Ejaculation and Orgasm Disorders

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Key Points:

1. Ejaculation and orgasm are distinct physiological events that are each coordinated by the nervous system. Disorders of ejaculation and orgasm are typically of complex and poorly understood etiology.
2. Premature ejaculation, a bothersome condition of poor ejaculatory control with decreased ejaculatory latency time, can be either lifelong or acquired. Although there are no FDA approved therapies, treatments include behavioral modifications, pharmacotherapy, and topical therapy. (**Table 2**)
3. Delayed ejaculation is an increased latency of ejaculation or inability to ejaculate that is bothersome. Though available treatment options are somewhat limited, cessation of any causative factors can be greatly beneficial. (**Figure 1**)

1. Introduction

Ejaculation is the process of semen expulsion from the urethra in individuals with a penis. **Orgasm** is the sensation of pleasure, relaxation, and/or satisfaction that accompanies sexual climax in men and women. It is believed that these pleasurable sensations are derived from central nervous system processing of afferent information from the pudendal nerve[1].

Orgasm and ejaculation are distinct physiological processes. Orgasm and ejaculation typically occur simultaneously in men, but one may occur without the other. Orgasm without ejaculation is most commonly observed in those who have had surgical treatment of the prostate; in these men ejaculation may be reduced or absent while orgasm is preserved[2].

Much of what is known about the neuronal and hormonal regulation of ejaculation has been gleaned from animal studies;[3] studies on the neurophysiology of orgasm/ejaculation in humans are difficult for logistical and ethical reasons.

The processes of ejaculation/orgasm are under the control of the nervous system. Ejaculation typically follows a period of sexual stimulation, which may be both **tactile** from stimulation of the penis and/or other body regions and **psychogenic** from emotional, mental, and sensory stimulation that accompany sexual activity. The precise triggers for orgasm are incompletely understood but appear to vary widely from person to person. **There is great heterogeneity in the amount and type of stimulation required to stimulate ejaculatory/orgasmic response**; this is thought to be related to biological, situational, interpersonal, genetic, neurochemical, and emotional factors[1].

Ejaculation is divided into two distinct events:[4]

1. *Emission*: During emission, sperm from the vas deferens are deposited in the posterior urethra. Simultaneously there is deposition of seminal fluid from the prostate and seminal vesicles. The bladder neck closes tightly to prevent retrograde flow of semen during the next phase of ejaculation. Most events in seminal emission are under the control of the sympathetic nervous system T10-L2 nerve roots extending to the pelvic plexus and from there to the hypogastric nerves[4]. Hence, they are not under voluntary control and may not produce distinct somatic sensations although most men will experience a sensation of "ejaculatory inevitability" during this phase. Oxytocin receptors have been identified in the epididymis; it is thought that these receptors may mediate epididymal contraction[5].
2. *Ejection*: During ejection, forceful contractions of the bulbospongiosus and ischiocavernous muscles in coordination with relaxation of the external urethral sphincter lead to expulsion of semen in an antegrade fashion from the urethra[1]. Tight coaptation of the bladder neck is essential in preventing retrograde ejaculation. This phase of ejaculation (other than bladder neck contraction) is mediated by the somatic nervous system from S2-S4 nerve roots and is therefore associated with distinct somatic sensation and orgasm[2].

2. Peripheral Control of Ejaculation

In men, tactile sensory input from the penis primarily arises from the glans, although stimulation of the entire external genitalia contributes to sexual response. The dorsal nerve of the penis conveys this afferent sensory information via the pudendal nerve to the

sacral spinal cord (S2-S4). The hypogastric nerve carries afferent sensory information to the thoracolumbar spinal cord (T10-L2)[3]. Efferent fibers are relayed from there to the pelvic (inferior hypogastric) plexus, the principle plexus that innervates the organs and muscles involved in emission and ejaculation[3]. This plexus is located posterolateral to the seminal vesicles and receives fibers from the hypogastric and pelvic nerves[3,6].

3. Central Nervous System (CNS) Control of Ejaculation

The pelvic processes of ejaculation are subject to substantial regulation at the level of the central nervous system.[3] **The medial pre-optic area (MPOA) of the brain appears to play a central role in ejaculation in animal models**. Electrical or hormonal stimulation of this area in animal models of sexual response induces ejaculation whereas ablation of this area prevents it.[3] The activity of the MPOA is driven by connections between the MPOA and various other brain regions salient to orgasm and ejaculation, such as the periaqueductal gray matter, the stria terminalis, the amygdala, and the thalamus[7]. Data on human brain regions relevant to ejaculation/orgasm are more controversial[7,8].

A marked decrease in pre-frontal cortical blood flow with sexual climax has been reported.[8] **The pre-frontal cortex controls executive functions and it thus seems that inhibition of this part of the brain is part of the orgasmic response**. This same study reported a marked increase in cortical blood flow to the left dentate nucleus, a region that may modulate pelvic contractions, and a moderate increase in blood flow to the ventrolateral transition zone of the midbrain and thalamus, a region associated with reward behaviors.

Stimulation of serotonergic 5-hydroxytryptamine (5-HT) receptors in the brain has variable effects on ejaculation. Whereas 5-HT 1A receptors appear to promote ejaculation by suppression of synaptic serotonin[9], 5-HT 2C receptors appear to suppress ejaculation.[10] **The general effect of serotonin in the CNS appears to be one of ejaculatory inhibition.**[3] This ejaculation delaying relationship underlies the suppression of ejaculation noted in men using serotonergic drugs, principally selective serotonin reuptake inhibitors (SSRIs)[3]. This side effect is used to beneficial effect in the management of men with premature ejaculation (PE).

Stimulation of dopaminergic D2 and D3 receptors in the CNS appears to stimulate ejaculation.[11] **Dopaminergic stimulation appears to increase a number of sexual behaviors (libido, erections)[11] in addition to clear effects on ejaculation.**[6]

Other signaling molecules and neurotransmitters known to play a role in central regulation of ejaculation and orgasm include oxytocin, acetylcholine, norepinephrine, prolactin, nitric oxide, glutamate, and gamma aminobutyric acid[7,11].

In the spine, thoracolumbar sympathetic fibers, the sacral parasympathetic nucleus, and Onuf's nucleus (somatic) are essential to regulation of ejaculation[12]. **Lumbar spinothalamic tracts (LST) appear to play a critical role as a pattern generator for ejaculation.**[13] These interneurons appear to be particularly essential for integrating afferent sensory and cortical information to produce motor and secretory neuronal activity that leads to ejaculation. The LST also appear to send fibers to the thalamus; this may play a role in central processing of orgasm[14].

4. Premature Ejaculation

4.1 Definitions

Over the last 50 years, numerous definitions of premature ejaculation have been proposed, used, and discarded. In an effort to further clarify the evaluation and management of ejaculatory and orgasmic dysfunction, the American Urological Association (AUA) and the Sexual Medicine Society of North America (SMSNA) jointly produced a **Guideline on Disorders of Ejaculation** in the summer of 2020.[15] In this guideline, lifelong (primary) premature ejaculation (PE) was defined as "poor ejaculatory control, associated bother, and ejaculation within about 2 minutes of initiation of penetrative sex that has been present since sexual debut."

This is in contrast to an older consensus definition by the International Society for Sexual Medicine (ISSM) in 2013 which centers on an intravaginal ejaculatory latency time of 1 minute. This definition does not define PE in terms of sexual behaviors other than vaginal intercourse due to absence of objective peer-reviewed data on ejaculation latency times in other contexts[16,17]. However, this does not address the sexual practices of many people, such as in men who have sex with men. Troublesome early ejaculation has been reported outside the setting of penis-in-vagina intercourse[17,18]. Moreover, studies on PE have been conducted mainly in Western countries and China and thus many ethnicities are not adequately represented. Data have also suggested that in addition to short ejaculation latency, men with PE are more likely than men without PE to report diminished pleasure and sensation with orgasm[19].

Importantly, an ejaculatory latency time (ELT) of less than 2 minutes is not sufficient to make a diagnosis; men must experience poor ejaculatory control and bother for the diagnosis to be applicable.

The **AUA/SMSNA 2020 Guideline** definition of acquired PE does not mention a specific cutoff for ELT.[15] Instead, to meet criteria for acquired PE, men must experience an ELT that is "markedly reduced" from prior sexual experience during penetrative intercourse. The expert panel notes a decrease of ELT by 50% or less than 2-3 minutes may be used as a rough marker of acquired PE, however given the paucity of data the panel recommends that clinicians exercise their own best judgment when making a diagnosis of acquired

PE. Again, bother is a necessary part of the diagnosis of PE.

It is important to acknowledge that men may complain of PE but not meet diagnostic criteria based on the ISSM 2013 or AUA/SMSNA 2020 definitions. Waldinger proposed that these men may be classified as having either “natural variable premature ejaculation” (NVPE, or variable PE) or “premature-like ejaculatory dysfunction” (PLED, or subjective PE). NVPE refers to situations in which a man may occasionally experience short ejaculation times as part of natural variation in his ELT. PLED refers to situations in which a man has an ELT within the normal range but experiences personal distress because the ELT is shorter than expected.[20] It is important to recognize that neither of these provisional diagnoses has been widely utilized nor validated.

4.2 Risk Factors and Pathophysiology

The **etiology of PE is unknown** although several risk factors have been hypothesized. These include: **depression,**[21] **psychological or interpersonal difficulties,**[22,23] **hypersensitivity of the glans penis,**[24] **robust cortical representation of the pudendal nerve,**[25] **disturbances in central serotonergic neurotransmission,**[26] **erectile difficulties and other sexual comorbidities,**[27] **prostatitis,**[28] **metabolic syndrome,**[29] **physical inactivity,**[30] **detoxification from prescribed medications,**[31] **recreational drugs,**[32,33] **chronic pelvic pain syndrome,**[34] **and thyroid disorders**.[35,36] It is important to recognize that lifelong and acquired PE likely have different physiological mechanisms; some of these conditions associated with PE may be relevant to just one of these PE sub-types. Though data are limited on the effects of COVID-19 on orgasm and ejaculation, no difference was found in intravaginal ejaculatory latency before and during the pandemic.[37]

4.3 Epidemiology

The prevalence of any form of PE has been estimated to be between 4% and 39% of men. This wide range can be attributed to the variability between incidence in stopwatch-based studies of ELT versus studies relying on single-item patient self-report.[38,39] Up to 60% of men self-report having either intermittent early ejaculation and/or other ejaculatory concerns.[40,41,42] Sense of control and/or bother is not routinely assessed and as such these higher estimates are likely not representative of true clinical PE.

In large stopwatch-based studies, ELT ranged from 0.5 minutes to 44 minutes (skewed to the right, with a median ELT of 5.4 minutes).[39] Epidemiological studies have suggested that SPE and NVPE are more common than either lifelong PE or acquired PE.[43,44] This relationship may be a driving factor for the relatively high prevalence of self-reported “PE” in large scale survey studies. The prevalence of clinical PE is likely <5%.[5]

4.4 Diagnosis and Evaluation

Diagnosis of PE is largely based on a detailed medical, psychological, relationship, and sexual history. **Table 1** lists questions that may be useful and relevant. In taking a detailed history, it is imperative to assess for erectile dysfunction, which may impact recommendations for treatment; the reader is referred to the **AUA Guideline on ED** and the Core Curriculum section on **Diagnosis** and **Treatment of ED** for more detail.

Patients often prefer that clinicians inquire about their sexual health; patients themselves may be hesitant to bring the topic up due to embarrassment, lack of time, or concern that the issue will not be taken seriously. A brief inquiry gives patients permission to discuss sexual concerns and also screens for associated health risks. Physical examination rarely contributes to the evaluation of PE, but a focused physical exam reassures patients and may reveal findings important for overall sexual function. The purpose of a targeted physical examination for the patient with acquired PE is to assess for associated/causal diseases.[45]

Additional testing, such as laboratory evaluation, is not necessary in the diagnosis of lifelong PE – history should be **sufficient**. However, laboratory testing may be considered if clinically indicated for other reasons. In acquired PE, laboratory testing is not a required element but can be utilized to obtain additional information if clinically **indicated**. Tests related to the hypothalamic-pituitary-testicular axis, thyroid function, glucose metabolism, prostatitis, or chronic pelvic pain syndrome can be employed if there is clinical suspicion for conditions which may impact a patient’s sexual and ejaculatory function.

Table 1: Questions that may aid in establishing a diagnosis of premature ejaculation
Focused sexual history related to PE
Do you have concerns about your ability to control ejaculation?
Do you ejaculate before you want to?
Is your premature ejaculation lifelong, or did it start after a period of “normal” ejaculation?
Do you feel you cannot postpone or delay ejaculation?
Do you experience negative interpersonal or relationship consequences because of PE?
Do you have anxiety because of PE?
Are you depressed because of PE?
Do you try to avoid sexual activity because of PE?
What is your estimated time to ejaculation (self-reported ELT)?
Does PE happen with every sexual encounter?
Does PE vary with different sexual partners?
Do you have PE with masturbation?
Does the use of a condom change your ELT?
Are there non-partner situational factors which alter your ELT (e.g., alcohol consumption, stress)?
Do you have difficulty achieving or maintaining an erection satisfactory for penetrative intercourse?
Questions about the patient’s sexual partner (questions can be directed to the partner if present and involved)
Has your partner mentioned your PE to you?
Has your partner expressed distress, bother, concern, or other feelings about your PE?
Has your partner requested you to get treatment for your PE?
What is your partner’s estimate of your ELT?
Does your partner have interest or lack of interest in sexual activity?

Does your partner have difficulty achieving climax?

Is there stress or strife in your relationship with your partner?

Relevant psychological history

Do you have (or have you ever had) a diagnosis of anxiety?

Do you have (or have you ever had) a diagnosis of a mood disorder, such as major depression or bipolar disorder?

Do you take (or have you taken) any psychiatric medications?

4.5 Counseling and treatment

A variety of pathways may be employed to counsel and treat men with PE. Psychotherapy, behavior modification, medications, and physical therapy may be used independently or in concert, depending on the patient's interest and **response**.[47,48,49]

Beyond these options, a small randomized controlled trial reported that moderate physical activity led to significant improvements in PE symptoms as reported on the Premature Ejaculation Diagnostic Tool; similar improvements were not seen in men randomized to minimal physical activity.[50] Although the evidence supporting this intervention is scant, the numerous health benefits of exercise make recommendations for increased physical activity a sensible course of action for any patient with or without symptoms of PE in concert with other forms of therapy.

4.5.1 Psychotherapy and Behavior Modification

The **AUA/SMSNA 2020 Guideline** recommends that clinicians consider referring men with PE to a mental health professional with expertise in sexual health.[15] Psychotherapy or sex therapy may be conducted in an individual, couple, or group framework. The essential premise is to focus on the psychological issues that have predisposed, precipitated or maintained PE symptoms. Anxiety, loss of self-confidence, and interpersonal tensions are examples of these issues.[51]

Behavioral therapy for PE focuses on intervening at the level of mounting sexual arousal to attempt to increase ELT. The most frequently used behavioral treatments are the **squeeze technique** and **stop-start technique**.[52,53] Both of these behavioral techniques are intended to help men recognize mid-level ranges of excitement that occur before ejaculatory inevitability. Men gain skills at identifying mid-level excitement by a series of graduated exercises beginning with self-stimulation, moving on to partner hand stimulation, then to intercourse without movement, and finally to stop-start penile thrusting with penetration. This process theoretically leads to gradual increase in ELT, sexual confidence, and self-esteem. There are few controlled studies to support this claim. However, animal studies have demonstrated that ejaculation latency time can be increased via training and that this is associated with changes to spinal centers critical to ejaculation.[54] This lends credence to the notion of behavioral training for management of PE.

4.5.2 Pharmacotherapy

There are currently no pharmacologic treatments that are approved by the United States Food and Drug Administration for management of PE; hence, all medications used for PE in the United States must be classified as "off-label" and patients should be advised as such. With that limitation in mind, several pharmacologic classes have gained traction for treatment of PE, including: traditional selective serotonin reuptake inhibitors (SSRIs), such as paroxetine, sertraline, or fluoxetine;[14,40] tricyclic antidepressants (TCAs), specifically clomipramine;[55] the short half-life SSRI dapoxetine (not approved for use in the United States but available in other countries);[52,56] topical penile local anesthetics;[57] and tramadol.[58] **Table 2** lists pharmacotherapies commonly utilized for PE, including dose ranges, adverse events, and half-life data.

Based on the AUA/SMSNA 2020 Guideline, **first-line offerings include daily SSRIs; on-demand clomipramine or dapoxetine; or topical penile anesthetics**.[15] For men who do not improve with first-line treatment, on-demand dosing of tramadol or daily dosing of alpha blocker agents (e.g., silodosin) may be considered. **For men with co-morbid ED and PE, the ED should be treated according to the AUA Guidelines on ED;**[59] **no specific guidance is provided regarding primacy of PE versus ED treatment**.

4.5.2.1 Selective Serotonin Reuptake Inhibitors (SSRIs) and Tricyclic Antidepressants (TCAs)

Daily treatment with the SSRIs **paroxetine** (10-40 mg), **sertraline** (50-200 mg), **fluoxetine** (20-40 mg), **citalopram** (20-40 mg), or the TCA **clomipramine** (12.5-50 mg), is usually effective in delaying ejaculation in men with PE. Of available SSRIs, **paroxetine appears to have the greatest degree of efficacy**.[60]

Ejaculation prolongation usually occurs within 5-10 days of starting treatment with SSRI or TCA but the full therapeutic effect may require 2-3 weeks of treatment and is usually sustained during long-term use.[49] A recent study suggested that there may be some variability in treatment efficacy based on polymorphisms of the dopamine transporter gene.[61]

Adverse effects of SSRIs are usually minor, start in the first week of treatment, and may gradually disappear within 2-3 weeks. Common adverse events include fatigue, yawning, sleepiness, mild nausea, diarrhea, or perspiration. There are anecdotal reports that decreased libido and ED are less frequently seen in non-depressed PE men treated by SSRIs compared to depressed men treated with SSRIs.[62] Men wishing to conceive with their partners should be advised that SSRIs may affect the motility of spermatozoa and therefore should weigh carefully the decision to start treatment with an SSRI for PE.[63] For patients who are concerned about the effect of SSRIs on sperm quality and overall fertility, a semen analysis and possible sperm banking may be recommended prior to initiation of treatment.

Neurocognitive adverse effects of SSRI include significant agitation and hypomania in a small number of patients; treatment with SSRIs should be avoided in men with a history of bipolar depression.[64] Caution should be exercised when prescribing SSRI to men with depression as suicidal ideation with initiation of therapy has been reported.[65] Providers should also be aware of the risk of serotonin

syndrome[66] with these agents even at low doses, particularly when combined with other medications. These agents include monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants, opioid drugs, antibiotics, herbal medications, antiemetics, recreational drugs, and other drugs with a serotonergic effect. The symptoms range from tremor, diarrhea, delirium, hypertension, seizures, hyperthermia and even death. Given the varied presentation, it can be missed with severe consequences.

On-demand administration of clomipramine, paroxetine, sertraline or fluoxetine 3-6 hours before intercourse is modestly efficacious and well tolerated but is associated with substantially less ejaculatory delay than daily treatment in most studies.[41,67,68]

4.5.2.2 Dapoxetine

Dapoxetine has received approval for the treatment of PE in over 50 countries worldwide but has not been approved by the United States Food and Drug Administration.[42-56] Dapoxetine is a rapid acting SSRI with short half-life (90-100 minutes); this pharmacokinetic profile underscores its efficacy as an on-demand treatment for PE.[69] No adverse drug interactions associated with dapoxetine have been reported.

In randomized controlled trials, dapoxetine 30 mg or 60 mg taken 1-2 hours before intercourse is more effective than placebo, resulting in a 2.5-3 fold increase in ELT, increased ejaculatory control, decreased distress, and increased satisfaction. Treatment related side effects were uncommon and dose dependent; the most common events included nausea, diarrhea, headache, and dizziness. There was no indication of an increased risk of suicidal ideation or suicide attempts and little indication of withdrawal symptoms with abrupt dapoxetine cessation. Although the drug has established efficacy, the discontinuation rate can be high (up to approximately 80% at 6 months). It is noteworthy that in these studies men with ELT greater than 2 minutes and those with concomitant symptoms of erectile dysfunction were more likely to discontinue.[70]

4.5.2.3 Topical Penile Local Anesthetics

Diminishing glans sensitivity may inhibit the spinal reflex arc responsible for ejaculation. The use of topical penile local anesthetics such as lidocaine and/or prilocaine as a cream, gel, or spray prior to intercourse is an established therapy and is effective in delaying ejaculation.[57,71,72,73] A meta-analysis of studies indicated that topical anesthetics were superior to placebo in prolonging ELT (six studies, mean difference in ELT 2.1-6.4 minutes depending on type of anesthetic).[74]

All topical anesthetics for PE carry the risk of significant penile hypoesthesia and possible transfer to the partner. This may result in numbness or irritation in the partner, which may be prevented by thoroughly washing the penis or covering it with a condom prior to any penetrative sexual activity.[71]

4.5.2.4 Tramadol

Tramadol is an opioid receptor agonist that also works as a serotonin and norepinephrine reuptake inhibitor. Given this mechanism of action there has been interest in this drug for use as an on-demand management option for PE. A meta-analysis indicated that tramadol is superior to placebo for management of PE with a pooled mean difference in ELT of 1.24 minutes versus placebo and improvement in various related parameters across different studies.[58] However, many experts have methodological concerns about one of the studies incorporated in this analysis.[75]

Common side effects of tramadol included constipation, dry mouth, nausea, and headache. In addition to minor side effects the opioid agonist activity of this medication raises concern regarding the potential for addiction and/or respiratory depression.[76] As this medication is indicated primarily for pain relief, in light of the ongoing opioid epidemic in the United States, extreme caution should be exercised when considering use of the drug off-label for management of PE. With caution, it may be used in patients who have failed first-line therapy per the 2020 AUA/SMSNA guideline.[18]

4.5.2.5 Other pharmacologic treatments

In patients who have failed first-line therapy of behavioral modification, SSRI/TCA, and topical anesthetics, the use of α1-Adrenoceptor antagonists is supported, though there is a paucity of high quality data.[77] A small randomized study of men with self-reported PE who failed dapoxetine suggested that the oral alpha-receptor antagonist silodosin, administered on demand, led to improvements in ejaculatory function.[78] Given that these patients self-reported PE and were not diagnosed based on an evidence based definition, these results should be interpreted with caution.

Phosphodiesterase type 5 inhibitors (PDE5I) can be used to treat comorbid ED[79] but do not have a role as first line monotherapy.[80]

A randomized controlled trial of testosterone supplementation in men with low serum testosterone levels demonstrated improvements in ejaculatory function but no changes in bother.[81] This was not a study of men with clinical PE and as such should not be interpreted as evidence for testosterone as a treatment for ejaculatory disorders.

Studies of oxytocin receptor antagonist cligosiban have been mixed, with one randomized trial finding no difference in ELT versus placebo.[82] And another finding a mean increase of ELT of 61.0 seconds for cligosiban compared to 16.4 seconds with placebo.[83]

Table 2: Summary of Recommended First-Line Pharmacological Treatments for Premature Ejaculation

Drug	Daily Dose/On Demand	Dose	ELT Fold Increase	Side Effect	Status	Half-Life
Oral Therapies						
Dapoxetine[69]	On Demand	30-60mg	2.5-3	Nausea Diarrhea Headache Dizziness	Approved in some countries	1.3-1.5hrs
Paroxetine[84]	Daily Dose	10-40mg	8	Fatigue Yawning Nausea Diarrhea Perspiration Decreased Sexual Desire Erectile Dysfunction	Off Label	
Clomipramine[85]	Daily Dose	12.5-50mg	6		Off Label	32 hrs
Sertraline[40]	Daily Dose	50-200mg	5		Off Label	23-26 hrs
Fluoxetine[86]	Daily Dose	20-40mg	5		Off Label	3-6 days
Citalopram[87]	Daily Dose	20-40mg	2		Off Label	35 hrs
Paroxetine[88]	Daily dose for 30 days and then On demand	10-40mg	11.6		Off Label	21-24 hrs
Clomipramine[55,88]	On Demand	12.5-50mg	4		Off Label	19-37 hrs
Tramadol[58,89]	On Demand	25-100mg	4-5		Off Label	6 hrs
Topical Therapy						

Lidocaine/Prilocaine[53]	On Demand	25 mg/gm Lidocaine 25 mg/gm Prilocaine	4-6.3	Penile numbness Partner genital numbness Skin irritation Erectile Dysfunction	Approved in some countries[73]	

4.5.3 Combining Pharmacotherapy with Psychotherapy and Behavioral Modification

Combining medical and psychological/behavioral interventions harnesses the power of both therapies to provide patients with rapid symptom amelioration, while the psychological and interpersonal issues that either precipitated or maintained the symptom are addressed.[90,91,92] The **AUA/SMSNA 2020** Guideline suggests that clinicians should advise men that the combination of approaches may be more effective than either modality alone.[15]

4.5.4 Physical Therapy

Physical therapy has been promoted by some authorities to enhance control of ejaculation. A recent meta-analysis indicated that physical therapy (primarily pelvic floor muscle training) was associated with clinically relevant improvement in ELT in men with PE.[47] Incorporation of masturbatory retraining may also be of benefit.[93] Studies included in the meta-analysis were heterogeneous and the overall evidence quality is low.[47] As the treatment is of relatively low risk (aside from potential cost), it may be considered as an option in settings where a qualified pelvic floor physical therapist is available.

4.5.5 Novel Therapies

There has been recent interest in oxytocin receptor antagonists for management of PE. The novel compound cligosiban represents an entirely new strategy for management of PE, relying on inhibition of oxytocinergic pathways rather than activation of serotonergic pathways. This drug is not yet approved for clinical use in any country. Preliminary publications have indicated that the drug appears safe in healthy volunteers.[94] Two similar phase II clinical trials of cligosiban (PEPIX trial and PEDRIX trial) were published simultaneously but reported contradictory results.[82,83]

5. Delayed Orgasm/Ejaculation and Anorgasmia

5.1 Definition

Delayed or absent orgasm is a poorly understood phenomenon. The 2020 SMSNA/AUA Guidelines on Disorders of Ejaculation characterize delayed ejaculation as either lifelong or acquired consistent, bothersome inability to achieve ejaculation, or an increased latency of ejaculation, despite adequate sexual stimulation and the desire to ejaculate.[15] This definition is similar to that of the **Diagnostic and Statistical Manual 5th edition (DSM-V), which likewise does not use a time-based definition.**[95] Ejaculation that takes more than two standard deviations above the mean ELT has been used to identify delayed ejaculation in population studies;[96] this equates to approximately 25-30 minutes although exhaustion prior to orgasm leading to cessation of sexual activity in otherwise healthy and fit individuals may also be taken as evidence for delayed orgasm.[97]

5.2 Risk Factors and Pathophysiology

Risk factors that have been associated with delayed ejaculation/orgasm include use of SSRI agents, increasing age, ED, diabetes, depression, lower urinary tract symptoms, low serum testosterone, penile sensory loss, idiosyncratic masturbation, and penile hyperstimulation.[98,99,100,101,102,103] Most studies to date have relied on patient self-report so caution should be exercised in interpreting the results.

Failure to achieve orgasm may be due to inadequate sexual stimulation (as may occur with loss of erection during penile stimulation, penile neuropathy, or absence of sexual excitement) leading to failure to initiate emission or due to disruption of the events of the emission phase. **Suppression of the normal central nervous system arousal responses which trigger sexual climax is also a prominent cause of ejaculatory dysfunction; the most common acquired etiology for this phenomenon is likely anti-depressants or other central nervous system acting drugs**[90] (ethanol,[1] antipsychotics,[104] opioids,[105] etc). Cerebrovascular accident has also been associated with impairment of orgasm response.[106] Hypothyroidism[107] and testosterone deficiency syndrome[10,108] are potential etiologies for delayed ejaculation/orgasm.

Conditions that are known to be associated with failure of emission include obstruction or ablation of the glandular elements that contribute to emission (e.g., transurethral resection of the prostate, transurethral needle ablation, etc),[109,110] neuropathic conditions such as diabetes or spinal cord injury,[111] and use of some alpha blocker medications.[112] **It is important to note that alpha blockers appear to lead to ejaculatory dysfunction by suppression of emission.**[113,114] A decline in ejaculate volume has also been reported as a side effect of 5-alpha reductase inhibitors although the phase of ejaculation impacted by these drugs is not entirely clear.[115]

Psychosocial variables are always important to consider in the setting of delayed ejaculation/orgasm. **Relationship stress, conflict with the partner, and personal antipathy towards sexuality may compromise sexual responses and inhibit sexual climax.**[1,85] Some authors have postulated that a history of intense penile self-stimulation (variably called idiosyncratic or traumatic masturbation) may predispose men to difficulty achieving orgasm with partnered intercourse; the hypothesis is that conditioning leads to insufficiency of any other form of stimulation to trigger climax.[116,117] While there is some evidence to support the association between reliance on intensive penile stimulation during masturbation and difficulty reaching climax with partnered sex, causality has not been

established. It is plausible to hypothesize that men who intrinsically require more intense stimulation to reach climax will develop intense masturbation styles to compensate.

5.3 Epidemiology

Difficulty attaining orgasm is a common sexual complaint. **In the Global Survey of Sexual Attitudes and Beliefs, over 14% of men aged 40-80 years worldwide reported difficulty achieving orgasm.**[102] An older study from the United States suggested a prevalence of difficulty achieving orgasm in approximately 8% of men aged 18-59 years.[103]

5.4 Diagnosis and Evaluation

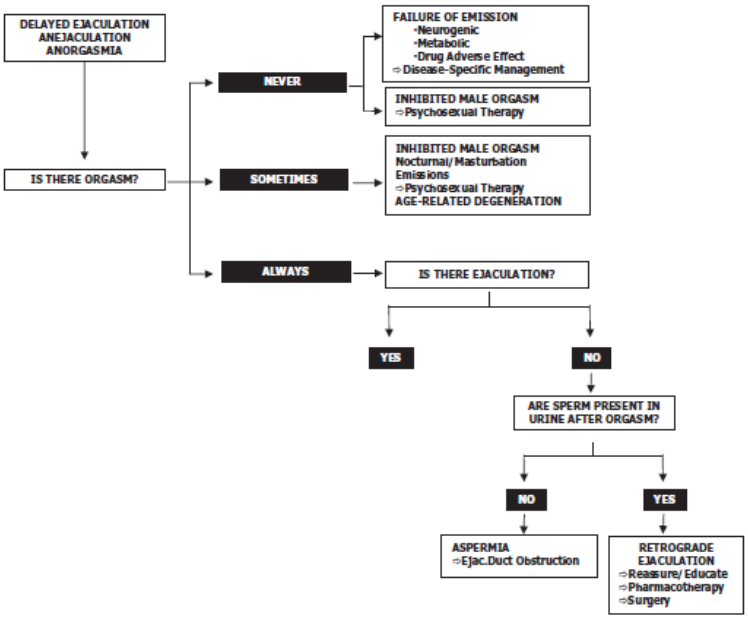

Figure 1: Algorithm for Assessment of Patient with Delayed Orgasm/Ejaculation, adapted from McMahon et al 2013

Evaluation of the man with delayed or absent orgasm/ejaculation should proceed along standard lines with a detailed history and physical examination. Precise characterization of the presenting concern is necessary as most men equate ejaculation and orgasm.[1] An algorithm for assessment of the patient with delayed ejaculation/orgasm (adapted from McMahon et al.)[1] is presented in **Figure 1**. Note that the recommendation for assessment of testosterone (T) is controversial; some studies have reported impairment of orgasm/ejaculation in men with low T[108] whereas others have not found such an association.[118,119]

5.5 Treatment

There are currently no US FDA approved medical therapies for delayed orgasm in men.[1]

5.5.1 Psychotherapy/Behavior Modification

Psychosexual counseling may be of great use in primary inhibited orgasm and as an adjunct in cases of delayed orgasm/ejaculation secondary to medical condition.[91] Attempts should be made to optimize erectile function as inadequacy of penile tumescence for satisfactory stimulation may contribute to many cases of orgasmic difficulty.[1] Men and their partners should also be encouraged to experiment with alternative forms of sexual stimulation (e.g., change in sexual position, manual stimulation of the penis by man or his partner, oral sex, use of sexual enhancement products such as lubricants or vibrators) as this may permit more intense stimulation of the penis and triggering of orgasm. Use of vibrators has been used to good effect in inducing ejaculation in men with spinal cord injury.[120]

5.5.2 Cessation of SSRI Agents

Cessation of drugs known to interfere with orgasm, most commonly anti-depressants of the SSRI class,[10,100] **should be considered; in some cases substitution or augmentation of the SSRI with a dopaminergic drug (e.g., bupropion, buspirone) may be of utility in restoring orgasmic response.**[121] Dopaminergic drugs may be useful even outside the context of SSRI induced sexual dysfunction.[122]

5.5.3 Hormone Therapy

Testosterone deficiency (hypogonadism) has been associated with blunted dopaminergic response in rat models; this effect can be

reversed by androgen supplementation.[123] Some human studies have also suggested a decline in orgasmic function with progressively lower serum androgens.[108] However, other studies have not found an association between testosterone and orgasmic delay,[118,119] supplementation should be considered only if indicated by other clinical signs of hypogonadism. There are some data on the clinical efficacy of exogenous testosterone supplementation for orgasmic dysfunction in humans[116,117] but further studies are needed.

5.5.4 Orgasmic Disorders

Cabergoline and bupropion have been used with some success in management of delayed ejaculation.[124] The largest study to date of cabergoline, a dopamine agonist, for male orgasmic disorders (n=131) reported subjective improvement in approximately 66% of cases.[125] Case reports have suggested that intranasal oxytocin,[107,126] amantadine,[127] and cryoheptidine,[128] may have utility in hastening orgasmic response but the dearth of robust evidence mandates that these be considered experimental therapies. Penile vibratory stimulation may also be useful for some men with delayed or absent orgasm.[124]

6. Miscellaneous Orgasm/Ejaculation Disorders

6.1 Retrograde and Anejaculation

Medical and surgical therapies for lower urinary tract symptoms (LUTS) and benign prostate hyperplasia (BPH) are frequently associated with disturbances of ejaculation. Medical and surgical therapies for LUTS/BPH may lead to anejaculation or retrograde ejaculation, the latter being particularly common with transurethral resection of the prostate (TURP).[129] The incidence of ejaculation disturbance after TURP has been reported as high as 70%.[130] Spinal cord injury, neurologic disease, retroperitoneal lymph node dissection and other retroperitoneal surgeries, are among other potential causes.[131] A number of options for medical management of retrograde and anejaculation have been described such as dextroamphetamine, imipramine, phenylephrine and pseudoephedrine.[132] Data are too limited at this point to clearly support the use of any medication over another.

6.2 Declining Orgasmic Function

Non-specific declines in “orgasmic function” are common after pelvic surgery, particularly endoscopic or open prostate procedures. Declines in orgasmic function may also be common in men treated with radical prostatectomy for prostate cancer. In one study, 60% of the men who were studied experienced declines in subjective orgasmic function. An age less than 50 years and better orgasmic function prior to surgery were predictive of better recovery. In most cases post-operative recovery of orgasmic function plateaued at two years post-operatively.[133] This has also been seen after radiation therapy for prostate cancer.[134]

6.3 Painful Orgasm

Pain with orgasm/ejaculation has been reported in 1-10% of men and may be localized to any part of the genitals and perineum.[131] Conditions commonly associated with ejaculatory pain include chronic pelvic pain syndrome,[135] ejaculatory duct calculi, BPH, prostatitis, prior hernia repair, and other etiologies.[131] Ejaculatory pain is typically treated as a pain syndrome; please refer to the Core Curriculum on **Chronic Pelvic Pain Core**.

6.4 Climacturia

Climacturia is the involuntary loss of urine during orgasm[134] and is typically associated with prostate cancer treatments. This has been found to occur in 5.2% of patients after prostate radiation therapy and 28.3% of men after radical prostatectomy, although it does appear to reduce over time after radical prostatectomy.[136] Treatments include behavioral modifications, such as urinating before sexual activity, using a condom, or using penile constriction rings or loops.[134] Pelvic floor muscle training may also be effective.[137] Surgical therapies for urinary incontinence can be helpful, such as male sling or artificial urinary sphincter placement.[134] More recently, placement of a “mini-jupette” sling at the time of penile prosthesis placement is designed to compress the urethra when the implant is inflated. Comparative studies are still needed to understand its role in climacturia.[138]

7. Conclusions

Disorders of ejaculation and orgasm in men are poorly understood. A careful history and physical examination is essential to evaluation. A limited number of medical therapies have been advanced as potential solutions for ejaculation disorders. Behavioral and psychotherapy interventions are often helpful in these cases. Often, a combination of treatments may be required for durable improvement in a patient’s sexual function. The AUA/SMSNA 2020 Guideline on Disorders of Ejaculation is a potent resource for clinicians seeking further information on how to evaluate and treat men with ejaculatory concerns.[45]

8. Patient Resources

Premature Ejaculation

https://www.sexhealthmatters.org/premature-ejaculation

https://www.issm.info/sexual-health-conditions/premature-ejaculation/

Delayed/Absent Ejaculation

https://www.sexhealthmatters.org/retrograde-ejaculation

https://www.issm.info/sexual-health-conditions/retrograde-ejaculation/

https://www.sexhealthmatters.org/delayed-ejaculation

https://www.issm.info/sexual-health-conditions/delayed-ejaculation/

https://www.sexhealthmatters.org/anejaculation

https://www.issm.info/sexual-health-conditions/retrograde-ejaculation/

9. Abbreviations

5-HT: 5-hydroxytryptamine
APE: Acquired Premature Ejaculation
BPH: Benign Prostate Hyperplasia
DSM-V: Diagnostic and Statistical Manual, 5th edition
ED: Erectile Dysfunction
ELT: Ejaculation Latency Time
ISSM: International Society for Sexual Medicine
LA: Local Anesthetic
LPE: Lifelong Premature Ejaculation
LST: Lumbar Spinothalamic Fibers
LUTS: Lower Urinary Tract Symptoms
MPOA: Medial Preoptic Area
NVPE: Natural Variable Premature Ejaculation
PDE5I: Phosphodiesterase type 5 Inhibitors
PE: Premature Ejaculation
PLED: Premature-Like Ejaculatory Dysfunction
SSRI: Selective Serotonin Reuptake Inhibitor
TCA: Tricyclic Antidepressant
TD: Testosterone Deficiency
TURP: Transurethral Resection of the Prostate

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