

The underlying pathophysiology and causes of erectile dysfunction

Michael G. Wyllie, MD

Urodoc Ltd., 46 Ridgeway Road, Herne Bay, Kent, CT6 7LN, UK

Physical organic causes are now thought to account for most cases of erectile dysfunction (ED), although there is often a psychogenic contribution to the condition. Atherosclerotic disease is estimated to account for 40% of ED in men over 50 years, and vascular disease, including diabetes, is a common cause of ED. ED may be considered an early marker for cardiovascular disease. Ageing is a strong risk factor, and both psychological conditions such as anxiety and depression and neurological conditions such as Parkinson's disease are also common risk factors. Pelvic surgery, with which there is a risk of nerve damage, may also result in ED. Other causes include endocrine disorders, and interactions from prescribed drugs such as antihypertensives, antidepressants, antipsychotics, hormone treatments, and histamine H₂ antagonists such as cimetidine. Anatomical features and anatomical conditions such as Peyronie's disease are a less common cause of ED. (*Clinical Cornerstone*. 2005;7[1]:19–26) Copyright © 2005 Elsevier BV.

Originally, erectile dysfunction (ED) was considered to have a predominant psychogenic (i.e. psychological) origin, with physical causes underlying only a minority of cases.¹ Perhaps as a consequence of this, until the 1990s ED was diagnosed and evaluated with psychological assessments, sometimes with biochemical or endocrine analyses, and only occasionally vascular investigations.

If there was no clear organic aetiology, and particularly if men reported involuntary erections during the night or early in the morning, as many did, the conclusion was that there was a psychological cause of the condition. The conclusion that the aetiology was psychological – however sensitively handled – was often distressing to men and their sexual partners.

It is now recognized, however, that organic causes are responsible for most cases of ED, particularly in those aged over 50 years. Indeed, of the men with ED who are older than 50 years, atherosclerotic disease is the primary cause of ED in 40%, and, in this large group of patients, the risk factors are not surprisingly, therefore, similar to those for cardiovascular disease.¹ A range of other diseases, from prostate conditions to rheumatic disease and allergy, have also been implicated either directly, as risk factors, or as relevant comorbidities.² In terms of diagnosis and patient management, there is an increasing

interest in the high degree of comorbid ED and benign prostatic hyperplasia (BPH).³

POSSIBLE CAUSES AND UNDERLYING PATHOPHYSIOLOGY

A wide range of causes of ED has been identified. These include ageing, psychological disorders such as depression and anxiety, neurological disorders such as cerebral disease and spinal cord injury, hormonal disorders such as hypogonadism, that depress libido, vascular disorders, drugs such as antihypertensives and antidepressants, and the use of marijuana, alcohol, and tobacco.¹

Age

Age is a strong risk factor for ED. The prevalence is high in older men, affecting between 20% and 45% of older men (see the article by J. Dean, p. 5–10), a figure likely to increase.

In 1 study, multivariate logistic regression analysis of data revealed that the risk of ED increased by 10% for every year of age in populations of men aged 40–70 years.⁴ The odds ratio (OR) for moderate or severe erectile dysfunction for every year of age was 1.10 (95% confidence interval [CI] 1.08–1.11).⁴ The prevalence of “complete impotence” in the Massachusetts Male Aging Study (MMAS) was 5% for men aged 40 years, and 15–25% for men aged 65 years; and age was the independent variable most strongly associated

with ED.^{5,6} However, it is pertinent to note that although ED is strongly associated with age, it is not necessarily an inevitable consequence of ageing.

As evidenced by the changes in the following parameters, overall sexual function tends to decline in “healthy normal” men as they age.⁷ The time taken for a healthy man to achieve an erection with sexual stimulation increases, erections are less turgid, ejaculations less powerful, and the volume of ejaculate decreases. The refractory time between erections increases when there is no reaction to sexual stimulus. The penis also becomes less sensitive to tactile stimulation. With age, there is usually a decrease in serum testosterone concentrations and a decrease in the tone of the corporal smooth muscle, either of which – or indeed one of several other age-related factors – could contribute to the development of ED.

In addition, there are a number of diseases that become more common in older men and could have an impact on erectile dysfunction. The prevalence and incidence of diabetes mellitus are increasing in many countries, both developed and developing, and up to one-half of all men with diabetes will have ED.⁷

Psychological disorders

Although most cases of ED are now believed to have a largely organic cause, there are a number of psychogenic factors that can per se cause ED or can contribute to the condition alongside one or more physical causes. Common psychological reasons for ED include anxieties about sexual performance, tension and stresses within the relationship, as well as common psychiatric conditions such as anxiety, depression, and schizophrenia.⁷ Persistent low mood, loss of interest and enjoyment, low energy, and sleep and appetite disturbances are the key characteristics of depression. Such illness is more commonly a cause of reduced sexual desire than an erectile problem, but the lack of desire may result in ED.⁸⁻¹⁰

Depression in particular has been well studied. In the MMAS, the OR for men with depression having ED was 1.82.^{6,10} The relationship was robust and independent of confounding factors, including demographic, anthropometric and lifestyle factors, health status, medication use, and serum hormone levels. A second study found that ED was associated with a high level of depressive symptoms (more than twice the incidence in men with BPH) regardless of age, marital status, or comorbidities.¹¹

Generalized anxiety states are characterized by heightened arousal, and feelings of fear, dread, and impending doom occurring in many situations or throughout the day. Patients may be aware of symptoms such as palpitations and hyperventilation, and may have panic attacks. ED as a symptom of a generalized anxiety needs to be distinguished from anxiety specific to sexual intercourse, or anxiety related to sexual performance.^{8,9}

Schizophrenia is associated with reduced libido. This may improve with neuroleptic drugs, but these treatments may themselves reduce a man’s ability to achieve and/or maintain an erection, have an orgasm, and otherwise achieve sexual satisfaction.⁷⁻⁹ People with schizophrenia may also have delusional beliefs about their erectile function, e.g. that their potency is controlled by outside forces.

KEY MESSAGE A WIDE RANGE OF FACTORS CAN CAUSE ED

ED is a common complication of alcohol dependency, as well as a consequence of acute consumption of an excess of alcohol. Patients who are dependent on alcohol frequently complain of ED and lack of libido, and they may, in addition, have serious physical sequelae of alcohol dependence that may contribute to ED.^{8,9} Other psychiatric conditions that may be involved include body dysmorphic disorder (BDD) and gender identity problem.^{8,9} BDD is a disorder of body image in which patients have abnormal beliefs about the anatomical structure and/or physiological function of specific body parts. If the genitalia are the focus of these beliefs, then ED may be a major feature of the condition.^{8,9} A man with a disorder of gender identity would not normally present with a complaint about ED, but would be seeking specialist treatment for the broader problem of feeling that he was trapped as the “wrong” gender and should really be a woman.^{8,9}

There are several factors that may suggest a psychogenic rather than a physical origin for ED. If the ED is of sudden rather than gradual onset, and if there is an early collapse of any erection achieved, the problem is more likely to be psychogenic. ED of psychogenic origin is also associated with good quality or “better” spontaneous, self-stimulated or waking erections,

and with early or otherwise problematic ejaculation. Relationship problems, major life events, and psychological problems are all more closely linked with psychogenic ED.^{8,9} There is more detail on clues to different types of ED in the article by F. Montorsi, p. 29–34.

Anxiety about sexual performance, a relationship under stress, and a lack of sexual arousability are also common causes of psychogenic ED.^{1,7-9} ED has also been significantly correlated with indices of anger, and of a dominant personality (someone with a submissive personality has a higher risk of ED).¹¹ ED of a psychogenic origin has an acute onset in contrast to ED of an organic/physical origin, which has a gradual onset.

Reduced libido is associated with ED, and there may be excessive neural inhibition that prevents the initiation of the erectile process. Impaired release of nitric oxide (see the article by D. Ralph, p. 13–17) is also believed to form part of the pathophysiology of psychogenic ED.⁷

Neurological disorders

A wide range of neurological disorders is associated with the development of ED.

Commonly, ED and a loss of sexual interest occur in those with cerebral diseases such as stroke, possibly because of over-inhibition of the spinal erection centres.¹

In those with spinal cord injury, the outcome depends on the location of the lesion. If upper motor neurons are affected, 95% of men can achieve reflexogenic erections. In cases of lower motor neuron lesions, 25% of men are capable of psychogenic erections, and more than 90% of those with incomplete lesions retain erectile function.¹ Treatment for prostate cancer, whether with surgery or radiotherapy, often damages the cavernosal nerve, and some degree of ED affects 80% of men treated for prostate cancer. Radical pelvic surgery for other reasons and pelvic injury can also cause neurogenic ED by damaging neural transmission.

Disorders such as Alzheimer's disease and Parkinson's disease can also result in ED by reducing libido and the initiation of an erection. Peripheral neuropathies from diabetes mellitus and alcohol abuse may also result in ED.

Endocrine disorders

The role of androgens in the development of ED is complex. Although men with hypogonadism and low levels of circulating androgens can still achieve erections in response to visual sexual stimulation,

androgen deficiencies reduce nocturnal erections and libido.^{1,7} In addition, testosterone supplementation has been shown to augment the response to phosphodiesterase-5 (PDE5) inhibitors.¹²

Hormonal disorders, or other conditions leading to hyperprolactinaemia, result in both sexual and reproductive dysfunction. Central dopaminergic activity is inhibited by prolactin. This in turn reduces the secretion of gonadotrophin-releasing hormone (GnRH), resulting in hypogonadotropic hypogonadism, a condition in which the testes are abnormally small because of low levels of GnRH, and which is associated with ED. ED is more common in those with thyroid hormone disorders. For example, unsuspected hypothyroidism has been found in 6% of a sample of 600 men with ED.¹³ Symptoms of hypothyroidism include low libido and depression, and neural reflexes slow down, all of which may affect erectile function. In hyperthyroidism, depression and nervousness may feature, which may increase performance anxiety. There is also an increase in β -adrenoreceptor levels, which may stimulate adrenergic tone, so preventing the relaxation of cavernosal smooth muscle, causing penile flaccidity.

ED may also be caused by Cushing's syndrome, or hypercortisolism, which is often associated with oral corticosteroid treatment for rheumatoid arthritis or severe asthma. Low levels of cortisol or aldosterone in Addison's disease are also associated with ED.^{8,9} Cortisol enhances the sympathetic stress response, and this may affect adrenergic tone, so keeping penile smooth muscle semi-contracted and inhibiting erectile function. High levels of cortisol reduce libido and can lead to psychological disorders ranging from mild euphoria to psychoses. In addition, cortisol may have an effect on ED through the hypothalamic-pituitary-adrenal axis, which affects the release of neurotransmitters including dopamine. Much of the pathophysiology of hormone-related ED is associated with a loss of libido, but there may also be a reduced and inadequate release of nitric oxide.

Vascular disorders

Vascular disorders are highly prevalent in the older population and have been linked to the appearance of ED. There is a wide range of risk factors associated with vascular insufficiency within the penis. These include hypertension, hyperlipidaemia, cigarette smoking, diabetes mellitus, and pelvic irradiation.⁷

In the development of atherosclerosis, as in the general systemic vascular tree, the arterioles within

the penis become gradually occluded by atherosclerotic plaques. The artery walls become less flexible, and, as a result of direct action or secondary to reduced tissue perfusion, the overall vascular and mechanical components of erectile function become less efficient.

ED is a common symptom in men with atherosclerosis, which may subsequently develop into more serious clinical end-points such as heart disease. Indeed, ED is now considered to be a marker or early warning of asymptomatic but potentially serious cardiovascular disease.¹⁴ A significantly higher probability of impotence was recorded in men with heart disease in the MMAS.⁶ ED was also found in men with other risk factors for atherosclerosis, including hypertension, diabetes, and low levels of high-density lipoprotein cholesterol.⁶ The association with hypertension is not a direct result of the high blood pressure, but is a result of stenotic lesions in the arteries associated with hypertension.

KEY MESSAGE ED MAY BE AN EARLY MARKER FOR CERTAIN DISEASES SUCH AS DIABETES AND CARDIOVASCULAR DISEASE

Venous problems can also cause ED. In particular, if the veins draining blood from the penis fail to close during an erection, there may not be enough blood in the penis to attain full rigidity and allow adequate sexual penetration. Such veno-occlusive dysfunction can have several causes. These include the development of large venous channels that drain the corpora cavernosa, and degenerative changes to the tunica albuginea (the sheath that surrounds the corpus cavernosum) caused by ageing, diabetes mellitus, and the formation of dense, fibrous scar tissue in the tunica albuginea in those with Peyronie's disease.^{8,9} The common penile artery can be partially and wholly blocked in accidents. Blunt pelvic or perineal trauma (e.g. from bicycling accidents) is the common reason for focal stenosis.^{8,9}

Other vascular problems may be caused by traumatic injury, changes to the structure of the cavernosal smooth muscle and endothelium, poor relaxation of trabecular smooth muscle (particularly in anxious men with excessive adrenergic tone), and surgical shunts from operations to correct priapism.

In summary, the sequelae of a compromised vascular system are easy to understand: inadequate arterial flow into the penis failing to produce adequate rigidity and/or excessive outflow because of impaired veno-occlusion.

Medications

Drugs – whether prescribed, legal (alcohol, tobacco), or illegal – affect sexual function in many ways, e.g. by inhibiting ejaculation, causing sedation, or resulting in depression, which in turn reduces libido. The adverse effects of drugs have been found to be an important risk factor for ED.^{2,6}

A wide range of commonly prescribed pharmaceutical treatments have adverse effects on erectile function. It has been estimated that 25% of all ED is attributable to the adverse effects of drugs.¹⁵ Central neurotransmitter pathways, whether involving serotonin, noradrenaline, or dopamine, are all involved in sexual and erectile function, and the many pharmaceutical treatments that act on, or interact with, such pathways may result in ED. Commonly prescribed drugs that are implicated in ED include almost all classes of antipsychotic drugs, antidepressants, and centrally acting antihypertensives.

In the case of antidepressants, the change in erectile function could be a consequence of the medication per se or a change in the depressive state.

Antihypertensive drugs such as the diuretics and β -blockers have been commonly associated with ED, and other types of drug associated with ED include digoxin, cimetidine, various hormonal medications, and anticancer drugs.⁶ Psychotropic drugs, described by patients as “medication for nerves” and “sleeping pills”, have also been identified as important risk factors for ED.²

Antihypertensives

β -adrenoreceptor antagonists (β -blockers) compromise erectile function whereas α adrenoreceptor antagonists (α -blockers) have little effect. A high level of adrenergic tone within the penile tissue prevents smooth muscle from relaxing. As described in the article by D. Ralph (p. 13–17), relaxation of trabecular smooth muscle is essential for erectile function. There may also be a direct effect on smooth muscle.¹⁵ The problem is more likely to occur with lipid-soluble β -blockers such as propranolol, but has also been reported with ophthalmic atenolol and timolol.

There have been isolated case reports of ED after

treatment with α -blockers, but the risk appears to be significantly less than with β -blockers, and it is mainly with older drugs such as methyldopa and reserpine. In a recent study, one α -blocker, doxazosin, was shown to have a positive effect on ED in patients with BPH,¹⁶ showing that the effect of α -blockers on erectile function may be dependent on comorbidities and may not invariably lead to sexual dysfunction. Thiazide diuretics, such as chlorothiazide and cyclopenthiiazide, have also been reported to cause ED. The mechanism for this is unclear because thiazides have no significant hormonal, autonomic, or central nervous system effects, although a direct effect on smooth muscle is thought to be responsible.¹⁵ The potassium-sparing diuretic spironolactone, which antagonizes aldosterone, can cause ED and has other sexual effects, e.g. inducing gynaecomastia and a decrease in libido.⁷ Cases of ED in men taking calcium-channel blockers are only rarely reported, and there does not seem to be any association with angiotensin-converting enzyme inhibitors.¹⁵

Cardiac and lipid-lowering drugs

Digoxin is among a number of other cardiac drugs found to have adverse effects on erectile function. Digoxin increases the force of contraction of myocardial cells and may have some effect on smooth-muscle contraction in erectile tissue, so preventing an erection.^{8,9} Others include the fibrate lipid-lowering drugs clofibrate and gemfibrozil, which reduce libido (although statins, such as simvastatin or atorvastatin are now widely used instead).^{8,9}

Antidepressants

Antidepressants are effective because they act on neurotransmitters such as serotonin, noradrenaline, and dopamine, but therefore they can also affect neurogenic sexual function. Most classes of antidepressant drug have been found to inhibit erectile function, from the older tricyclics, lithium, and monoamine oxidase inhibitors to the newer selective serotonin reuptake inhibitors (SSRIs), and the serotonin and noradrenaline reuptake inhibitors (SNRIs) that affect more than one pathway. Antidepressants may lead directly to ED, and by inhibiting ejaculation may also contribute indirectly.^{8,9} It is this propensity of SSRIs that has led to the development of a new generation, e.g. dapoxetine, specifically for the treatment of premature ejaculation.

Antipsychotic drugs

Tranquilizers such as phenothiazine and haloperidol, commonly used to manage schizophrenia and other psychotic conditions, often result in ED alongside their strong sedative effects, as a result of their effects on the central nervous system.^{8,9}

Hormones: oestrogens and antiandrogens

Treatments that affect sexual hormones can also affect erectile function. Luteinizing-hormone-releasing hormone agonists, used in the hormonal modulation of malignant and benign disease including prostate cancer, have effects on the androgenic system and therefore may induce ED. The antiandrogen flutamide used to treat prostate cancer can also have ED side-effects.

Histamine H₂ antagonists

The histamine H₂ antagonists, available over the counter in many countries and used to treat ulcers, oesophagitis, and other gastrointestinal conditions, reduce libido and may cause ED. Most reports have been for cimetidine, but the problem may also affect other members of the class.⁸ The mechanism is an antiandrogenic effect that may result in hyperprolactinaemia.

Anticholinergic therapies

Therapies that have anticholinergic action, e.g. those used in treatment of urinary incontinence and respiratory disease, may also have effects on erectile function.^{8,9} They interfere with the cholinergic system, which has some neural influence on erectile function.

Finasteride and dutasteride

The 5- α -reductase inhibitors used to treat BPH and male pattern baldness have their effect by interfering with androgen metabolism, and so may have effects on ED and sexual activity. A high prevalence has been found in some studies. One study reported an ED prevalence of 33% in men treated with finasteride for 6 months.¹⁷ None of the men had reported sexual dysfunction at the beginning of the study.

Dutasteride, a newer dual inhibitor of 5- α -reductase, differs from finasteride because it inhibits both isoenzymes of 5- α -reductase and results in near-complete suppression of serum dihydrotestosterone. ED, decreased libido, gynaecomastia, and ejaculation disorders are the main side-effects of dutasteride treatment.¹⁸

Neurological treatments

Treatments used to treat neurological conditions such as epilepsy (e.g. phenytoin and carbamazepine) and Parkinson's disease (levodopa) are associated with ED.

Others

A range of other drugs also affect erectile function. They include non-steroidal anti-inflammatory drugs such as naproxen; indomethacin; allopurinol, a common treatment for gout; the alcoholism drug disulfiram; phenothiazines used as antihistamines and as antiemetics; the tuberculosis antibiotic ethionamide; and the anaesthetic nitrous oxide ("laughing gas").

Structural abnormalities of the penis

Abnormalities in the anatomy of the penis can result in reduced erectile function. The fibrosis and scarring in the corpora albuginea in patients with Peyronie's disease can cause venous leakage and impair the maintenance of an erection.

Priapism, an erection that lasts an abnormally long time (typically several hours) that is painful, and usually not the result of sexual stimulation, does not usually allow normal erectile and sexual function. Priapism may be idiopathic or associated with sickle cell anaemia, leukaemia, or other malignancies. Other structural abnormalities may be caused by trauma, e.g. from road traffic or occupational accidents.

Diabetes mellitus

ED is common in men with diabetes mellitus. More than 50% of men with diabetes are likely to experience ED within 10 years of their initial diagnosis.¹⁹ Men with diabetes have more than a 3-fold increased prevalence of ED compared with men without diabetes.²⁰

Given that the prevalence of diabetes is high in most developed countries, and rising fast in both the developed and developing world, diabetes is important in ED.

In diabetes, poor glucose control commonly leads to damage to the small blood vessels, and this may include those in the penis resulting in damage to erectile function. In addition, one of the common complications of diabetes is peripheral autonomic neuropathy, and this can affect the neural erection centres (see the article by D. Ralph, p. 13–17). Furthermore, the lipid abnormalities common in patients with diabetes promote the development of atherosclerosis.

Other diseases and conditions

ED in patients with renal disease is common and may be caused by hypogonadism due to dysfunction of Leydig's cells. Low serum testosterone concentrations, vascular insufficiency, use of multiple medications, and autonomic and somatic neuropathy may all contribute alongside psychological stress. Other possible explanations for ED in patients with severe renal disease include hyperprolactinaemia, hyperparathyroidism, anaemia, protein malnutrition, and zinc deficiency.⁷

Hyperlipidaemia is the key cause of atherosclerosis, which impairs vascular function. Because erectile function relies on effective vasculature, atherosclerotic damage can result in ED by limiting arterial blood flow into the penis and allowing venous blood to flow from the penis during an erection.

KEY MESSAGE A MULTIVARIATE LOGISTIC ANALYSIS OF AN INTERNATIONAL STUDY OF MEN AGED 40–70 YEARS FOUND THAT ED INCREASED BY 10% WITH EVERY YEAR OF AGE.

ED is also found at high levels in men with hypertension, angina, previous myocardial infarction, and heart failure. Anxiety, depression, and penile arterial insufficiency may occur in these conditions. The pathophysiology of hypertension includes the development of inadequate arterial flow and veno-occlusion.

Chronic obstructive pulmonary disease (COPD) has also been linked to sexual problems including ED. It was an independent predictor of ED in a study of 1,688 Dutch men aged 50–78 years.²¹ In a small study of 49 men with COPD and chronic respiratory failure who were on long-term oxygen therapy, over two-thirds reported sexual dysfunction including impotence.²² The mechanism for the association with COPD is not clear, but it may be through vascular damage brought on by the pathology of COPD. In addition, anticholinergic bronchodilator treatment for COPD may contribute to ED.

An increased risk of ED has been found in men with lower urinary tract symptoms (adjusted OR 2.05–5.75).⁴ This increased risk may be

attributable to prostate disease or surgery, which have repeatedly been found to be linked with ED. A high proportion of men with BPH also have ED, but the association may arise because BPH is, similarly to ED, strongly associated with age. What is clearer is that many treatments for BPH, both surgical and medical, contribute to ED. Obesity has been found to be a significant and independent risk factor for ED.²³ The MMAS found that baseline obesity was a predictor of ED whatever the weight loss after an average 8.8 years of follow-up.²³ Obesity is associated with hyperlipidaemia, high blood pressure, diabetes, and atherosclerosis, and the long-term vascular effects, including the effects on blood flow within the penis, may not be reversible. There may also be a psychological effect of obesity on ED.

ED AS A MARKER OF DISEASE

ED may be an early presenting symptom of diseases such as diabetes, coronary artery disease, hyperlipidaemia, hypertension, spinal cord compression, and pituitary tumour. A thorough medical, sexual, and psychosocial history needs to be taken when a man presents with ED, with an appropriate physical examination and laboratory tests to see whether the ED is part of a broader clinical picture.

Cardiovascular disease and ED share risk factors, and ED can be viewed as a manifestation of cardiovascular disease. The vascular and endothelial lesions, which occur in the coronary artery, are also likely to occur in the cavernosal artery. Even mild ED may be the first clue of an otherwise silent progressive cardiovascular condition, including hypertension and diabetes. Some researchers now say that men presenting with ED should be screened for hypertension, and that ED is a marker of cardiovascular complications.^{14,24}

LIFESTYLE AND SOCIAL STATUS

Lifestyle and social status may play a role in the development of ED and should be considered by clinicians during diagnosis and consultation. Smoking was found to be 2.5 times more common in men with ED (after adjusting for age) in a Spanish study, and 1.7 times more common in current compared with non-smokers in an Italian study.^{4,25}

Alcohol has long been recognized as a cause of ED. In a large study of Italian men with ED, those drinking more than the equivalent of 3 glasses of wine per day had a 40% increased risk of ED,

although there was no increased risk for lighter drinkers.²⁴

Illegal drugs such as cannabis, cocaine, and heroin have their mood-altering effects by interfering with neurotransmission. They can cause temporary and permanent neurological damage and may cause central neural suppression resulting in neurogenic ED.

Low levels of physical activity have been found to be significantly associated with ED. In a study that followed up men for nearly 9 years, those who remained sedentary throughout the period of the study were at highest risk, whereas those who remained active, or took up physical activity, were at significantly lower risk (about half) compared with those who stayed inactive.²³ There was a trend suggesting that more physical activity may be more protective against ED ($p = 0.07$). Change in physical activity was the only modifiable risk factor in this study that reduced the risk of ED if initiated in middle age. In an Italian study, men who were physically active for more than 2 hours per week had a 20% reduced risk of ED.²⁵ Physical activity is associated with psychological benefits including an improved libido and improved mood, as well as physical improvements to the vasculature.

Social status

In a large Italian study, men with ED were less educated than those without ED; about 50% fewer men with ED had a university education (14.6% versus 20.7%).²⁴ In general, more education is associated with better health, through a whole range of complex socio-economic factors, including having better-paid employment and a healthier lifestyle. Social status may affect erectile function in other ways. Job insecurity and disappointment in self, for example, may contribute to performance anxiety.

REFERENCES

1. Fazio L, Brock G. Erectile dysfunction: management update. *CMAJ*. 2004;170:1429-37.
2. Martin-Morales A, Sanchez-Cruz JJ, Saenz de Tejada I, Rodriguez-Vela L, Jimenez-Cruz JF, Burgos-Rodriguez R. Prevalence and independent risk factors for erectile dysfunction in Spain: results of the Epidemiologia de la Disfuncion Erectil Masculina Study. *J Urol*. 2001;166:569-74.
3. Rosen R, Altwein J, Boyle P, Kirby RS, Lukacs B, Meuleman E, et al. Lower urinary tract symptoms and male sexual dysfunction: the multinational survey of the aging male (MSAM-7). *Eur Urol*. 2003;44:637-49.
4. Nicolosi A, Moreira ED Jr, Shirai M, Bin Mohd Tambi MI, Glasser DB. Epidemiology of erectile dysfunction in four

- countries: cross-national study of the prevalence and correlates of erectile dysfunction. *Urology*. 2003;61:201-6.
5. NIH Consensus Development Panel on Impotence. NIH Consensus Conference. Impotence. *JAMA*. 1993;270:83-90.
 6. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical and psychosocial correlates: results of the Massachusetts Male Aging Study. *J Urol*. 1994;151:54-61.
 7. Lue TF. Erectile dysfunction. *N Engl J Med*. 2000;342:1802-13.
 8. Erectile Dysfunction Alliance UK. Management guidelines for erectile dysfunction. London: The Royal Society of Medicine Press; 1999.
 9. Ralph D, McNicholas T. UK management guidelines for erectile dysfunction. *BMJ*. 2000;321:499-503.
 10. Araujo AB, Durante R, Feldman HA, Goldstein I, McKinlay JB. The relationship between depressive symptoms and male erectile dysfunction: cross-sectional results from the Massachusetts Male Aging Study. *Psychosom Med*. 1998;60:458-65.
 11. Shabsigh R, Klein LT, Seidman S, Kaplan SA, Lehrhoff BJ, Ritter JS. Increased incidence of depressive symptoms in men with erectile dysfunction. *Urology*. 1998;52:848-52.
 12. Shabsigh R, Kaufman JM, Steidle C, Padma-Nathan H. Randomized study of testosterone gel as adjunctive therapy to sildenafil in hypogonadal men with erectile dysfunction who do not respond to sildenafil alone. *J Urol*. 2004;172:658-63.
 13. Baskin HJ. Endocrinologic evaluation of impotence. *South Med J*. 1989;82:446-9.
 14. O'Kane PD, Jackson G. Erectile dysfunction: is there silent obstructive coronary artery disease? *Int J Clin Pract*. 2001;55:219-20.
 15. MacLean F, Lee A. Drug-induced sexual dysfunction and infertility. *Pharmaceutical Journal*. 1999;262:780-4.
 16. Kirby RS, O'Leary MP, Carson C. Efficacy of extended-release doxazosin and doxazosin standard in patients with concomitant benign prostatic hyperplasia and sexual dysfunction. *BJU Int*. 2005;95:103-9; discussion 109.
 17. Shabbir M, Mikhailidis M, Morgan RJ. Erectile dysfunction: an underdiagnosed condition associated with multiple risk factors. *Curr Med Res Opin*. 2004;20:603-6.
 18. Djavan B, Milani S, Fong YK. Dutasteride: a novel dual inhibitor of 5alpha-reductase for benign prostatic hyperplasia. *Expert Opin Pharmacother*. 2005;6:311-17.
 19. Vinik A, Richardson D. Erectile dysfunction in diabetes. *Diabetes Reviews*. 1998;6:16-33.
 20. Dey J, Shepherd DM. Evaluation and treatment of erectile dysfunction in men with diabetes mellitus. *Mayo Clin Proc*. 2002;77:276-82.
 21. Blanker MH, Bohnen AM, Groeneveld FP, Bernsen RM, Prins A, Thomas S, et al. Correlates for erectile and ejaculatory dysfunction in older Dutch men: a community-based study. *J Am Geriatr Soc*. 2001;49:436-42.
 22. Ibanez M, Aguilar JJ, Maderal MA, Prats E, Farrero E, Font A, et al. Sexuality in chronic respiratory failure: coincidences and divergences between patient and primary caregiver. *Respir Med*. 2001;95:975-9.
 23. Derby CA, Mohr BA, Goldstein I, Feldman HA, Johannes CB, McKinlay JB. Modifiable risk factors and erectile dysfunction: can lifestyle changes modify risk? *Urology*. 2000;56:302-6.
 24. Mirone V, Ricci E, Gentile V, Basile Fasolo C, Parazzini F. Determinants of erectile dysfunction risk in a large series of Italian men attending andrology clinics. *Eur Urol*. 2004; 45:87-91.
 25. Prazzini F, Menchini Fabris F, Bortolotti A, Calabro A, Chatenoud L, Colli E, et al. Frequency and determinants of erectile dysfunction in Italy. *Eur Urol*. 2000;37:43-9.

Dialogue Box

EDITORIAL BOARD

Is there evidence that men treated for depression with antidepressants have improved sexual function afterwards? Do antidepressants counteract natural benefits of lifting depression in ED?

WYLLIE

The evidence is equivocal and situational. Depending on the type of antidepressant, there can either be a positive or negative effect.

EDITORIAL BOARD

There is a real problem in men who have had treatment for cancer of the prostate in that some would benefit from testosterone. Is testosterone contraindicated after radical prostatectomy even if there was no evidence of spread of the cancer?

WYLLIE

Although there is no definite link between testosterone replacement and increase in cancer of the prostate, in general, testosterone replacement should be avoided in high-risk individuals.

EDITORIAL BOARD

Does vascular “stenting” have any role to play in the treatment of ED?

WYLLIE

In the post PDE inhibitor era, almost certainly not.

EDITORIAL BOARD

Does treatment with antihypertensives improve or worsen long-term prognosis of ED?

WYLLIE

Certain antihypertensives, particularly thiazide diuretics and to a certain extent beta-blockers, can exacerbate ED. Most antihypertensives have little or no effect. There is some recent evidence that alpha-blockers may cause a modest improvement in erectile function.

EDITORIAL BOARD

Does treatment of hyperlipidaemia improve the long-term prognosis of ED?

WYLLIE

Hyperlipidaemia, like obesity and hypertension, is one of the major risk factors for ED. On this basis, although objective clinical evidence may be lacking, restoration of normal lipid profile should improve erectile function.

EDITORIAL BOARD

Does losing weight through dieting improve ED?

WYLLIE

As above, but there is good clinical evidence to show that weight loss in obese ED patients does improve erectile function.

EDITORIAL BOARD

I am not aware of any cardiovascular disease risk table that includes ED as a marker – should ED be included to calculate risk of cardiovascular disease?

WYLLIE

There are now several studies showing that ED may be a sentinel of early stage vascular dysfunction. On this basis, it would not be unreasonable to include it as one of the indices of certain types of cardiovascular dysfunction.