KEYPOINTS:

- Although the number of men in an ED prevalence study who have neurological disease will be low, the incidence of ED and other types of sexual dysfunction in men with neurological disease is very high.

CHAPTER 4

NEUROGENIC SEXUAL DYSFUNCTION IN MEN AND WOMEN

INTRODUCTION

Physiological sexual function depends on both central and peripheral neurological pathways. Neurological disease of many different types can, therefore, adversely affect function in both men and women.

In general terms, sexual libido and arousal depend upon psychological factors and on the integrity of higher brain centers, whereas function of the spinal cord and peripheral pathways is essential for effecting sexual responsiveness. Central centers which determine drive include the basal hypothalamus and limbic system, and the frontal and fronto-temporal regions where testosterone, dihydrotestosterone and estrogen may have important modulatory effects. Spinal pathways and the peripheral nervous system conveying efferent and afferent activity to pelvic parasympathetic, sympathetic and somatic innervated structures are critical for the voluntary and autonomically mediated aspects of genital responses.

Study of male sexual function and the many disorders, both neurological and non-neurological, which can affect it, is a relatively new medical subject, little being known, researched or discussed before the mid 1970s. The change in public attitude towards sexuality which occurred in Europe and the US at that time, together with the appearance of some effective therapies, has altered the situation, and male sexual dysfunction is now an area of intense research and active treatment. Female sexual dysfunction (FSD) is only just beginning to be scientifically studied, driven by the hope that some of the therapies which have proved to be so effective in men might be extended to women. Still much less is now known and possible therapies lag significantly behind.

The focus of treatment of sexual dysfunction so far has been the treatment of erectile dysfunction (ED). This chapter follows the traditional approach and deals first with male sexual dysfunction, ED in particular, before covering the lesser studied topic of FSD.

ERECTILE DYSFUNCTION

A definition of ED is the persistent inability to develop and maintain an erection sufficient for satisfactory sexual activity [1]. The term "impotence" should now be avoided because of its broader, negative connotations.

General prevalence. In the late 1980s, a large study was carried out of men aged 40-70 years living around Boston, USA which showed that ED was a common problem and that its incidence increased with age [2]. More than 1000 men completed a self-administered questionnaire which asked, if they had impotence, to rate the problem. Their ED was then categorized as "minimal", "moderate" or "complete". The combined prevalence of all categories of ED was 52%. Figure 1 shows a break down of severity with aging. Other general associated factors were identified, which are summarized in Table 1.

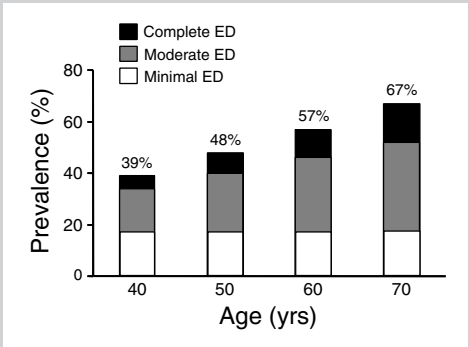

FIGURE 1 Association between age and prevalence of erectile dysfunction.

From the Massachusetts Male Aging Study (*n*=1290) [2].

TABLE 1 General factors known to predispose to ED

Aging
(as shown in Figure 1 [2])

Chronic illness
Atherosclerosis, diabetes, cardiovascular disease, renal disease, hepatic failure, depression, endocrine disorders and neurological disease

Surgery and trauma
Spinal cord injury, pelvic injury/surgery, prostatectomy

Drug and other modifiable factors
Alcohol, tobacco, medication (antihypertensives, antidepressants, hormones, tranquilizers, H2 antagonists, nonsteroidal anti-inflammatory drugs

Because the subject population of the Massachusetts study was racially unmixed and unusually well educated, further epidemiological studies are now being carried out to reassess the prevalence of ED globally. Early results are producing figures of the same order of magnitude as those of the Massachusetts study, although there are some regional differences.

Prevalence of ED in neurological disease. Although the number of men in an ED prevalence study who have neurological disease will be low, the incidence of ED and other types of sexual dysfunction in men with neurological disease is very high. The data are sparse, but Table 2 gives some published incidences from various small studies of specific neurological illnesses.

Physiology of penile erection and ejaculation. Erection results from filling of the paired corpora cavernosa with blood at systolic pressure. The lacunar spaces within the corpora are fed by the numerous helicine arteries which branch off the cavernosal arteries. Smooth muscle relaxation of the trabecular smooth muscle in this vascular system is mediated by the release of nitric oxide from the vascular endothelium in response to pelvic parasympathetic activity. Reduction of corporeal venous drainage is critical in the erectile response and occurs as a result of compression of the subtunical draining veins against the rigid tunica albuginea (Figure 2).

Ejaculation involves emission of semen from the vas and seminal vesicles into the posterior urethra, closure of the bladder neck and rhythmic contractions of the ischiocavernosus and bulbocavernosus. Bladder neck closure and emission are under sympathetic control from the thoracolumbar sympathetic outflow, whereas the contraction of the pelvic floor muscles is under somatic nerve control.

Following orgasm and ejaculation, sympathetic tone returns and causes the cavernosal and helicine arteries to contract, restricting blood flow into the lacunar spaces. The falling intralacunar pressure then decompresses the subtunical venules and allows increased venous outflow so that detumescence occurs.

Neurological control of male sexual function and penile erection. Central control of sexual response is currently an area of intense research and animal experiments, often in the rat, have now defined the importance of regions in the hypothalamus. Visual, olfactory, auditory, tactile and imaginative stimuli are integrated in the medial pre-optic area (MPOA), but there is no direct connection demonstrable between this structure and the spinal cord. The paraventricular nucleus (PVN) is the origin of descending, oxytocinergic autonomic pathways to the sacral cord which mediate erectile responses and this receives input from the MPOA. Dopaminergic receptors, probably D2 receptors in the PVN

KEYPOINTS:

- Smooth muscle relaxation of the trabecular smooth muscle in this vascular system is mediated by the release of nitric oxide from the vascular endothelium in response to pelvic parasympathetic activity.
- Visual, olfactory, auditory, tactile and imaginative stimuli are integrated in the medial pre-optic area (MPOA), but there is no direct connection demonstrable between this structure and the spinal cord. The paraventricular nucleus (PVN) is the origin of descending, oxytocinergic autonomic pathways to the sacral cord which mediate erectile responses and this receives input from the MPOA.

TABLE 2 Incidence of sexual dysfunction, including ED, in neurological disease

Hypothalamic-pituitary disorders	78% [3]
Parkinson's disease	60% [4]
MSA	98% [5]
Spinal cord injury	25-95% [1] [6]
MS	62-83% [7-9]
Diabetic neuropathy	approx. 100% [2]

[1] Depending on level and completeness of lesion.

[2] The extent to which micro-vascular disease and metabolic factors contribute to the common problem of ED in diabetics is uncertain, but a man with diabetic neuropathy is highly likely to have ED.

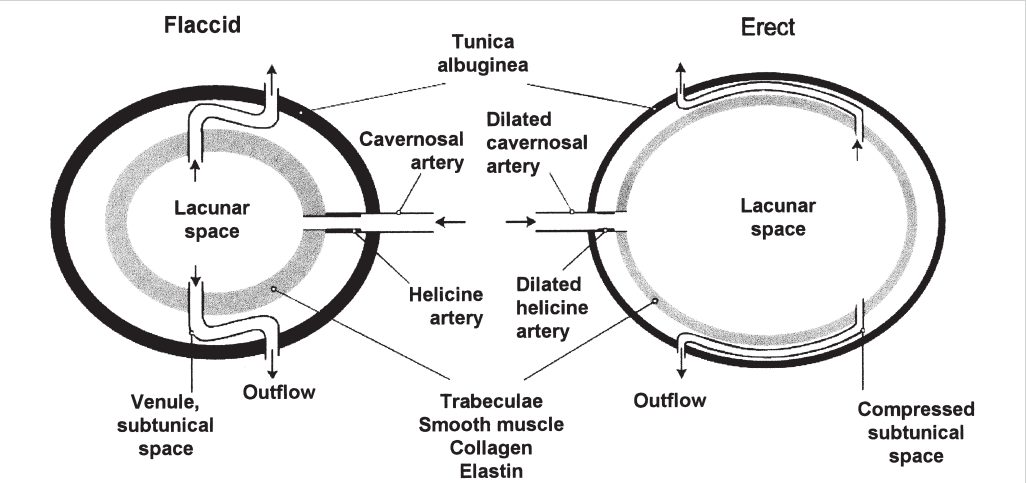

FIGURE 2 Physiology of penile erection.

From [24].

induce erection in animals, which is the rationale for the therapeutic use of apomorphine (a mainly D2 agonist) as an erectogenic agent. Many inhibitory, mainly serotoninergic, pathways have also been identified within the diencephalon.

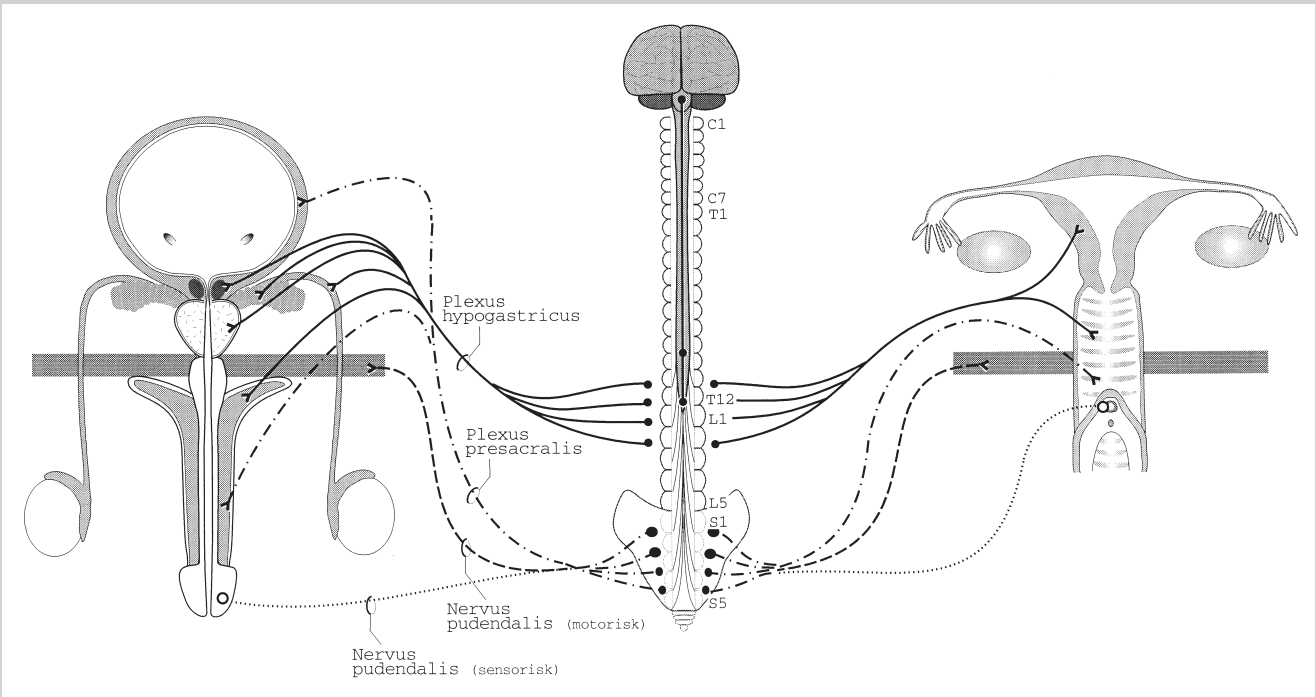

FIGURE 3 Diagram showing the peripheral innervation of the male and female sexual organs.

Reproduced by courtesy of Petter Hedlund and Axel Brattberg.

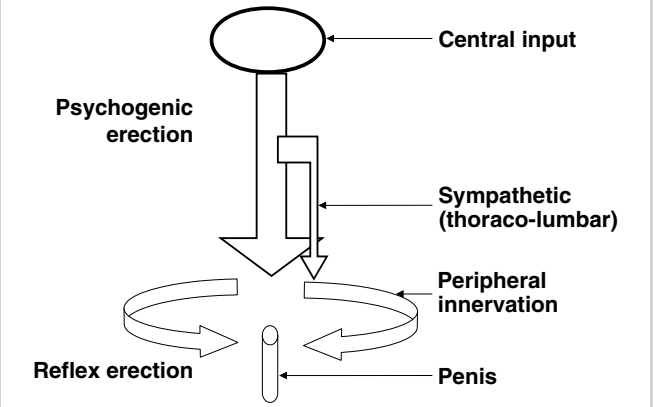

FIGURE 4 Neurological pathways involved in erectile response.

The parasympathetic innervation travels to the genital region in the pelvic nerves, the so called "nervi erigentes" and pudendal nerves. Sympathetic innervation of the genital region originates in the thoracolumbar chain (T11-L2) and travels in the hypogastric nerves to the confluence of neural tissue which lies either side of the rectum and the lower urinary tract — the pelvic plexus. This also receives input from the pelvic nerves and it is from the pelvic plexus that the very fine cavernous nerves pass to innervate the corpora cavernosa (Figure 3).

There are essentially two neurological pathways for erection: a sacral segmental pathway which subserves reflex erections and a spinal pathway which is necessary for psychogenic erections (Figure 4). Reflex erections result from cutaneous genital stimulation with afferent impulses conveyed in the pudendal nerve to S2- S4 the efferent activity travelling through the same-level sacral roots. Psychogenic erection requires cortical activation of erectogenic pathways via the spinal cord and the sometimes preservation of this type of responsiveness in men with low spinal cord lesions suggests that it may be mediated by sympathetic pathways. In health, psychogenic and reflex erections reinforce one another.

Ejaculation depends on descending spinal pathways which are predominantly excitatory, although there may also be an inhibitory spinal input. Very little is known about the neurophysiology of orgasm — the sensation is blocked by bilateral anterolateral (i.e. spinothalamic tracts) cordotomy. A SPECT study showed an increase in activity in the right frontal lobe region during ejaculation in healthy male subjects, but no focal activation in the medial anterior parietal lobe corresponding to somatosensory cortex of the genital projection area. This was interpreted as implying that the right prefrontal cortex is important for the emotional responses of male sexuality.

Neurological diseases causing ED. Figure 5 and Table 3 show the various different neurological diseases that may adversely affect sexual function, penile erection, in particular. A detailed description of what is known about sexual dysfunction in both sexes with each disease is given under the appropriate headings of Chapters 5-9.

History in men with neurogenic ED. In men with established neurological disease and ED, laboratory investigations are rarely indicated. It is usually clear from the history how the onset of ED relates to the development of their neurological disability.

TABLE 3 Neurological causes of ED

Temporal lobe epilepsy
Hypothalamic pituitary disorders
Parkinson's disease
Multiple system atrophy
Spinal cord injury
Multiple sclerosis
Spina bifida
Cauda equina
Peripheral neuropathy (especially small fiber)
Surgical damage to cavernosal innervation

KEYPOINTS:

- There are essentially two neurological pathways for erection: a sacral segmental pathway which subserves reflex erections and a spinal pathway which is necessary for psychogenic erections.
- In men with established neurological disease and ED, laboratory investigations are rarely indicated.

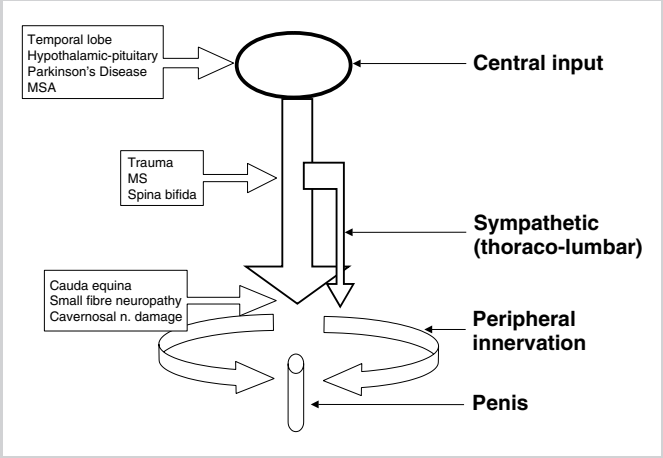

FIGURE 5 Sites at which neurological disease can affect pathways necessary for erectile response.

KEYPOINTS:

- The sexual function deficit resulting from spinal cord disease (either traumatic or MS) depends on the level and extent of the lesion: typically, a man with a cervical or high thoracic lesion will have preserved reflex erections, but not be able to sustain erection for penetrative intercourse.
- Bladder dysfunction occurs considerably later and evidence of relevant neuropathy is best detected by testing small fiber function in the feet, since many of the small fiber neuropathies are length-dependent.
- In the general population, ED often has a significant vascular component.

Temporal lobe disease and hypothalamic-pituitary disease often causes loss of desire as an early symptom, which the patient may not complain of, although ED can occur with preserved libido with pathology at those sites.

The sexual function deficit resulting from spinal cord disease (either traumatic or multiple sclerosis (MS)) depends on the level and extent of the lesion: typically, a man with a cervical or high thoracic lesion will have preserved reflex erections, but not be able to sustain erection for penetrative intercourse. The teaching that if a man had nocturnal penile erections or reflex erections, but could not sustain an erection for intercourse, his impotence was psychogenic, is no longer thought to be correct, particularly in the case of spinal cord disease.

Ejaculation and orgasm are likely to be affected by spinal cord lesions. ED is very rarely the only symptom and the complaint is usually part of a symptom complex accompanied by a spastic paraparesis and neurogenic bladder dysfunction.

If ED occurs as a result of a cauda equina lesion, somatic sensation in the S2-S4 dermatomes is also likely to be impaired. Small fiber peripheral neuropathies, i.e. diabetes and amyloid disease, are particularly likely to cause ED, and this may occur early in the condition without disturbances of ejaculation. Bladder dysfunction occurs considerably later, and evidence of relevant neuropathy is best detected by testing small fiber function in the feet, since many of the small fiber neuropathies are length-dependent.

Following pelvic trauma or surgery which injures the pelvic nerves or cavernosal nerves, ED occurs, but with preservation of somatic sensation, unless the pudendal nerve is also damaged.

Clinical examination. Following a careful history, clinical examination focussing on the points shown in Table 4 will identify concomitant spinal cord disease, root lesions or peripheral neuropathy. In general, if a clinical neurological examination fails to discover evidence of neurological disease, sophisticated neurophysiological investigations are unlikely to be contributory.

Investigations. Now that there are simple and effective symptomatic treatments for ED, the emphasis on investigations has shifted. In former times, these were carried out to establish whether the problem was psychogenic or organic and, if organic, whether surgical intervention was indicated.

In the general population, ED often has a significant vascular component. A history of coronary or peripheral vascular disease suggests a vascular cause. This may be is investigated by andrologists using a variety of techniques including color Doppler ultrasonography imaging with intracavernosal injections, cavernosometry and cavernosography if surgery is being considered. A brief description of these investigations of penile hemodynamics, usually only performed in non-neurogenic ED, is given in Pullout 1.

Useful insight as to the cause of ED in a patient comes from observing their response to intracavernosal injection of an erectogenic agent, such as prostaglandin E1. A good response from a low-dose injection suggests the cause is likely to be neurogenic,

TABLE 4 **Clinical neurological examination for ED**

Lower limb reflexes
Plantar responses
Sensation (thermal testing) of feet

psychogenic or endocrine, whilst a poor response using a high dose suggests there may be a vascular cause and those investigations described in Pullout 1 may be indicated. However, false-negatives with this test do occur as the psychological inhibition caused by the anxiety of a penile injection in an impersonal setting, such as at a hospital clinic, may inhibit the response to intracavernosal injection.

There is continuing discussion as to the minimum biochemical investigations necessary, and some authorities recommend measurement of serum total and free testosterone, prolactin, glucose and cholesterol [10]. If there is reason to suspect a hypothalamic-pituitary lesion, measurement of hormone levels is mandatory.

The use of neurophysiological tests to investigate genital innervation has been advocated in the past, but none of them is now used routinely. The various tests are described in Chapter 1, (Pullout 1) since many of them were promoted as being appropriate for investigating pelvic organ dysfunctions other than ED. Evaluation of the test specific for ED, so-called "corpus cavernosum EMG" is still ongoing, and although it may prove to be of

KEYPOINTS:

- If there is reason to suspect a hypothalamic-pituitary lesion, measurement of hormone levels is mandatory.

PULLOUT 1 Investigation of penile hemodynamics

These investigations are sometimes requested by urologists and andrologists when a vascular cause for ED is suspected and they may be particularly indicated in patients who have not responded to oral agents.

Methods of investigating arterial supply

Color Doppler ultrasonography (CDU) is considered to be an ideal screening method for both functional and anatomic evaluation of penile arterial blood flow. Following intracavernosal injection, components of the penis, including the corpora cavernosa, corpus spongiosum, septum, urethra, cavernous artery, and dorsal vein, can be visualized. Cavernosal artery diameter and peak systolic arterial velocity can be measured, although there is no general agreement as to what is regarded as normal, partly due to lack of control data in healthy volunteers and partly because arterial inflow is dependent on the degree of smooth muscle relaxation which may be determined by factors such as patient's anxiety.

Selective pudendal arteriography is technically difficult and invasive and is rarely used, except in men with erectile failure secondary to pelvic trauma in whom pudendal arterial reconstruction is being considered.

Methods of investigating venous leakage

Failure of the veno-occlusive mechanism to trap arterial blood within the penis results in ED. The underlying etiology, diagnosis and treatment of venous leakage remains controversial, but many different pathological processes have been described. The majority of patients with "venous leak" have normal venous anatomy, but fail to compress the emissary veins as they exit from the cavernosal bodies.

CDU, cavernosometry and cavernosography are all used in the diagnosis of venous leak. Following an intracavernosal injection of a vasodilator, flow should stop in diastole or even reverse if the veno-occlusive mechanism is functioning adequately. Excessive forward flow in the cavernosal arteries during diastole with failure to obtain a firm erection is taken as evidence for a venous leak.

Cavernosometry is the technique whereby intracavernosal pressure is measured in response to corporeal perfusion and cavernosography is the technique whereby abnormal venous outflow is seen radiologically following perfusion of contrast.

Smooth muscle degeneration, as occurs in diabetes, may result in inadequate sinusoidal relaxation with inadequate inflow and failure of the intracavernosal pressure to rise sufficiently to occlude the emissary veins. A healthy tunica albuginea that stretches and kinks the emerging emissary veins as the penis engorges is also necessary for veno-occlusion. In Peyronie's disease, firm fibrous plaques form at random on the tunica preventing full elongation of the penis with consequent penile curvature and venous leak in some patients. The treatment of erectile dysfunction secondary to venous leak is not straightforward as the underlying pathogenesis is often unclear. Attempts to reduce leakage by dividing draining veins have some short-term success, but the longer term results are poor.

KEYPOINTS:

- An effective oral treatment has meant that treatment of ED can now be offered by primary care physicians as well as specialists not previously therapeutically empowered, such as neurologists.

value in assessing penile autonomic innervation, it is unlikely to assume importance as anything other than a research investigation.

Treatment. With the introduction of the orally active agent sildenafil (Viagra®, Pfizer) in 1998, the treatment of ED was transformed. Prior to then, intracavernosal injection pharmacotherapy was the most used treatment, usually administered by urologists or andrologists. Before that, what help that was available was the provenance of psychotherapists or those surgeons who implanted penile prostheses. An effective oral treatment has meant that treatment of ED can now be offered by primary care physicians as well as specialists not previously therapeutically empowered, such as neurologists.

Oral medication: Sildenafil citrate (Viagra®) is a potent and highly selective inhibitor of type 5 cGMP phosphodiesterase (PDE5). Its action is to augment nitric oxide-mediated relaxation pathways in penile tissues by increasing available cGMP in the corpus cavernosum (Figure 6). The effect of the medication is therefore not to cause erection, but to enhance the response to sexual arousal. Sildenafil is rapidly absorbed with a maximal plasma concentration occurring within 1 hour, so that it is necessary for it to be taken about 1 hour before intended sexual activity.

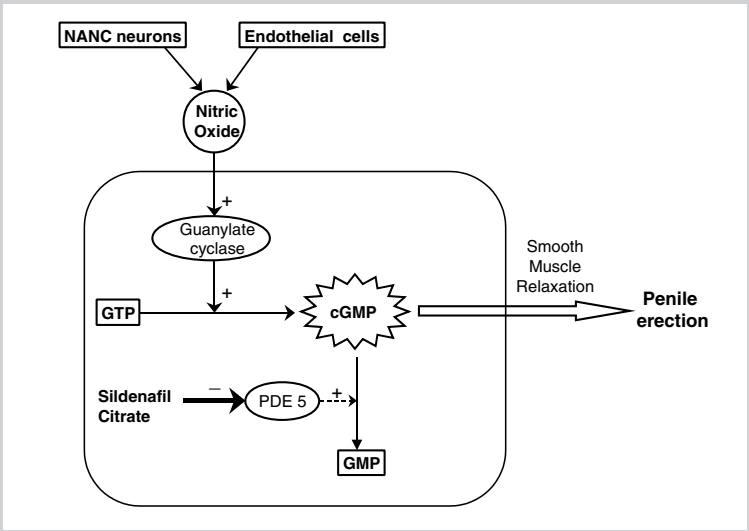

FIGURE 6 Nitric oxide-cGMP mechanism of corpus cavernosal smooth muscle relaxation and penile erection. Sexual stimulation results in the release of nitric oxide from corporal vascular endothelium and nonadrenergic-noncholinergic (NANC neurons). PDE 5 = cGMP-specific phosphodiesterase type 5.

More than 6000 men with many different causes of ED have now participated in placebo-controlled trials of sildenafil citrate, and the medication was demonstrated to be effective, with few side effects or adverse events. The pivotal study was a large placebo-controlled, flexible dose-escalation study with an open label extension in men with organic, psychogenic or mixed etiology ED [11]. Efficacy was assessed using the self-administered International Index of Erectile Function (IIEF) questionnaire which showed significantly higher mean scores for frequency of penetration and maintenance of erection in the sildenafil-treated group compared with men receiving placebo. Sexual desire was not increased in the active agent-treated group, but the scores for orgasmic function, intercourse satisfaction and overall satisfaction were all better. Adverse effects were headache, flushing, dyspepsia, nasal stuffiness and visual disturbances, but these were usually mild and were dose-related. Only 2% withdrew from the open-label study because of adverse effects. Similar findings for efficacy have been demonstrated since in other studies, although the response rate is variable, being less good in vasculopaths and diabetics and better in patients with neurogenic ED. The side-effect profile has also been consistent, with few patients discontinuing medication because of adverse reactions.

However, initially, there was public concern about the medication's safety prompted by reports of death following the use of Viagra®, as monitored by "spontaneous" reports to the US Food and Drug Administration. This anxiety has now lessened and studies have shown that although the cardiovascular risk profile for myocardial infarction is similar to that which predisposes to ED, there has not been a higher rate of serious cardiovascular events in the treated groups than in the placebo groups in controlled studies. Epidemiological studies have shown that the incidence of serious events has been consistent with the expected background frequency in the treated population [12], and there is no evidence that sildenafil adds to the overall risk in patients with or without cardiovascular disease [13]. Sildenafil is contraindicated with concurrent use of

nitrates as it interacts to cause severe acute hypotension. Sildenafil is contraindicated in severe hepatic impairment and in conditions that predispose to priapism and bleeding disorders.

The efficacy of sildenafil in several neurological conditions has now been demonstrated. Following spinal cord injury, reflex erections may be preserved, but these are often not suitable for satisfactory sexual activity. In a placebo-controlled, cross-over study, 76% of 168 patients who had had traumatic spinal cord injury, reported improved erections and a preference for sildenafil [14]. The majority of the subjects had some residual erectile function, although in 25 of those who did not, sildenafil also improved erections in 16.

Preliminary analysis of a placebo-controlled trial of sildenafil in 217 men with MS has likewise demonstrated excellent efficacy, with 90% of 104 patients on sildenafil and 24% of 113 patients on placebo, reporting improved erections [15] as well as a measurable improvement in quality of life. A placebo-controlled trial in eight men with spina bifida showed improved erectile function in 63% [16]. Thus, the present evidence points to this form of treatment being particularly effective in men with ED caused by spinal pathology. Any pre-existing neurological difficulty with ejaculation, however, persists.

Abstract reports of an open label study of men with Parkinson's disease have also shown sildenafil to be effective [17], although this study showed that in men with parkinsonism due to multiple system atrophy (MSA) who had ED and either symptomatic or asymptomatic autonomic failure, hypotension was significantly exacerbated by sildenafil. It is therefore important to check for postural hypotension in men with parkinsonism before prescribing sildenafil.

The efficacy of sildenafil in treating ED in diabetics is less than in most other patient groups with ED. In a study of 131 diabetics, 56% reported improved erections on active treatment compared with 10% of 127 in the placebo group [18]. The peripheral vascular component as well as the effect of advanced glycosylated end products which decrease nitric oxide activity are thought to be contribute to the severity and relative intractability of ED in diabetics.

In men who have ED following radical prostatectomy, sildenafil is ineffective in those in whom it was not possible to carry out a nerve-sparing procedure on either side [19].

At the time of writing, sildenafil is the only available orally active erectogenic agent, but preliminary studies have demonstrated an erectogenic effect with oral apomorphine [20], although nausea is a frequent side effect, particularly in those using higher dosages. However, it is certain that in the near future, other orally active treatments for ED will become available, either other phosphodiesterase inhibitors or agents which act on some other stage of the process of the erectile response.

Intracavernosal pharmacotherapy: Prior to the availability of an orally active treatment, injection of medication into the corpus cavernosum was the preferred treatment. The first used agent was papaverine, but this was subsequently replaced by alprostadil [21], a prostaglandin PGE1. Various combinations of injectable agents have also been tried.

The main side effect of alprostadil is penile pain, which occurs in about half of the patients. Priapism is characterized by a persistent erection that generally lasts 4-6 hours and can be associated with severe pain. When this condition occurs, it should be considered a medical emergency as permanent damage can be sustained after 12 hours of persistent erection. Treatment involves immediate injection of phenylephrine hydrochloride at 500 µg into the corpora cavernosum. This administration can be repeated at 20-minute intervals. Alternately, blood can be aspirated from the corpora via a 23-gauge butterfly needle along with α-adrenergic irrigation (1 mg phenylephrine HCl to 1 liter of normal saline). The main late complication is the appearance of fibrotic nodules or scarring within the corpora, but in most cases, these disappear after temporary discontinuation of the treatment.

Intracavernosal injection therapy still has a continuing role in treatment of patients who do not respond to sildenafil, although the determining features for responsiveness are not yet known. Patients with neurogenic ED responded well to low doses of alprostadil therapy, while those with vascular disease required higher doses.

KEYPOINTS:

- It is therefore important to check for postural hypotension in men with parkinsonism before prescribing sildenafil.
- Patients with neurogenic ED responded well to low doses of alprostadil therapy, while those with vascular disease required higher doses.

KEYPOINTS:

- Similar erection mechanisms to those that occur in men also operate in women, including NO- and cGMP-mediated vascular events.
- The clitoris is homologous to the glans penis and is the most densely innervated area of the skin with an innervation density, approximately twice that of the male dorsal penile nerve, so that clitoral sensory thresholds are lower than that of the glans penis.

A high attrition rate for using the treatment was found in several studies, thought to be due to dislike of injections, the artificiality of the therapy and the practical difficulties preparing and administering the solution. In order to overcome some of these problems, several easy self-injection devices have been manufactured.

Intraurethral pharmacotherapy and topical creams: Although intraurethral administration of alprostadil as a medicated pellet (MUSE®), which obviated the need for injection, was theoretically an attractive option, the efficacy of the preparation is much less, despite higher doses. Its use in clinical practice has been somewhat disappointing.

Topically acting vasodilator creams have been developed, some with a mixture including nitric oxide donors [22].

Vacuum devices: A vacuum device consists of a vacuum chamber, a vacuum pump that creates negative pressure within the chamber, and a constrictor or tension band that is applied to the base of the penis after the erection is achieved. Vacuum-induced erections are due to venous turgidity and the penis is only rigid distal to the constricting band. These devices have been successfully used in older men and have the advantage of having limited side effects, although these may include pain, hematoma, petichiae, and numbness. The use of this device is contraindicated in patients with bleeding disorders, Peyronie's disease, and in those with intracavernosal scarring. Vacuum devices may also be useful to enhance the effects other treatment modalities (intracavernosal, intraurethral).

Penile prosthesis: Penile prostheses are generally much less used nowadays. The complication rate in men with spinal cord disease was higher than in other patients, and, in general, a prosthesis is not suitable for a man who has progressive neurological disease.

FEMALE SEXUAL DYSFUNCTION

Similar erection mechanisms to those that occur in men also operate in women, including NO- and cGMP-mediated vascular events. Arousal and hyperalgesia of the genital tissues can be provoked by imagery and fantasy, or by stimulation of vaginal or cervical tissues or of other erogenous zones. During this process, blood flow is increased to the vagina which results in lubrication and erection of the female cavernous tissues and clitoris. Women experience a period of REM-sleep-associated augmentation of vaginal blood flow and increased lubrication, analogous to male nocturnal tumescence.

Lubrication is derived mainly from a transudate from the vaginal tissues, although secretion from Bartholin's glands, the cervix, and uterus also contribute [23]. Diminished lubrication can impair sexual function and can be caused by estrogen deficiency states, pituitary insufficiency, antiestrogen therapy, and anticholinergic agents.

Neurological control of sexual function in women. The clitoris is homologous to the glans penis and is the most densely innervated area of the skin with an innervation density approximately twice that of the male dorsal penile nerve, so that clitoral sensory thresholds are lower than that of the glans penis. The clitoris contains three different types of nerve endings, including free endings that mediate response to pain, submucosal fibers that respond to pressure and movement, and onion bulbs that are involved in sensing pressure and vigorous movements. These latter two types of nerve endings are localized in close proximity to cavernous tissue and are thereby stimulated during the phase of vascular engorgement. The clitoral nerves join the pudendal nerves, which ultimately transmit information to the sacral spinal cord.

Two clitoral reflexes characterize the neurophysiology of the clitoris. The bulbocavernosus reflex is a phasic response that can be triggered by pinching the clitoris and involves contraction of the bulbocavernosus muscle and the external anal sphincter. Vibratory stimulation evokes a tonic reflex involving sustained contraction of the pelvic floor musculature. The bulbocavernosus muscles surround the vaginal introitus and insert on the dorsal surface of the clitoris forming an anatomical sling. During the process of muscle contraction, the dorsal vein is compressed and the cavernous tissue becomes engorged with blood, leading to clitoral erection.

In addition to the clitoris, there are areas on the anterior vaginal wall which respond to sexual stimulation, and some have claimed the existence of a highly localized area, the so-called "Grafenberg spot" (G-spot).

TABLE 5 Types of female orgasm

Clitoral or vulval
Uterine or vaginal
Blended
Anal
Erogenous zones (breasts/neck/hands)
Psychogenic

With appropriate stimulation and rising sexual excitement, orgasm may be reached. The female orgasm is characterized by the experience of a spreading sensation of warmth followed by up to 20 synchronous contractions of the vaginal musculature and sphincters lasting for 10-50 seconds. There are several forms of female orgasm, which provides for a broad diversity of stimulation sites (Table 5). Some women can experience multiple orgasms in sequence in response to repeated or persistent sexual stimulation.

Neurological causes of FSD. Much less is known about neurogenic FSD than is known about male sexual dysfunction and, furthermore, most female patients are still very much more reticent about discussing sexual problems, although that may change. However, based on considerations of the homologous nature of neurological control of sexual responses, it is reasonable to assume that the diseases shown in Figure 5 and listed in Table 3 adversely affected women in much the same way as men. Each of these and what therapy is available is discussed in the appropriate chapters (Chapters 5-9).

SEXUAL HEALTH AND REHABILITATION

The ready availability of simple, effective treatment for ED has made both patients and their doctors more willing to talk about sexual dysfunction. The high incidence of ED in neurological disease (Table 2) means that every neurologist is taking care of many patients who have sexual dysfunction amongst their complaints. Ignoring this aspect of the patient's health should be regarded as being as neglectful as failure by the physician to attend to some other major neurological dysfunction.

In treating sexual dysfunction, irrespective of the cause, the physician may or may not become involved in the extent to which the problem has affected partner relationships. In progressive neurological disease, the disease itself may have a considerable impact on a relationship, and restoring erectile function may have complicated repercussions when a patient's partner has become their carer. Following traumatic spinal cord injury, the problems are quite different and may include sexual rehabilitation of an otherwise fit young man, so that he is able to enjoy a full dyadic relationship.

A sympathetic and encouraging approach of enquiry is necessary, with the level of detail of discussion determined by the extent to which patient and doctor feel comfortable with the topic. Often the subject can be easily introduced following discussion of neurogenic bladder dysfunction, pointing out to the patient that, as is often the case, the same parts of the nervous system are needed for control of the bladder and sexual function. The neurologist must be sensitive to the patients' situation and be nonjudgmental. Provided this approach is taken, the successful treatment of

KEYPOINTS:

- The high incidence of ED in neurological disease means that every neurologist is taking care of many patients who have sexual dysfunction amongst their complaints.

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