

Erectile dysfunction

CVD, drug cross-talk and testosterone in ED



Bill Alexander,
Consultant
Physician
Western General
Hospital, Glasgow

Men's health is currently a focus of attention, with sexual health being an important component. Erectile dysfunction (ED) is being increasingly recognised, not only as a consequence of known cardiovascular disease (CVD) and associated risk factors, but also as a marker of these, and often

as the first overt manifestation of endothelial dysfunction. ED is being increasingly managed by primary and secondary care physicians rather than urologists, which is clearly appropriate. To maximise availability of treatment, and also to help identify men with occult CVD, physicians practising in 'high-risk' specialties, such as diabetes and cardiovascular medicine, should probably now be screening all men for ED. Men with severe ED should undergo intensive cardiovascular assessment.

The first of this series of papers is relevant in this respect. The second looks in depth at the association between CVD, cardiovascular drugs and erectile failure. Two articles then focus on testosterone and its association with ED.

Although debate continues, it is still generally accepted that testosterone replacement therapy is only indicated in men with proven hypogonadism. Intracavernosal injection treatment with vasoactive drugs remains an important option for men who fail to respond to oral phosphodiesterase (PDE) 5 inhibitors or for whom they are contraindicated. This is a relatively common situation in men with diabetes and CVD. Topical and intraurethral therapies alone are relatively useless. Vacuum devices are now available on NHS prescription. Some of my tips from the ISSIR meeting are:

- Men who experience painful erections with injected PGE1 might be helped by the concomitant use of sublingual or other GTN preparations. GTN as an activator of guanylyl cyclase is a synergistic vasodilator yet antagonises PGE1-induced signalling in nociceptive neurons. The combination appears to be well tolerated.
- Invicorp (VIP + phentolamine) injection therapy is again available on a named patient basis from Senetek and can be useful in men who are unresponsive to, or intolerant of, alprostadil injections.
- Combination treatments might be worth trying, although they are currently unlicensed.

THE JOURNAL OF UROLOGY



Diagnosing ED

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

- 1 The use of effective oral therapies for erectile dysfunction, such as sildenafil, has led to the non-specific use of this agent irrespective of the aetiology of the condition, eliminating the baseline diagnostic evaluation.
- 2 This has led to questioning of the necessity for a complete diagnostic evaluation in all patients with ED.
- 3 This study sought to determine the impact of different diagnostic steps on the management strategy for ED.
- 4 In 1276 patients, medical history revealed ED associated with medical conditions in 57%, blood tests identified previously undiagnosed medical conditions in 6.2%, and physical examination and the intracavernous injection test were diagnostic in 13.9% and 2.6%, respectively, of patients.
- 5 Initial screening was negative in 20.3%, in whom specific diagnostic procedures identified an underlying vascular pathology in 12.9% and unfavourable penile geometry in 1.3%. The remaining 6.1% had no evidence of organic disease.
- 6 Baseline diagnostic evaluation for ED can identify the underlying pathological condition or associated risk factors in 80% of patients. This is cost-effective as it eliminates unnecessary diagnostic procedures.
- 7 Such screening might diagnose reversible causes of ED and also reveal medical conditions that manifest with ED as the first symptom.
- 8 In conclusion, the article proposes that a minimal diagnostic evaluation is necessary in all patients with ED.
- 9 The proposed baseline evaluation for ED is simple and cost-effective, and has a high diagnostic reliability.

Hatzichristou D, Hatzimouratidis K, Bekas M et al (2002) Diagnostic steps in the evaluation of patients with erectile dysfunction. *The Journal of Urology* 168: 615–20

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

Drug cross-talk

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓✓

- 1 The prevalence of ED is higher in patients with cardiovascular disease than in the general population because of the presence of overlapping arterial risk factors.
- 2 It is therefore difficult to distinguish the effect on erectile function of underlying disease, and of the multiple cardiovascular drugs the patient is taking.
- 3 This increases the risk of drug treatments for ED affecting cardiovascular function and vice versa.
- 4 This review focuses on the effects of cardiovascular drugs on erectile function.
- 5 The known interactions of systemically administered drugs for ED with drugs for CVD are mainly pharmacodynamic.

- 6 Most studies of cardiovascular drugs on erectile function suggest that the treatment of CVD worsens erectile function.
- 7 All drugs for ED reaching sufficiently high plasma concentrations have the potential to induce systemic hypotension. Therefore, pharmacodynamic interactions that enhance the systemic vasodilator effect, or pharmacokinetic interactions that lead to accumulation of the drug applied for treatment of ED, are of major concern.
- 8 In clinical trials of cardiovascular drugs, it is also important to address the effect on erectile function. Moreover, the mechanisms by which cardiovascular drugs affect erectile function will enhance our understanding and help us to choose the therapy with most advantages with respect to both CVD and erectile/sexual function.

Simonsen U (2002) Interactions between drugs for erectile dysfunction and drugs for cardiovascular disease. *International Journal of Impotence Research* 14: 178–88

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

Testosterone levels and ED

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! factor	✓✓✓

- To examine the relationship between severity of ED and total testosterone (TT) serum levels in a normal population, the authors of this study assessed 965 men during screening for the early diagnosis of prostate cancer.
- Subjects were given the Simplified International Index of Erectile Function questionnaire, and their serum TT levels were recorded.
- ED was defined as severe, moderate, mild-moderate, mild or no ED.
- The prevalence of all degrees of ED was 53.9%. This was mild in 21.5%, mild-moderate in 14.3%, moderate in 6.3% and severe in 11.9%.
- ED was associated with age: whereas 36.4% of 40-49-year olds mentioned some degree of ED, this rose to 79.4% in the 70-79 age group.
- TT level variation was similar in different age groups, similar in people with and without ED, and similar in people with different severities of ED. Rhoden EL, Teloken C, Mafessoni R, Vargas Souto CA (2002) Is there any relation between serum levels of total testosterone and the severity of erectile dysfunction? *International Journal of Impotence Research* 14: 167-71

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

Male andropause

Readability	✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓

- Andropause syndrome is characterised by diminished sexual desire and erectile capacity, as well as by depression and obesity, and by changes in lean body mass, skin, bone mineral density and visceral fat.
 - Current treatments for androgen supplementation include oral tablets, intramuscular injections, and scrotal and nonscrotal patches.
 - This article discusses the diseases associated with testosterone levels, and the changes in androgen levels that accompany normal male aging.
 - Clinical manifestations are described, as are various androgen supplementations.
 - Because of the lack of relevant controlled clinical trials of sufficient duration, it is not possible to propose an ideal therapeutic regimen for androgen substitution in aging men.
 - Several studies suggest that these could benefit from testosterone replacement therapy, although larger clinical studies are needed to assess adverse effects.
- Wespes E, Schulman CC (2002) Male andropause: myth, reality, and treatment. *International Journal of Impotence Research* 14(Suppl. 1): S93-8

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

Local penile therapy

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! factor	✓✓✓✓

- Oral pharmacotherapy currently represents the first-line option for most patients with ED. Patients who do not respond to oral therapy, or who are not eligible for this treatment, are considered for second-line treatments.
- Second-line treatments include intracavernosal and intraurethral injections, and topical agents.
- Despite the well-established safety of injection treatments, patients receiving either injection therapy eventually drop out of the treatment.
- Newer agents with better efficacy-safety profiles, and improvements in devices for drug administration, might increase the long-term satisfaction rate.
- Topical therapy with vasoactive agents could become first-line treatment for ED because it acts locally and is easy to use. However, so far, the crossing of the barrier caused by the penile skin and tunica albuginea has limited the efficacy of the drugs used.
- This article reviews the latest results with these therapeutic options, and demonstrates the correct approach to determining which patients are candidates for these therapies.
- Results and complications of the therapies are discussed, and trials of intracavernosal and intraurethral therapy are compared.

Montorsi F, Salonia A, Zanoni M, Pompa P et al (2002) Current status of local penile therapy. *International Journal of Impotence Research* 14(Suppl. 1): S70-81

'Variations in total testosterone were similar in people with and without ED, and similar in people with different severities of ED.'

Therapy direction

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓
WOW! factor	✓✓✓✓✓

- Ongoing research suggests that current ED therapies can and will be improved. This article discusses some directions for the future.
- Research: there have been recent improvements in current therapeutic principles and in orally active PDE inhibitors. There are also new dopamine receptor agonists.
- The combination of existing therapeutic principles might have a therapeutic potential in patients who do not respond satisfactorily to single-drug treatment.
- New CNS targets: e.g. melanocortin receptor agonists, oxytocin agonists

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- and growth hormone releasing peptides.
- New peripheral targets: e.g. guanylyl cyclases and rho-kinase.
 - The use of intracavernosal somatic gene therapy to augment a missing or decreased relaxation-mediating component in the corpus cavernosum.
 - Prevention strategies: e.g. decreasing risk factors such as smoking, hypertension and dyslipidaemia, and possibly obesity, sedentary behaviour and chronic alcoholism.
- Andersson K-E, Hedlund P (2002) New directions for erectile dysfunction therapies. *International Journal of Impotence Research* 14(Suppl. 1): S82-92