



Premature Ejaculation and MS: A Review

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Introduction and Overview

Sexual dysfunction (SD) is one of many symptoms affecting persons with a diagnosis of multiple sclerosis (MS). SD in men encompasses both erectile and ejaculatory disorders. The prevalence of SD in men with MS ranges from 75 to 91% (Ref 1, 2, 3). Erectile dysfunction appears to be the most common form of SD documented in MS (Ref 4, 5, 6, 7).

In contrast, premature ejaculation (PE) is the most common and most problematic form of sexual dysfunction among men throughout the world. It is estimated that between 21 to 30% of men worldwide report this condition across all age groups (Ref 8, 9). This number is greater than the number of men in the United States who report erectile dysfunction (ED), estimated to be between 7 and 20 million, or 5 to 15% of the population, with the majority of cases occurring after age 40. (Ref 10 Laumann)
PE is a self-reported condition and there are a variety of definitions. According to the American Urological Association, PE is defined as the persistent or recurrent onset of orgasm and ejaculation with minimal stimulation before or shortly after penetration AND before the person wishes it to occur, causing distress to one or both partners (Ref 11 Montague)

Neurophysiology of ejaculation

The process of ejaculation requires two sequentially distinct actions: emission and expulsion. The first phase, emission, involves the deposition of seminal fluid from the ampullary vasa deferens, seminal vesicles & prostate gland into the posterior urethra (Ref 12 Bohlen). During the second phase, expulsion, semen is forcefully propelled along the urethra by the rhythmic contractions of the striated pelvic floor muscles and the bulbospongiosus muscle and out past the closed bladder neck, during which time there is intermittent relaxation of the external urethral sphincter(Ref 13, Master and Turek,).

Both the central and peripheral nervous systems are involved in the ejaculatory process. Sympathetic motor neurons control the emission phase of the ejaculation reflex. The expulsion phase is executed by somatic and autonomic motor neurons. These motor neurons are located in the thoracolumbar and lumbosacral spinal cord and are activated in a coordinated manner when sufficient sensory input to reach the ejaculatory threshold has entered the central nervous system (Ref 14, de Groat and Booth 1980; Ref 15, Truitt and Coolen 2002). Several areas in the brain, and especially the nucleus paragigantocellularis, have been identified as involved in ejaculatory control (Ref 16, Coolen, et al., 2004). In the absence of descending inhibitory input from the cerebral ejaculatory center, the spinal ejaculatory center functions as its own system as seen in men with complete spinal cord injury (Ref 17 Kuhr).

Multiple neurotransmitter systems at both the spinal and supraspinal regions have been implicated in regulation of the ejaculatory reflex. The most significant of these seem to be the central serotonergic

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and dopaminergic neurons. Dopamine signaling has been implicated in the physiology of arousal and orgasm as dopamine levels in the medial preoptic area of the hypothalamus increase during excitation and intercourse (Ref 18 Hull). Serotonin (5-HT) is involved in the ejaculatory process as demonstrated in 1981 by Ahlenius et al. (Ref 19).

Acetylcholine, adrenaline, neuropeptides, oxytocin, γ -aminobutyric acid (GABA), and nitric oxide have all been shown to play a secondary role. GABA-receptor antagonists have demonstrated an inhibitory effect on sexual behavior in animal models, and muscular contractions during ejaculation seem to be mediated by oxytocin (Ref 20 Bancroft). The multifactorial and complex nature of ejaculation continues to be poorly understood and the precise role of each individual neurotransmitter is yet to be clearly defined.

Types of PE

A. Lifelong

Many men admit to lack of control early in their sexual experiences. With time, control is achieved by the majority of men; however, one-third may complain of rapid ejaculation throughout their entire life. In the early 1900s PE was assumed to be only of psychological origin. Today the neurophysiological evidence demonstrates the ejaculation reflex cannot always be controlled. A hereditary component also appears to exist per Waldinger et al as 10 % of men with PE have a relative with PE (Ref 21).

B. Acquired

There are both physical reasons and psychological reasons why men will develop PE after a period of normal control. Certain physical conditions, such as prostatitis and urinary infections, and endocrinopathies, specifically hyperprolactinemia and hyperthyroidism, may result in PE (Ref 22 El-Sakka, 23, Carani). Withdrawal from opiates, tranquilizers and cold medications can result in PE (Ref 24 Metz). PE may appear after insertion of an intrathecal baclofen pump (Ref 25 Denys). Psychological issues such as stress, anxiety, or conflicts within relationships, cultural and religious beliefs, and intercourse with particular partners may impact the ability to perform sexually. Any of these issues can precipitate PE. Without resolution, this may occur repeatedly.

C. Mixed

The level of comorbidity between PE and ED may be as high as 30% (Ref 26 Lue) PE may occur first or may be a result of ED. Mistakes may occur during the initial patient assessment as patients may self-report impotence when in fact they may also be describing symptoms of PE or symptoms of PE alone. This may be a result of public acceptance of ED and its terminology, combined with less public information on PE. In relation to treatment order of PE and ED, ED should be the first symptom to which treatment is directed per Shindel et al. (Ref 27).

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Diagnosis of PE

The AUA Guideline (Ref 11 Montague) has determined that the diagnosis of PE is typically a self-reported diagnosis and recommends that it be based solely on past sexual history. Laboratory and physiologic testing is not required unless indicated in the sexual and medical history. Questions to consider according to the guidelines include:

- The frequency and duration of this condition
- Whether or not the PE is related to specific partners
- Whether PE occurs with all or some sexual events
- The nature and frequency of sexual activity
- The impact on quality of life and sexual activity

A review of the sexual history, including questions relating to the frequency and duration of PE, are important in determining whether the condition is acquired or lifelong. The impact of PE on the relationship should be assessed. A medical examination may be required to rule out any acute or chronic illness. Previous injuries, surgeries or deformities may impact sexual function. Neurological and endocrine disturbances and the impact of drugs or alcohol on sexual function should be assessed to help differentiate any medical cause of the condition.

An objective parameter that can also be used to evaluate for PE is the use of the intravaginal ejaculatory latency time (IELT). The IELT is measured using a stopwatch at the start of vaginal intromission and the start of intravaginal ejaculation (Ref 28 Shabsign). Men who report lifelong PE often report times of less than 60 seconds. Because this may be an impractical approach within the clinical setting, questionnaires have been developed and validated for use within clinical trials and in clinical practice. The Index of Premature Ejaculation is an example of a reliable and valid questionnaire for the assessment of control, satisfaction, and distress with ejaculation (Ref 29 Althof). This questionnaire has been translated into 13 languages. Caution should be exercised when using assessment tools tested in the general population as they may not have been tested for validity and reliability in the population of neurologically impaired men.

Treatment Options

A. Behavior Modification Techniques

The stop-start method or the squeeze techniques are often recommended as self-help methods both in the literature and on the internet. Patients with PE find that these can be difficult to initiate during intercourse and therefore men and their partners continue to search for more effective treatments. Use of a condom during intercourse is another way to increase time to ejaculation.

B. Pharmacologic

The use of anesthetic creams applied to the penis can increase time to ejaculation. A recent phase II study conducted in Great Britain published by Dismore (Ref 30) describes a new effective topical agent TEMPE, a combination of lidocaine and prilocaine in an aerosol form that significantly increased time to ejaculation. One of the oldest and most popular topical

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agents is SS cream which contains a blend of nine natural herbs, several of which produce an anesthetic effect (Ref 31 Choi). Side effects of topical products include skin irritation to the penis and numbness in one or both partners. The use of a condom with or without any anesthetic cream may also increase ejaculatory control.

The selective serotonin uptake inhibitor (SSRI) antidepressants such as fluoxetine, paroxetine, sertraline, and citalopram, and the serotonergic TCA clomipramine (Ref 32 Hellstrom) have been found to have a beneficial side effect of delayed ejaculation. As a result, physicians will prescribe such medications “off label” to manage PE. Due to side effects including dry mouth, gastrointestinal symptoms, and complaints of hypoactive sexual desire which may develop with regular daily dosing, some of these medications may be used for only days or weeks within a month.

Recently Phase II and III clinical trials were completed for an on-demand SSRI known as dapoxetine (Priligy™ , Johnson & Johnson). Results of the studies demonstrated efficacy and tolerability and favorable pharmacokinetics (Ref 32 Helstrom). At the time of this writing, the FDA has not given approval for this drug. Future studies using dapoxetine within a population of men with MS could determine if this is an effective agent.

An on-demand nutraceutical product produced by Delithe Nutraceuticals Inc. known as Prolasta is available for men with symptoms of PE. This product contains a proprietary blend of *Hypericum perforatum*. Its effect occurs quickly and lasts for several hours. Studies in men both with and without PE showed a delayed time to ejaculation (Ref 33). Prolasta is available within several retail outlets and via the internet at www.prolasta.com.

C. Pelvic Floor Rehabilitation

Excessive pelvic floor muscle spasticity is a feature in men with PE. This is also a common finding in persons with MS. With the assistance of a trained physical therapist, patients are taught to contract and relax pelvic floor muscles. Treatment may include internal rectal muscle facilitation via the rectum, biofeedback, electrical stimulation, and soft tissue techniques aimed at improving pelvic muscle tone and strength. For maximum effect the pelvic floor exercises must be performed several times per day.

D. Counseling

In men with PE, anxiety may be an immediate problem, or as lack of control over ejaculation continues over time, anxiety over intimate situations may appear. In some situations, PE is acquired and a result of a larger problems within a relationship. Counseling from a psychologist, therapist or trained social worker for direction as to how to change the situation may be considered. Methods of communication, negotiating and conflict resolution strategies are explored in these sessions (Ref 34 Foley).

If the problem with sexual function is identified as sexual in origin, counselors trained in this area and certified through the American Association of Sex Counselors and Therapists

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(www.asect.org) can help identify new strategies to improve sexual function with attention to any special needs as a result of MS. These therapists can help a couple review their thoughts, experiences and beliefs about sexual encounters. The goal is to help the couple learn to focus on what is important to each of them in a sexual relationship and to assist with new methods of sexual expression.

PE and MS

In the limited number of studies documenting the incidence of PE in MS it is difficult to distinguish if symptoms occurred or worsened as a result of MS or if the incidence is lifelong. A PubMed search of the keywords words “premature ejaculation” and “multiple sclerosis” provided two references. Expanding the keyword search to include “ejaculation”, “sexual dysfunction”, and “multiple sclerosis” provided more opportunity to find related articles to assess prevalence. The incidence of PE in all articles reviewed documents the rate of PE in MS to be less than 10% and much lower than the incidence of ED in all articles (Ref 4-7). This may be due to the questions used to assess SD and the lack of valid and reliable instruments available at the time of the study to assess PE. Symptomatic treatment for depression, fatigue, pain and sensory disturbances, other frequent symptoms of MS, includes the use of SSRI treatments. The use of SSRI’s impacts not only PE but sexual desire. Therefore, the incidence of PE in MS may be significantly different when compared to the general population due either to disease or other treatments such as antidepressent use.

Conclusion

Future studies and clinical assessments of sexual function in all age groups of men with MS should accurately capture this condition, and other ejaculatory disturbances such as anejaculation, delayed ejaculation, retrograde ejaculation or any mixed dysfunction. Appropriate questions can identify if symptoms were lifelong, worsened or improved through the course of MS. At this time, due to the lack of standardization related to PE terminology, any documentation of this health problem in the literature must be accurately described. As the interest and understanding of neurophysiologic mechanisms expands, the actual pathology that results in PE or other ejaculatory disorders specifically related to MS will be better understood. Treatment and education of PE in men with MS may become a new market opportunity as it has become with men in the general population.

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Illustration

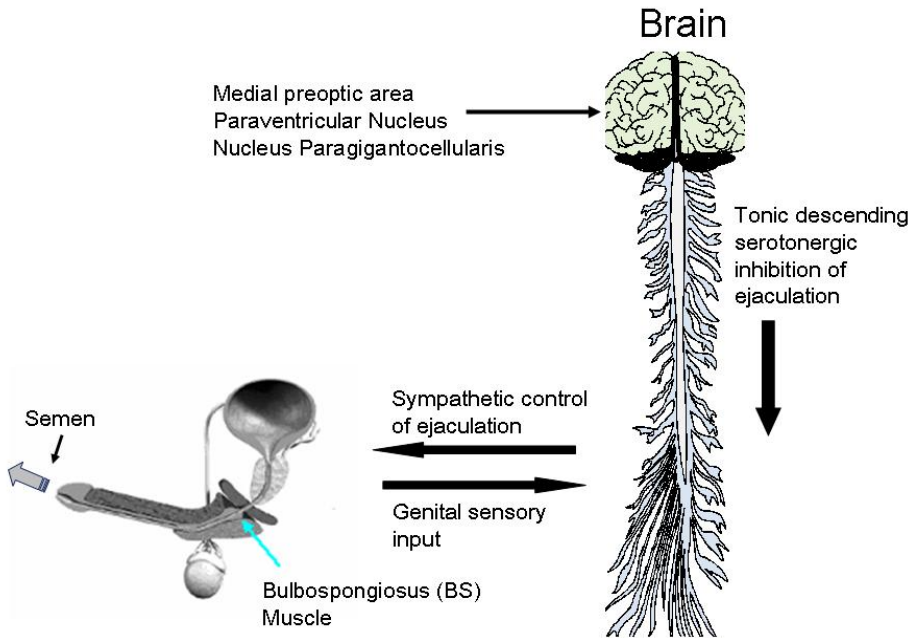


Figure 1: Ejaculation is a spinal sympathetic reflex generated in the lumbosacral spinal cord. Ejaculation is influenced by genital sensory input and by tonic descending inhibitory serotonergic control from the nucleus paragigantocellularis in the brain. Expulsion of semen is due to the activation of rhythmic contractions of bulbospongiosus (BS) muscles.



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