

# Neurogenic sexual dysfunction

Sexuality is an important function both for procreation and for quality of life. To talk about sexuality, make the necessary diagnosis and give a proper treatment is part of the comprehensive management of many individuals who suffer a pathology of the nervous system. In this manuscript we will describe actual knowledge about this topic and give practical advice on how sexual problems can be dealt with in this group of individuals.



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## Introduction

Till the 1970s very little attention was given to this function in people who suffered a neurologic pathology. The reason may have been lack of knowledge, influence of certain society rules or underestimating the importance. It was not rare that following statements were made: "Paralyzed people have no sex; why bother these patients by talking about sex. It is like showing them ice cream when you know they can't eat it; you should not love or marry a person incapable to have children in a 'normal' way." Times have changed and with a different attitude towards sexuality in general and also in neurologic patients the subject has become part of overall comprehensive management. Both in men and in women different topic will need to be discussed: sexual arousal and libido, sexual play and intercourse, fertility and reproduction. In literature more is to be found about male sexuality than about female sexuality though the latter subject gets an increasing attention.

## Innervation in sexual function

More extensive research has given a better idea of what may be involved in

sexuality in the brain. MRI images have shown regions activated while patients viewed erotic videos with abstraction of regions activated while viewing sexually neutral videos.<sup>1</sup> Activity has been shown in anterior cingulate gyros, prefrontal cortex, thalamus, occipital temporal lobes, insula and claustrum, hypothalamus and amygdale, illustrating how broad involvement exists in the brain. The peripheral innervation in both sexes includes hypogastric, pelvic and pudendal nerves, both afferent and efferent nerve pathways and thus very much running together with information from the other pelvic organs as bladder and bowel. A review has recently discussed the control of male sexual responses, highlighting studies in spinal cord injured step by step.<sup>2</sup> Denis et al recently report the data from the literature concerning male sexual disorders in cases of acquired brain lesions (stroke, cranial trauma), extrapyramidal symptoms, medullar lesions, multiple sclerosis, peripheral lesions of the cauda equina or more distal.<sup>3</sup> Perrouin-Verbe et al made recently a review on sexuality in women with spinal cord injury.<sup>4</sup> Aisen made another overview published in 2013.<sup>5</sup> However it is important to realize that sexuality mechanisms in human are not as yet completely understood.

## Influence of neurologic lesion on sexual function

It is clear that the level of the neurologic lesion, its extent and progression will be mostly responsible for the individual type of dysfunction. Lesions in the brain, brainstem and spinal cord will in a different way affect sexuality. But also general factors as ageing, atherosclerosis, cardiovascular disease, previous surgery, alcohol abuse, smoking, intake of medication will have an influence. Sexuality in an individual with neurologic deficit will have personal expressions depending on gender, age, preference and partner, body image and overall quality of life. As a direct consequence of the neuropathy men and women can suffer from libido disturbance, sensory problems and difficulties to obtain orgasm. Men can experience problems with erection and/or ejaculation. Women can notice less vaginal lubrication, loss of tonicity of the pelvic floor muscles, problems with swelling of the clitoris. Secondary problems related to sexuality can be bladder and bowel function, fatigue, spasticity, muscle weakness, shaking of hand and body, diminished attention and concentration, sensory disturbances.

Tertiary sexuality related dysfunction can be cultural and psychosocial with loss of self-esteem, body image problems, demoralization, depression, changes of mood. If one partner takes up a heavy role of health care provider to the other, the relationship can change. Problems in employment and changed role pattern in the household can have a negative influence.

## KeyPoints

- Sexuality in the individual with neurologic lesion is important and its diagnosis and treatment should be part of the comprehensive overall management.
- Technical testing is often not needed unless specific deficits need to be documented.
- Be careful in patients with symptoms of parkinsonism as erectile dysfunction in MSA patients is best not treated with PDE5.

It is very important to realize that individual variations prevent using lesion characteristics to predict patient's individual potential.<sup>6</sup> It is unwise to speak in definite terms regarding sexual prospects early after the onset of a neurologic lesion. To predict what will be one individual's sexuality is impossible for a function that relates to so many other functions and is by definition very personal and individual.

### Epidemiology

Are patients with neurologic deficit sexual active? Data are available for spinal cord lesion individuals. 87% of the patients report participating in sexual activity before injury and 67% after injury. The likelihood of participating in intercourse increases with time after the injury. Many patients are sexually inactive. Erection problems have been described in 60% in Parkinson, 98% in multiple system atrophy, 25-95% after spinal cord injury, 62-83% in multiple sclerosis and  $\pm$  100% in diabetic neuropathy. Sexual problems in women have been described between 40 and 80% dependent on different factors. Overall it is clear that sexuality is very often affected and needs full attention as part of comprehensive management. There is a gender difference in importance given to sexuality: in men it has the second place on 11 for importance and satisfaction. In women it has the 10<sup>th</sup> place on 11. But here again individual differences exist.

### Start of diagnosis

It is usually more easy for the physician or allied professional to start discussing the subject than to leave all initiative with the patient. Best is to propose to discuss it. But the patient can give a negative reply which needs to be respected. But most will be eager to discuss a problem that they carried already for some time and that created worries and/or questions.

### History taking

It is good to have sufficient information from the beginning. If the individual already had sexual activity before the neuropathy the way this was done and how it was experienced is a good starting

point. Does the patient have a regular partner? What has been tried out since the neurological problems started and what was noticed as problematic?

It has proved useful to ask for expectations early. They will in most cases result in hoping for regaining most of the previous sex life, some to have children. For adolescents without previous sexual experience the approach will be somewhat different but to explain and reply to questions they may have is of great importance. Many individuals in acute rehabilitation settings discuss sexuality with allied professionals and other patients. If something important is reported to the allied professional this should best be communicated to the physician in charge as it will permit to guide the management.

### Management

Which diagnostic tests are needed will depend on each individual case and the reported problems. But from a clinical point of view, as treatment options do not differ much, directly going into conservative treatment without performing many technical tests may be a good way to start. Educating will create knowledge of what is the probable cause behind the symptoms, what will be possible as treatment and why. In specialized spinal units this often starts with group lessons as applied since many decades. They have proved to be of value for all different aspects including sexuality. Counseling on an individual basis is the next step. Post injury hospitalization periods and rehabilitation are excellent times to go for initial management by discussing the topic. The PLISSIT model<sup>7</sup> with consecutive Permission, Limited Information, Specific Suggestions and Intensive Therapy stands as the classical way of approach.

### Male sexuality

#### Erection problems

An algorithm for diagnostic evaluation of erectile dysfunction (Lue TF et al, J Sex Med 2004; 1: 6-23; <http://onlinelibrary.wiley.com/doi/10.1111/j.1743-6109.2004.10104.x/full#f1>) gives a very complete overview.

### Drugs

After counseling, treatment will start mostly with PDE 5 inhibitors, but L-arginine/Yohimbine (NO and alfa blocker), Apomorfine (dopamine agonist), Fentolamine (alfa blocker), Yohimbine (alfa blocker) have all been used. PDE 5 inhibitors are absorbed quickly. Time to maximum effect is 1 hour for Sildenafil and Vardenafil, 2 hours for tadalafil. The time of action is 4-5 hours for Sildenafil and Vardenafil and >17.5 hours for tadalafil.

With these medications interaction can occur with CYP3A4 inhibitors (itraconazol as Sporanox<sup>®</sup>, ketoconazol as Nizoral<sup>®</sup>, indinavir as Crixivan<sup>®</sup> and ritonavir as Norvir<sup>®</sup>), nitroglycerines and molsidomine (Coruno<sup>®</sup>, Corvatar<sup>®</sup>, Corvaton<sup>®</sup>). Vardenafil should not be taken with 1A (Rythmodan<sup>®</sup>) or type 3 antiarrhythmics (Amiodarone<sup>®</sup>, Cordarone<sup>®</sup>) or in cardiologic problems.

There have been studies in men with different types of neuropathy:

- Traumatic spinal cord injury: 76% of the patients reported improved erections and a preference for sildenafil. Treatment with sildenafil can significantly improve key quality of life parameters. Dosis of sildenafil is often 50 mg but sometimes a higher dosage is needed. Either sacral 2-4 or thoracic 10-lumbar 2 must be spared.<sup>8-11</sup>
- Multiple sclerosis: a placebo controlled trial with sildenafil in 217 men. The efficacy was excellent with 90% of 104 sildenafil patients and 24% of 113 placebo patients reporting improved erections as well as a measurable improvement in quality of life.<sup>12</sup>
- Spina bifida: placebo controlled trial in 8 men showed improved erectile function in 63%.<sup>13</sup>
- Parkinson's disease: in a randomized, cross over, placebo controlled study 50 mg sildenafil proved to be effective, (n=12) although in parkinsonism due to multiple system atrophy who had erectile dysfunction and either symptomatic or asymptomatic autonomic failure, hypotension was significantly exacerbated by sildenafil. It is therefore important to check for postural hypotension in these patients before prescribing sildenafil.<sup>14</sup>

- Diabetic: in a study of 131 men, 56% reported improved erections on active treatment compared with 10% of 127 in the placebo group. The peripheral vascular as well as the effect of advanced glycosylated end products which decrease NO activity are thought to contribute to the severity and relative intractability of erectile dysfunction in diabetics.<sup>15</sup> Vardenafil improved erectile function in men with erectile dysfunction associated with diabetes mellitus.<sup>16-17</sup> Tadalafil has a similar effect.<sup>18</sup>
- When peripheral nerve lesions with radical prostatectomy are the neurologic cause of erectile dysfunction the use of sildenafil was ineffective but with preserved innervation good results were seen.<sup>19</sup>

The possible side effects are well known: headache, flushing, dyspepsia and running nose. The use of PDE5 is contraindicated in severe hepatic impairment, conditions that predispose to priapism, bleeding disorders, cardiologic high risk. PDE5 has been studied in new indications: sildenafil as cognitive enhancer in age related cerebral conditions; PDE5A to improve recovery of cerebral function after stroke; sildenafil delays intestinal ulceration and has a protective effect in reducing gastric damage.<sup>20</sup>

#### *Intracavernosal injections*

Intracavernosal injections existed before the drugs came into clinical use. Intracavernosal injections with papaverine, phentolamine are mostly replaced now by alprostadyl PGE1 in a dosage between 5-40µg. Sometimes combinations of products are used. After injection at a proper dose erection appears quickly within 5-15 min. Rigidity occurs in both corpora cavernosa but not to a major extent in the corpus spongiosum and the glans penis.

Drawbacks can be some pain in patients with preserved sensation and the risk for priapism which occurs more with injection of products other than alprostadyl. But patients must be made aware in any case that such risk exists and that treatment is an emergency. Good training and accurate application can help to avoid the development of scarring and the formation of fibrotic nodules at the injection

site. The attrition rate is higher due to dislike or fear of injections, difficulty in preparing and administration, and impression that it is overall artificial.<sup>21, 22</sup>

#### *Vacuum device*

Devices gave 50% satisfaction when used for treating erectile dysfunction after spinal cord injury.<sup>23</sup>

#### *Other treatments and combinations*

Almost no data are available on MUSE®, PDE5 plus vacuum device, PDE5 plus intraurethral alprostadil, PDE5 plus intracavernosal injection, PDE5 plus androgen supplementation, PDE5 plus alpha adrenergic receptor antagonist.

#### *Penile prosthesis*

Implantation of penile prosthesis is used less now. Studies showed that over a period of 17 years in 245 men with neurologic pathology those who had the implant for erection were successful in 75%. Other series give success of 89%, satisfaction 81%. Reinterventions are not rare.<sup>24, 25</sup>

#### **Ejaculation problems**

Older studies<sup>26</sup> gave in large groups of patients with spinal cord injury ejaculation possible in 10% and 3.4% who fathered children. More recently<sup>27</sup> 80% could become ejaculation with therapy.

#### *Vibration*

Is quiet successful with frequency between 60 and 120Hz. Amplitude is important and 2.5mm peak to peak. The session is usually short with ejaculation occurring within minutes. Studies give positive results between 65 and 96%,<sup>28</sup> and improvement of sperm quality after spinal cord injury.<sup>29</sup> Attention must be given to possible autonomic dysreflexia which one can try to prevent with nifedipine.<sup>30</sup>

#### *Electroejaculation*

Has been used for more than 60 years.<sup>31</sup> Brindley has studied it and Seager has produced a well evaluated equipment for this purpose.<sup>32</sup> As guideline, differentiation can be made on which technique to be used after spinal cord injury: if T12-L2 is intact both masturbation and mostly vibration may be successful. If T12-L2 is not intact electroejaculation can be used or fertilization techniques.

After spinal cord injury sperm quality gets quickly lower. That can be one of the reasons to start fertility techniques soon and also to make the utmost effort to avoid infections in the lower urinary tract/prostate and genital organs. When the basic techniques are successful they can be used at home and series of pregnancies have been described, obtained in these conditions. Is time available limited because of age and if basic techniques are not easily successful the couple may decide to search for help in the setting of a fertility clinic fairly rapidly after the neurologic problem started.

There are several other aspects on fertility, many psychological and it is needed to discuss an eventual parenthood with the couple before starting the fertilization process. Stability in the relation, financial situation, possibility to give proper care and education to eventual children are all important to discuss. Active fertility treatments should be considered if major risk factors are planned as rhizotomies or bladder neck surgery.

#### **Treatment of sexual sensory deficiency**

There is not much one can do if sensation has been lost. Possible treatment may be sexual counseling and using stimulation of the erogenic non genital zones. Kegel exercises and physiotherapy have been tried for incomplete deficits but the results remain not well documented.

#### **Orgasm**

Orgasm can be obtained by many patients. It will need a long and strong genital stimulation if the genital organs are not decentralized. Caution about autonomic dysreflexia is needed. Patients who can have orgasm often report improvement of their spasticity. Treatment can be with sexual counseling and vibration, Midodrine (alfa agonist) has been used with some success.<sup>33</sup>

#### **Female sexuality**

It is noteworthy that studies show that 75% of women with neurologic deficit seem to adjust well without sexual counseling. The reasons for this remain speculative. But 80% reported being engaged in sexual activity after spinal cord injury,

but with many changes and many factors giving a negative influence.<sup>34</sup> Several authors have reported on sexual function in women with spinal cord injury in relation to the level and completeness of the lesion and linked these with parts of the genital reactions seen during stimulation and intercourse.<sup>34-38</sup> Problems mentioned by the women and limitations for having intercourse are difficulty with positioning, increased spasticity, bladder incontinence, autonomic dysreflexia and problems with Foley catheters.

#### *Treatment of vaginal lubrication problems*

Sexual activity in a proper environment, relaxation is mandatory. Other techniques are: Stimulating massage during prelude. Long foreplay. Increasing reflex lubrication with oral or manual stimulation of the sexual organs, allocation of hydrosoluble lubricants. Vaseline is not recommended because of danger of infection of residual gel.

#### *Treatment for loss or diminished sensation of the genitals and loss of orgasm*

Study a drawing of the sensorial chart of the body can help to understand. Strong stimulation with vibrator or oral stimulation; treatment of genital or other body pain with drugs; avoidance of antidepressant drugs can all help. Sildenafil was studied and results are reported different in different study groups but with indication that one can not expect an overwhelming positive effect.<sup>39-40</sup>

#### *Advice for intercourse*

It may be worthwhile to discuss sex habits in a more specific way. Different positions for good contact and at the same time good comfort; special hygiene; bladder, bowel and skin care.

#### *Fertility, pregnancy and childbirth*

In most women fertility will not be overall changed after an initial period of neurogenic shock. This means that pregnancy is possible and there are sufficient publications showing that this happens. During pregnancy and childbirth, as well as during the post delivery period close active surveillance and care is needed. The obstetrician should be informed of things that need special attention. For

very severe neurologic lesions as high complete tetraplegia, specific monitoring might be needed. Delivery can happen transvaginally and it is not necessary to decide on cesarean unless indicated. If there is no wish for a child anticonception is needed. This can be done with the classical techniques. The pill gives the highest risk for developing thrombosis. An intrauterine device can cause increased spasticity. Sterilization can be considered if no further child is wanted. Other techniques can be used, all with their advantages and shortcomings. ■

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