Chapter 7
Anejaculation, Retrograde Ejaculation, and Anorgasmia

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Introduction

Antegrade transit of sperm through the male genital ductal system and ultimately out the anterior urethra is among the most basic and essential biological processes for male reproduction. Neither natural conception nor assisted reproduction is possible unless sperm-containing semen can be delivered into the female reproductive tract or to the embryology laboratory. Disorders that impair semen delivery should be broadly categorized as either anorgasmia or absence of antegrade ejaculation, which may result from retrograde ejaculation or anejaculation. Anorgasmia, as the term suggests, refers to inability to achieve climactic pleasure during sexual activity. Retrograde ejaculation refers to the absence of antegrade ejaculate but presence of sperm in a postorgasmic urinalysis. Anejaculation refers to absence of antegrade or retrograde ejaculate despite achievement of orgasm. Anorgasmia, retrograde ejaculation, and anejaculation are pathophysiologically distinct disorders that warrant specific diagnostic and therapeutic approaches.

Physiology

Basic understanding of the male sexual response cycle provides an essential framework for conceptualizing and treating disorders of orgasm and ejaculation in men. Desire and arousal comprise the first two phases of the male sexual response cycle and are critical for normal male reproductive function [1]. Desire depends upon cortical processing of environmental factors, partner factors, and prior sexual

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experiences. Though incompletely understood, serotoninergic, dopaminergic, and sex steroid signaling play integral roles [2].

In the arousal phase, peripheral afferent genital and nongenital tactile, auditory, visual, and olfactory stimuli are integrated and centrally processed. The main genital tactile input is derived from receptors and free nerve endings located in the glans of the penis, the penile shaft skin, and the scrotum. Sensory information from the penis is carried by the paired dorsal penile nerves (sensory branches of the pudendal nerves) to the sacral segments of the spinal cord.

Penile tumescence results from both a spinal reflex arc and higher-order efferent central signals, which may be excitatory but are tonically inhibitory. Increased rigidity of the corpora cavernosa during erection enables higher levels of sexual stimulation (i.e., through penetrative sexual activity) and pushes free nerve endings within the penile skin closer to the surface, thereby increasing the level of afferent input. However, it should be noted that erection is not required for orgasm or ejaculation. Ultimately a threshold of arousal is reached that triggers the orgasmic and ejaculatory responses, which constitute the effector phase of the male sexual response cycle that in normal cases results in passage of semen out the urethral meatus. Orgasm and ejaculation are integrated but incompletely interdependent processes, as orgasm may occur in the absence of ejaculation (but not vice versa). This is commonly the case after surgical removal of the prostate and seminal vesicles for prostate cancer.

Ejaculation consists of two distinct phases: emission and expulsion. Seminal emission refers to deposition of seminal fluid, prostatic fluid, and sperm into the posterior urethra. Emission is mediated by sympathetic fibers that originate in the thoracic spinal cord at levels T10–L2, course through the paraspinal sympathetic ganglia that comprise the sympathetic chains, and ultimately travel to the prostate, seminal vesicles, vasa deferentia, and epididymis as the pelvic nerves. Alpha-1 receptor signaling is critical for emission.

Expulsion refers to rhythmic, forcible contractions of striated periurethral muscles including the bulbospongiosus muscle while the bladder neck is closed, resulting in projectile expulsion of semen out the urethral meatus. The bulbocavernosus and other periurethral muscles are innervated by the pudendal nerve, which is therefore thought to be integral for the expulsive phase. It is important to note that contraction of the bladder neck is necessary to prevent retrograde ejaculation during expulsion.

Effective ejaculation of semen requires precise regulatory coordination of emission and expulsion that occurs at the spinal level. A neural circuit known as the ejaculatory central pattern generator (CPG) integrates supraspinal modulatory input with peripheral sensory input and initiates coordinated action of the many effectors of the ejaculatory response, including the prostate, seminal vesicles, vasa deferentia, epididymis, bladder neck, and periurethral muscles [3]. It is important to note that supraspinal input is modulatory and not required, as men with complete spinal cord injuries above T10 can ejaculate in response to vibratory stimulation.

Orgasm is a distinct supraspinal, higher-order cognitive event that occurs after a threshold level of arousal is attained. The neurobiological basis of orgasm remains

incompletely understood. It may require central integration of ascending signaling from the ejaculatory CPG or may be the result of central processing of proprioceptive input derived from the rhythmic contractions of the periurethral and bulbocavernosus muscles during the expulsive phase of ejaculation.

Pathophysiology

Conceptualization of anorgasmia, retrograde ejaculation, and anejaculation within the framework of the male sexual response cycle enables logical formulation of differential diagnoses, informs selection of diagnostic tests, and ultimately guides therapeutic intervention. Disorders that inhibit the desire and arousal phases result in anorgasmia, whereas anejaculation results from failure of emission and/or expulsion, and retrograde ejaculation results from disordered expulsion. Table 7.1 lists physiologic drivers and facilitators of each phase of the male sexual response cycle and commonly clinically encountered factors that disrupt each phase. Though in-depth discussion of each clinical disruptor is beyond the scope of this chapter, most cases of absent antegrade ejaculate result from several common clinical scenarios.

Pharmacologic Disruptors

Medications are among the most commonly encountered causes of orgasmic and ejaculatory dysfunction. Any pharmacotherapy that interferes with dopaminergic, serotoninergic, adrenergic, or gamma aminobutyric acid (GABA) signaling can impair the desire, arousal, or ejaculatory phases of the male sexual response cycle. Antidepressant medications that disrupt serotoninergic signaling affect all three phases of male sexual response, though in men the desire and orgasm phases seem to be preferentially disrupted [4]. The selective serotonin reuptake inhibitors (SSRIs) and the serotonin-norepinephrine reuptake inhibitors (SNRIs) are the most commonly implicated agents. Antipsychotic medications predominantly target dopaminergic signaling and may impair sexual arousal or orgasm in up to 70 % of patients [5]. Alpha-1 adrenoreceptor antagonists inhibit contracture of the bladder neck and thus may cause retrograde ejaculation through interference with the expulsion phase of ejaculation, though these agents may also exert peripheral or central effects that impair emission and thus result in anejaculation [6]. Antiepileptic drugs and neuromodulatory agents including gabapentin have also been implicated in ejaculatory and orgasmic dysfunction [7].

Table 7.1 Conceptual framework for disorders of absent antegrade ejaculation

Phase of male sexual response	Physiologic drivers/ facilitators	Clinical disruptors	Result
Desire	Environment	Stress/anxiety	Anorgasmia
	Sex steroid signaling	Endocrine disorders	
	Dopamine signaling	Antipsychotic drugs	
	Serotonin signaling	SSRIs	
		Brain disorders	
		Depression	
Arousal	Dorsal penile nerves	Peripheral neuropathy (DM)	Anorgasmia
	Pudendal nerves	Brain disorders	
	Central processing	Depression	
	Erection	Erectile dysfunction	
		Spinal cord injury	
Emission	Sympathetic chain	Peripheral neuropathy	Anejaculation
	Pelvic nerves	Sympathetic nerve injury (RPLND, radiation)	
	Alpha adrenergic signaling	Spinal cord injury	
		Multiple sclerosis	
		Alpha-blockers	
		Ejaculatory duct obstruction	
Expulsion	Bladder neck	Bladder neck surgery	Anejaculation
	Pudendal nerve	Peripheral neuropathy (DM)	Retrograde ejaculation
		Spinal cord Injury	
		Pelvic nerve injury (RPLND, radiation)	
		Antipsychotic drugs	
		Alpha-blockers	

Neurogenic Disruptors

Spinal cord injury is a commonly encountered etiology of orgasmic and ejaculatory dysfunction. Most spinal cord-injured men are unable to ejaculate without therapeutic intervention [8]. Complete or partial injury at any level usually results in multiphase disruption of the male sexual response cycle. Low self-esteem and psychosocial dysfunction may impair sexual desire. Absent or reduced afferent sensory input affects arousal. Disruption of the spinal ejaculatory CPG and spinal reflex arcs that control emission and expulsion can result in anejaculation or retrograde ejaculation.

Retroperitoneal lymph node dissection (RPLND) is an integral component of multimodality treatment for testicular cancer and a common cause of neurogenic ejaculatory dysfunction. Retroperitoneal lymph nodes near the aorta, vena cava, and iliac blood vessels are excised to remove any sites of potential retroperitoneal nodal metastases. During RPLND the sympathetic chains, the postganglionic branches of the thoracolumbar sympathetic nerves, and the autonomic nerves of the pelvis are at risk of injury or excision. Injury to these structures can result in

complete failure of emission with resultant anejaculation or in discoordination of emission and bladder neck closure with resultant retrograde ejaculation. The development of limited operative templates and nerve-sparing procedures has greatly reduced the incidence of ejaculatory dysfunction after RPLND to under 5 % [9]. However, nerve sparing is difficult in some clinical scenarios (i.e., after chemotherapy), and RPLND remains a common cause of ejaculatory dysfunction [10].

Diabetes mellitus is a common cause of peripheral and autonomic neuropathy that may interfere with orgasm and ejaculation. Decreased genital and nongenital sensation from loss of afferent sensory fibers may inhibit arousal and orgasm. Autonomic neuropathy may affect emission, bladder neck closure, or both. Affected men often progress from decreased semen volume to complete absence of antegrade ejaculation, which usually reflects either retrograde ejaculation or more commonly complete failure of emission [11].

Mechanical Disruptors

Mechanical disruption of the bladder neck or prostate from prior surgery is yet another cause of ejaculatory dysfunction. Transurethral resection of the prostate and reconstruction of the bladder neck for outlet obstruction are common acquired causes of retrograde ejaculation, as these surgeries often render the bladder neck partially incompetent and unable to fully close during the expulsive phase of ejaculation. Up to 30–40 % of men report retrograde ejaculation after transurethral prostate surgery [12].

Clinical Evaluation

History

The clinical evaluation should begin with a focused history. The initial focus should be to distinguish anorgasmia from absence of antegrade ejaculation by direct questioning about whether or not the patient is able to achieve a climactic pleasurable experience during sexual activity. This may be difficult in patients with limited sexual awareness or experience. It is important to determine if absence of antegrade ejaculate is a lifelong or acquired problem. Patients should be queried about whether or not there is any situational variability in their ability to produce antegrade ejaculate and if nocturnal emissions are present. Situational variability in orgasmic function suggests a disorder of desire or arousal, as opposed to a pharmacologically induced or neurogenic failure of emission or expulsion. Patients should be screened for signs and symptoms of hypogonadism (i.e., low energy, low

libido), erectile dysfunction, diabetes (i.e., polyuria), psychiatric illness (i.e., depression), and neurological disease (i.e., sensory abnormalities, bowel or bladder dysfunction). Obtaining detailed sexual, medical, and surgical histories is critically important, as is identification of all prescribed medications.

Physical Examination

The focused physical examination should include examination of the penis and scrotum for assessment of the location of the urethral meatus, penile development, testicular size, and presence of the vasa deferentia and a full neurological exam. Body habitus, gynecomastia, and/or thyroid abnormalities may indicate the presence of endocrinopathy and should be noted. Assessment of penile vibratory sensory thresholds with biothesiometry is a useful adjunct that may be helpful to identify decreased penile sensation [13].

Additional Testing

Additional testing should be directed by findings in the history and physical examination. There should be a low threshold for serum testing to screen patients for diabetes (hemoglobin A1c), hypogonadism (early morning total testosterone), or hypothyroidism (thyroxine- and thyroid-stimulating hormone). Postorgasm urinalysis should be performed in all patients who are able to achieve orgasm to distinguish anejaculation from retrograde ejaculation. The diagnosis of retrograde ejaculation can be made if sperm, fructose, or seminal fluid are observed in the postorgasm voided urine sample [14]. Postorgasm urinalysis should be performed after at least 2 days of ejaculatory abstinence. The patient should first empty his bladder, after which he should perform self-stimulation to achieve orgasm. Any antegrade ejaculate is collected in its own specimen container. The patient should then be instructed to void after waiting 15–20 min. The postorgasm urine sample is then centrifuged, and the derived pellet is microscopically examined for the presence and quantity of sperm.

Medical Management

Withdrawal of Disruptive Medications

The first step in the medical management of anejaculation is cessation or adjustment of medications that interfere with the emission or expulsion phases of

Table 7.2 Drug classes implicated in orgasmic and ejaculatory dysfunction

Drug class	Phase of male sexual response affected
Antidepressants	Desire, arousal, orgasm
Antipsychotics	Arousal, orgasm
Alpha-blockers	Orgasm, emission, expulsion
Antiepileptics	Anorgasmia
Neuromodulators	Anorgasmia

ejaculation (Table 7.2). In patients on alpha-blockers who cannot discontinue alpha-blocker therapy, switching to the highly selective agent alfuzosin may be beneficial [15].

Sympathomimetic Therapy

In some patients, therapy with oral sympathomimetic agents may improve bladder neck contraction during the expulsive phase of ejaculation and thereby convert retrograde ejaculation to antegrade ejaculation [16]. In some cases sympathomimetic therapy is effective for anejaculatory patients and results in either induction of retrograde or antegrade ejaculation. Commonly used sympathomimetic agents include the tricyclic antidepressant imipramine (25–75 mg daily), pseudoephedrine (60 mg four times daily), and midodrine (7.5–30 mg daily) [17].

Sperm Harvesting from Postorgasm Urine

Collection of sperm from a postorgasm voided urine sample can be considered for acquisition of sperm to be used for assisted reproduction techniques. The urine is typically alkalinized with sodium bicarbonate (50 mg 12 and 2 h prior to sperm harvest) to minimize the toxic effect of acidic urine on sperm. The bladder is catheterized or the patient is asked to void immediately prior to orgasm to minimize the volume of urine in the bladder. After orgasm the voided or catheterized urine is centrifuged for collection of sperm, which are then resuspended in appropriate media for use in assisted reproduction [18].

Assisted Ejaculation Procedures

Assisted ejaculation procedures can be used to obtain sperm for assisted reproduction in anorgasmic and anejaculatory men. Surgical sperm retrieval from the seminal vesicles, epididymis, or testes is another option that may be considered, though discussion of these techniques is outside the scope of this chapter. Two

assisted ejaculation procedures are available: penile vibratory stimulation and electroejaculation.

Penile vibratory stimulation (PVS) refers to use of a vibrator applied to the frenular surface of the penis to induce ejaculation. PVS activates an ejaculatory reflex arc that results in a normal ejaculation when all components of the reflex arc are intact and descending cortical inhibitory input is absent. The reflex arc begins with afferent sensory input from the dorsal penile nerves that travels through the pudendal nerve to enter the sacral spinal cord (S2–S4) and travels through spinal interneurons to the thoracolumbar spinal cord (T10–L2). There is then simultaneous sympathetic outflow from T10–L2 to the effector organs of emission (the prostate, seminal vesicles, vas deferens, epididymis, and bladder neck) and efferent motor outflow from S2 to S4 via the pudendal nerve to the periurethral muscles, which mediate expulsion.

The best candidates for PVS are those men with a complete spinal cord injury above the level of T9–T10 in whom the ejaculation reflex arc is intact and inhibitory cortical input is disrupted. Optimal vibration parameters are 2.5 mm amplitude and 100 Hz frequency [19], though simple vibrators without adjustable amplitudes and frequencies may also be used effectively. PVS may also be used in non-spinal cord-injured patients with idiopathic anorgasmia or peripheral neuropathy, though reported experience in such patients is limited. Possible side effects of PVS include abrasions of the penile skin and autonomic dysreflexia in at-risk spinal cord-injured men. Such men should be treated prophylactically with nifedipine (10–20 mg) prior to the procedure. Ejaculated sperm retrieved via PVS have been used successfully for in vitro fertilization, intrauterine insemination, and intravaginal insemination [8].

Electroejaculation (EEJ) is a more invasive assisted ejaculation procedure in which a specialized transrectal probe is used to deliver rhythmic electrostimulation directly to the prostate and seminal vesicles. EEJ is effective for inducing ejaculation in the vast majority of men with anejaculation or anorgasmia of any etiology [20]. It may be performed in the office in spinal cord-injured men but requires general anesthesia for those with intact sensation. Pre-procedure bladder catheterization is performed to empty the bladder, after which sperm transport media is instilled through the catheter. Rectoscopy is recommended before and after EEJ to identify rectal pathology that might preclude or result from the procedure. EEJ should be aborted if rectal ulcerations or other mucosal abnormalities are identified. After rectoscopy the EEJ probe is inserted and held firmly against the prostate and seminal vesicles. An escalating amplitude of rhythmic electrostimulation is administered until ejaculation is achieved, which may be retrograde or antegrade and is collected for use in assisted reproduction. As is the case for PVS, patients at risk for autonomic dysreflexia should receive prophylactic nifedipine prior to EEJ. Sperm harvested during EEJ have been used to successfully achieve pregnancy via intrauterine insemination and in vitro fertilization [21].

Conclusion

Failure of the male sexual response cycle at various points may result in anorgasmia, retrograde ejaculation, and anejaculation. These disorders each present with absence of antegrade ejaculation. However, each is a pathophysiologically distinct disorder that warrants a specific diagnostic and therapeutic approach. An informed, logical multimodal approach to affected men is successful in the majority of cases.

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