Orgasm and Ejaculation Disorders

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7.1 Anatomy and Physiology of Orgasm and Ejaculation

There is no standard definition of orgasm, although it has been defined as an intense transient peak sensation of pleasure alternating the state of consciousness and associated with reported physical changes. It is commonly combined with ejaculation [1] although the experience of orgasm is a distinct cortical event, associated with the perception of striated muscle contractions and resulting in semen expelled during ejaculation, mediated through sensory neurons in the pelvic region. During orgasm, hyperventilation up to 40 breaths/min, tachycardia, and high blood pressure could occur [1]. Both ejaculation and orgasm are based on a complex interplay between the central nervous system and the peripheral nervous system, with the involvement of several neurotransmitters, thus including dopamine, norepinephrine, serotonin, acetylcholine, gamma-aminobutyric acid (GABA), and nitric oxide (NO) [2]; moreover, hormonal pathways may influence the process of ejaculation with an active role played by oxytocin, prolactin, thyroid hormones, glucocorticoids, and sexual steroid hormones [2]. Different studies using positron emission tomography (PET) have identified areas of activation in the brain during orgasm. Primary intense activation areas are noted to be in the mesodiencephalic transition zones, which include the midline, the zona incerta, ventroposterior and intralaminar thalamic nuclei, the lateral segmental central field, the suprafascicular nucleus, and the ventral tegmental area. Strong increases were seen in the cerebellum. Decreases were noted at the entorhinal cortex and the amygdala [3]. In men, a period of inhibition normally follows orgasm, called the refractory period. This is a poorly understood phenomenon, with some investigators suggesting a central rather than spinal mechanism to be involved [4].

Ejaculation is a different physiological process mainly under the regulation of the autonomic nervous system. It consists of two main phases: emission and expulsion. The first step in the emission phase is the closure of bladder neck to prevent retrograde spillage of the seminal fluid into the bladder. This is followed by the ejection of prostatic secretions, mixed with spermatozoa from the vas deferens into the prostatic urethra [5]. The organs involved in the ejaculation process receive dense autonomic nerve supply, both sympathetic and parasympathetic, from the pelvic plexus. The sympathetic neurons play the pre-

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dominant role in the ejaculation process. Input from genital stimulation is integrated at the neural sacral spinal level to produce emission [6]. The emission phase of ejaculation is also under a considerable cerebral control, and can be induced through physical or visual erotic stimulation [7]. Expulsion follows emission and refers to the ejection of semen through the urethral meatus. The semen is propelled through a number of rhythmic contractions of the pelvic striated muscles in addition to the bulbospongiosus and ischiocavernosus muscles [1]. To achieve antegrade semen expulsion, the bladder neck remains closed, whereas the external urethral sphincter is open.

7.2 Premature Ejaculation (PE)

7.2.1 Aetiology

The International Society for Sexual Medicine (ISSM) elaborated the most comprehensive and widely considered definition of PE, which indeed is defined as a male sexual dysfunction where ejaculation always or almost always occurs prior to or within about 1 min of penetration. It is a condition characterized by the inability to delay ejaculation during sexual activity all (or nearly all) of the time, that causes personal distress and may even lead to the avoidance of sexual intimacy [8]. Overall, the most widely used classification for PE is as follows:

1. Lifelong PE (LPE): occurring since an individual's first sexual encounter.
2. Acquired PE (APE): it begins occurring at some point later in a person's life.

According to this definition, PE prevalence could affect about 4% of the male population [9–13]. Few of these men typically seek treatment for their condition. Up to approximately 30% of men with PE suffer from concurrent erectile dysfunction (ED), which typically may result in early ejaculation without full erection [11, 14, 15]. A wide range of severity is seen, with patients ejaculating on or prior to penetration in the most severe cases. Although this holds true, PE pathophysiology remains an undoubtedly complex topic even though compelling evidence has accumulated over the years, both on animal and human models.

7.2.1.1 Hereditary PE

Hereditary and genetic factors have been supported and correlated with PE onset, thanks to results of familial studies, whereby the risk of PE between family members was higher than the risk expected solely based on prevalence rates in the population [16]. Furthermore, other studies investigating twins, demonstrated a substantial genetic effect on LPE, representing 22% [17] to 28% [17–19] of the variance, as well as on undifferentiated PE observed in young adults (mean age 29.9 years), representing 28–31.5% of the variance [17, 18].

7.2.1.2 Neurobiology of PE

Serotonin (5-HT) is the neurotransmitter of greatest interest in the control of ejaculation. Robust data on animal and human models have been published over the years. As such, it has been hypothesized and subsequently demonstrated that LPE in humans may be explained by a hyposensitivity of the 5-HT2C and/or hypersensitivity of the 5-HT1A receptors. In this context, serotonin per se is known to delay ejaculation; in fact, men with low circulating levels of 5-HT or with 5-HT2C receptor hyposensitivity are known to have lower ejaculatory thresholds. Indeed, it has been demonstrated the presence of a neural network at the peripheral level (within the spinal cord) responsible for the ejaculatory reflex whereby serotonin plays a major role in controlling ejaculation [20]. From this, many therapeutic approaches have been tried and validated. Additionally, both dopamine and oxytocin also appear to play important roles in ejaculation; the biology of these neurotransmitters in relation to ejaculation is less well studied, but in animal models, both appear to have a stimulatory effect on ejaculation [21]. To conclude, the well-documented efficacy of selective serotonin reuptake inhibitors (SSRIs)—such as paroxetine and the on-demand on label molecule dapoxetine—in

increasing intravaginal ejaculatory latency time (IELT) in men with PE supports the role of an impairment over the serotonergic inhibitory control of the ejaculatory process, at least in some men with PE [21].

7.2.1.3 Hormones and PE

Animal studies show the biological interactions between 5-HT, dopamine, and the hypothalamic-pituitary axis. Specifically, the hypothalamic-pituitary-thyroid axis is involved [22–24]. Corona et al. and Carani et al. reported a significant correlation between APE and suppressed thyroid-stimulating hormone (TSH) and high thyroid hormone values [25–28]. After normalizing thyroid function in hyperthyroid men, the prevalence of APE fells from 50% to 15% [26]. Interestingly, no case of hyperthyroidism was found in 620 men with LPE, demonstrating that the association of PE with hyperthyroidism is obviously restricted to men with APE [29]. Furthermore, more recently published studies indicate that prolactin (PRL) hormone is somehow connected with ejaculatory control. Particularly, by analysing data of 25,321 patients seeking first medical help for sexual dysfunctions, lowest interquartile levels of PRL were registered with APE and anxiety symptoms [30]. Lastly, testosterone levels have also been correlated with PE onset. More in details, lower levels of testosterone have been linked with delayed ejaculation [31]. Even though the aforementioned statements are true, hyperprolactinemia and high testosterone levels cannot be considered causative factors for APE onset.

7.2.1.4 Chronic Prostatitis and Chronic Pelvic Pain Syndrome (CPPS)

It has been shown how men with chronic prostatitis or CPPS have a higher probability of reporting PE [32, 33]. Studies investigating prevalence of PE among patients with lower urinary tract symptoms (LUTS) associated with CPPS, showed a prevalence of PE in LUTS ranging from 12% to 77% [34]. In this context, the pathophysiological mechanism remains unclear with many hypotheses postulated. Although this holds true, considering the role of the prostate in the ejaculatory mechanism, a direct influence of the local inflammation in the pathogenesis of a few cases of APE seems possible [33, 35–38].

7.2.1.5 Psychological Factors

Psychological and interpersonal factors may cause or exacerbate symptoms of APE and LPE [39]. In this context, robust data exist regarding the true association of a specific psychological distress and PE onset. As such, the well-known bidirectional influence of PE and psychological distress makes it extremely difficult to detect the true causative agent. Although this holds true, sexual abuse, attitudes toward sex internalized during childhood, individual psychological factors (e.g., body image, depression, performance anxiety, alexithymia), and/or relationship factors (e.g., decreased intimacy, partner conflict) have all been related to PE [40–42].

7.2.1.6 Pharmacology and PE

Possible interactions between opioid withdrawal and APE onset have been postulated [43]. As such, endogenous opioids have been demonstrated to influence (in rats) the inhibition of the ejaculatory reflex at the spinal level. Furthermore, in several placebo-controlled trials, tramadol per se, significantly improved the IELT of men with LPE. Lastly, it has been reported that APE could occur when SSRIs or norepinephrine re-uptake inhibitors are interrupted without a proper decalage.

7.2.2 Diagnosis

7.2.2.1 History and Questionnaires

The diagnosis of PE should start with a comprehensive and detailed medical and sexual history. Moreover, classification of APE, LPE situational, and consistent PE should be made at first clinical assessment. Specific focus should be put on the duration of ejaculation, the impact on patient's quality of life (QoL), and any concomitant use of specific drugs or the abuse of recreational substances. As a whole, IELT alone is not sufficient for the diagnosis of PE. In fact, it has been reported that there is a significant overlap

between men with PE and without PE by using the IELT [44]. In this context, the correct evaluation of QoL is mandatory for the diagnosis. As such, notwithstanding not indicated for diagnosis in clinical practice, a number of questionnaires have been developed over the years. Of those, two validated questionnaires are suggested by the clinical guidelines, such as:

1. Premature Ejaculation Diagnostic Tool (PEDT) [45]: a five-item questionnaire based upon interviews made in USA, Germany, and Spain. A score of >11 is suggestive of PE. A score of 9 or 10 shows a probable PE, whereas a score <8 is indicative of non-PE.
2. Arabic Index of Premature Ejaculation (AIPE) [46]: a seven-item questionnaire developed in Saudi Arabia. A cut-off of 30 shows PE. Severity of PE can also be assessed using the AIPE.

7.2.2.2 Physical Examination

Physical examination should be part of the initial assessment of a patient complaining of PE. As such, penile and genital abnormalities should be carefully assessed, along with other urological, endocrinological, and neurological conditions [44]. Other urological disorders such as ED, Peyronie's disease (PD), urethritis, and prostatitis should be carefully assessed. Lastly, there is no need to ask for laboratory exams unless an underlying aetiology that should be confirmed or excluded is present (e.g., dysthyroidism). During assessment, checking for specific triggers of APE is recommended (e.g., anxiety, guilt, and fear of being caught). As such, the involvement of the partner is often strongly suggested [44].

7.2.3 Treatments

Management depends upon the aetiology, but the most useful available drugs include:

1. *Selective Serotonin Reuptake Inhibitors (SSRIs)* [39]. SSRIs include Paroxetine (10–40 mg/day), Sertraline (50–200 mg/day), Fluoxetine (20–40 mg/day), Citalopram (20–40 mg/day), and Escitalopram (10–20 mg/day) [47]. SSRIs should be started at the lowest dose and up-titrated as needed at 3- to 4-week intervals. Among those, in a meta-analysis, paroxetine has been found to be the most effective in delaying ejaculation when considered as a continuous daily treatment [48]. Additionally, dapoxetine was the first drug patented for the specific treatment of PE; evidence has accumulated upon five trials (including over 6000 men) who were randomly assigned to placebo vs. dapoxetine (30 mg or 60 mg/prn) [49]. Unlike other SSRIs, which are most effective when taken daily, dapoxetine is taken on-demand, ideally 2–3 h before intercourse in the everyday scenario. Specific attention should be maintained regarding the full therapeutic effect of SSRIs. It is typically not seen if not after 2–3 weeks of continuous therapy, and symptoms return if treatment is stopped (although is strictly recommended not to abruptly discontinue any SSRI). Lastly, if SSRIs are not well tolerated or they are ineffective, serotoninergic tricyclic antidepressants (TCA) (e.g., tricyclic clomipramine (12.5–50 mg/day)) could be tried as a second-line alternative [50].
2. *Topical Anaesthetics* [51]. Among this class of available PE treatments, lidocaine-prilocaine spray is the predominant topical treatment given to PE patients in routine clinical-practice [52]. In this context, multicentric trials have shown its superior efficacy at improving ejaculatory control, ejaculatory latency, and eventually overall patients' satisfaction [52].
3. *Psychotherapy*, when psychogenic and/or relationship factors are predominant or co-existing [53]. In this context, behavioural and psychological therapies are effective in some men. These interventions are designed to achieve several goals: improve self-confidence and communication in the relationship and, ultimately, increase the ejaculation latency. Of note, combination therapy (e.g., topical therapy + behavioural therapy) has been shown to be more effective when psychological distress is particularly predominant.

Other available treatments are as follows:

1. *Phosphodiesterase type 5 inhibitors (PDE5i)* [54]. This class of drugs is particularly relevant whenever PE is coexisting with ED. In this context, two meta-analyses have shown the efficacy of PDE5i for PE [55, 56]. The main findings were: (a) both SSRIs and PDE5i are more effective than placebo; (b) PDE5i are either as effective as SSRIs or slightly more effective; and (c) combined therapy is more effective than either therapy alone.
2. *Topical Alprostadil cream (200/300 μg)* [57]. In this context, one available study (multicentre, open-label, long-term study) analysing 1161 patients has shown beneficial effects in terms of delaying ejaculation.
3. *Tramadol* [58, 59]. Tramadol exerts its effect on the opioid receptors along with weak inhibition of serotonin and norepinephrine reuptake. Tramadol can be used as an alternative to SSRIs and TCA anti-depressants. In this context, tramadol's effects on PE have previously been evaluated by three systematic reviews [60–62], two of which have pooled data in a meta-analysis [61, 62]. Of the two meta-analyses, one [60] pooled data across different study types (observational studies and RCTs) [60]. The other one reviewed pooled IELT effect estimates across studies using a standardized mean difference [61]. In conclusion, tramadol appeared to be more effective than placebo or behavioural therapy in the treatment of PE. However, these findings should be interpreted with caution given the observed levels of between-study heterogeneity and the methodological quality of the available evidence. Overall, meticulous attention should be used when prescribing this drug in the everyday clinical setting.
4. *Alpha Blockers* [63]. Patients with LUTS are often diagnosed with sexual dysfunctions (thus including PE) [36]. As such, treatment of LUTS with Alfuzosin has been shown to reduce ejaculatory dysfunctions.

7.3 Delayed Ejaculation (DE)

7.3.1 Aetiology

The American Psychiatric Association defines delayed ejaculation (DE) as requiring one of two symptoms as follows: marked delay, infrequency, or absence of ejaculation on 75–100% of occasions, that persists for at least 6 months, and which causes personal distress [64]. Although this holds true, the definition of DE remains of clinical debate; in this context, compelling evidence has accumulated regarding the true prevalence of DE, thus revealing a 3% prevalence among sexually active men [65, 66]. According to the National Health and Social Life Survey (NHSLS), involving a national probability sample of 1749 women and 1410 men aged 18–59 years, and assessing the prevalence and risk of experiencing sexual dysfunction across various social groups, the prevalence of men having the inability to achieve orgasm climax and ejaculation is around 7.78% [66]. Likewise, another national probability sample study reporting sexual function problems among 11,161 men and women aged 16–44 years in Britain found that 0.7% of men reported inability of achieving an orgasm [67]. Additionally, in an international survey of sexual problems among 13,618 men aged 40–80 years from 29 countries, 1.1–2.8% of men reported that they frequently experience inability to reach orgasm [68]. Although the evidence is limited, the prevalence of lifelong and acquired DE is estimated around 1% and 4%, respectively [69]. Regarding the pathophysiology of DE, experimental evidence shows how 5-HT, throughout brain interconnection pathways (descending), exerts an inhibitory role on ejaculation. Up to date, three main serotonin receptor subtypes (5-HT1A, 5-HT1B, and 5-HT2C) have been postulated to control the ejaculatory reflex. It has been suggested that the presynaptic 5-HT1A somatodendritic auto-receptors, located in the mesencephalic and medullary raphe nuclei and responsible for decreasing 5-HT release into the synapse, decrease ejaculatory latency. In contrast, the postsynaptic 5-HT1B and 5-HT2C receptors have been shown to prolong

ejaculatory latency [70, 71]. In this context, the true pathophysiological mechanisms behind DE remain unclear. There are mainly three aetiological factors which are well-recognized in the context of DE [44].

1. Aging: degeneration of penile afferent nerves inhibits ejaculation.
2. Congenital: Mullerian duct cyst, Wolffian duct abnormalities, Prune Belly Syndrome, imperforate anus, and genetic abnormalities.
3. Anatomic causes: transurethral resection of prostate, bladder neck incision, circumcision, and ejaculatory duct obstruction (can be congenital or acquired).
4. Neurogenic causes: diabetic autonomic neuropathy, multiple sclerosis, spinal cord injury, radical prostatectomy, proctocolectomy, bilateral sympathectomy, abdominal aortic aneurysmectomy, and para-aortic lymphadenectomy.
5. Infective/inflammatory causes: urethritis, genitourinary tuberculosis, schistosomiasis, prostatitis, and orchitis.
6. Endocrine causes: hypogonadism, hypothyroidism, and prolactin disorders.
7. Medications: antihypertensives, thiazide diuretics, alpha-adrenergic blockers, antipsychotics, antidepressants, alcohol, antiandrogens, ganglion blockers, and SSRIs.
8. Psychological: acute psychological distress, relationship distress, psychosexual skill deficit, disconnect between arousal and sexual situations masturbation style.

7.3.2 Diagnosis of DE

Patients should be assessed with a full medical and sexual history. Comprehensive physical examination should exclude anatomical and congenital abnormalities of male genitalia. Understanding the details of patients' ejaculation, as well as sexual habits, might be useful during the patients work-up. In this context, the impact of the disease is also useful to better tailor the therapeutic approach. Psychological evaluation might be useful if psychological distress appears to be relevant [44].

7.3.3 Treatment

1. *Psychological support:* patients with DE should be counselled by a psychology expert dealing with sexual issues. A basic understanding of the sexual cycle for their respective partners can assist men and women in managing expectations and evaluating their own sexual practices [72].
2. *Pharmacotherapy:* many therapeutic options exist in the context of DE. As such, even though neither the European Medicine Agency (EMA) nor the Food and Drug Administration (FDA) approval exist, agents like cabergoline, bupropion, alpha-1-adrenergic agonists, buspirone, oxytocin, testosterone, bethanechol, yohimbine, amantadine, cyproheptadine, and apomorphine have been used to treat DE, with varied success rates [73].
3. *Penile vibratory stimulation:* this should be used in selected cases (e.g., men with spinal cord-injuries) in conjunction with pharmacological therapy [74]. In this context, penile vibrators fall into two categories; (a) high-amplitude vibrators (tend to be more effective because they cover more surface area) and (b) low-amplitude vibrators. In this context, the Miami Project to Cure Paralysis estimated that 30–40% of men with spinal cord injury can ejaculate using a low-amplitude vibrator [75]. For men using a high-amplitude vibrator, the estimate is 55–85%. Penile vibratory stimulation may take place in a doctor's office or at home.

7.4 Retrograde Ejaculation

7.4.1 Aetiology

Retrograde ejaculation is a condition in which patients are unable to release semen since in the posterior urethra, it flows back into the bladder, as diagnosed by five or more spermatozoa/HPF in the urine sediment immediately after masturbation. Among the different causes of RE is possible to find spinal cord injuries, diabetic

neuropathies, colorectal surgeries, aortic aneurysm surgeries, thoracolumbar sympathectomies, retroperitoneal lymph node dissection surgeries, transurethral prostatectomies, and transurethral bladder neck incisions. Transurethral prostatectomies (e.g., TURP, THULEP, or HOLEP) are probably the most common surgical causes of RE. It affects more than 80% of patients undergoing these procedures [76]. Also, bladder neck surgery may cause RE, especially if performed in childhood [77]. Pharmacological aetiology is mainly related to antihypertensives, thiazide diuretics, α-1-adrenoceptor antagonists, antipsychotics, and antidepressants [73].

7.4.2 Diagnosis of RE

Men with RE present with reduced ejaculation or dry orgasm, cloudy urine post orgasm, due to the mixing of semen in the bladder with urine. A thorough history is essential in order to identify the underlying cause. The lower reference limit for semen volume is 1.5 mL (fifth centile, 95% confidence interval (CI) 1.4–1.7) as defined by the World Health Organization (WHO) [78]. Hypospermia or aspermia should highlight to the clinician the possibility of RE. Vroege et al. suggested that the analysis and confirmation of sperm in a post orgasmic urine sample could help differentiate between a failure of semen emission and RE [79]. Presence in the post-orgasmic urine of 10–15 sperm per high-power field would confirm the diagnosis of RE [80].

7.4.3 Treatment

Several medical approaches have been investigated in order to achieve antegrade ejaculation for natural reproduction in patients with RE. The tested substances include imipramine (tri-cyclic antidepressant), amoxapine (tri-cyclic antidepressant), B12 vitamin, pseudoephedrine (stimulation of α and β receptors in the urinary tract) as well as injection of collagen within the bladder neck [81–85]. One cross-over RCT treated 26 patients with amoxapine (50 mg daily) and B12 vitamin (500 μg three times per day), separately for a period of 4 weeks with each drug [82]. Amoxapine, which acts as a noradrenaline reuptake inhibitor, was effective in 80% of patients compared to only 16% success obtained in the vitamin B12 group. In another study, comparing the effects of imipramine 25 mg twice per day and pseudoephedrine 120 mg twice per day on RE in diabetic men, Arafa et al. [84] found a more moderate success rate of 38.5% with imipramine. However, the use of pseudoephedrine resulted in almost half of the patients having antegrade ejaculation and this increased to 61.5% when combining the two drugs. Of note, the side effects of sympathomimetics include dryness of mucous membranes and hypertension. Exploring a different approach to the problem, Kurbatov et al. injected collagen into the bladder neck to increase the constriction of the internal sphincter [83]. A total of 24 diabetic men were randomized to either a collagen or a saline injection, showing a small increase in antegrade ejaculate with a mean difference of 0.71 mL in favour of patients receiving collagen ($p < 0.05$).

Beyond the use of drugs, other methods have been proposed in order to manage infertility in RE. Standard sperm-retrieval techniques, such as testicular sperm extraction (TESE), and two different methods of sperm acquisition have been proposed [44]. Those include the following:

1. Centrifugation and resuspension of post-ejaculatory urine specimens: post-orgasmic urine sample is collected by introducing a catheter or spontaneous voiding. This sample is then centrifuged and suspended in a medium. The resultant modified sperm mixture can then be used in assisted reproductive techniques. A systematic review of studies is done in couples in which male partner had RE found a 15% pregnancy rate per cycle (0–100%) [86].
2. The Hotchkiss (or modified Hotchkiss) technique, which involves emptying the bladder prior to ejaculation, using a catheter, and then washing out and instilling a small quantity of Lactated Ringers to improve the ambient condition of the bladder. The patient then

ejaculates, and semen is retrieved by catheterization or voiding [87]. Modified Hotchkiss methods involve variance in the instillation medium. Pregnancy rates were 24% per cycle (0–100%) [86].

7.5 Anejaculation and Anorgasmia

7.5.1 Aetiology

The Diagnostic Manual of Mental Disorders defines inhibited ejaculation as the persistent or recurrent absence of attaining orgasm following sufficient sexual stimulation, which causes personal distress [64]. On the other hand, anejaculation can be classified as either a lifelong or acquired, or as global or situational. Any single or combination of psychological or medical disease, surgical procedure or drug which interferes with either central control of ejaculation, the afferent or efferent nerve supply to the vas, bladder neck, pelvic floor, or the penis, can result in inhibited ejaculation, anejaculation, and anorgasmia. Among the different aetiologies, a prominent role is occupied by multiple sclerosis, a demyelinating disease affecting the central nervous system—both the brain and the spinal cord [88]. Its effect on sexual function depends on the location of plaques in the central nervous system with ejaculatory dysfunction appearing in almost 50% of men with this condition [89].

7.5.2 Diagnosis

Medical/psychosexual history, social/religious history, medication list, and physical exam are the main part of the diagnosis. Penile sensitivity must be addressed, especially in men at risk for penile sensation loss such as those with diabetes mellitus. Symptoms and signs of endocrinopathies, such as testosterone deficiency, hypothyroidism, and hyperprolactinemia, should be sought. Masturbatory style is another useful line of inquiry as frequent masturbation or idiosyncratic masturbatory styles may play a role. Furthermore, identifying the onset is critical, whether lifelong or acquired. Next, understanding whether the condition is generalized or situational is also critical to understand the pathophysiology [90]. The role of laboratory testing, such a testosterone and TSH levels, is optional and is applied depending on patient symptoms. In patients complaining of loss of penile sensitivity, bio-thesiometry and/or pudendal somatosensory evoked potentials (SSEP) might be warranted [91].

7.5.3 Treatment

Although multiple psychodynamic and behavioural treatments for anorgasmia and anejaculation have been suggested, empirical evidence to support treatment efficacy is lacking [92]. Most reports are uncontrolled case reports with treatment ranging from a few brief sessions of sex education to the nearly 2 years of multiple-modality treatment in more complex multiple aetiologic cases. There has been limited success with pharmacologic therapies for the treatment of anejaculation. Cabergoline and bupropion are the two most trialled medications, though neither has been officially approved. Cabergoline is a potent dopamine receptor agonist. By increasing dopamine neurotransmission, it is thought to promote ejaculation. One study found that cabergoline in the treatment of 72 anorgasmic men showed improvement in 69% of men [93]. On the other hand, Bupropion blocks the reuptake of both norepinephrine and dopamine, is commonly used in depressed men when SSRIs cause delayed or anejaculation [94].

Another proposed therapeutic approach is the vibratory stimulation of the dorsal penile nerve. Three studies have investigated success rates and achieved successful retrieval in 32–96% of the patients [95–97]. Success was primarily dependent on amplitude of the stimulation. In a cohort of 66 men with spinal cord injury and anejaculation, Sønksen et al. [97] found better success rates with a 100 Hz frequency and an increasing amplitude of the stimulation plate spanning from 32% with an amplitude of 1 mm,

to 96% with an amplitude of 2.5 mm. In a similar setting with 211 spinal cord injury men, Brackett et al. [96] managed good results using an amplitude of 2.5 mm, resulting in sperm retrieval in 54.4% of the cases. Interestingly, there seem to be a better sperm quality with PVS as compared to EEJ [98].

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