

Erectile dysfunction

ADAM easily treated with testosterone replacement therapy



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Do you believe in ADAM? I do not mean the creationist theory, but the syndrome of androgen deficiency in the aging male. In the past referred to as the andropause, this syndrome is now referred to as ADAM or P(partial)ADAM (mild androgen deficiency of the aging male does not have an acceptable acronym!).

There has been much controversy and debate about testosterone replacement therapy for middle-aged or elderly men with only slight or modestly reduced levels of testosterone, and treatment has largely been reserved only for men with unequivocal and severe testosterone deficiency. However, a milder degree of testosterone deficiency is fairly common in aging men and also

commoner in men with diabetes.

Testosterone deficiency produces diverse effects, including decreased libido and erectile function, depression, irritability and apathy, osteoporosis, decreased muscle mass and stamina, and maybe can even contribute towards type 2 diabetes. Symptoms, however, are vague and easily overlooked.

Undoubtedly testosterone replacement can reverse some of these effects and improve quality of life. It can also be useful in combination in men whose erectile dysfunction initially fails to respond to phosphodiesterase type-5 inhibitors. ADAM is easily treated with testosterone replacement therapy.

Do you believe in thyroid replacement therapy for the 'symptomatic' with minimally abnormal or even normal thyroid function tests? Well, whether you do or you don't, read on!

BRITISH JOURNAL
OF UROLOGY
INTERNATIONAL

Pathophysiology and management of ED in elderly men

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

1 ED is common in the aging man, and reliable therapies are needed. This article reviews the data on the epidemiology, pathophysiology and management of ED in elderly men.

2 An association between aging and ED was shown in several epidemiological studies. Thus it is mandatory that physicians include sexual matters in dealing with their aging patients as an essential part of assessing their quality of life.

3 The pathophysiology of ED in elderly men is mainly associated with atherosclerosis-induced cavernosal ischaemia leading to cavernosal fibrosis and veno-occlusive dysfunction. Abnormalities in circulating levels of hormones controlling the sexual organs seem to have an important effect, at least in some patients.

4 Managing ED in the aging male is first based on extensively evaluating the patient's sexual and medical history, and assessing the patient's and couple's needs and expectations.

5 Although several therapeutic options are available to treat the patient's symptoms, it seems that in most men oral pharmacotherapy is the first choice because it is effective and safe.

6 Future drugs will further increase the medical choices available to effectively treat aging men with ED.

INTERNATIONAL JOURNAL OF
IMPOTENCE RESEARCH

Gene transfer technology could be used to treat ED

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

1 The use of sophisticated genomic technologies has important implications for the understanding, diagnosis and treatment of ED.

2 This report reviews one aspect of the impact of the genomic revolution in urology — the preclinical evidence emerging from several laboratories indicating that gene therapy for ED may well provide the first safe and effective application of gene therapy to the treatment of smooth-muscle disease.

3 The molecular targets explored so far have largely concentrated on manipulating various aspects of the nitric oxide/guanylate cyclase/cGMP

system, although genetic modulation of growth factors, calcium sensitisation mechanisms and potassium-channel expression have also been explored.

4 The apparent preclinical success of virtually all of these gene-based strategies reflects the multifactorial nature of ED, as well as the numerous regulatory mechanisms available for restoring erectile capacity.

5 The ultimate goal of gene therapy is to provide a safe, effective and specific means for altering intracavernous pressure 'on demand', while simultaneously eliminating the necessity for other forms of therapy, and moreover, without altering resting penile function or the physiology of other organ systems.

6 It is in these arenas that the groundbreaking potential of gene transfer technology for the treatment of ED will be fully tested. In fact, the potential benefits of the application of gene transfer techniques to this important medical problem is just now beginning to be recognised.

Christ GJ (2003) Frontiers in gene therapy for erectile dysfunction. *International Journal of Impotence Research* **15**(suppl 5): 33–40

Montorsi F, Briganti A, Salonia A et al (2003) The aging male and erectile dysfunction. *British Journal of Urology International* **92**: 516–20

‘One study indicated that the major age-related changes in testosterone levels are caused by changes at the testicular level, and that the hypothalamic-pituitary responsiveness is maintained in aging men.’

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH



Low testosterone levels in type 2 diabetes

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

- 1 Clinicians have been aware of the increased prevalence of low testosterone levels in patients with type 2 diabetes for several years, but how these two conditions are associated is difficult to determine. This review examines current understanding.
- 2 Older age and obesity may be factors, as both are associated with type 2 diabetes and both decrease testosterone levels.

- 3 Sex hormone-binding globulin (SHBG), the major serum carrier protein for testosterone, may also have an impact.
- 4 One study indicated that the major age-related changes in testosterone levels are caused by changes at the testicular level, and that the hypothalamic-pituitary responsiveness is maintained in aging men.
- 5 SHBG levels fall with obesity and increase with aging.
- 6 Some studies indicate lower SHBG levels in type 2 diabetes. Most of the differences in testosterone levels between patients with and without diabetes may be related to reduced SHBG, rather than reduced testosterone production.
- 7 However, free testosterone levels fall with increasing age and obesity, rendering many patients with type 2 diabetes testosterone deficient.

- 8 Testosterone replacement may improve insulin sensitivity in hypogonadal, overweight men with type 2 diabetes by altering body composition, but studies are conflicting.
- 9 While it appears that testosterone replacement may have beneficial effects on cardiovascular risk factors, one must recognise that testosterone replacement in aging men has the potential risks of excessive erythrocytosis and adverse effects on benign prostatic hyperplasia and prostate cancer.
- 10 Understanding the risk/benefit ratio requires a large clinical trial. Until such a trial is conducted, one must discuss the potential benefits and risks with patients before giving testosterone replacement therapy.

Betancourt-Albrecht M, Cunningham GR (2003) Hypogonadism and diabetes. *International Journal of Impotence Research* **15**(suppl 4): 14–20

‘Even though the pathogenetic relationship between LUTS and ED is not yet completely understood, one has to postulate a direct association between these two typical symptom complexes in the aging male.’

EUROPEAN UROLOGY



Direct association between LUTS and ED in the aging male

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

- 1 From many epidemiological studies we know that the prevalence of benign prostatic hyperplasia (BPH) and the loss of erectile function increase with advancing age.
- 2 The aim of this study was to determine to which degree do voiding problems and impotence influence each other, and should they be considered true co-morbidities?
- 3 A newly developed and validated questionnaire on male ED (KEED) and a set of questions pertaining to voiding problems (IPSS) were mailed to a representative population sample

- of 8000 men from 30–80 years of age residing in the city of Cologne.
- 4 The responses included 4489 evaluable replies (56.1%). The response rates in the different age groups ranged from 41–61%. The mean age of the men who answered was 51.8 years.
- 5 The overall prevalence of ED was 19.2% (n=862), with a steep age-related increase from 2–53%.
- 6 Furthermore, 31.2% (n=1957) of all men complained of lower urinary tract symptoms (LUTS), the prevalence and intensity of which increased with age.
- 7 Interestingly, a high co-morbidity was found between ED and voiding problems.
- 8 Prevalence of LUTS in men suffering from ED was about 72.2% (n=621) vs 37.7% (n=1367) in men with normal erections. The odds ratio was evaluated with 2.11.
- 9 The trivariate analysis showed that the occurrence of LUTS can be considered as an age-independent risk factor for the development of ED

- (P<0.001).
- 10 Even though the pathogenetic relationship between LUTS and ED is not yet completely understood, one has to postulate a direct association between these two typical symptom complexes in the aging male.
- 11 In conclusion of the review, the question of whether and how often BPH treatment results in ED cannot be answered conclusively by the current literature.
- 12 So, is it simply the normal male aging process that is responsible for the pathophysiology of both diseases? Is the shift in hormones responsible for both typical male ailments? Can these changes then be reversed by means of hormonal therapy? These questions must be answered to allow for a causal therapy or even a special prophylaxis for these symptoms of the aging male.

Braun MH, Sommer F, Haupt G, Mathers MJ, Reifenrath B, Engelmann UH (2003) Lower urinary tract symptoms and erectile dysfunction: co-morbidity or typical ‘aging male’ symptoms? Results of the ‘Cologne male survey’. *European Urology* **44**: 588–94

‘Testosterone replacement therapy is generally safe in aging men and may improve libido, cognition, bone mineral density, body mass composition and serum lipoproteins.’

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH



Declining testicular function and aging

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

1 Age-related decline in male sex hormones, particularly testosterone, is referred to as andropause. Like menopause, andropause is associated with physical and emotional changes that may be alleviated by hormone replacement therapy.

2 As with women, selecting an appropriate hormone replacement therapy has the

potential to ameliorate some of these symptoms and improve overall well-being in aging men.

3 Hypogonadism in aging men, as defined by a low free testosterone index, is caused by declining testosterone production and increased sex hormone-binding globulin levels.

4 About 30% of men in their 60s, and more than 80% of men over 80 years may have a low free testosterone index.

5 Diagnosis of hypogonadism is based on clinical symptoms (e.g. decreased muscle mass, fractures and loss of libido) and laboratory determinations of serum testosterone — usually total testosterone levels.

6 Measuring bioavailable testosterone, or free testosterone, is expensive and time consuming, but may more accurately detect hypogonadism.

7 Testosterone replacement therapy is generally safe in aging men and may improve libido, cognition, bone mineral density, body mass composition and serum lipoproteins.

8 More studies are required to confirm these benefits; however, the available data suggest that, as the population ages, testosterone replacement therapy may play a role in preserving a high quality of life in some aging males.

9 Any of the available testosterone formulations can be used, but injectable forms have certain advantages, including excellent dose adjustability, lack of skin irritation and low cost — features that may be particularly important to older patients.

Tenover JS (2003) Declining testicular function in aging men. *International Journal of Impotence Research* **15**(suppl 4): 3–8

‘Except for young patients with traumatic arterial lesions, this study demonstrated the poor sexual satisfaction rate in impotent patients treated with the vasculogenic approach and the high rate of satisfaction in those treated with penile implants.’

JOURNAL OF UROLOGY



Vascular surgical treatment for impotence

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

1 Non-surgical treatment alternatives for ED include psychological, endocrinological, neurological and pharmacological therapy, including oral, topical and intraurethral delivery agents, and external device modalities.

2 Surgical interventions have consisted primarily of penile prosthesis insertion and arterial bypass surgery. Venous leakage surgery for corporeal veno-occlusive dysfunction came later in the mid-1980s–early 1990s.

3 This article compares the sexual satisfaction rate in patients with

arterial and/or venous impotence treated with four surgical techniques with long-term follow up.

4 Surgery was performed in 130 patients with vascular erectile dysfunction by one surgeon. Two young patients (2%) with traumatic arterial lesions underwent penile revascularisation (group 1), while 128 with arterial and/or venous impotence were also treated with surgery, including 11 of 130 (8%) with deep dorsal penile vein resection (group 2), 39 (30%) with arterialisation of the deep dorsal penile vein (group 3) and 78 (60%) with penile implants (group 4).

5 Sexual satisfaction, defined as the possibility of satisfactory sexual intercourse without any additional treatment or pain, was evaluated by patient interview.

6 Of the 130 patients, 111 (85%) participated in the sexual life events interview, including both patients (100%) in group 1, 7 of 11 (63.6%) in group 2, 33 of 39 (85%) in group 3 and 69 of 78 (88%) in group 4.

7 Mean follow up was 50, 48, 46 and 54 months for groups 1–4, respectively.

8 The sexual satisfaction rate was 2 of 2 (100%) for penile revascularisation, 1 of 7 (14%) for venous resection, 4 of 33 (12%) for arterialisation and 64 of 69 (93%) for penile implantation.

9 Complications occurred in 9.5%, 12.5% and 20.5% of the patients in groups 2–4, respectively.

10 Except for young patients with traumatic arterial lesions, this study demonstrated the poor sexual satisfaction rate in impotent patients treated with the vasculogenic approach and the high rate of satisfaction in those treated with penile implants.

11 Better selection criteria must be applied for vascular surgical treatment for impotence.

Wespes E, Wildschutz T, Roumequere T, Schulman CC (2003) The place of surgery for vascular impotence in the third millennium. *Journal of Urology* **170**: 1284–86

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH



Correlation between PDE-5 inhibitors

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

1 Phosphodiesterase type-5 (PDE-5) is the major cGMP-hydrolysing enzyme in penile corpus cavernosum and is an important regulator of nitric-oxide-mediated smooth muscle relaxation.

2 The critical role of PDE-5 in penile erection and the recent availability of specific and potent inhibitors of PDE-5 have enabled

the development of effective oral treatment strategies that have been widely accepted by both healthcare professionals and the lay public.

3 This article examines the correlation between the available biochemical and clinical data for the PDE-5 inhibitors sildenafil (Viagra), tadalafil (Cialis) and vardenafil (Levitra).

4 Data from studies using a single PDE-5 inhibitor suggest that differences in biochemical potency may be carried forward to the clinical setting. However, at normally prescribed doses, the efficacy all three PDE-5 inhibitors is similar.

5 The biochemical characterisation of sildenafil, vardenafil and tadalafil indicates that these compounds are all potent and selective inhibitors of PDE-5. Vardenafil was found to be the

most potent, followed by sildenafil and tadalafil.

6 By virtue of the major role of PDE-5 in regulating cGMP metabolism in penile cavernosal tissue, this potency and selectivity on the molecular level translates to drugs that are highly efficacious and safe.

7 Patients over 65 years or those with hepatic or severe renal impairment may experience elevated levels of plasma PDE-5 inhibitors. Thus, the use of lower doses is deemed advisable in these patients.

8 Overall, sildenafil, vardenafil and tadalafil exhibit low adverse event profiles and are well tolerated by patients.

‘Overall, sildenafil, vardenafil and tadalafil exhibit low adverse event profiles and are well tolerated by patients.’

Kim N (2003) Phosphodiesterase type 5 inhibitors: a biochemical and clinical correlation survey. *International Journal of Impotence Research* **15**(suppl 5): 13–19

EUROPEAN UROLOGY



Many patients with coronary artery disease have ED

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

1 The aim of this study was to assess the prevalence of ED, time of onset and association with risk factors in 300 patients with acute chest pain and angiographically documented coronary heart disease.

2 Mean patient age was 62.5 years. Mean duration of symptoms or signs of myocardial ischaemia before enrolment in the study was 49 months.

3 Coronary angiography showed 1-, 2- and 3-vessel disease in

98 (32.6%), 88 (29.3%) and 114 (38%) patients, respectively.

4 The prevalence of ED among all patients was 49% (147/300). ED was scored as mild in 21 (14%), mild to moderate in 31 (21%), moderate in 20 (14%) and severe in 75 (51%) patients.

5 In the 147 patients with co-existing ED and coronary artery disease, ED symptoms were reported as having become clinically evident before symptoms of coronary artery disease by 99/147 (67%) patients.

6 The mean time interval between the onset of ED and coronary artery disease was 38.8 months (range 1–168).

7 There was no significant difference in terms of risk factor distribution and clinical and angiographic characteristics between patients with the onset of ED before vs after coronary artery disease diagnosis.

8 All patients with type 1 diabetes and ED actually developed sexual

dysfunction before the onset of coronary artery disease ($p < 0.001$).

9 The study suggests that a significant proportion of patients with angiographically documented coronary artery disease have ED, and that this latter condition may become evident before angina symptoms in almost 70% of cases.

10 The major limitation of this study is the lack of a control group, ie, patients with ED and no clinically evident coronary artery disease. Thus further research is required to test the hypothesis that ED is a predictor for coronary artery disease.

11 Future studies including a control group of patients with coronary artery disease and normal erectile function are required in order to verify whether ED may be considered a real predictor of ischaemic heart disease.

‘There was no significant difference in terms of risk factor distribution and clinical and angiographic characteristics between patients with the onset of ED before vs after coronary artery disease diagnosis.’

Montorsi F, Briganti A, Salonia A et al (2003) Erectile dysfunction prevalence, time of onset and association with risk factors in 300 consecutive patients with acute chest pain and angiographically documented coronary artery disease. *European Urology* **44**: 360–5