The physiology of erection and its relationship to the management of erectile dysfunction

The physiology of erection is central to the management of erectile dysfunction.

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There is a growing population of men with erectile dysfunction (ED), which is probably closely related to increasing age of the population, but also the result of the epidemic of conditions associated with the metabolic syndrome.

Physicians have to understand the basics:

• How an erection occurs
• What can cause ED?
• How this translates to management of patients.

Erectile function is a balance between 2 contrasting forces (with orgasm sometimes happening in between).

ED was first described about 2000 BC on Egyptian papyrus. Later Hippocrates described the condition in wealthy horseback riders. Erections were initially thought to occur from air entering the penis but Da Vinci noted large amounts of blood in the penis of hanged prisoners in 1504, which began the more modern understanding of the process.

However, it was not until the 1990s that nitric oxide (NO) was recognised as the major factor in tumescence and the phosphodiesterases (PDEs) in detumescence.

Neuro-anatomy and neurophysiology

The penis is essentially composed of 3 cylindrical tubes – the paired corpora cavernosa and the urethra, housing the corpus spongiosum, which also forms the glans penis.

Blood supply comes from terminal branches of the pudendal artery, which is a branch of the internal iliac artery, with venous drainage following the same reverse route.

Nerve supply is both somatic and autonomic (sympathetic nerve roots T10 - L2 and parasympathetic and somatic arising from roots S2 - 4) which all contribute to the pelvic plexus.

Erectile function (EF) is a balance between 2 contrasting forces (with orgasm sometimes happening in between). These are flaccidity/detumescence, an active smooth-muscle process with vasoconstriction of the arterial bed mainly a postsynaptic alpha-sympathetic function but with contributions from other neurovascular factors, including angiotensin II, prostaglandin EF2 (PGEF2) and endothelins. Aligned to this is breakdown of NO by PDE5 inhibitors.

Tumescence relies on NO action on the efflux of calcium (Ca++) and hyperpolarisation of the smooth-muscle cell potassium (K+) to cause relaxation of the arteries with a decrease in venous drainage. This is both active and passive as a result of kinking of veins on the tunica albuginea.

Orgasm appears to be controlled centrally in the right cerebrum (in right-handed individuals) and the cerebellum, with some contribution from ‘reward’ centres in the frontal area. As ED is a neurovascular event the nerves and their vascular-modulating transmitters cannot be described in isolation. There is a delicate balance between but with major contributions from the medial pre-optic area (MPOA) using dopaminergic/adrenergic stimulation

• Reflexogenic – utilising parasympathetics in Onuf’s nucleus (S2 - 4)
• Nocturnal – associated with the pons during rapid eye movement (REM) sleep.
Erectile dysfunction

Common causes include ageing, medications, operations and comorbid conditions, notably those related to other vascular events such as diabetes mellitus (DM), especially in the context of the metabolic syndrome.

The most important modifiable lifestyle associations for ED are smoking, physical inactivity and high caloric intake.

ED can be organic, psychogenic and mixed, although the majority of cases will be the latter.

It is important to separate these categories:
- Organic ED (vascular, neurogenic, anatomical, endocrinological) can occur in up to 80% of patients and may be the precursor of various life-threatening conditions, notably cardiac events (CEs). Studies have shown that the lag time from a first episode of ED to a CE can be as high as 50% within 5 years. It has also been shown that identifying and treating ED and its underlying cause(s) can prevent morbidity and mortality.
- Psychogenic – symptoms can be present as a precursor or sequelae of ED, including depression, schizophrenia and lethargy, which impacts on psychiatric therapy. Studies have shown that up to 50% of men with a first diagnosis of depression after the age of 40 years have testosterone deficiency syndrome (TDS).

Treatments for either organic or psychogenic conditions may cause/exacerbate ED (e.g. selective serotonin re-uptake inhibitors (SSRIs), anti-androgens) or in some cases improve it (e.g. alpha-blockers).

Evaluation and management of ED
Modern management includes:
- Early detection
- Goal-directed management
- Partner interaction
- Cardiac risk assessment
- Directed investigations (e.g. psychiatric, testosterone levels, prostate check)
- Shared decision-making
- Rigorous follow-up
- Specialist referral when necessary.

Use of questionnaires and sexual function symptoms scores (e.g. International Index of Erectile Function (IIEF), sexual encounters profile (SEP)) are practical and useful but are not essential for every practice.

Evaluation should include standard history and examination, and blood pressure related to age, with recommended blood tests being glucose, total serum testosterone and lipogram. Full blood count (FBC), prostate-specific antigen (PSA), liver function tests (LFTs), prolactin and luteinising hormone (LH) may also be assessed as indicated.

Specialised investigations (e.g. Doppler ultrasound, dynamic stimulation tests) are often helpful but may not be within the scope or expertise of every practitioner.

Similarly, more intensive neurological, endocrinological and psychophysiological evaluation may be indicated in a select group.

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Treatment considerations
Try to adhere to the patient’s goal-directed focus to therapy and specify that therapeutic options are presented in a step-wise management approach as follows, when indicated:
- Lifestyle modifications
- Medication change if possible or necessary (e.g. blood pressure medication)
- Psychosexual therapy (minimal or more)
- Testosterone therapy
- Oral therapy (mainly PDE5 inhibitors)
- Intracavernous injections and penile pumps
**Erectile dysfunction**

- Surgical interventions (prostheses, revascularisation – reserved for urological/vascular specialists).
- Investigation of iatrogenic causes, basic scientific research into endothelial and smooth-muscle function and newer medications for ED need to be identified and addressed.

**Future directions**

Sexual dysfunction is a priority research area and numerous components including epidemiological, pathogenic mechanisms, investigation of iatrogenic causes, basic scientific research into endothelial and smooth-muscle function and newer medications for ED need to be identified and addressed.

Finally, outcomes research for the field needs to be bolstered to raise the profile of sexual dysfunction to the more mainstream practice.

References are available on request.

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**IN A NUTSHELL**

- Erectile function is a balance between flaccidity and tumescence (with orgasm sometimes happening in between).
- Erectile dysfunction (ED) is defined as the inability to attain or maintain an erection sufficient for satisfactory penetration or sexual performance.
- Tumescence relies on nitrous oxide (NO) action on the efflux of calcium (Ca++) and hyperpolarisation of the smooth-muscle cell potassium (K+) to cause relaxation of the arteries with a decrease in venous drainage.
- Three types of erection are recognised, depending on where the central control is situated. Not all are affected equally in different cases of ED:
  - Psychogenic – cortical sexual stimulation modulated in various parts of the brain but with major contributions from the medial pre-optic area using dopaminergic/adrenergic stimulation.
  - Reflexogenic – utilising parasympathetics in Onuf’s nucleus (S2 - 4).
  - Nocturnal – associated with the pons during rapid eye movement (REM) sleep.
- Common causes include ageing, medications, operations and comorbid conditions, notably those related to other vascular events such as diabetes mellitus, especially in the context of the metabolic syndrome.
- The most important modifiable lifestyle associations for ED are smoking, physical inactivity and high caloric intake.
- ED can be organic, psychogenic and mixed, although the majority of cases will be the latter.