MedicineToday 2012; 13(8): 50-57

PEER REVIEWED FEATURE
POINTS: 2 CPD/2 PDP

Delayed ejaculation: a management challenge

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Key points

- The causes of delayed ejaculation and anejaculation are manifold.
- Failure of ejaculation can be a lifelong problem (25%) or an acquired problem (75%). It may be global and occur in every sexual encounter, or be intermittent or situational.
- Treatment of men with delayed ejaculation should be aetiology specific and address the issue of infertility in men of reproductive age.
- Drug treatment of men with delayed or inhibited ejaculation has met with limited success.

Delayed ejaculation and anejaculation are probably the least understood of the male sexual dysfunctions. However, their impact is significant because they may result in a lack of sexual fulfilment for both the man and his partner.

Ejaculatory dysfunction is one of the most common male sexual disorders. The spectrum of ejaculatory dysfunction extends from premature ejaculation, through delayed ejaculation (anorgasmia) to a complete inability to ejaculate (anejaculation) and also includes retrograde ejaculation (when semen enters the bladder instead of exiting through the urethra).

Delayed ejaculation, anejaculation and anorgasmia can result from any psychological or medical disease or surgical procedure that interferes with:

- central control of ejaculation
- peripheral sympathetic nerve supply to the vas deferens and bladder neck
- somatic efferent nerve supply to the pelvic floor
- somatic afferent nerve supply to the penis.

As such, the causes of delayed ejaculation and anejaculation are manifold (Table 1).

ANATOMY AND PHYSIOLOGY OF THE EJACULATORY RESPONSE

The ejaculatory reflex comprises sensory receptors and areas, afferent pathways, cerebral sensory areas, cerebral motor centres, spinal motor centres and efferent pathways. Neurochemically, this reflex involves a complex interplay between central serotonergic and dopaminergic neurons, with secondary involvement of cholinergic, adrenergic, oxytocinergic and gamma aminobutyric acid (GABA) neurons. Serotonin, which inhibits emission/ejaculation, and dopamine, which promotes seminal emission/ejaculation, have emerged as key neurochemical factors.[1]

DEFINITION AND CHARACTERISTICS OF DELAYED EJACULATION/ ANEJACULATION

Delayed ejaculation (also known as inhibited or retarded ejaculation) and anejaculation

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TABLE 1. CAUSES OF DELAYED EJACULATION, ANEJACULATION AND ANORGASMIA

Category	Cause
Ageing	• Degeneration of penile afferent nerves
Psychogenic	• Inhibited ejaculation
Congenital	• Mullerian duct cyst • Wolfian duct abnormality • Prune belly syndrome
Anatomical	• Transurethral resection of prostate • Bladder neck incision
Neurogenic	• Diabetic autonomic neuropathy • Multiple sclerosis • Spinal cord injury • Radical prostatectomy • Proctocolectomy • Bilateral sympathectomy • Abdominal aortic aneurysmectomy • Para-aortic lymphadenectomy
Infective	• Urethritis • Genitourinary tuberculosis • Schistosomiasis
Endocrine	• Hypogonadism • Hypothyroidism
Medication	• Alpha-methyldopa • Thiazide diuretics • Tricyclic and SSRI antidepressants • Phenothiazine • Alcohol abuse

ABBREVIATION: SSRI = selective serotonin reuptake inhibitor.

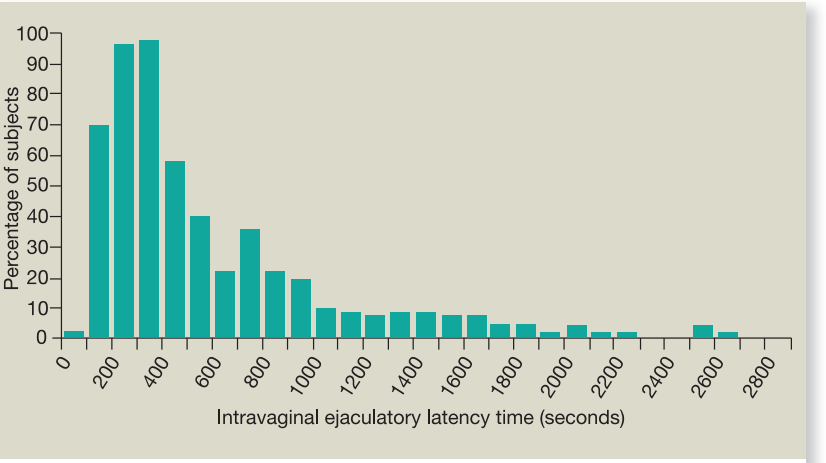


Figure. Distribution of intravaginal ejaculatory latency times (IELT) values in a random cohort of 491 men with a median IELT of 5.4 minutes.[4]

are probably the least common, least studied and least understood of the male sexual dysfunctions. However, their impact is significant in that they typically result in a lack of sexual fulfilment for both the man and his partner, an effect further compounded when procreation is among the couple's goals of sexual intercourse.

The *Diagnostic and Statistical Manual of Mental Disorders (DSM) IV-TR* defines delayed ejaculation as '…the persistent or recurrent delay in, or absence of, orgasm after 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 disturbance causes marked distress or interpersonal difficulty; it should not be better accounted for by another Axis I (clinical) disorder or caused exclusively by the direct physiologic effects of a substance or a general medical condition.'[2]

There are no clear criteria for when a man actually meets the conditions for delayed ejaculation, because operationalised criteria do not exist. Given that most sexually functional men ejaculate within about 5.4 minutes following intromission,[3] a clinician might assume that men with latencies beyond 25 to 30 minutes (about two standard deviations above the mean) who report distress or men who simply cease sexual activity due to loss of erection, exhaustion, irritation or partner request qualify for this diagnosis (Figure).[4]

Failure of ejaculation can be a lifelong problem (about 25% of affected men) or an acquired problem (the remainder). It may be global and occur in every sexual encounter, or be intermittent or situational. Many men

TABLE 2. RECOMMENDED AND OPTIONAL QUESTIONS TO ESTABLISH THE DIAGNOSIS OF DELAYED EJACULATION

Aim of questions	Questions
Recommended questions	
To aid diagnosis	• How often can you ejaculate during sexual intercourse? • During intercourse, how long after penetration does it take for you to either ejaculate or stop intercourse? • When you cannot ejaculate during sexual intercourse, how often do you feel that you are close to ejaculation? • If you cannot ejaculate, why do you stop intercourse? • Do you ever feel that you have ejaculated but fail to release semen? • Do you feel bothered, annoyed and/or frustrated by your delayed ejaculation? • How often can you ejaculate during masturbation by yourself or with your partner?
Optional questions	
To differentiate between lifelong and acquired delayed ejaculation	• When did you first experience delayed ejaculation? • Have you experienced delayed ejaculation since your first sexual experience on every or almost every attempt and with every partner?
To assess erectile function	• Is your erection hard enough to achieve penetration? • Do you have difficulty in maintaining your erection during intercourse?
To assess relationship impact	• How upset is your partner with your delayed ejaculation? • Do you or your partner avoid sexual intercourse? • Is your delayed ejaculation affecting your overall relationship?
To assess previous treatment	• Have you received any previous treatment for your delayed ejaculation?
To assess impact on quality of life	• Do you feel anxious, depressed or embarrassed because of your delayed ejaculation?

with acquired delayed ejaculation can masturbate to orgasm, whereas others, for multiple reasons, will or can not. Loss of masturbatory capacity secondary to emotional or physical trauma is also seen. About 75% of men with delayed ejaculation can reach orgasm through solitary masturbation, whereas the remainder fail to ejaculate.

PATHOPHYSIOLOGY OF DELAYED EJACULATION

Several pathophysiologies have been associated with ejaculatory problems. These include congenital disorders as well as ones caused by trauma, infection, disease and treatment for other disorders (Table 1). When a medical history or symptomatology so indicates, investigation of such possible aetiologies may be necessary.

The most common causes of delayed ejaculation seen in clinical practice are:

- degeneration of psychogenic factors, penile afferent nerves and Pacinian corpuscles in the ageing male
- diabetic autonomic neuropathy
- use of selective serotonin reuptake inhibitor (SSRI) antidepressants and major tranquillisers
- radical prostatectomy or other pelvic surgery.

Psychogenic delayed ejaculation is usually related to sexual performance anxiety, which may draw the man's attention away from erotic cues that normally serve to enhance arousal. Other psychodynamic explanations emphasise psychosexual development issues and have attributed lifelong delayed ejaculation to a wide range of conditions, including fear, anxiety, hostility, orthodoxy of religious belief and relationship difficulties.[5,6] Idiosyncratic and vigorous masturbation styles that cannot be replicated during intercourse with a partner or an 'autosexual' orientation where men derive greater arousal and enjoyment from masturbation than from intercourse are risk factors for delayed ejaculation.[7] Disparity between the reality of sex with the partner and the sexual fantasy used during masturbation may inhibit sexual arousal and thus represent another contributor to delayed ejaculation.

Delayed ejaculation and anejaculation are commonly seen in men with hypothyroidism and occasionally in men with hypogonadism. The ability to ejaculate may be severely impaired in men with multiple sclerosis, diabetic autonomic neuropathy or a spinal cord injury.[8] Fewer than 5% of patients with a complete upper motor neuron lesion and almost all with incomplete lower motor neuron lesions retain the ability to ejaculate.

EVALUATION OF MEN WITH DELAYED EJACULATION

Evaluation of men presenting with delayed ejaculation or anejaculation should include

a full medical and sexual history, a focused physical examination, determination of serum testosterone levels and any additional investigations suggested by these findings.

Assessment begins by determining whether delayed ejaculation is lifelong or acquired and global or situational (Table 2). Evaluation includes establishment of how often a man can ejaculate during intercourse and the intravaginal ejaculation latency time (the time elapsed between penetration and ejaculation). If the patient reports a failure to ejaculate, the duration of intercourse before it is suspended, the reasons for suspension of intercourse (e.g. fatigue, loss of erection, a sense of ejaculatory futility or partner request) and whether ejaculation can occur during postcoital self or partner-assisted masturbation must be determined. The presence or absence of premonitory ejaculatory sensation during intercourse or masturbation suggests achievement of sufficient arousal to almost attain the ejaculation threshold. Variables that the patient thinks improve or worsen performance should be noted. The man's ability to relax, sustain and heighten arousal and the degree to which he can concentrate on sensations should also be noted.

The presence and extent of patient-, partner- or interpersonal-related negative psychological consequences, such as bother, distress, frustration or the avoidance of sexual contact, should be established. The frequency of intercourse and the identity of the initiator of sexual contacts are useful surrogate measures for these negative psychological consequences. The quality of the nonsexual relationship should also be explored.

In men with acquired delayed ejaculation, previous illness, surgery and medication use, and life events and circumstances should be reviewed. The events may include a variety of life stressors and other psychological factors – for example, following his wife's mastectomy where the man is afraid of hurting her and therefore is only partially aroused. Societal and religious attitudes that may interfere with excitement should be noted, such as the 'spilling of seed as a sin'.

A focused physical and genital examination to determine whether the testes and epididymes are normal and whether the vasa deferentia are present or absent on each side, supported by a screening morning total testosterone level and any other hormonal or imaging investigations indicated by either history or physical examination will identify or exclude organic disease. Digital rectal examination to determine prostate size, anal sphincter tone and quality of the bulbocavernous reflex is indicated in most men with the exception of young men with situational and clear psychogenic inhibited ejaculation. The presence of a neuropathy may require electrophysiological evaluation of neural pathways controlling ejaculation, pudendal somatosensory and motor evoked potentials, the sacral reflex arc and sympathetic skin responses.

The occurrence of orgasm in the absence of prograde ejaculation suggests a diagnosis of retrograde ejaculation and can be confirmed by the presence of spermatozoa in postmasturbation first-void urine. If the aetiology of delayed ejaculation is unclear, culture of expressed prostatic secretion and urine, urine cytology and measurement of serum prostate specific antigen levels will exclude prostatitis and bladder and prostatic cancers. An ultrasound scan of the testicles and epididymes may define any local disease.

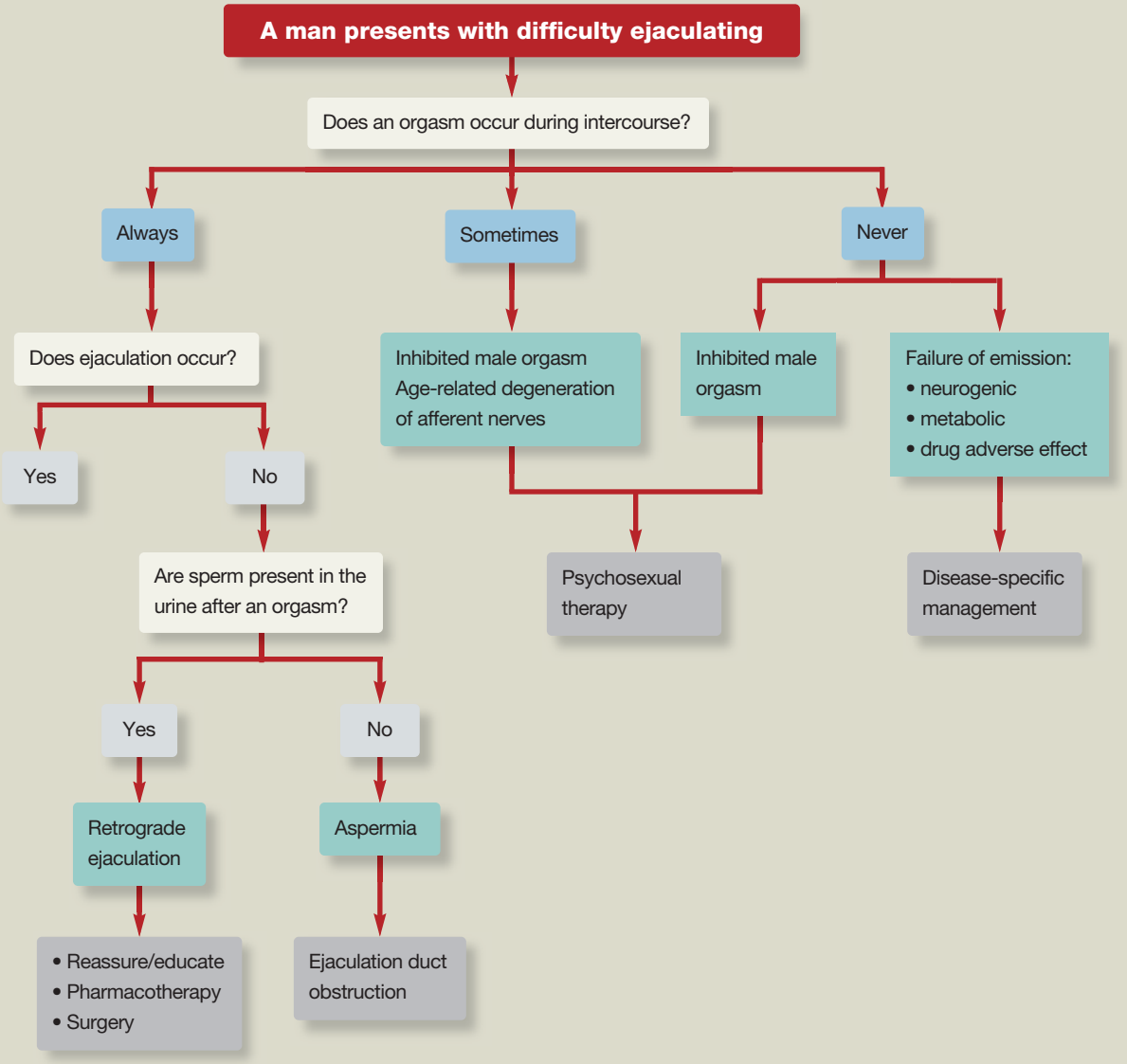
Patients with unilateral or bilateral ejaculatory duct obstruction or congenital absence of vasa deferentia usually present with a thin/runny low volume of semen, aspermia and infertility. Seminal analysis demonstrates azospermia or oligospermia with a low concentration of fructose and a low pH. Ultrasound scanning of the entire urinary system and referral of the patient to a urologist is indicated as coexisting renal anomalies may be present. Bilateral absence or malformation of the vasa deferentia may be associated with the cystic fibrosis gene.[9] A flowchart showing an approach to the management of men having difficulty ejaculating is provided on page 54.[10]

TREATMENT OF MEN WITH DELAYED EJACULATION

Treatment of men with delayed ejaculation should be aetiology specific and address the issue of infertility in those of reproductive age. It may also include patient or couple psychoeducation and/or psychosexual therapy, pharmacotherapy or integrated treatment. Men of reproductive age undergoing pelvic surgery and their partners should be informed of the risk of infertility due to anejaculation and the availability of sperm harvesting and assisted reproductive techniques.

Whether a clear pathophysiological cause is present or absent, patients may be counselled to consider lifestyle changes, including enjoying more time together to achieve greater intimacy, minimising

AN APPROACH TO THE MANAGEMENT OF MEN HAVING DIFFICULTY EJACULATING



alcohol consumption, making love when not tired and practising techniques that maximise penile stimulation, such as pelvic floor training.[5] Neuropathic delayed ejaculation is usually irreversible and therefore the patient might be counselled to seek alternative methods to achieve mutual sexual satisfaction with his partner.

Psychological strategies

If organic and pharmacological causes of delayed ejaculation have been eliminated, referral of the patient to an expert psychosexual therapist is usually indicated to evaluate the causative psychological and behavioural issues. Beneficial effects through psychotherapy depend on the severity of the delayed ejaculation and the individual's receptiveness to engage in counselling and adhere to the counsellor's recommendations.

The man's partner and the quality of the relationship warrant exploration. Numerous psychotherapeutic processes are described for the management of men with delayed or inhibited ejaculation[11,12] and some appear to be effective,

TABLE 3. PHARMACOTHERAPY FOR DELAYED OR INHIBITED EJACULATION

Drug*	Dose	Dosing instructions
Amantadine	100 to 200 mg	On demand, for 2 days prior to intercourse
	100 to 200 mg	Twice daily
Bupropion	150 mg	Once or twice daily
Buspirone	5 to 15 mg	Twice daily
Cabergoline	2.5 to 5 mg	Twice weekly
Cyproheptadine	2 to 6 mg	On demand, 3 to 4 hours prior to intercourse
Pseudoephedrine	60 to 120 mg	On demand, 1 to 2 hours prior to intercourse
Reboxetine	4 to 8 mg	Once daily

* All drugs are used off label for the treatment of men with delayed or inhibited ejaculation.

but none has been properly evaluated in large-scale samples.[13] These psycho - therapeutic strategies include:

- sex education
- reduction of goal-focused anxiety
- increased and more genitally-focused stimulation
- patient role playing an exaggerated ejaculatory response on his own and in front of his partner
- masturbatory retraining
- re-alignment of sexual fantasies and arousal strategies.

Most current sex therapy approaches to delayed ejaculation emphasise the importance of masturbation in the treatment of delayed ejaculation, with most of the focus on 'masturbatory retraining' integrated into sex therapy.[14] Typically, self-stimulation techniques incorporating fantasy can be used to achieve incremental increases in arousal that eventually enable orgasm. Fantasy can serve the purpose of increasing arousal and blocking inhibiting thoughts that might otherwise interfere. Once the man's ejaculatory ability is established through masturbation, the same skill set can be incorporated into sex with his partner.

An important component in the treatment of men with any type of delayed ejaculation is the removal of the 'demand' (and thus anxiety-producing) characteristics of the situation.[11] 'Ejaculatory performance' anxiety can interfere with the erotic sensations of genital stimulation and may result in levels of sexual excitement insufficient for climax (although they may be more than adequate to maintain an erection). To reduce anxiety, treatment of men with delayed ejaculation may include recognition of their over-eagerness to please their partners, validation of (although not necessarily encouragement of) their autosexual orientation, removal of stigmas suggesting hostility or withholding towards their partner, and general anxiety-reduction techniques such as relaxation and desensitisation.

The man's partner also needs to collaborate in the therapeutic process, finding ways to enhance the man's arousal and accepting the use of erotica and various (harmless) sexual fantasies that also might be incorporated into the couple's lovemaking. Furthermore, because inter - ventions used in the treatment of delayed ejaculation may be experienced by the man's partner as mechanistic (e.g. using a step-wise program) and insensitive to his or her sexual needs, the therapeutic challenge is to facilitate the rapport between the partners while maintaining a therapeutic alliance with both partners and simultaneously optimising the patient's response to his partner's manual, oral and vaginal stimulations.

The success of treating men with delayed ejaculation is difficult to assess from the literature[13] because evidence on the effectiveness of various treatments is limited[15] and both successful and unsuccessful case reports have been cited.[11]

Pharmacotherapy

Drug treatment of men with delayed or inhibited ejaculation has met with limited success. Drugs used facilitate ejaculation through either a central dopaminergic, antiserotonergic or oxytocinergic mechanism of action or a peripheral adrenergic mechanism of action. However, no drugs have been approved by regulatory agencies for this purpose, and most drugs that have been identified for potential use have limited efficacy, impart significant side effects or are yet considered experimental in nature. Results are relatively poor in men with psychogenic or neuropathic delayed ejaculation. Table 3 lists some drugs that are used off label for the treatment of men with delayed or inhibited ejaculation.

Alpha-1 adrenergic receptor agonists such as on-demand precoital pseudo - ephedrine (60 to 120 mg one to two hours prior to intercourse) or the selective noradrenaline reuptake inhibitor (SNRI) antidepressant reboxetine (4 to 8 mg/day), which inhibits synaptic noradrenaline reuptake, have limited efficacy in men with delayed ejaculation. The antihistamine cyproheptadine, a central serotonin antagonist, is anecdotally associated with the reversal of anorgasmia induced by the use of SSRI antidepressants but no controlled studies have been reported.[16,17]

An effective dose range of 2 to 16 mg has been suggested, with administration on a chronic or 'on-demand' basis. However, significant dose-related sedative effects are likely to diminish the drug's overall efficacy.

Amantadine, an indirect stimulant of dopaminergic nerves both centrally and peripherally, has been reported to stimulate sexual behaviour and ejaculation in men with SSRI antidepressant-induced anorgasmia. It may be administered on demand (100 to 200 mg five to six hours before intercourse) or chronically (100 to 200 mg twice a day).[18]

A variety of other pharmacological agents including bromocriptine, cabergoline, bupropion and buspirone have been anecdotally reported as potential delayed ejaculation pharmacotherapies for men with delayed ejaculation, despite an absence of large population randomised controlled trials. Of interest is the recent single case report of the intracoital administration of intranasal oxytocin in a case of treatment-resistant anorgasmia.[19] However, in the absence of robust data from randomised controlled trials, oxytocin cannot be recommended as a treatment for men with delayed ejaculation.

CONCLUSION

Delayed ejaculation and anejaculation have manifold organic and psychogenic causes and occur more commonly in men as they age. These conditions have a significant impact upon sexual fulfilment for both the man and his partner and may result in infertility. Treatment of men with delayed ejaculation represents one of the most significant challenges in sexual medicine and outcome results are often disappointing. MT

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COMPETING INTERESTS: Associate Professor McMahon is a consultant, investigator and/or member of speakers panels for Janssen Cilag, Bayer Schering and Plethora UK.