Erectile dysfunction

Central and peripheral factors and general health

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The initial paper by Sachs is useful in discussing the false distinction between psychogenic and organic ED. It contains a useful classification table, as recommended by the nomenclature committee of the International Society for Sexual and Impotence Research (ISSIR), and continues with an interesting discussion, followed by an alternative taxonomy of ED free of the organic–psychogenic distinction. This taxonomy divides ED into organic and situational. Organic ED is then subdivided into:

A. Peripheral
- *Vascular*
- *Neural*
- *Anatomical*
- *Endocrine*

B. Central
- *Neural*
- *Endocrine*
- *Generalised – lack of arousal, age, sexual inhibitions*
- *Psychological stress.*

Situational ED is subdivided into:
A. Partner-related
B. Performance-related
C. Environment-related.

The discussion continues and provides stimulating food for thought. There is some brain physiology from Montorsi and colleagues that is relevant to apomorphine and other centrally acting treatments.

There are also three papers related to cardiovascular disease. Siroky and Azadzoi discuss risk factors and underlying mechanisms causing ED in cardiovascular disease and their relevance to potential therapy. Exercise testing is a useful if not essential means of identifying the 'cardiac risk category' (as per Princeton guidelines) and this is important in a significant number of our patients.

Laboratory investigations in men with ED have been much debated but there is no consensus. Bodie et al argue for testosterone, cholesterol, HbA_{1c} and thyroid-stimulating hormone tests, to identify modifiable systemic factors. Finally, Steers et al discuss combination treatment regimens and their rationale (although there is still little evidence regarding enhanced efficacy).

THE JOURNAL OF UROLOGY

Treatment strategies for vasculogenic ED

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

1 Current therapy for vasculogenic ED is relatively ineffective in permanently reversing the condition.

2 This paper explores the mechanisms behind vasculogenic ED and potential therapies to permanently reverse or prevent it.

3 Penile erection is a complex neurovascular phenomenon that may be affected by hypercholesterolaemia, atherosclerotic vascular occlusive disease, veno-occlusive dysfunction and cavernosal fibrosis.

4 Penile revascularisation represents the only currently feasible cure of arteriogenic ED. However, success rates are variable.

5 Permanent reversal of impaired cavernosal relaxation requires control of hypercholesterolaemia and lifestyle changes, such as smoking cessation.

6 Strategies aimed at improving cavernosal relaxation or fibrosis may also improve veno-occlusive dysfunction.

7 Although there is evidence to support a role for hypoxaemia in cavernosal dysfunction and fibrosis, little attention has been paid to the use of oxygen to treat ED.

8 Further research into possible long-term treatments for vasculogenic ED is needed.

Siroky MB, Azadzoi KM (2003) Vasculogenic erectile dysfunction: newer therapeutic strategies. *The Journal of Urology* **170**: S24–30

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

A non-traditional classification system for ED

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

1 The traditional distinction between organic and psychogenic ED does not take into account knowledge of the neurobiology of psychological disorders, and has become counterproductive in the diagnosis, classification and treatment of ED.

2 This paper presents an alternative classification, based on the proposals of the nomenclature committee of the International Society for Sexual Health and Impotence Research.

3 The category psychogenic ED is based on an obsolete view of mind-body distractions.

4 The term psychogenic ED disregards the fundamental meaning of psychosomatic. Psychological processes should be viewed as bound with organic processes of erectile function rather than as separate pigeonholes to which relative causation can be assigned.

5 The diagnosis of psychogenic ED is often by exclusion. Disorders in the organic basis of erection in one context may or may not be predictive of ED in another context.

6 The alternative taxonomy reclassifies as organic several of the causes of ED now considered to be psychogenic, and considers others as situational ED, a class reserved for episodic occurrences of ED clearly due to attributes of sexual encounters.

7 The traditional division between organic and psychogenic ED should be discarded.

Sachs BD (2003) The false organic-psychogenic distinction and related problems in the classification of erectile dysfunction. *International Journal of Impotence Research* **15**: 72–78

'Since ED often reflects the development of endothelial dysfunction and atherosclerosis, it may be a forerunner of coronary artery disease.'

THE JOURNAL OF UROLOGY

Frequency of ED in people with coronary artery disease

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

1 Although the association between ED and risk factors for cardiovascular disease is well established, most cardiologists do not routinely ask about ED.

2 This paper sought to determine the frequency of ED in patients with stable coronary artery disease in a private practice cardiology setting.

3 A total of 76 men were given a questionnaire – the validated Sexual Health Inventory for Men (SHIM).

4 The mean patient age was 64 years and 47% of patients were on β–blockers, 92% on statins and 28% on diuretics.

5 The SHIM score was 17–21 in 14 men, which suggests mild ED. There was mild to moderate ED in 16 men (SHIM = 11–16), moderate ED in four (SHIM = 8–10) and severe ED in 19 (SHIM ≤ 7).

6 Of the study population, 75% had difficulty in achieving erections and 67% had problems in maintaining an erection after penetration.

7 According to the responses to the questionnaire, sildenafil treatment was successful in four patients.

8 If these four men are included as having had ED, then 75% of men with chronic stable coronary artery disease had ED or a recent history of ED.

9 ED is very common in men with chronic coronary artery disease.

10 The SHIM is a useful, quick and inexpensive tool for diagnosis of ED.

11 Since ED often reflects the development of endothelial dysfunction and atherosclerosis, it may be a forerunner of coronary artery disease.

12 It is unclear whether treating the risk factors for cardiovascular disease will also treat the ED.

13 Changes in lifestyle in midlife may be too late to effect a change, and some antihypertensive and lipid-lowering drugs may actually exacerbate ED.

14 The American College of Cardiology/American Heart Association and Princeton Guidelines may be useful in the approach to treatment of ED in the cardiac patient.

Kloner RA, Mullin SH, Shook T et al (2003) Erectile dysfunction in the cardiac patient: how common and should we treat? *The Journal of Urology* **170**: S46–50

'There are some concerns about the use of combination therapy. Many agents used to treat ED cause relaxation of smooth muscle, hence gastroesophageal reflux could occur following the use of such therapy.'

THE JOURNAL OF UROLOGY

Combination drug therapy for ED

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

1 Lack of efficacy with monotherapy using a non-selective α–adrenergic antagonist or a non-selective phosphodiesterase (PDE) inhibitor has led to the use of a combination of intracavernous therapies for ED.

2 However, a lack of randomised controlled trials means that it is not clear whether combinations of intracavernous drugs are more effective than prostaglandin E1 alone.

3 There are at least eight classes of drugs acting either on the corpus cavernous smooth muscle or within the central nervous system with suspected or proven efficacy for the treatment of ED.

4 There are also three other classes of drugs and six gene therapies that have shown promise experimentally.

5 A popular approach has been to use sildenafil with intraurethral prostaglandin E1 (the Medicated Urethral System for Erection – MUSE), or with intracavernous prostaglandin E1.

6 Although there is evidence to suggest that these combinations are more effective than using sildenafil alone, true safety and efficacy must be evaluated in a double-blind, placebo-controlled randomised trial.

7 The coexistence of psychogenic factors of ED suggests that the combination of psychotherapy and drugs that act within the brain may facilitate the actions of drugs within the penis. However, there are common adverse effects associated with such combinations.

8 Other strategies have been to reduce tone in corpus cavernous smooth muscle or alter neural input to the penis. A reduction in sympathetic tone by sympathectomy or α–adrenergic blockage in animals enhances the effects of intracavernous drugs that work through cyclic adenosine monophosphate mediated mechanisms.

9 Another approach to the treatment of ED could be the use of drugs that take advantage of two different mechanisms to achieve penile erection.

10 There are some concerns about the safety of combination therapy. Many agents used to treat ED cause relaxation of smooth muscle, hence gastroesophageal reflux could occur following the use of such therapy.

11 Although preliminary observations support the use of combination therapy in patients in whom single therapy has failed, these reports must be viewed with some scepticism.

Steers WD (2003) Viability and safety of combination drug therapies for erectile dysfunction. *The Journal of Urology* **170**: S20–23

'Psychogenic impotence may be associated with previously unrecognised underlying functional abnormalities of the brain.'

INTERNATIONAL JOURNAL OF IMPOTENCE RESEARCH

Brain modulation during sexual stimulation

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

1 Sexual stimulation leading to penile erection is known to be controlled by different areas in the brain.

2 Apomorphine sublingual is the first centrally acting agent approved for the treatment of ED.

3 Apomorphine has been shown to act on neurons located within the paraventricular nucleus and the medial preoptic area of the hypothalamus in rats.

4 However, the mechanisms of action of apomorphine in humans are not clear.

5 The aim of this study was to use magnetic resonance imaging to evaluate the functional effect of apomorphine versus placebo in the brains of patients with psychogenic ED.

6 Eight patients with psychogenic ED and four controls underwent two magnetic resonance sessions after receiving apomorphine and placebo in this double-blind, randomised crossover trial.

7 Patients were shown neutral and erotic video sequences during the acquisition of magnetic resonance images.

8 Six out of eight patients reported penile erection after administration of apomorphine. Two of the four controls reported erection during the erotic videotape projection.

9 There was apomorphine induced modulation of cortical and subcortical brain structures in patients with psychogenic ED.

10 Compared with controls, patients with ED showed increased activity in frontal limbic areas, which was downregulated by apomorphine.

11 Psychogenic impotence may be associated with previously unrecognised underlying functional abnormalities of the brain.

12 Functional magnetic resonance imaging may be an essential new tool in the assessment of cerebral areas of penile erection that are functionally activated during stimulation by means of different neurochemical agonists.

Montorsi F, Perani D, Anchisi D et al (2003) Apomorphine-induced brain modulation during sexual stimulation: a new look at central phenomena related to erectile dysfunction. *International Journal of Impotence Research* **15**: 203–9

'There is an increased frequency of ED in men with diabetes who already have clinical evidence of neuropathy, retinopathy, nephropathy and coronary artery disease.'

THE JOURNAL OF UROLOGY

Future goals for the treatment of ED

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

1 Between 25% and 75% of men with type 2 diabetes will complain of ED.

2 A man with diabetes has an odds ratio of having ED 1.9–4 times greater than a person without diabetes.

3 This paper reviews the research relating to prevention and treatment strategies for ED in diabetes and identifies future goals to enhance our understanding of the unique pathophysiological attributes of diabetes and ED.

4 No single mechanism is responsible for diabetes induced ED. Evidence suggests that multiple mechanisms interact and lead ultimately to cavernosal damage.

5 The goal of research into diabetes-induced ED is to translate present animal research into clinical paradigms that will be useful in optimising treatment.

6 There is an increased frequency of ED in men with diabetes who already have clinical evidence of neuropathy, retinopathy, nephropathy, and coronary artery disease.

7 The rate of ED is also higher in men with diabetes who also have hypertension or hyperlipidaemia, or use tobacco.

8 It is unclear whether there are abnormalities in the hypothalamic-pituitary-gonadal axis of patients with diabetes-induced ED.

9 Most studies in patients with diabetes, with or without ED, show an intact hypothalamic-pituitary-gonadal axis with normal levels of serum testosterone, luteinising hormone and follicle-stimulating hormone.

10 Since early and aggressive treatment of diabetes has been shown to significantly decrease the incidence of other complications, perhaps early treatment of diabetes induced ED could decrease its severity.

11 There have been few prospective studies on the development of ED and its relation to control of diabetes.

12 Lifestyle modification such as stopping smoking and control of high blood pressure is likely to decrease the chances of developing ED.

13 Attempts to prevent end-stage cavernosal injury must occur early and have an effect on protecting nitric oxide synthase levels and activity as well as cavernosal and endothelial function.

14 A multilevel approach which includes a variety of treatment strategies must be used to effectively diagnose and treat diabetes-induced ED.

Costabile RA (2003) Optimising treatment for diabetes mellitus induced erectile dysfunction. *Journal of Urology* **170**: S35–39

HEART

Exercise treadmill testing in the management of ED

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

1 Men with hypertension have a 15% probability of developing complete ED, while those with diabetes have a 28% chance of developing ED.

2 Fear of resuming sexual activity after a cardiac event may deter men from seeking medical advice.

3 The Princeton and British consensus panels have assessed the evidence for risk of sexual activity in cardiac patients. Specific guidelines have been produced on the basis of this.

4 This paper reports on the success of the implementation of the guidelines, and the use of exercise treadmill testing in the management of ED in particular.

5 Patients (n = 112) with cardiovascular disease complaining of ED were referred to a specialised ED/cardiovascular clinic.

6 Men who had exercise-limiting symptoms were referred for exercise treadmill testing and/or echocardiography.

7 Eighty-five (75%) men underwent exercise treadmill testing. Of these, 58% achieved more than 4 minutes (without any symptoms and with a normal blood pressure response) on the test and were classified as low risk and given treatment for ED.

8 Fourteen per cent of men did not reach 4 minutes on the treadmill. These men, apart from three in whom coronary angiography showed minimal disease, were classified as intermediate/high risk and had priority specialised cardiac investigations.

9 The Princeton and British guidelines are extremely valuable in managing ED in patients with cardiovascular disease.

Solomon H, Man J, Martin E, Jackson G (2003) Role of exercise treadmill testing in the management of erectile dysfunction: a joint cardiovascular/erectile dysfunction clinic. *Heart* **89**: 671–2

THE JOURNAL OF UROLOGY

Evidence-based approach to laboratory screening of ED

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

1 The usefulness of routine testing for laboratory abnormalities in men presenting with ED is not clear.

2 The authors of this paper undertook a retrospective review of the computerised charts of 3547 men with erectile dysfunction to assess the prevalence of laboratory abnormalities.

3 Standard laboratory tests were performed. These included tests for serum testosterone, prolactin, luteinising hormone, thyroid-stimulating hormone, HbA_{1c}, prostate-specific antigen, haemoglobin, cholesterol and creatinine levels.

4 Of the study population, 8.7% of patients had low testosterone, 4.6% had increased prolactin, 14.6% had abnormal luteinising hormone, 4.0% had increased thyroid-stimulating hormone, 8.3% had increased prostate-specific antigen, 26.5% had anaemia and 11.9% had renal insufficiency.

5 A high number of patients with a primary complaint of ED had increased HbA_{1c} and total serum cholesterol levels.

6 Testosterone deficiency is a common condition, which is treatable, and therefore warrants routine evaluation.

7 These findings provide evidence to support routine screening of total serum cholesterol but further studies are needed to establish which cholesterol fractions and lipid levels correlate with ED.

8 Routine screening of thyroid-stimulating hormone, total serum cholesterol and HbA_{1c} is warranted in men presenting with ED.

9 An evidence-based approach to standardisation of laboratory evaluations for men presenting with ED is recommended. Screening should be directed to identify those risk factors that may benefit from lifestyle modification and pharmacological intervention.

Bodie J, Lewis J, Schow D, Monga M (2003) Laboratory evaluations of erectile dysfunction: an evidence based approach. *The Journal of Urology* **169**: 2262–64