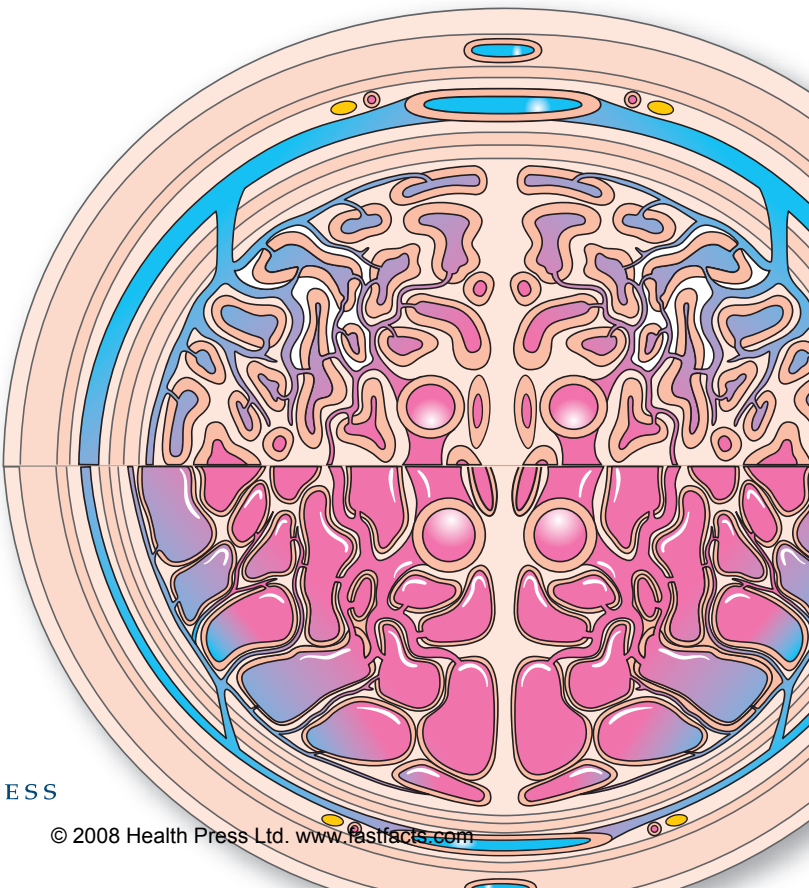
Fast Facts

Fast Facts: Erectile Dysfunction

Culley Carson and Chris G McMahon

Fourth edition



HEALTH PRESS

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Declaration of Independence
This book is as balanced and as practical as we can make it. Ideas for improvement are always welcome: feedback@fastfacts.com

HEALTH PRESS

Fast Facts: Erectile Dysfunction
First published 1997
Second edition 1998; third edition 2002
Fourth edition June 2008

Health Press Limited, Elizabeth House, Queen Street, Abingdon,
Oxford OX14 3LN, UK
Tel: +44 (0)1235 523233
Fax: +44 (0)1235 523238

Book orders can be placed by telephone or via the website.
For regional distributors or to order via the website, please go to:
www.fastfacts.com
For telephone orders, please call 01752 202301 (UK), +44 1752 202301 (Europe), 1 800 247 6553 (USA, toll free), +1 419 281 1802 (Americas) or +61 (0)2 9351 6173 (Asia–Pacific).

A CIP record for this title is available from the British Library.

ISBN 978-1-903734-67-4

Carson C (Culley)
Fast Facts: Erectile Dysfunction/
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Medical illustrations by Dee McLean, London, UK.
Typesetting and page layout by Zed, Oxford, UK.
Printed by Latimer Trend & Company Ltd, UK

Text printed with vegetable inks on biodegradable and recyclable paper manufactured from sustainable forests.

Glossary

ACE: angiotensin-converting enzyme

cAMP: cyclic adenosine monophosphate, secondary pathway for corpus cavernosum smooth muscle relaxation

cGMP: cyclic guanosine monophosphate, the second messenger molecule that facilitates the vasodilatation that leads to erection

Corpora cavernosa: paired columns of erectile tissue in the penis

Detumescence: loss of turgidity and erection, usually caused by active sympathetic stimulation

ED: erectile dysfunction

Intracavernosal self-injection: technique in which the patient injects vasoactive drugs into his own corpora cavernosa

MUSE®: medicated urethral system for erection

NAION: non-arteric anterior ischemic optic neuropathy

NO: nitric oxide, a neurotransmitter that produces an erection

NPT: nocturnal penile tumescence

Organic erectile dysfunction: erectile dysfunction caused by the failure of one or more of the essential stages in penile erection, namely the arterial blood supply, venous occlusion or neurological control

PDE5: phosphodiesterase type 5, the substance that breaks down cGMP, resulting in detumescence

PGE_1: prostaglandin E_1, a neurotransmitter resulting in erection

Priapism: a persistent erection that lasts for more than 4 hours

PSA: prostate-specific antigen

Psychogenic erectile dysfunction: erectile dysfunction caused by higher brain center influences in the presence of a normal erectile mechanism

SHBG: sex-hormone-binding globulin

Spinal erection center: an area in the spinal cord through which the spinal erection reflex passes, and which is under neural control from higher brain centers

SSRIs: selective serotonin-reuptake inhibitors

Tumescence: vasodilatation in the corpora cavernosa resulting in erection

Vasoactive agents: drugs that have a dilatory effect on blood vessels

VED: vacuum erection device

Veno-occlusive mechanism: the mechanism by which the venous drainage of the erectile tissues is occluded to allow filling of the lacunar spaces resulting in penile turgidity

VIP: vasoactive intestinal polypeptide – a neurotransmitter in the corpora cavernosa

Introduction

Just 30 years ago, male sexual health was considered to be the exclusive domain of the psychologist. Since then, surgeons have introduced penile prostheses and vacuum devices as mechanical treatments for erectile dysfunction (ED). More recently, basic scientists have determined the physiology of the erectile mechanism, leading to the development of a number of pharmacological treatment alternatives.

This progress has coincided with an increased understanding of the nature of male sexual health problems, and epidemiological data have confirmed that such problems are widely prevalent and the source of considerable morbidity, both for individuals and within relationships. ED is not a necessary part of the aging process, but may occur as a result of a specific illness or as a consequence of the medical treatment of another unrelated illness. Healthcare professionals involved in all aspects of care need to be aware of these risks.

Patients now realize that simple, effective treatments are available and are demanding access to these therapies. The range of healthcare workers involved in the treatment of men with ED continues to expand with specialist nurses, nurse practitioners, primary care physicians and doctors from a variety of secondary care specialties expected to diagnose and treat patients and offer support and advice confidently and confidentially to these individuals. Therefore, it is essential that all healthcare professionals keep apace with developments to provide the best advice about the safety and effectiveness of treatment.

In response to these rapid advances in treatment, several sets of guidelines have been developed to help manage patients with ED. The guidelines include identification, assessment and diagnosis of the condition, modification of risk factors and provision of first- and second-line therapies. This fourth edition of *Fast Facts: Erectile Dysfunction* provides an in-depth view of the overall management of ED and will be valuable to any healthcare professional who encounters men with the condition, particularly as the number of therapeutic options is increasing and patients expect to receive straightforward and effective treatment.

1 Epidemiology and pathophysiology

Epidemiology

Accurate figures for the prevalence of erectile dysfunction (ED) in populations around the world are difficult to obtain. However, data from a number of US and UK studies are similar, so are regarded as the best estimate. The prevalence of complete ED is estimated to be approximately 5% among 40-year-olds, 10% among men in their 60s, 15% among men in their 70s and 30–40% among men in their 80s. From these figures it has been estimated that there may be 20 million men in the USA, and perhaps as many in Europe, who have significant problems with erectile function. It is projected that, by 2025, 322 million men worldwide will have ED.

Prevalence studies show that, when controlling for other factors, increasing age is a strong risk factor for ED, especially after 50 years of age (Figure 1.1). In addition, conditions such as obesity, diabetes, hypertension, hypercholesterolemia and vascular disease – all present in Western populations in epidemic proportions – are causative factors.

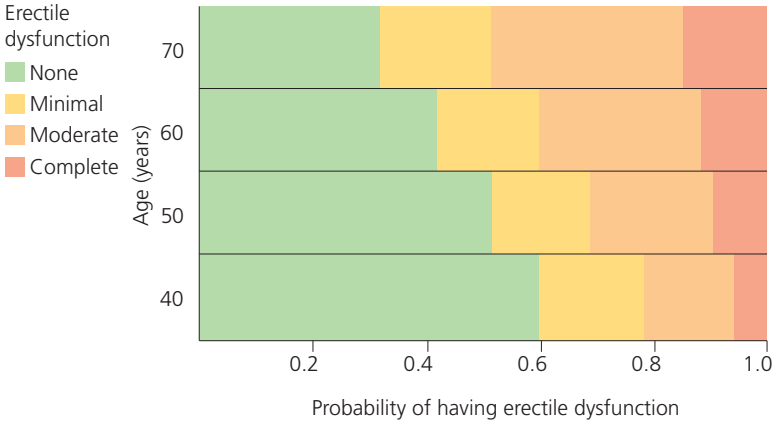

Figure 1.1 Relationship between age and the probability of erectile dysfunction. Data from the Massachusetts Male Aging Study, Feldman et al. 1994.

Endothelial dysfunction appears to be the final common pathway for many cases of ED. Recent studies support the notion that ED may be an early manifestation, and a predictor, of generalized endothelial dysfunction, as well as being a precursor for other forms of cardiovascular disease. Two-thirds of men with hypertension have some degree of ED; 60% of men presenting to an ED clinic had undiagnosed lipid abnormalities. More than half of men with ED who have no cardiac symptoms have an abnormal stress test, and 40% have been found to have significant coronary artery disease when studied. Of men hospitalized for their first myocardial infarction, 64% had ED with onset 3 years or more before infarction. These data strongly support the onset of ED as an early indicator for vascular disease in men. However, the condition remains a source of embarrassment for many men and their doctors and therefore continues to be under-reported, under-recognized and undertreated.

Risk factors for erectile dysfunction. Apart from age, the main risk factors are those for vascular disease (smoking, hypertension, abnormal lipid profile, obesity and lack of exercise). Essentially, any condition that damages endothelial function can result in ED. Other factors include diabetes mellitus and depression (Table 1.1). A study of over 270 000 men with ED showed them to have a higher incidence of hypertension, hyperlipidemia, diabetes and depression.

TABLE 1.1

Prevalence of ED with specific medical conditions

Condition	Prevalence (%)
Overall (age 40–70 years)	10
Severe depression	90
Post myocardial infarction	40
Diabetes	35
Hypertension	25
Cigarette smokers	20

Topical intraurethral therapy

A pellet of alprostadil has been developed for insertion into the urethra through a specific polypropylene applicator. Once delivered, the pellet dissolves into the urethral mucosa and from there enters the corpora.

Alprostadil is a synthetic form of prostaglandin E_1; it acts via the adenylate cyclase system to reduce intracellular calcium and induce smooth-muscle relaxation. The administration system is marketed as MUSE® (Medicated Urethral System for Erection; Figure 3.6). Men are asked to urinate before use, as this aids insertion of the applicator and facilitates the intraurethral dispersion of the drug. While in the sitting position, the patient inserts the applicator and then depresses the ejector button, releasing the alprostadil pellet. The penis is then held upright and gently rolled to disperse the drug. Erections develop about 10–15 minutes after application and last for approximately 30 minutes.

Early results with this treatment reported a dose–response effect with 66% of men with ED (all causes) obtaining a full erection, though subsequent studies have reported a lower efficacy. The doses required to achieve this ranged from 125 to 1000 µg. The side effects of this treatment are those of penile pain (7%) and minor urethral trauma

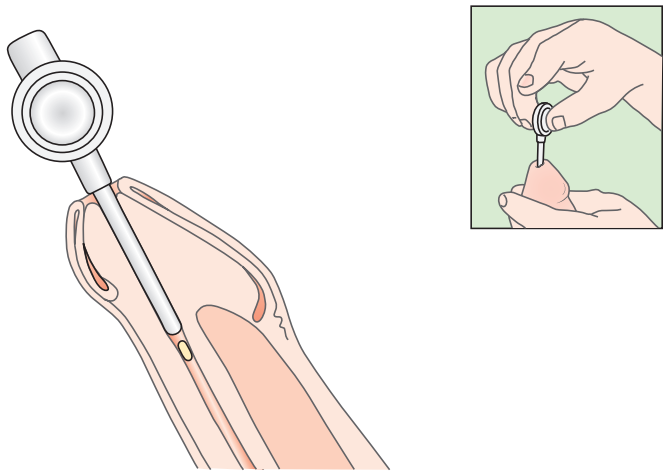

Figure 3.6 Intraurethral administration of alprostadil using the MUSE® system.

(1%). In a comparative study of intracavernosal and intraurethral application of alprostadil, the intracavernosal administration was shown to be more effective though there was a slightly higher incidence of local side effects than with the intraurethral route of administration. It would thus seem that while the intraurethral route of administration is associated with a lower overall success rate, the improved side-effect profile and acceptability to patients may make it a preferred option for some patients. MUSE may also be effective in men with failed penile implants.

A new topical alprostadil preparation is under development that is applied to the glans penis. Early reports suggest effectiveness in as many as 75% of patients with few side effects.

Androgen replacement therapy for hypogonadal men

In men with a proven testosterone deficiency, testosterone replacement therapy can be effective, not only in improving sexual function, but also enhancing well-being and libido. Reliable diagnosis of hypogonadism requires a pool of two or three morning samples to minimize the effect of the diurnal rhythm of testosterone secretion. Approximately 1% of men with ED have hypogonadism but it is unlikely to be present unless the plasma testosterone level is less than 8 nmol/liter. Delivery methods include oral administration, intramuscular injection, skin patches and gels.

All forms of androgen replacement carry the theoretical risk of stimulating prostate growth and promoting the development of latent foci of prostate cancer. Although it is difficult to quantify these risks, and they are probably small, it is important that any patient receiving this treatment is fully informed and his prostate-specific antigen (PSA) level is monitored. Other side effects may include hepatotoxicity, polycythemia, changes in lipids and worsening sleep apnea.

Oral administration. Two types of oral testosterone are available – modified and unmodified. Unmodified testosterone is rapidly absorbed and degraded by the liver, making it difficult to achieve satisfactory serum concentrations. Modified 17-alkyltestosterones, such as methyltestosterone or fluoxymesterone, usually require large doses