.

How and when to take phosphodiesterase type 5 inhibitors

How to take (BNF and CKS, November 2020):

- Take before sex; timing matters (see table below). Sexual stimulation is still required to facilitate an erection.
- Best taken on an empty stomach; if taken with food, may not work as well/onset of action may be delayed, especially with fatty food (sildenafil especially).
- Avoid excessive alcohol as this stops/decreases erections.
- Grapefruit juice should also be avoided (drug interaction).

The table below summarises when to take different PDE5is and their half-lives (BNF and CKS, November 2020):

	When to take	**Half-life**
Sildenafil (cheapest)	Stat dose 1h before expected sexual activity.	4h
Avanafil	Stat dose 15–30min before expected sexual activity.	6–17h
Vardenafil	Stat dose 25–60min before expected sexual activity.	4h
Tadalafil (most expensive)	Stat dose at least 30min before expected sexual activity.	17.5h

	Also comes as a once-daily preparation if anticipate sexual activity at least twice a week (expensive).	

Phosphodiesterase inhibitors: side-effects and interactions

Adverse events with PDE5is:

- Common: flushing, nausea, dizziness, vomiting, dyspepsia, back pain.
- Less common: chest pain, palpitations, tinnitus, vertigo, eye complications or priapism.

Dose adjustments of PDE5is may be needed if:

- >65y, hepatic impairment or renal impairment.
- Concomitant use of potent cytochrome P450 3A4 *inhibitors*: erythromycin, cimetidine, ritonavir (we usually think about P450 *inducers*, but *inhibitors* delay the metabolism of PDE5is and increase the risk of a prolonged erection).

PDE5i-related eye complications

A JAMA Ophthalmology case–control analysis involving 213 000 males reported an association between regular use of PDE5i drugs and an increased incidence of:

- Serous retinal detachment.
- Retinal vascular occlusion.
- Ischaemic optic neuropathy.

The results were adjusted to take account of hypertension, diabetes, coronary artery disease and smoking. The increased incidence was small (15 extra cases of this composite endpoint/10 000 person years), but the authors concluded that those taking regular PDE5is should report any visual abnormalities promptly (JAMA 2022;327:2066).

The BNF also reminds us that PDE5i drugs can cause (BNF 2022):

- Dry eye.
- Eye discomfort.
- Eye inflammation.
- Glaucoma.
- Scleral discolouration.

PDE5i-associated hypotension

All PDE5is cause a small drop in blood pressure when taken on demand but, in combination with certain medications, this drop in blood pressure can be significant – or, at extreme, catastrophic (BNF, accessed January 2021):

PDE5i use with…	Risks
Alpha-blockers.	May cause orthostatic hypotension; caution if used together. Specific dose reductions for some preparations are outlined in the BNF.
Riociguat (a medication for pulmonary hypertension).	Contraindicated.
Any nitrates (e.g. isosorbide mononitrate, isosorbide dinitrate, GTN, amyl nitrate poppers) or nicorandil.	Contraindicated: associated with a risk of hypotension, which (at extreme) may be catastrophic.

If a man with erectile dysfunction takes a nitrate/GTN/nicorandil, do not start a PDE5i. Refer for advice on the best treatment for their erectile dysfunction.

Eroxon

In June 2023, The New York Times reported that a new treatment for erectile dysfunction was available: Eroxon. Eroxon is now available over the counter in the UK.

As a topical ED therapy, this treatment appears quite unique. At Red Whale, we were keen to review the literature to find out what's in it and if it really works.

We did some digging. Lots of digging. Despite our best efforts, we were unable to find any good-quality published evidence proving efficacy. Here's what we did find:

- A topical 0.2% GTN treatment (GTN in DermaSys) was produced and trialled (without success). Following on from these trials, the manufacturer proceeded to market the PLACEBO from the trial (DermaSys). The idea is that the

rapid cooling (presumably from evaporative loss) was effective (J Urol 2018 199:1378, Int J Impot Res. 2020;32:569, J Sex Med, 2018; 15:167).

- The manufacturer write-up suggests that DermaSys alone has "comparable efficacy to PDE5s (Cialis)", but we were unable to see any head-to-head trial data with a PDE5i drug to support this statement.
- The product is approved under the EU CE mark and UKCA (UK conformity assessed) mark as a 'medical device' rather than a medical drug. The product website clarifies that "the product does not contain an active pharmaceutical agent" and that it works through a rapid cooling action.

Does it work? Based on the evidence we could find: we don't know. But it only gets 2.4 stars on a well-known online retailer (n=672, accessed November 2023).

	**Erectile dysfunction** • ALL men with chronic cardiovascular disease, diabetes (T1 or T2) or hypertension (new or at review) should be asked about erectile dysfunction. Consider asking about ED in cancer survivors. • ED can affect men with both pelvic and non-pelvic cancers due to a combination of factors. • ALL men presenting with erectile dysfunction should have fasting glucose/HbA1c, lipid profile and fasting morning total testosterone checked. Offer PSA with shared decision-making. • Assess for underlying cardiovascular, metabolic and endocrine conditions. • Refer if testosterone low or prolactin raised. • Treatment includes a combination of lifestyle, psychological and pharmacological interventions.
	Audit your patients coded as having 'erectile dysfunction'; have they had the suggested bloods carried out? If you do not have many patients coded as having erectile dysfunction, run the search on those prescribed PDE5is in the past 12m. Audit patients with known cardiovascular disease; have they been asked about erectile dysfunction? If not, consider adding this to your templates.
	**Useful resources:** Websites (all resources are hyperlinked for ease of use in Red Whale Knowledge) • BAUS - sexual health inventory for men questionnaire • BAUS - international index of erectile function • MAZE Men's Health - aging male symptom score • British Heart Foundation - sex and heart conditions