

## Erectile dysfunction

### Lower urinary tract symptoms and ED



Bill Alexander,  
Consultant  
Physician,  
Western General  
Hospital, Edinburgh

This compilation continues with some of the topics from the last issue including ADAM (mild androgen deficiency of the aging male) and LUTS (lower urinary tract symptoms), two important associations of age and ED.

There is also an update on experience with sildenafil in a staggering 20 million men. The comprehensive review of female sexual dysfunction is an important and useful reference.

LUTS collectively represent a common age-related condition in men with or without diabetes and significantly affects quality of life. LUTS and ED have a mutual association with aging but a number of studies have shown LUTS to be independently associated with sexual dysfunction. This association becomes particularly relevant when considering surgical and pharmacological

treatments that may have an impact on erectile and ejaculatory function. This not only applies to prostatic surgery but also to 5 $\alpha$ -reductase inhibitors, such as finasteride and the  $\alpha$  blockers. Although doxazosin may have a beneficial effect on LUTS and ED, caution is required when it is used in combination with phosphodiesterase 5 (PDE5) inhibitors. The selective  $\alpha$ 1 blockers are safe in combination with PDE5 inhibitors, but tamsulosin may cause abnormal ejaculatory function. Alfuzocin, however, has been reported to improve erectile and ejaculatory dysfunction in men with LUTS and may be worth considering in combination with PDE5 inhibitors in men with both LUTS and ED.

Female sexual dysfunction a complex and neglected area. The update review by Berman, Berman and Kanaly provides a comprehensive look at this whole topic including anatomy, physiology, clinical evaluation and treatment and is an important read.

### INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH



### Role of testosterone therapy for ED and hypogonadism

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

- The role that low testosterone levels play in erectile function remains unclear.
- This article explores the aetiology and evaluation of ED, and looks at potential new therapies.
- Uncertainty about the impact of testosterone on ED is fuelled by observations that some severely hypogonadal men continue to have an erectile response and that testosterone replacement in hypogonadal men with ED results in improvement in only 40–60% of patients.

4 However, improvements in sexual function have been seen in hypogonadal men with ED who have had testosterone replacement therapy.

5 The oral agents sildenafil, tadalafil and vardenafil are the most frequent choice for first-line therapy.

6 About 30–40% of patients do not have a satisfactory response to treatment with sildenafil. Local therapies such as intracavernous or intraurethral alprostadil, or vacuum devices can be used in such patients.

7 There is evidence to suggest that the addition of testosterone may improve the response to sildenafil monotherapy.

8 The future role of testosterone in treating ED may be substantial. Other combination therapies that exploit multiple pathways, such as phosphodiesterase 5 inhibitors plus alprostadil, may also provide valuable treatment options for patients refractory to monotherapy for ED.

Shabsigh R et al (2003) Hypogonadism and erectile dysfunction: the role for testosterone therapy. *International Journal of Impotence Research* 15(Suppl 4): S9–S13

### BJU INTERNATIONAL



### Treatment of hypogonadism and ED

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

1 The fundamental importance of androgens at most levels of the pathways that serve penile erection means that consideration of androgen status has a significant place in the management of most patients with ED.

2 Hypogonadal men are capable of sexual erections, however, successful hormonal supplementation that results in normal testosterone values does not always restore libido and erectile function.

3 This article discusses the diagnosis of hypogonadism and treatment of the condition relevant to erectile dysfunction.

4 Androgen replacement therapy should ideally maintain not only

physiological levels of serum testosterone but also the metabolites of testosterone to optimise maintenance of libido, virilisation and sexual function.

5 Current treatments include oral, buccal, transdermal, intramuscular and implantable pellets. Most of these use molecular testosterone or salts and the clinical effects of the treatment depend on the mode of delivery.

6 More recent evidence suggests that dihydrotestosterone (DHT) could be used instead of testosterone for treating late-onset hypogonadism and improvements in sexual function have been reported.

7 The evidence for efficacy of dehydroepiandrosterone (DHEA) is inconclusive but reports suggest that it is safe to use.

8 The theory that androgens may work synergistically with other pharmacological agents is an attractive possibility for further research.

Morales A, Heaton JPW (2003) Hypogonadism and erectile dysfunction: pathophysiological observations and therapeutic outcomes. *BJU International* 92: 896–99

‘The combined use of sildenafil and a VED may satisfy patients more than when either of these treatments is used alone.’

## THE JOURNAL OF UROLOGY



### Use of sildenafil and a vacuum entrapment device

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

- 1 Sildenafil is considered first-line treatment for most men with ED. Use of a vacuum entrapment device (VED) is offered to men who are not completely satisfied with erectile function following treatment with sildenafil.
- 2 The aim of this study was to assess the efficacy of combined use of sildenafil and a VED. Satisfaction rates were also compared.

- 3 Patients (n=161) were randomly assigned to treatment with sildenafil or a VED. Men who were not satisfied with sildenafil were offered a VED and those not satisfied with a VED were given sildenafil.
- 4 After 2 months, men (n=41) who were not satisfied with either sildenafil or VED alone were given a combination of both.
- 5 The International Index of Erectile Function questionnaire and a global assessment questionnaire were used to evaluate satisfaction before and after treatment.
- 6 A total of 45 of 80 patients were satisfied with treatment on sildenafil alone, whereas 30 of 81 patients were happy with the VED.
- 7 All 41 patients stated on the global assessment questionnaire that they had a greater level of satisfaction with the results of

- combined treatment than with each treatment alone.
- 8 There was greater overall satisfaction among older men (age > 60 years).
- 9 No correlation was observed between treatment outcome and erectile dysfunction aetiology or between treatment satisfaction and the order in which the treatments were given and the pretreatment scores for the International Index of Erectile Function domains.
- 10 The combined use of sildenafil and VED may satisfy patients more than when either of these treatments is used alone. This option could obviate the need for more invasive therapy.

Chen J, Sofer M, Kaver I, Matzkin H, Greenstein A (2004) Concomitant use of sildenafil and a vacuum entrapment device for the treatment of erectile dysfunction. *The Journal of Urology* **171**: 292–95

‘These results demonstrate the high prevalence of ED in hypertensive patients from Spanish specialised hypertension units.’

## AMERICAN JOURNAL OF HYPERTENSION



### ED in essential arterial hypertension

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

- 1 A high prevalence of ED has been reported in patients with controlled arterial hypertension.
- 2 The aim of this study was to evaluate the prevalence of ED in a large population of men with hypertension seen in specialised hypertension units (SCHUs) and to assess the effectiveness and tolerability of sildenafil for the treatment of ED.
- 3 A total of 2130 men, who were being treated for essential hypertension, were recruited to this multicentre, prospective and observational study.

- 4 Only 291 patients (with a Sexual Health Inventory for Men [SHIM] score  $\leq 21$ ) were included in the study and received 50 mg sildenafil a day as required 30–60 minutes before sexual activity.
- 5 Sildenafil improved the SHIM score in the erectile function domain in 232 patients (83.2%).
- 6 There was a reduction in the percentage of hypertensive patients with severe (22.3% to 7.7%), moderate (23% to 5.6%), and mild (36.3% to 44.8%) ED after treatment.
- 7 The International Index of Erectile Function (IIEF) was normalised in 39% of patients who completed post-treatment IIEF.
- 8 The efficacy of sildenafil could only be determined in the 237 patients who completed the erectile function domain of the IIEF. Of these patients, 208 agreed that erectile function had improved as a result of treatment and showed a score increase in this domain.

- 9 There were no significant reductions in blood pressure as a result of treatment, and no changes were required in the dose or number of antihypertensive agents used in any of the patients. Sildenafil was equally effective with all types of antihypertensive agent or multiple agents.
- 10 Efficacy of sildenafil was significantly lower in patients with a high BMI.
- 11 There was no significant association between prevalence of any side-effects and single drug or combination antihypertensive treatment.
- 12 These results demonstrate the high prevalence of ED in hypertensive patients from Spanish SCHUs.
- 13 Sildenafil was safe to use and produced an excellent response in these patients.

Aranda P, Ruilope LM, Calvo C, Luque M, Coca A, De Miguel AG, for the Sildenafil Study Group (2004) Erectile dysfunction in essential arterial hypertension and effects of sildenafil: results of a spanish national study *American Journal of Hypertension* **17**: 139–45

## EUROPEAN UROLOGY SUPPLEMENTS



### Treatment options for ED and lower urinary tract symptoms

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

- The prevalence of lower urinary tract symptoms (LUTS) associated with benign prostatic hyperplasia (BPH) in older and middle-aged men is significant and is growing. LUTS is a major risk factor for ED.
- This literature review examines the data on the impact of

surgical and pharmacological treatments for LUTS on male sexual function. Key studies and newer studies on treatments for BPH and/or LUTS were reviewed.

**3** The most common surgical procedures for the treatment of BPH are currently transurethral resection of the prostate and transurethral incision of the prostate.

**4** Pharmacological treatment interventions for BPH are associated with a relatively lower risk of consequential sexual dysfunction compared with surgical intervention.

**5** Finasteride, which inhibits the conversion of testosterone to 5 $\alpha$ -dihydrotestosterone (DHT), improved symptoms in patients with BPH. However, it was also associated with increases in the incidence of

impotence.

**6** Most  $\alpha_1$ -adrenoceptor blockers have a minimal adverse impact on sexual function and improve urinary symptoms.

**7** The observed differences in action between  $\alpha_1$ -blockers could be explained by their differential selectivity for the various  $\alpha_1$ -adrenoceptor subtypes.

**8** Preservation of sexual function is important in the maintenance of quality of life for men with LUTS and should be considered when treatment choices are made. Potential effects of treatment choices on sexual function should be discussed with the patient before therapy is started.

van Moorselaar J (2003) LUTS and sexual dysfunction: implications for management of BPH. *European Urology Supplements* 2: 13–20

**‘Preservation of sexual function is important for quality of life for men with LUTS and should be considered when treatment choices are made.’**

## EAU UPDATE SERIES



### Treatment of female sexual dysfunction

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

- Female sexual dysfunction affects 30–50% of American women. Evidence suggests that the same disease processes and risk factors that occur in male ED are involved in female sexual dysfunction.
- This article describes the American Foundation of Urologic Disease (AFUD) Consensus Panel classification of female sexual dysfunction.
- There are a number of different types of female sexual dysfunctions, including hypoactive

sexual desire disorder, sexual aversion disorder, sexual arousal disorder, orgasmic disorder, and sexual pain disorders.

**4** A strong understanding of female pelvic anatomy, the neurogenic mediators of the female sexual response, the impact of hormones of female sexual function and the aetiologies of female sexual dysfunction is required before treatment choices can be made.

**5** High blood pressure and cholesterol, smoking and heart disease are all associated with sexual dysfunction in men and women.

**6** The same neurogenic aetiologies that cause ED in men can also cause female sexual dysfunction. These include: (1) spinal cord injury or disease of the central or peripheral nervous system, including diabetes and (2) complete upper motor neuron injuries affecting sacral spinal segments.

**7** Female sexual responses are difficult to quantify objectively in the clinical setting.

**8** Aside from hormonal replacement therapy, the best approach to medical management of female sexual dysfunction is unclear.

**9** Treatment with oestrogen, methyltestosterone, sildenafil, L-arginine, prostaglandin E1, phentolamine and apomorphine are options currently under investigation.

**10** The ideal approach to female sexual dysfunction should involve the collaborative efforts of therapists and physicians. A complete medical and psychosocial evaluation should be done.

**11** A comprehensive approach should be taken, which includes both psychological and physiological factors.

**12** Whether sildenafil or other vasoactive agents are effective in women with arousal disorder remains to be demonstrated.

Berman JR, Berman LA, Kanaly KA (2003) Female sexual dysfunction: new perspectives on anatomy, physiology, evaluation and treatment. *EAU Update Series* 1: 166–77

**‘The ideal approach to female sexual dysfunction should involve the collaborative efforts of therapists and physicians.’**

**‘The 4 years of availability of sildenafil has changed the treatment of ED in men.’**



## CURRENT UROLOGY REPORTS

### Four year update on use of sildenafil

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

- 1 Sildenafil was the first internationally approved drug for the treatment of ED.
- 2 In the past 5 years, more than 20 million men worldwide have been treated with the drug, and it has become the gold standard for treatment of ED.
- 3 Sildenafil is a phosphodiesterase type 5 inhibitor which is

selective for corpus cavernosum smooth muscle tissue and produces excellent erectile function.

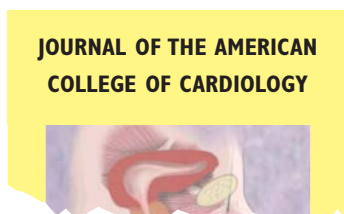
- 4 The clinical efficacy of erectogenic agents can be assessed in a number of ways. The global assessment questionnaire asks patients whether treatments have improved their erections. Other assessments include the International Index of Erectile Function (IIEF).
- 5 Sildenafil has been evaluated clinically and experimentally using each of these endpoint measurements with positive outcomes.
- 6 Sildenafil has also been effective across multiple aetiologies of ED.
- 7 Although sildenafil has a mild hypotensive effect it has been shown to be safe and effective in men

with treated and untreated hypertension.

- 8 Studies have shown that patients with mild untreated depression and ED who were given sildenafil showed a decrease in their depression scores.
- 9 There have been concerns about the possible cardiac effects of sildenafil. It is thought that sildenafil is contraindicated in patients taking nitrate medications for cardiac disease, but is effective and safe for other patients with cardiovascular disease.
- 10 The 4 years of availability of sildenafil has changed the treatment of ED in men. With few adverse events, sildenafil can be prescribed safely and reliably with a high degree of patient satisfaction.

Carson CC (2003) Sildenafil: a 4-year update in the treatment of 20 million erectile dysfunction patients. *Current Urology Reports* 4: 488–96

**‘ED could be an early clinical marker for the presence of systemic vasodilator abnormalities.’**



## JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

### Vascular defect in patients with ED but no CV disease

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

- 1 Although vascular disease of the penile arteries is the most common cause of ED, studies have shown that the many young patients with ED do not have clinical cardiovascular disease.
- 2 The aim of this study was to determine if patients with vascular ED and no clinical cardiovascular disease have structural and functional abnormalities of other vascular beds.

3 Systemic vascular structure and function was assessed in 30 patients with ED and 27 age-matched controls.

- 4 The following vascular parameters were measured: (1) carotid and brachial artery diameters, intima-media thickness, compliance and distensibility; (2) aortic pulse wave velocity; (3) coronary calcification and (4) brachial artery endothelium-dependent and independent vasodilation.
- 5 Apart from a significantly increased heart rate in the group with ED there were no differences in baseline characteristics between the two groups.
- 6 Most structural and functional vascular parameters were similar in the two groups.
- 7 Brachial artery flow-mediated vasodilation and vasodilation to nitroglycerin were significantly reduced in patients with ED compared with controls. There was

also a significant association between flow-mediated vasodilation and vasodilation to nitroglycerin in patients with ED, which was not seen in the control group.

- 8 This study has demonstrated the presence of a defect in the peripheral vascular nitric oxide-cyclic guanosine-3'5'-monophosphate pathway in patients with ED and with no clinical cardiovascular disease.
- 9 This abnormality is not usually associated with traditional cardiovascular risk factors. ED could be an early clinical marker for the presence of systemic vasodilator abnormalities.
- 10 It is still unclear whether patients with this abnormality will progress to clinically significant systemic cardiovascular disease or will go on to have acute cardiovascular events such as stroke or myocardial infarction.

Kaiser DR, Billups K, Mason C et al (2004) Impaired brachial artery endothelium-dependent and -independent vasodilation in men with erectile dysfunction and no clinical cardiovascular disease. *Journal of the American College of Cardiology* 43(2): 179–84