The Evaluation and Treatment of Delayed Ejaculation

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ABSTRACT

Introduction. Delayed ejaculation is a small but important subsection of ejaculatory dysfunction, with prevalence estimated at 1–4%. It is most commonly defined by *DSM-IV-TR* criteria, as "a persistent delay in, or absence of, orgasm in a male following a normal sexual excitement phase during sexual activity that the clinician, taking into account the person's age, judges to be adequate in focus, intensity, and duration." The pathophysiology of delayed ejaculation is related to disruptions in ejaculatory apparatus, nervous transmission, hormonal or neurochemical ejaculatory control, or psychosocial factors.

Aim. To update the clinician on the evaluation and treatment of delayed ejaculation.

Methods. The keywords "delayed ejaculation" and "retarded ejaculation" were utilized to search Pubmed for relevant publications.

Main Outcome Measures. 319 results were generated from the search, and those publications judged relevant to the pathophysiology, epidemiology, evaluation, and treatment of delayed ejaculation were included in the review.

Result. 110 articles were ultimately selected for inclusion in this review.

Conclusion. The evaluation of this condition requires a focused history and physical, which includes a detailed sexual history, examination of the genitalia, and inquiry into the status of the partner. Laboratory tests are aimed at the detection of abnormalities in the blood count, glucose level, hormone levels, or kidney function. If a correctable etiology is discovered, treatment is directed towards the reversal of this condition. In some cases, the delayed ejaculation may be a lifelong problem. Also, in some cases the etiology of the delayed ejaculation may be irreversible, such as in the case of age-related sensation loss or diabetes-related neuropathy. In these instances treatment may require a combination of behavioral modification, sexual therapy, or perhaps pharmaceutical drugs. Participation of the partner in therapy may sometimes be necessary. Future investigations will continue to elucidate the complex biological and psychosocial factors which contribute to delayed ejaculation, leading to more effective treatments.

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Introduction

Ejaculatory dysfunction is one of the most common male sexual disorders. It is best envisioned as a spectrum of disorders, with one extreme being premature ejaculation, and the other extreme including delayed ejaculation, anejaculation, and retrograde ejaculation. Worldwide surveys show high prevalence of ejaculatory dysfunction, with estimates of premature ejaculation alone reaching 30% prevalence among males 40–80 years of age [1–3]. Delayed ejaculation is much less commonly reported, with best estimates showing it to have approximately 1–4% prevalence [4,5]. When encountered, however, delayed ejaculation can cause a lack of sexual fulfillment for the male and pose a difficult problem for a couple, especially when conception is desired.

In this article, we will first review the definitions of delayed ejaculation and the various approaches to its diagnosis. Next, we will briefly review the

physiology of ejaculation and use this as a basis to explain the proper approach to the evaluation of delayed ejaculation (DE). We will then provide etiology-specific treatment recommendations based on the most recent literature. Finally, we will highlight future directions for research.

Male Sexual Response

Masters and Johnson delineated the human sexual response as encompassing four distinct phases, including excitement, plateau, orgasm, and resolution [6]. In males, the orgasm phase is typically associated with ejaculation, in which the striated bulbocavernosal muscles rhythmically contract to expel semen. The time period from the beginning of sexual stimulation to ejaculation is the latency period, and varies greatly across different men, and within men as a result of variation in sexual environment including novelty, frequency, and masturbatory habits.

Ejaculatory Physiology

The two phases of ejaculation are emission and expulsion. In emission, peristaltic contractions of the smooth muscles of the seminal tract deposit semen via the ejaculatory ducts and verumontanum into the posterior urethra. Next, rhythmic contractions of the pelvic floor muscles (bulbospongiosus, bulbocavernosus, and levator ani muscles) expel the ejaculate through the urethra and out through the urethral meatus. Antegrade ejaculation relies on closure of the internal sphincter of the bladder neck and relaxation of the external urethral sphincter. Failure in the closure of the bladder neck, from urological surgery or neuropathic failure, can lead to retrograde ejaculation [7,8]. The sensation of expulsion is usually associated with the pleasurable experience of orgasm, which is the result of cognitive processing, in part, of sensory nerve stimuli from increased pressure in the posterior urethra and contractions of the urethral bulb and accessory sexual organs [9]. Orgasm and ejaculation are mediated by independent neural mechanisms, though, and may occur separately from each other [10–12].

The sexual response of ejaculation relies on both central and peripheral stimuli with involvement of both the sympathetic and parasympathetic nervous systems. Investigation of ejaculation in rats has elucidated its neurophysiology. The spinal ejaculatory center is composed of thoracolumbar sympathetic fibers, sacral parasympathetic fibers, and somatic fibers (Onuf's nucleus, S2–S4) [13]. These areas collectively integrate peripheral and central stimuli and coordinate the two phases of ejaculation via the pelvi-perineal musculature. Investigation in rats has shown that application of electrical stimuli to these spinal nuclei will trigger the ejaculatory reflex [14,15].

Neurotransmitter/Hormonal Control of Ejaculation

The spinal ejaculatory center is centrally controlled mainly by serotonin and dopamine, with secondary involvement of many neurotransmitters/hormones including acetylcholine, norepinephrine, nitric oxide, GABA, prolactin, and oxytocin [9,16]. Serotonin plays mainly an inhibitory role in ejaculation via the action of two serotonin receptors: 5-HT2C and 5-HT1A [17]. Stimulation of 5-HT2C results in delay of ejaculation and longer ejaculatory latency time, while stimulation of 5-HT1A results in shorter ejaculatory latency time [18]. It has been theorized that men with premature ejaculation may have hyposensitivity of the 5-HT2C receptor, potentially combined with hypersensitivity of the 5-HT1A receptor [19,20]. The respective balance of these receptors may help establish an ejaculatory latency "set point," which varies naturally across a wide distribution.

More recent investigations into oxytocin have found evidence that 5-HT receptors on central oxytocin-releasing neurons may also play a role in establishment of the ejaculatory set point. Review of animal studies in 2007 noted that selective serotonin reuptake inhibitors (SSRIs), over time, decrease the release of oxytocin by desensitization of the 5-HT receptors which reside on these oxytocin-releasing neurons [21]. Rat studies have shown that central oxytocin has a pro-erectile effect [22,23]. Furthermore, case studies have shown that men with lifelong premature ejaculation often report rapidly occurring erections [19,24]. Taken together, it has been argued that this evidence points to a role for oxytocin in establishment of the ejaculatory set point as well, with central oxytocin excess contributing to premature ejaculation and central oxytocin deficiency leading to delayed ejaculation [21].

In contrast to serotonin, dopamine facilitates ejaculation, with rat studies showing that dopamine levels increase steadily through copulation until ejaculation [25]. Prolactin has also been implicated in influencing ejaculatory latency, with severe hyperprolactinemia associated with adverse effects on sexual function and desire, both through suppression of testosterone production