

Physiology and management of erectile dysfunction



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Anatomy and Physiology

The physiology of erections is a complex interaction between the penile anatomical compartments, vessels and nerves. The penile anatomical compartments involved in erections are principally the corpora cavernosa. These are paired cylinders of smooth muscle encased in the tunica albuginea which function as the erection chambers and are separate from the glans penis (see Figure 1). The blood supply comes from the internal pudendal artery which separates into 3-4 branches into the penis. Just beneath the tunica albuginea is the subtunical venous plexus which drains into emissary veins and eventually forms the dorsal veins of the penis. The autonomic nervous system plays an integral role with parasympathetic nerves involved in tumescence and the sympathetic nerves controlling detumescence.

The key steps involved are (see Figure 2):

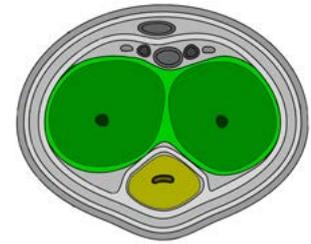
1. Sexual stimulation triggers release of neurotransmitters (nitrous oxide)
2. Dilatation of arterioles within the corpora
3. Engorgement of corpora with compression of subtunical venous plexus thereby "trapping" blood in the penis
4. Detumescence occurs when there is arteriolar contraction which results in the venous plexus "opening up" and blood effluxes from the penis

Epidemiology

The Massachusetts Male Aging study demonstrated an overall prevalence of erectile dysfunction (ED) of 52% in men aged 40-70 in the Boston Area [1]. An Australian study demonstrated that 1 in 5 men over the age of 40 had ED with 10% being completely unable to attain an erection [2]. In another study, it was found that one in four men first sought medical help for ED when they were aged less than 40 yrs old.

Classifications/causes

The aetiology of erectile dysfunction is broad and can very often be multifactorial (Figure 3).



Corpus cavernosa

Corpus spongiosum

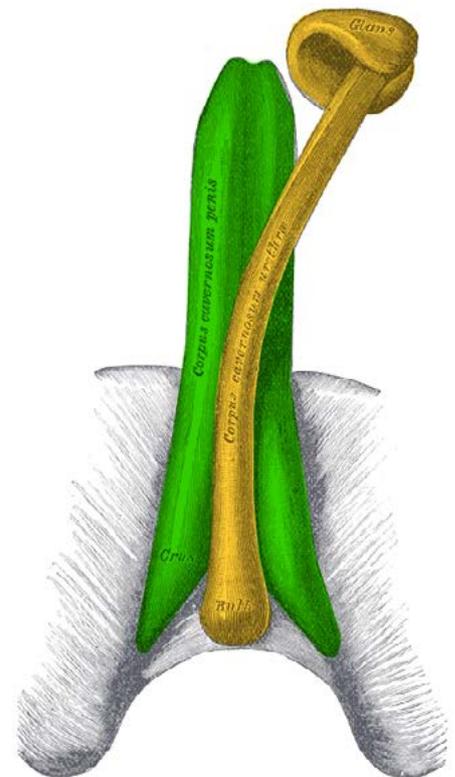


Figure 1. Accessed from: https://en.wikipedia.org/wiki/Corpus_cavernosum_penis#/media/File:Gray1154.png

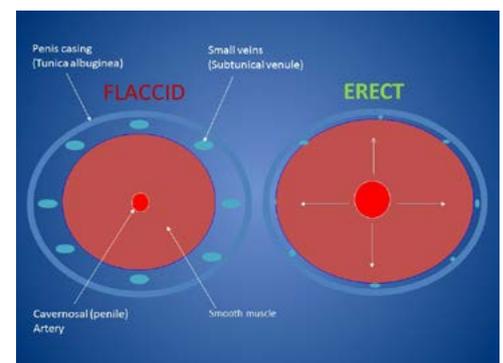


Figure 2: Steps involved in an erection: Engorgement of smooth muscle with blood swells and compresses small veins against penis casing. Blood is trapped.

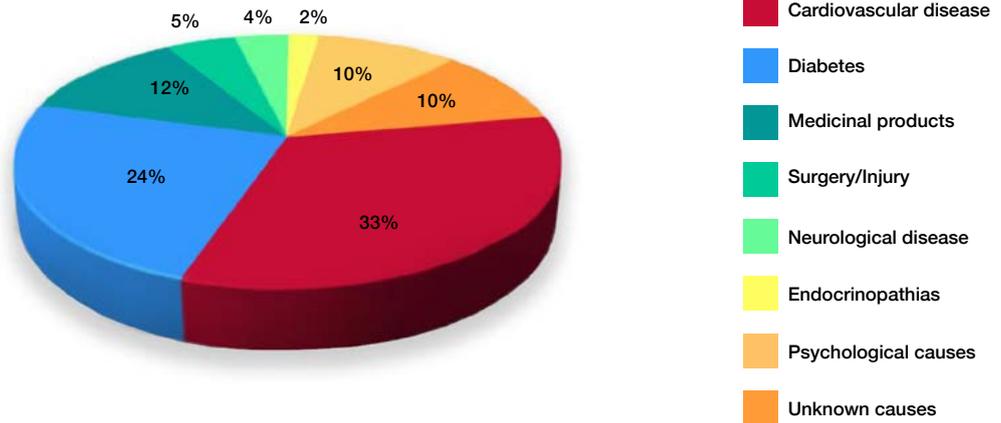


Figure 3: Aetiology of ED:

Sourced from: <http://www.for-us-2.com/en/erectile-dysfunction/causes-of-erectile-dysfunction/>

Management of ED

History

Much can be ascertained from a complete medical and sexual history and this is the first key step in management. It is preferable if the partner is available and willing to be present at the consultation. Validated questionnaires such as the SHIM (Sexual Health Inventory of Men) can be very useful to assess baseline function and also response to treatment [3].

Examination

Given the multiple aetiologies and various systems that can be involved in ED, the physical examination should be focused, yet must take into account the relevant genitourinary, vascular, endocrine and neurological areas. Measuring testis size with an orchidometer is useful. The presence of penile plaques (Peyronie's disease), androgenisation (or lack thereof) and blood pressure is important to note.

Investigations

General

Depending on the patient's age, risk factors and physical examination findings, testing can be individualised. However, most men should be screened for hypogonadism (morning testosterone), diabetes (HbA1c or fasting blood glucose) and dyslipidaemia.

Specialised

Most patients will not need specialised investigations. For patients for which the aetiology is unclear, or first/second line treatments have not worked, consideration should be made of a penile duplex Doppler ultrasound [4]. This should be done with an intracavernosal vasoactive agent and can help to classify the aetiology of ED and may help direct if further sub-specialised tests are needed. A penile duplex Doppler ultrasound may also predict which treatments may be beneficial. If arteriogenic ED is diagnosed, consideration of referral to a cardiologist for assessment of occult ischemic heart disease is warranted.

Treatment of Erectile dysfunction

The different steps in treatment are shown in Table 1

If there is any type of reversible cause identified in the assessment, this should be treated initially (sometimes in combination with first line therapy). Typical reversible causes include hormonal imbalance (e.g. low testosterone), medication induced ED and psychogenic ED. Modifiable risk factors such as diabetes, hypertension, smoking and dyslipidaemia should be optimised as well. This should be performed in consultation with a general practitioner. Rare treatable causes include internal pudendal artery stenosis.

Table 1: Step wise approach to ED treatment*

Step	Options	Notes
1	Treat reversible causes Optimise modifiable risk factors	May augment with drug therapy
2	First line therapies	PDE5 Inhibitors
3	Second line therapies	Penile injections Vacuum erection devices External Shock Wave lithotripsy
4	Third line therapies	Penile prosthesis

*At each step consider psychological support/referral

Physiology and management of erectile dysfunction: continued

Psychological support

Not only can ED be caused by psychological problems, ED is a condition which can cause psychological distress in its own right to both the patient and the partner. This can create a negative feedback loop whereby it exacerbates the ED. This needs to be screened for at each consultation and a referral to a qualified allied health professional (ideally with an interest in sexual dysfunction) should be made if necessary.

First line therapy

The most common first line therapy is PDE5 inhibitors. The commercially available drugs in Australia are Sildenafil (Viagra®), Tadalafil (Cialis®) and Vardenafil (Levitra). Key differences between the drugs are shown in Table 2. The side effect profile is outlined in Table 3. All side effects cease with cessation of medication. Occasionally, with frequent daily administration (especially 5mg Tadalafil), the side effects can resolve.

The choice of which PDE5 inhibitor to use takes into account several variables: frequency and timing of intercourse, cost (Sildenafil is the cheapest as it is "off patent"), side effect profile, spontaneity required, previous use etc. There are no large scale good quality comparative studies of these drugs. Because of its prolonged half-life Tadalafil can maintain efficacy for up to 36 hours and hence a daily dose of 5mg will allow for constant blood levels. Tadalafil has also been shown to improve lower urinary tract symptoms (LUTS) and hence may be useful in men who have ED and LUTS.

Contraindications include patients on topical nitrates, severe CCF, unstable angina (or angina with sexual intercourse), resting hypotension, recent stroke or myocardial infarction.

Before classifying a patient as "non-responsive to PDE5 inhibitors", a discussion with the patient should be had to clarify if:

- The medication was sourced from accredited pharmacy (ie not online, overseas etc)
- Taken on empty stomach (Sildenafil, Vardenafil)
- Adequate duration until sexual stimulation
- Sexual stimulation attempted
- Taken maximum dose
- Tried at least 3 times
- Trialed at least 2 PDE5 inhibitors

Table 2: Comparison of the 3 commercially available PDE5 Inhibitors in Australia

	Sildenafil	Tadalafil	Vardenafil
Dosage	25mg, 50mg, 100mg	5mg, 10mg, 20mg	5mg, 10mg, 20mg
Administration	On demand	On demand or daily	On demand
Absorption affected by fatty meal	Yes	No	Yes
Effective from	30-60 mins	30 mins	30 mins
Tmax (approx.)	1 hour	2 hours	1 hour
T 1/2 (approx.)	3 hours	18 hours	4 hours
Off patent	Yes	No	No
Improve avoiding symptoms	Not assessed	Yes (daily dose)	Not assessed

Adapted from European Guidelines on Male Sexual Dysfunction 2015 [5].

Table 3: Comparison of side effects the 3 commercially available PDE5 Inhibitors in Australia

	Sildenafil	Tadalafil	Vardenafil
Headache	13%	15%	16%
Flushing	10%	4%	12%
Dyspepsia	5%	12%	10%
Nasal congestion	1%	4%	10%
Abnormal vision	2%	0%	<2%
Back pain	Not assessed	7%	Not assessed
Myalgia	Not assessed	6%	Not assessed

Adapted from European Guidelines on Male Sexual Dysfunction 2015 [5].

If the previous points have been determined regarding administration of PDE5 inhibitors and the patient does not achieve an adequate response, second line therapies should be instituted.

Second line therapies

Vacuum erection devices (VED)

These devices draw blood into the corpora and an occlusion ring is placed at the base of the penis to sustain the erection. A certain level of dexterity is needed to use a VED however, when used in the correct fashion, an erection suitable for penetration is often the result. Most men cease using a VED in the long term because of the potential side effects such as pain, inability to ejaculate, bruising, “hinging” and paraesthesia.

Penile injections

Penile injections can be a useful treatment for non-responders to PDE5 inhibitors. It allows a “natural” erection to occur within 10-15 mins of administration and, with correct dosage, should last less than 1 hour. There is only one widely available commercial product in Australia (Caverject®) which is Alprostadil. It can be administered in dosages of 2.5-20 mcg. It does not need to be refrigerated and is available in “all-in-one” package (ie drug, needle, alcohol swab). Caverject is expensive (~\$20 AUD per injection) and cheaper options can be sourced via compounding pharmacies. However, many of these compounded medications do need to be refrigerated.

Structured training of patients in how to administer penile injections (especially with compounded medications) and monitoring for efficacy and side effects can help increase the success of penile injection therapy.

The side effects of penile injections include pain (10% - especially with alprostadil), prolonged erections (5%) and fibrosis (2%).

Low Intensity External Shock Wave Lithotripsy (LiESWL)

Li-ESWL applied to the penis has recently been shown to have short term efficacy in up to 50% of patient who were non-responders to PDE5Is [6]. The mechanism of action is still debated and may involve recruitment of stem cells and/or angiogenesis. The results to date have involved small numbers of patients and many of the trials have been industry sponsored. However, this is a treatment with no known side effects and so some patients are keen to “give it a shot” even though the evidence for its use is not very strong.

Third line therapies

Penile prosthesis

Penile Prostheses (penile implants) are a concealed, surgically implanted device, generally reserved for patients who have failed other conservative therapies. Penile prostheses offer patients a permanent solution to their ED. For this reason, and combined with a low complication rate seen in high volume penile implant surgeons, the patient satisfaction rate for this procedure is >90% [7].

Summary

ED has a complex multifaceted pathophysiological mechanism. Assessment should be focused on determining the cause and any modifiable risk factors. For most patients, simple testing will suffice, but occasionally a penile duplex Doppler ultrasound can help to direct treatment options. There is a well-established step-wise approach to ED treatments. Involvement of allied health professionals can help with managing the psychological impacts of ED on patient and partner.

References

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