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Ejaculatory Disorders
Diagnosis, and Management

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Disclosures

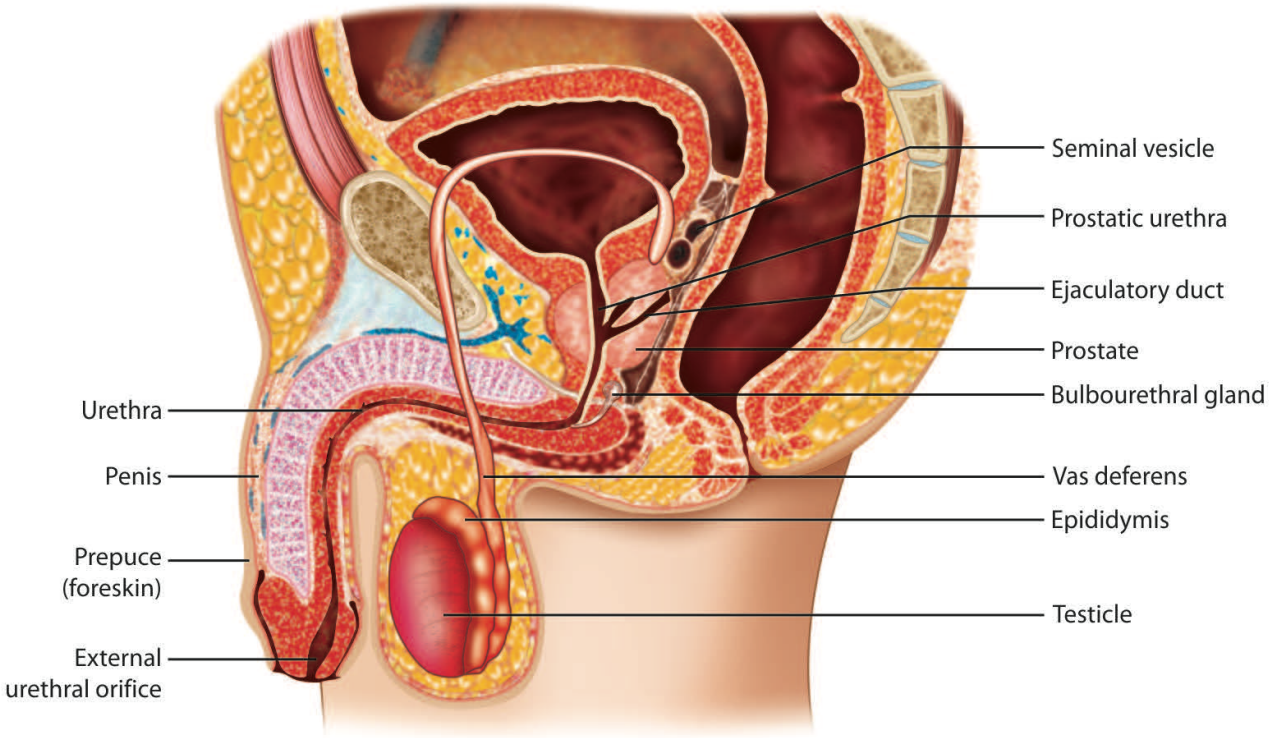
Drs. Sadri and Howards have *no financial disclosures or conflicts of interest* to report relevant to this presentation.

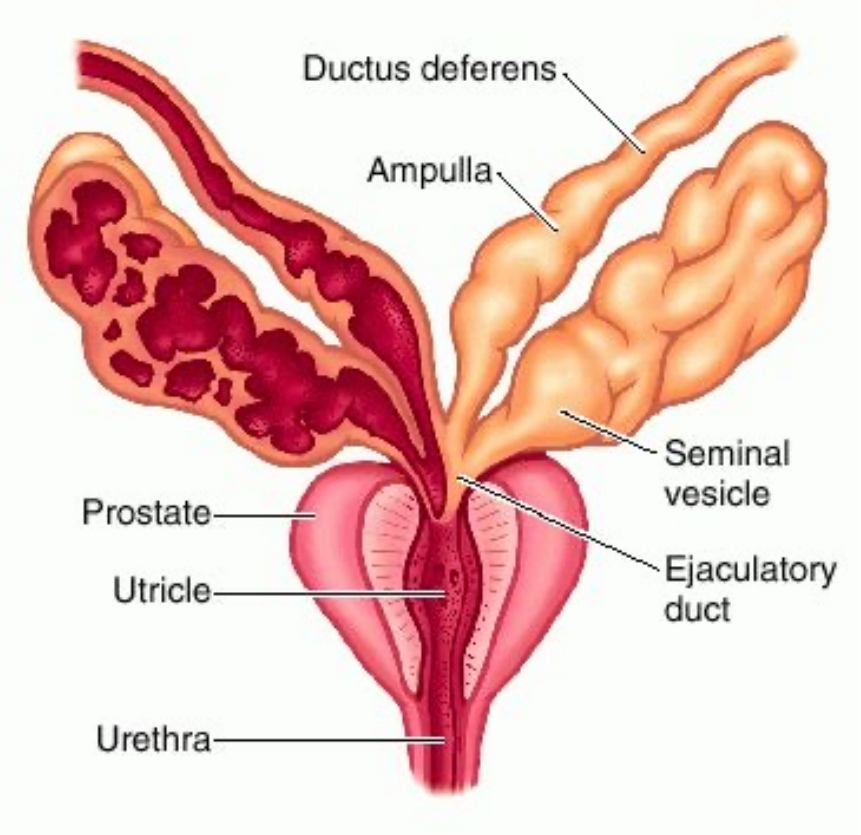
Learning objectives

After this presentation, the learner should be able to:

- Understanding the normal ejaculation pathway
- Identify the etiologies and different categories of ejaculation disorders
- Apply the latest recommendations of AUA on evaluation and management of the ejaculation disorders

ANATOMY AND PHYSIOLOGY OF EJACULATION

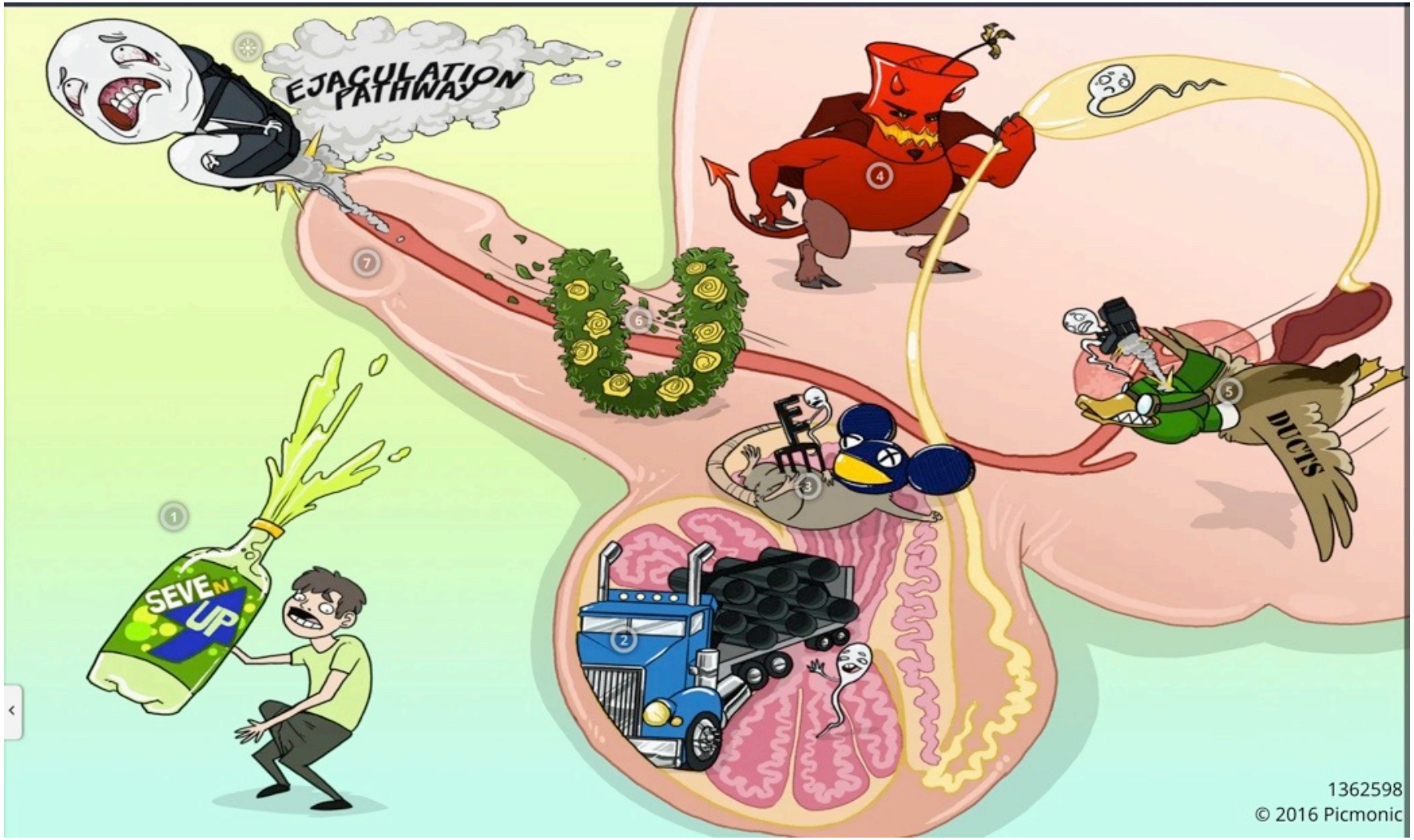




Ejaculation Pathway

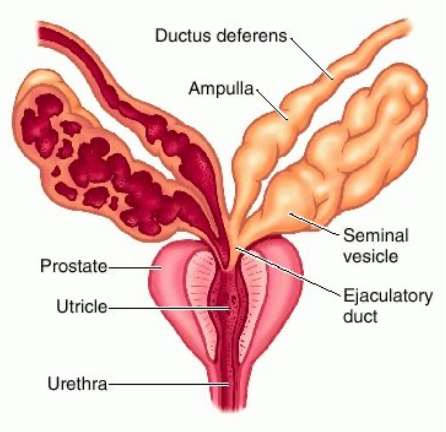
Ejaculation Pathway
Ejecting-sperm
Picmonic

1. SEVEn UP
   SEVEn UP-arrow Soda
2. Seminiferous Tubules
   Semi-tubes
3. Epididymis
   E-pick-dead-mouse
4. Vas Deferens
   Vase Devil
5. Ejaculatory Ducts
   Ejecting Ducks
6. Urethra
   U-wreath
7. Penis
   Penis



Components and contributions of semen (seminal fluid)

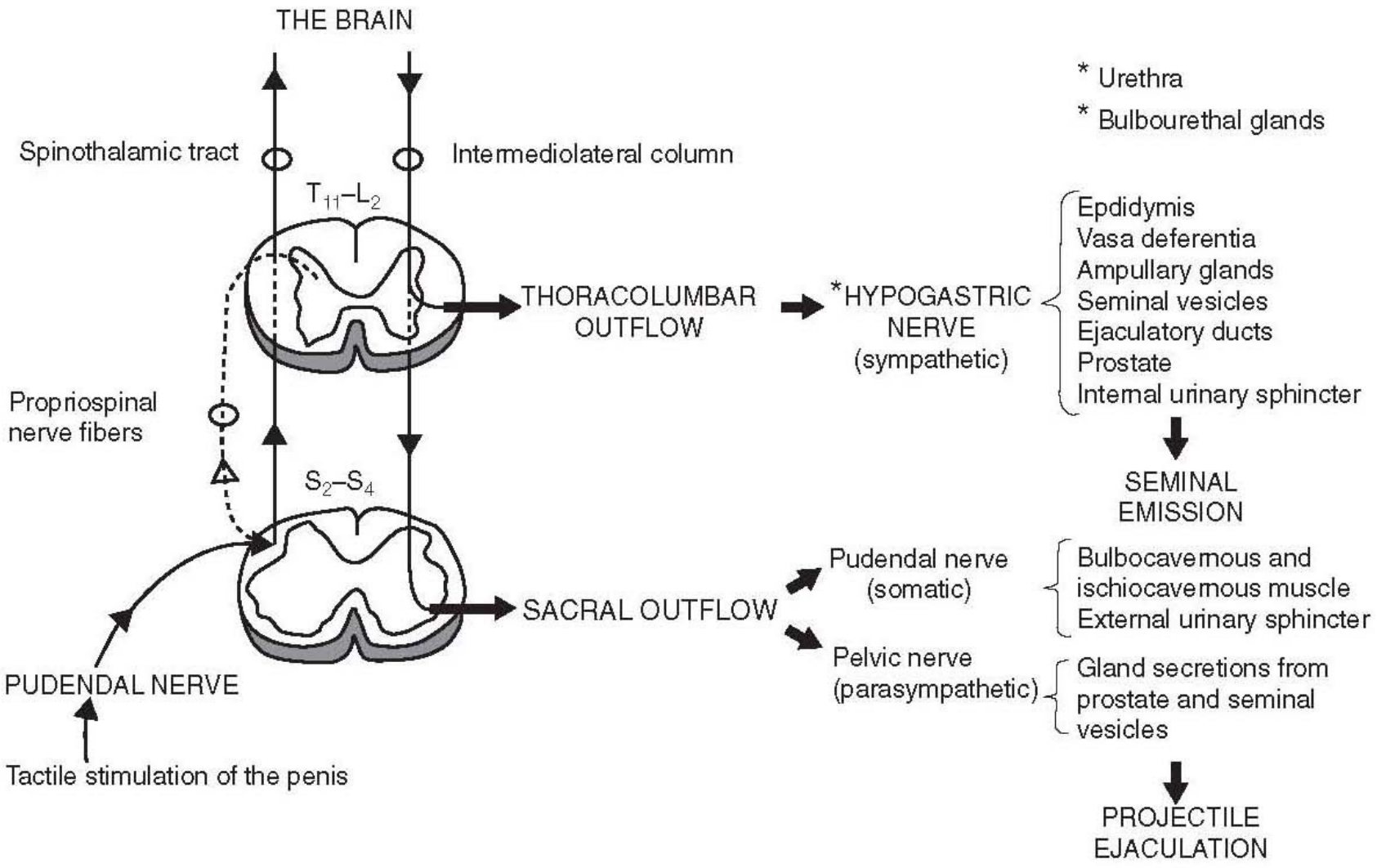
Gland	Approximate %	Description
testes	2–5%	Approximately 200- to 500-million spermatozoa (also called *sperm* or *spermatozoans*), produced in the testes, are released per ejaculation. If a man has undergone a vasectomy, he will have no sperm in the ejaculation.
seminal vesicle	65–75%	amino acids, citrate, enzymes, flavins, fructose (2–5 mg per mL semen,[3] the main energy source of sperm cells, which rely entirely on sugars from the seminal plasma for energy), phosphorylcholine, prostaglandins (involved in suppressing an immune response by the female against the foreign semen), proteins, vitamin C
prostate	25–30%	acid phosphatase, citric acid, fibrinolysin, prostate specific antigen, proteolytic enzymes, zinc (the zinc level is about 135±40 micrograms/ml for healthy men.[4] Zinc serves to help to stabilize the DNA-containing chromatin in the sperm cells. A zinc deficiency may result in lowered fertility because of increased sperm fragility. Zinc deficiency can also adversely affect spermatogenesis.)
bulbourethral glands	< 1%	galactose, mucus (serve to increase the mobility of sperm cells in the vagina and cervix by creating a less viscous channel for the sperm cells to swim through, and preventing their diffusion out of the semen. Contributes to the cohesive jelly-like texture of semen.), pre-ejaculate, sialic acid



Spinal Innervation of Ejaculation

- Sympathetic nervous system stimulation (lumbar splanchnic nerves) mediates movement of mature spermatozoa from the epididymis and vas deferens into the ejaculatory duct.
- Accessory glands such as the bulbourethral (Cowper) glands, prostate, and seminal vesicles secrete fluids that aid in sperm survival and fertility
- Somatic motor efferent (pudendal nerve) that innervate the bulbospongiosus and ischiocavernous muscles at the base of the penis stimulate the rapid ejection of semen out the urethra during ejaculation. Peristaltic waves in the vas deferens aid in a more complete ejection of semen through the urethra

Spinal Innervation of Ejaculation



Clinical Andrology: EAU/ESAU Course Guidelines 2011 (Chapter 41 Bracket et al)

Atrium Health Wake Forest Baptist

AUA Guideline Article

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American Urological Association

RECOMMENDATION

Disorders of Ejaculation: An AUA/SMSNA Guideline

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Abbreviations and Acronyms

AUA = American Urological Association
BPH = Benign prostatic hyperplasia
CNS = Central nervous system
DE = Delayed ejaculation
DSM-V = American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders 5th edition
ED = Erectile dysfunction
ELT = Ejaculation latency time
GABA = Gamma aminobutyric acid
IELT = Intravaginal ejaculatory latency time
ISSM = The International Society of Sexual Medicine
LUTS = Lower urinary tract symptoms
MSM = Men who have sex with men
PE = Premature ejaculation
RCT = Randomized controlled trial
SMSNA = Sexual Medicine Society of North America
SNRI = Serotonin noradrenaline reuptake inhibitors
SSRI = Selective serotonin reuptake inhibitors
T = Testosterone
TCA = Tricyclic antidepressants

Purpose: Men who ejaculate before or shortly after penetration, without a sense of control, and who experience distress related to this condition may be diagnosed with premature ejaculation (PE), while men who experience difficulty achieving sexual climax may be diagnosed with delayed ejaculation (DE). The experience of many clinicians suggest that these problems are not rare and can be a source of considerable embarrassment and dissatisfaction for patients. The role of the clinician in managing PE and DE is to conduct appropriate investigation, to provide education, and to offer available treatments that are rational and based on sound scientific data.

Materials and Methods: The systematic review utilized to inform this guideline was conducted by a methodology team at the Pacific Northwest Evidence–based Practice Center. A research librarian conducted searches in Ovid MEDLINE (1946 to March 1, 2019), the Cochrane Central Register of Controlled Trials (through January 2019) and the Cochrane Database of Systematic Reviews (through March 1, 2019). An update search was conducted on September 5, 2019. Database searches resulted in 1,851 potentially relevant articles. After dual review of abstracts and titles, 223 systematic reviews and individual studies were selected for full-text dual review, and 8 systematic reviews and 59 individual studies were determined to meet inclusion criteria and were included in the review.

Results: Several psychological health, behavioral, and pharmacotherapy options exist for both PE and DE; however, none of these pharmacotherapy options have achieved approval from the United States Food and Drug Administration and their use in the treatment of PE and DE is considered off-label.

Conclusion: Disturbances of the timing of ejaculation can pose a substantial impediment to sexual enjoyment for men and their partners. The

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The complete unabridged version of the guideline is available at https://www.jurology.com.
This document is being printed as submitted, independent of standard editorial or peer review by the editors of *The Journal of Urology®*.
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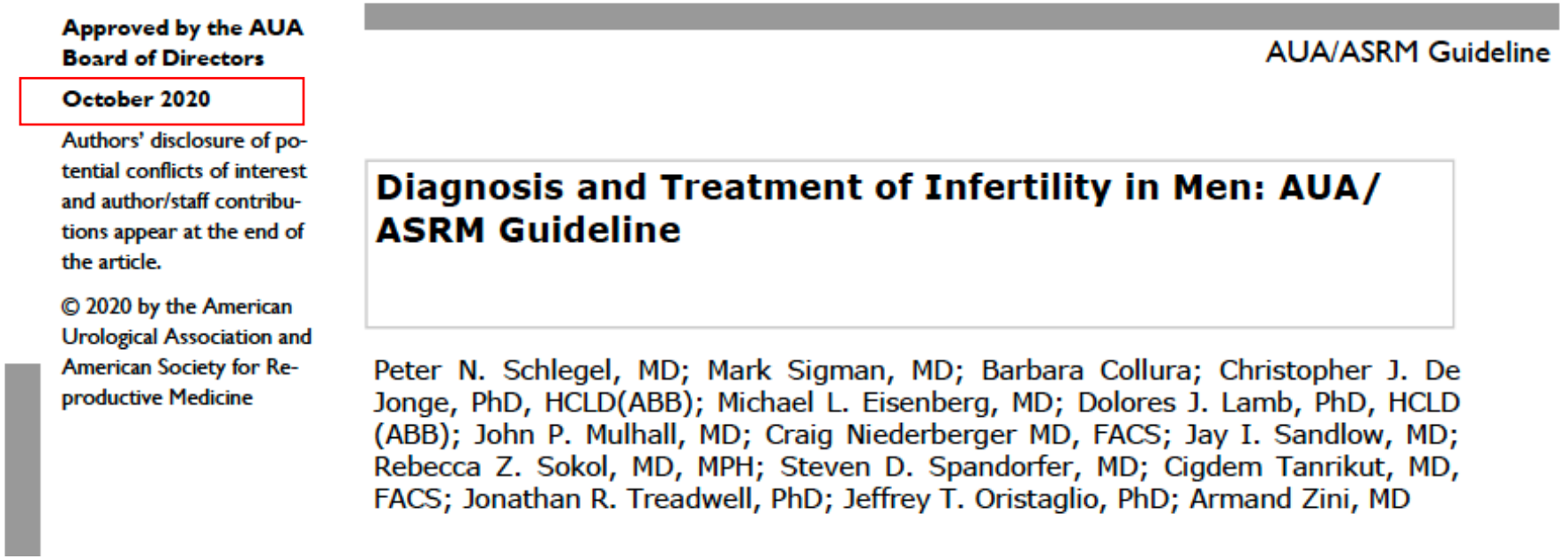
AUA/ASRM Guideline



Approved by the AUA Board of Directors

October 2020

Authors' disclosure of potential conflicts of interest and author/staff contributions appear at the end of the article.

Diagnosis and Treatment of Infertility in Men: AUA/ASRM Guideline

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Best Practice Statement (16 Pages) → **Clinical Guideline (53 Pages)**

American Urological Association

asrm American Society for Reproductive Medicine

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ABNORMALITIES OF EJACULATION

ABNORMALITIES OF EJACULATION

- **Anatomic Abnormalities of Ejaculation**
  - Ejaculatory Duct Obstruction
  - Congenital Bilateral Absence of the Vas Deferens (CBAVD)
  - Bladder Neck Incompetence
- **Neuropathic Abnormalities of Ejaculation**
  - Diabetes
  - Low abdominal/pelvic surgery
  - Multiple sclerosis
  - Retroperitoneal lymph node dissection
  - Spinal cord injury
  - Stroke/traumatic brain injury
- **Functional Abnormalities of Ejaculation**
  - Delayed Ejaculation (Retarded Ejaculation, Primary Anejaculation, and Anorgasmia)

Ejaculatory Duct Obstruction

- Obstruction of the ejaculatory ducts may be complete or partial

- **Complete ejaculatory duct obstruction** (EDO) as a condition caused either by
  - Obstruction of the distal ends of the ejaculatory ducts such as by midline prostatic cysts (usually originating in the prostatic utricle)
  - Atresia of the ends of the ejaculatory ducts
- Men with atretic distal prostatic ducts may have **cystic fibrosis gene mutations** as seen also in men with congenital bilateral absence of the vas deferens
- The **clinical findings** are: azoospermia, low seminal fluid volume (<1 cc), absence of fructose in the seminal fluid, and an acidic pH of the seminal fluid
- A carefully performed transrectal ultrasound of the prostate can often demonstrate **dilated ejaculatory ducts** as they course through the prostate or he midline cysts

- **Partial EDO** is a controversial diagnosis. It is thought that some problems of abnormal sperm morphology and motility previously thought to be idiopathic (and with sperm volumes > 1 cc) may be explained by partial EDO
- However the diagnosis is presumptive and that the treatment, **transurethral resection of the ejaculatory ducts** (TURED), may have significant morbidity, including reduced fertility

Congenital Bilateral Absence of the Vas Deferens (CBAVD)

- Congenital bilateral absence of the vas deferens (CBAVD) is usually associated with mutations of the cystic fibrosis gene (the cystic fibrosis transmembrane conductance regulator gene, CFTR).
- More than 80% of men with CBAVD will have at least one mutation of the gene.
- Over 95% of men with cystic fibrosis will have an abnormality of the Wolffian duct structures, **primarily absences of the vasa.**
- Men with CBAVD will also have varying degrees of malformation of the epididymis although the caput is usually intact
- The seminal vesicles are commonly hypoplastic or atretic and may appear absent or abnormal on transrectal ultrasound
- Clinically, men with CBAVD present as do men with **complete EDO**; azoospermia, low ejaculate volume, absence of seminal fructose, and an acid seminal pH
- The vasa are not palpable.
- CBAVD is not re-constructible. Usually testicular function is normal and sperm retrieval coupled with IVF/ICSI is commonly employed to achieve pregnancy. Prior to commencing attempts at pregnancy, both the man and his partner should undergo testing for CFTR gene mutations and receive genetic counseling.

Bladder Neck Incompetence

- The bladder neck must close in order for an orderly sequence of antegrade ejaculation to occur
- Bladder neck incompetence results in retrograde ejaculation
- Occasionally, this condition is a spontaneous problem.
- More commonly, retrograde ejaculation, due to an incompetent internal sphincter, is a result of medication (adrenergic antagonists), diabetic neuropathy or other neurogenic causes, or anatomic causes.
- In the past, Y-V plasty of the bladder neck had been employed to surgically treat young boys for a variety of conditions, such as vesicoureteral reflux, urinary tract infections, dysfunctional voiding, and enuresis
  - It was not effective and has been abandoned. However, an occasional patient will still be seen with this condition

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Diabetes

- Genital urinary (GU) dysfunction is **common** in Type I diabetics
- Diabetic "cystopathy" and **erectile dysfunction** have been well described, occurring in up to 87% and **75%**, respectively, of men with Type I diabetes
- Ejaculatory dysfunction is **not** as well described. In surveys, it may be included as a part of ED
- Clinically, ejaculatory dysfunction will be recognized as an **absence of ejaculate**. This condition will be caused either by **retrograde ejaculation** (poor closure of the bladder neck) or by anejaculation (failure of emission), and is now considered part due to diabetic sympathetic autonomic neuropathy
- Ejaculatory dysfunction is present in **up to 40%** of men with Type I diabetes
- To produce an antegrade ejaculate and/or attempt a pregnancy through normal intercourse, almost any sympathomimetic drug may be used to close or "tighten" the bladder neck, although results are variable and usually disappointing
- For most couples, some sort of assisted conception will be necessary, and usually protocols for retrieving and using retrograde sperm will be satisfactory
- Men more severely affected who are truly anejaculatory (failure of emission) will usually require electroejaculation or surgical sperm retrieval to obtain sperm for assisted conception.

Low Abdominal/Pelvic Surgery

- Surgery in the retroperitoneum and pelvis in proximity to the sympathetic and parasympathetic plexus that supply the GU organs often injures to those structures
- The **superior hypogastric plexus**, rich in sympathetic fibers, lies in a midline presacral position just below the aortic bifurcation and isvulnerable to injury during classic open surgery for abdominal aortic aneurysm, aorto bifemoral bypass, and some colorectal and pelvic tumors
- Injury to this structure may lead to **denervation of the bladder neck**, which can result in retrograde ejaculation
- The pelvic splanchnic nerve(s) in the perirectal area, rich in parasympathetic fibers, may commonly be injured during radical rectal surgery
- In addition to erectile and urinary dysfunction, 36% to 60% rates of ejaculatory dysfunction have been reported after this type of surgery

Multiple Sclerosis

- Multiple sclerosis (MS), a demyelinating disease, **affects both the brain and spinal cord**. Autonomic dysfunction, may be an early sign of MS but as the disease progresses the GU system is heavily involved
- Voiding dysfunction is present in up to 97% of patients, erectile dysfunction in up to 73%, and ejaculatory and/or orgasmic dysfunction in 50%, while libido is reduced in only 40%
- The autonomic nervous system symptoms may wax and wane along with the somatic symptoms
- Men with MS who are anejaculatory respond to assisted ejaculation in much the same way as men with spinal cord injury, although certain caveats must be followed
- Men with MS are generally sensate, and if electroejaculation is employed, heavy conscious sedation or general anesthesia will be necessary
- Similarly, penile vibratory stimulation (PVS), if performed with the degree of intensity required to induce ejaculation, may be intolerable, due to preserved penile sensation
- Additional considerations are that treatment regimens for men with MS include steroids and/or immunosuppressive medications with accompanying effects on testicular function and spermatogenesis

Retroperitoneal Lymph Node Dissection (RPLND)

- The paravertebral sympathetic ganglia at the thoracolumbar levels are in close proximity to the para-aortic and paracaval lymph nodes involved in metastatic spread from testicular cancers and may be injured and/or resected during RPLND
- The superior hypogastric plexus, comprised of postganglionic fibers from these ganglia, lies approximately in a midline presacral position and may also be involved to some degree in the dissection
- These structures contain sympathetic fibers responsible for seminal emission and bladder neck closure
- Retrograde ejaculation or anejaculation is an sequelae of concern after this procedure
- Surgical templates designed to spare at least a part of these structures have reduced the risk of loss of ejaculatory function
- The highest rates of success in preserving ejaculatory function have been reported with nerve sparing RPLND
- When the surgical anatomy and findings are favorable, ejaculation can be preserved in up to 95% of patients undergoing this procedure
- With the advent of laparoscopic lymph node dissection, there have been some reports of laparoscopic RPLND successfully in preserving ejaculation in all of the patients in which the procedure was successfully complete

Spinal Cord Injury

- In men with a conus or cauda equina injury occurring below sacral cord levels responsible for ejaculation, up to 18% retain their ability to ejaculate
- These very low lesions are uncommon and the vast majority of men with SCI cannot ejaculate without technical or medical assistance
- The two most studied and reliable methods of assisted ejaculation are penile vibratory stimulation (PVS) and electroejaculation (EEJ)

Stroke and Traumatic Brain Injury

Patients who have sustained either a stroke or traumatic brain injury (TBI) will complain of the same types of sexual disorders, which include a decline in libido, sexual satisfaction, coital frequency, erection, and orgasmic ability

- Ejaculatory dysfunction is usually not reported and is implied in reports and discussions of orgasmic dysfunction. Because of the profound effects of brain injury/dysfunction on the patients' psychological, cognitive, and social functions, it is not clear what role these factors or any resultant or residual physical disability may play in the sexual dysfunctions so often reported

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  - Premature Ejaculation
  - Delayed Ejaculation (Retarded Ejaculation, Primary Anejaculation, and Anorgasmia)

Functional Abnormalities of Ejaculation

- It is typical for men to have partial control of ejaculation

- If a man does not feel that he has control of when ejaculation occurs, he has either
  - premature ejaculation (PE) or
  - delayed ejaculation (DE) may be present

- Either PE or DE could be
  - Lifelong
  - Acquired

- Ejaculation latency time (ELT), defined as the time between penetration and ejaculation

- The experience of many clinicians suggest that these problems are not at all rare.

Premature Ejaculation (PE)

- PE is a common. 31% of men ages 18 to 59 report this problem
- PE is characterized by a lack of voluntary control over ejaculation with concomitant distress in which the sexual or emotional well-being of one or both partners is negatively affected
- Because there is great variation in both how long it takes men to ejaculate and how long both partners want sex to last, researchers have begun to formulate a quantitative definition of PE

American Urological Association

<u>Lifelong</u> premature ejaculation is 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 (Expert Opinion)

American Urological Association

Acquired premature ejaculation is defined as consistently poor ejaculatory control, associated bother, and ejaculation latency that is **markedly reduced from prior sexual experience** during penetrative sex. (Expert Opinion)

American Urological Association

Clinicians **may utilize** additional testing as clinically indicated for the evaluation of the patient with **acquired** premature ejaculation. (Conditional Recommendation; Evidence Level: Grade C)

High serum testosterone (T), hyperthyroidism, elevated serum glucose or HbA1c

American Urological Association

Clinicians should not use **additional testing** for the evaluation of a patient with **lifelong premature** ejaculation. (Conditional Recommendation; Evidence Level: Grade C)

High serum testosterone (T), hyperthyroidism, elevated serum glucose or HbA1c

American Urological Association

Clinicians should advise patients that **ejaculatory latency** is not affected by **circumcision status**. (Conditional Recommendation; Evidence Level: Grade C)

Delayed Ejaculation

- Delayed ejaculation is present when a man is unable to ejaculate, either during intercourse, or with manual stimulation in the presence of a partner
- Men with delayed ejaculation may be entirely unable to ejaculate in some circumstances (e.g., during intercourse), or may be able to ejaculate only with great effort and after prolonged intercourse (e.g., 30–45 minutes)
- Delayed ejaculation may be lifelong or acquired, occurring in 8% of men aged 18 to 59
- Evaluation should rule out neurological conditions and confirm the presence of nocturnal emissions, suggesting that the ejaculatory reflex can function normally
- Many cases of lifelong anorgasmia are thought to be due to psychological factors, such as strict religious upbringing, lack of attraction for a partner, traumatic events, or conditioning caused by unique or atypical masturbation patterns
- Various medications may also contribute to delayed ejaculation

MANAGEMENT OF ABNORMALITIES OF EJACULATION

American Urological Association

Several **psychological health**, **behavioral**, **and pharmacotherapy** **options** exist for both PE and DE; however, none of these pharmacotherapy options have achieved approval from the United States Food and Drug Administration andtheir use in the treatment of PE and DE is considered **off-label**.

Premature ejaculation

Nonsurgical Management

American Urological Association

Clinicians should recommend daily SSRIs; on demand clomipramine or dapoxetine (where available); and topical penile anesthetics as first-line agents of choice in treatment of pre-mature ejaculation. (Strong Recommendation; Evidence Level: Grade B)

Table 1. *Pharmacotherapies for the treatment of Premature Ejaculation*

Drug	Daily Dose	On-demand dosing
First Line:		
Paroxetine	10–40 mg	20 mg (+/-10 mg daily)
Clompramine	12.5–50 mg	25–50 mg
Sertraline	50–200 mg	50–100 mg
Fluoxetine	20–40 mg	
Citalopram	20–40 mg	
Second Line:		
Tramadol		25–100 mg
Terazosin	5 mg	
Alfuzosion	6–10 mg	
Sildosin	4 mg	
Tamsulosin	0.4 mg	
Doxazosin	4 mg	

American Urological Association

Clinicians may consider treating men with premature ejaculation who have failed first line therapy with α1-adrenoreceptor antagonists (Expert Opinion)

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Clinicians should treat **comorbid erectile dysfunction** in patients with premature ejaculation according to the AUA Guidelines on Erectile Dysfunction. (Expert Opinion).

American Urological Association

Clinicians should advise men with **premature ejaculation** that combining behavioral and pharmacological approaches may be more effective than either modality alone. (Moderate Recommendation; Evidence Level:Grade B

American Urological Association

Clinicians should inform patients that surgical management (including injection of bulking agents) of premature ejaculation should be considered experimental and only be used in the context of an ethical board approved clinical trial. (Expert Opinion)

Delayed ejaculation

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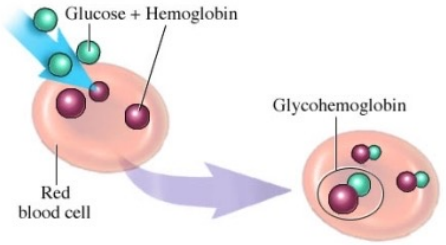
Clinicians should assess medical, relationship, and sexual history and perform a focused physical exam to evaluate a patient with delayed ejaculation. (Clinical Principle)

American Urological Association

RECOMMENDATION

Clinicians may utilize additional testing as clinically indicated for the evaluation of delayed ejaculation. (Conditional Recommendation; Evidence Level: Grade C)

- Morning T
- Electrolytes, Lipids, and Glycosylated Hemoglobin (HBA1C)



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RECOMMENDATION

Clinicians should suggest replacement, dose adjustment, or staged cessation or of medications that may contribute to delayed ejaculation. (Clinical Principle)

Table 2. *Agents known to be associated with Delayed Ejaculation*

Alcohol	Clomipramine	Mebanizine	Phenelzine Sulfate
Alprazolam	Demethylimpiramine	Mesoridazine	Prazosin
Amiocaproic Acid	Fluoxetine	Methadone	Protriptyline
Amitriptyline	Fluvoxamine	Methyldopa	Reserpine
Amoxapine	Guanadrel	Naproxen	Sertraline
Baclofen	Guanethidine	Nortriptyline	Thiazides
Bethanidine	Haloperidol	Pargyline	Thioridazine
Butaperazine	Hexamethonium	Paroxetine	Trazodone
Chlordiazepoxide	Imipramine	Perphenazine	Trifluoperazine
Chlorimipramine	Iproniazid	Phenotiazine	
Chloropromazine	Isocarboxazid	Phenoxybenzamine	
Chlorprothixene	Lorazepam	Phentolamine	

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RECOMMENDATION

Clinicians should inform patients that there is insufficient evidence to assess the risk-benefit ratio of oral pharmacotherapy for the management of delayed ejaculation.(Expert Opinion)

Table 3. *Pharmacotherapies with potential efficacy for the treatment of Delayed Ejaculation*

Drug	PRN Dosage	Daily Dosage
Oxytocin	24 IU intranasal/SL during sex	—
Pseudoephedrine	60–120 mg (120–150 minutes prior to sex)	—
Ephedrine	15–60 mg (1 hour prior to sex)	—
Midodrine	5–40 mg daily (30–120 minutes prior to sex)	—
Bethanecol	20 mg daily	
Yohimbine	—	5.4 mg TID
Cabergoline	—	0.25–2 mg BIW
Imipramine	—	25–75 mg Daily

BIW: twice a week; IU: international units; PRN: pro re nata; SL: sublingual; TID: three times a day

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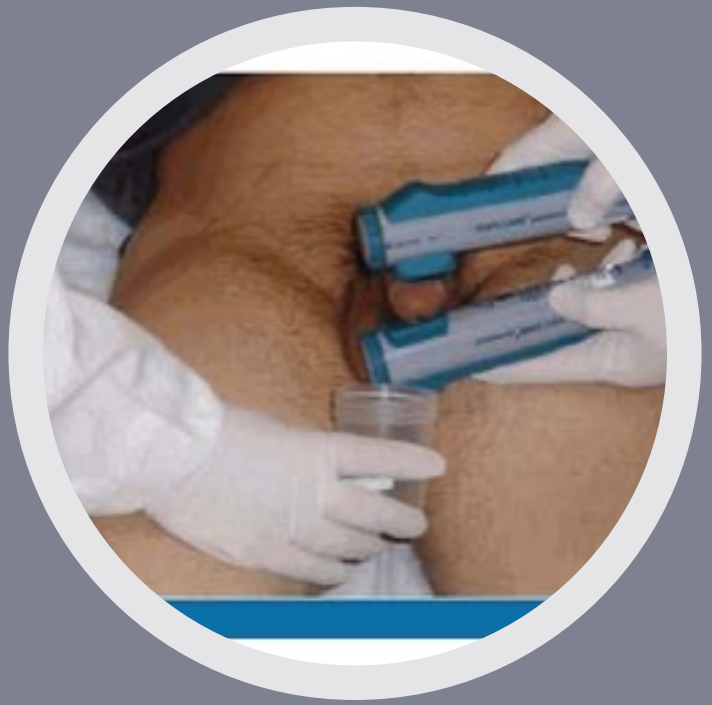
Clinicians may offer treatment to normalize serum testosterone levels in patients with delayed ejaculation and testosterone deficiency. (Expert Opinion)

American Urological Association

Clinicians should treat men who have delayed ejaculation and comorbid erectile dysfunction according to the AUA Guidelines on Erectile Dysfunction. (Expert Opinion)

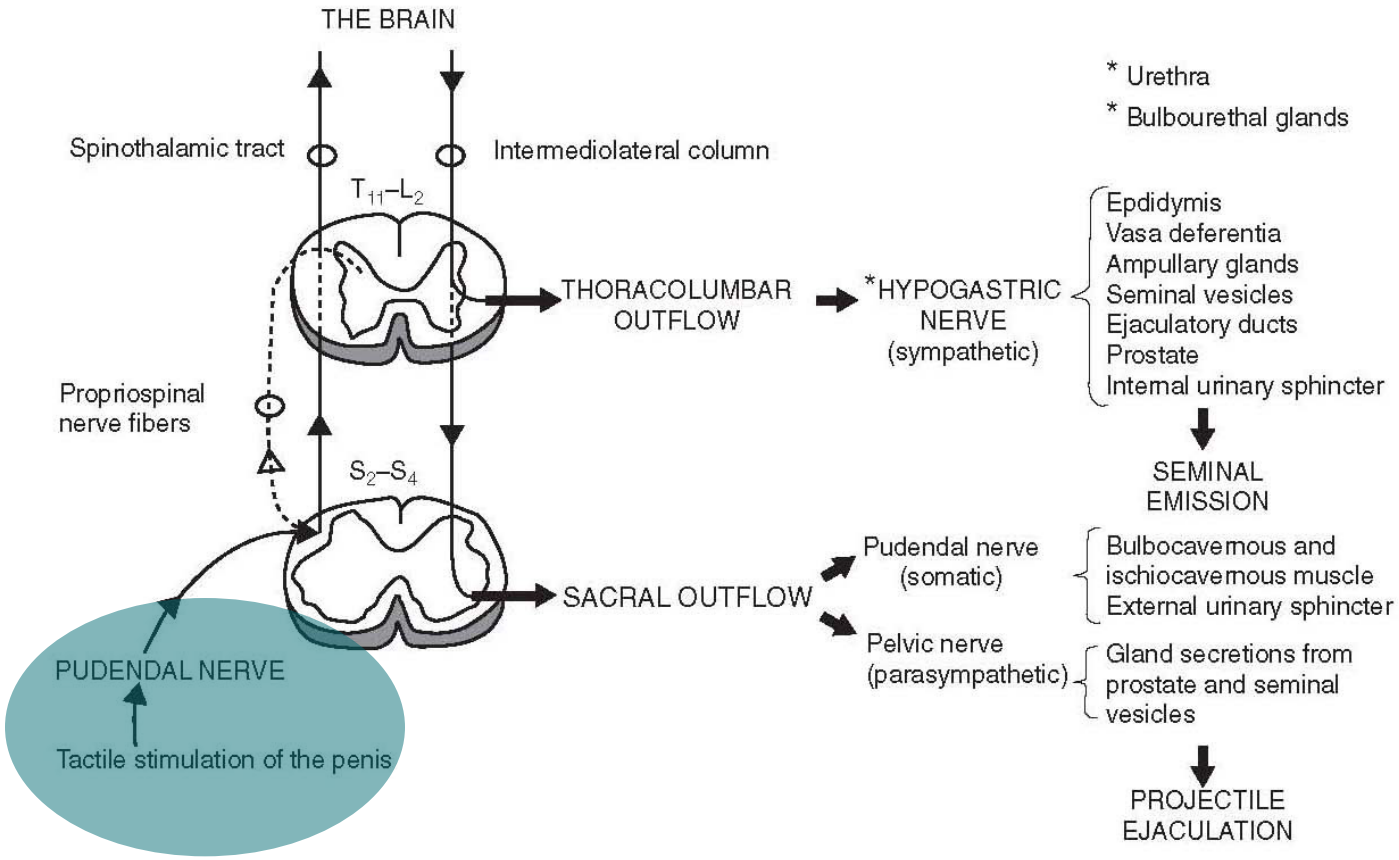
American Urological Association

Clinicians should counsel patients with delayed ejaculation that no currently available data indicates that **invasive nonpharmacological** strategies are of benefit. (Expert Opinion)



Penile Vibration Stimulation (PVS)

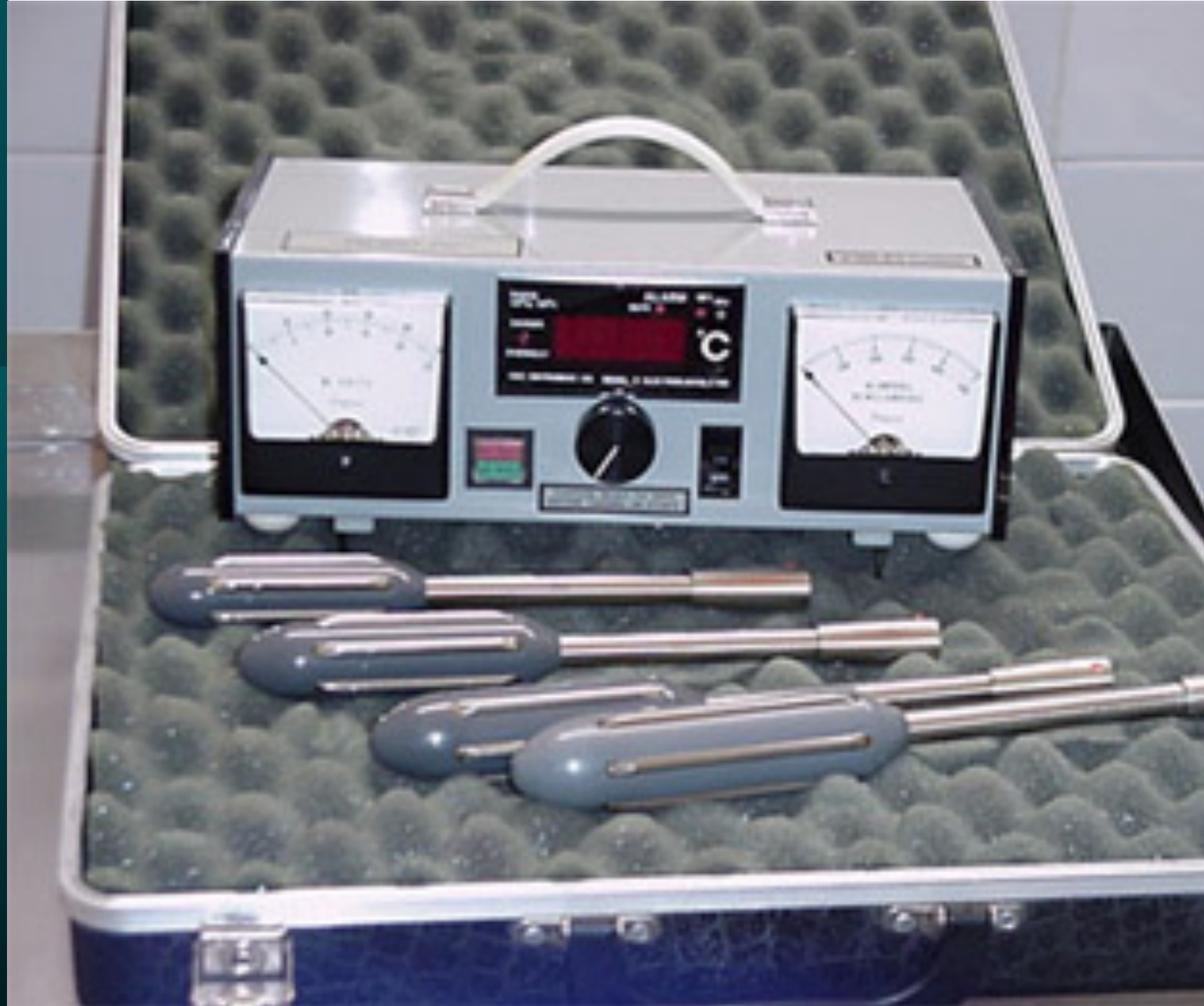
Spinal innervation of ejaculation



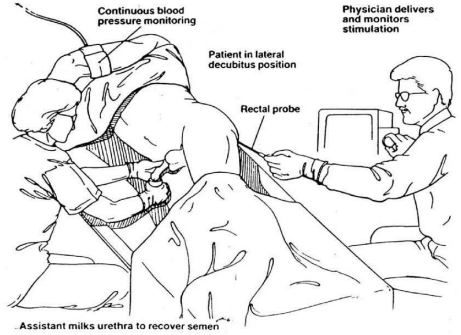
How to use?

- Placing a vibrator on the glans penis
- Goal: recruiting the ejaculatory reflex to induce ejaculation
- Patients whose level of injury is T6 or rostral should be administered 20 mg Nifedipine orally 30 minutes before PVS
- Supine position
- 2–5 min stimulation, interspersed by 1–2 min rest period (maximum 3 trials).
- Another person holds the semen collection container close to the urethral meatus

Electroejaculation (EEJ)

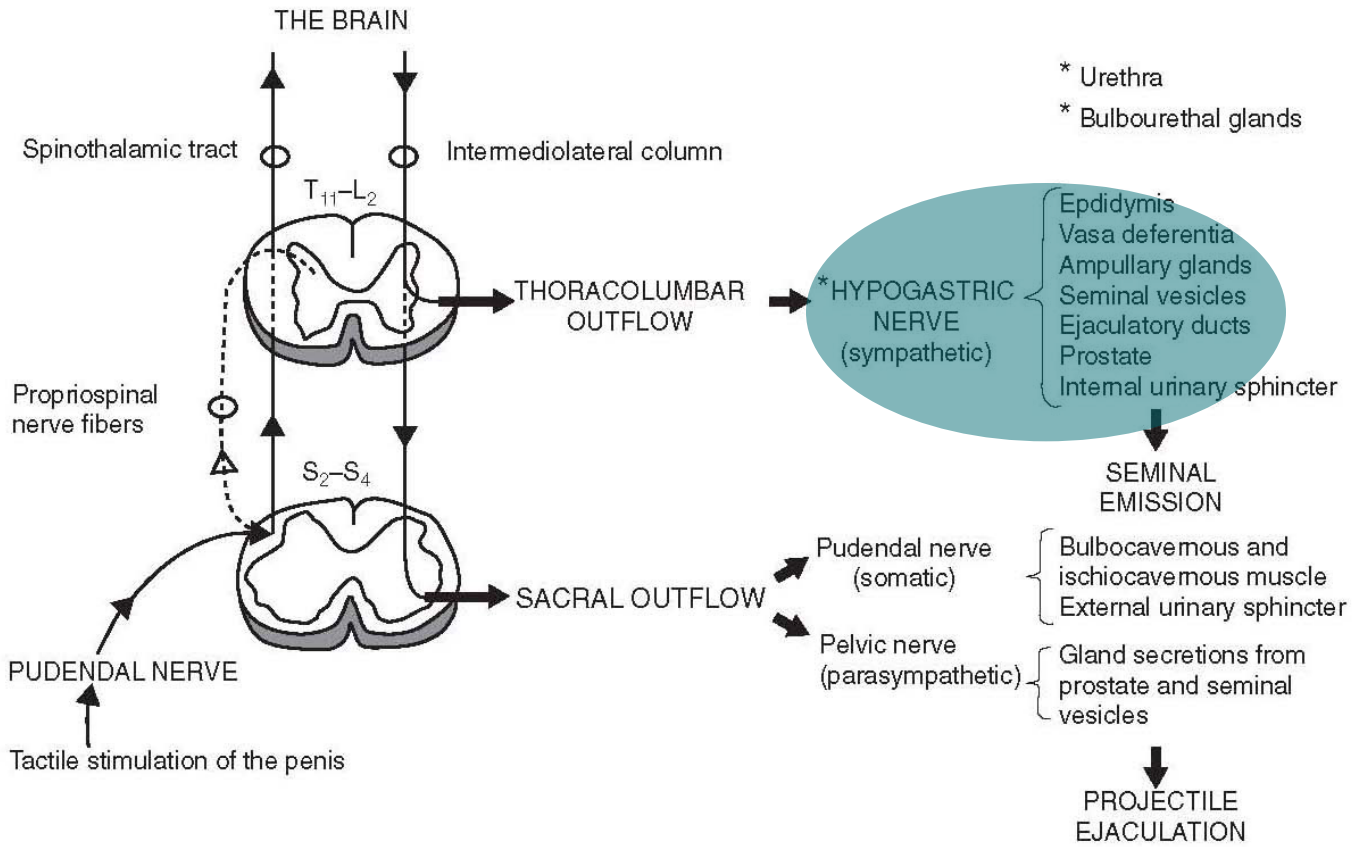


How to use?



- Placing a probe in the rectum
- Goal: electric stimulation toward prostate and seminal vesicles
- Patients whose level of injury is T6 or rostral should be administered 20 mg Nifedipine orally 30 minutes before PVS
- Lateral decubitus position
- Anesthesia?
- Bladder Catheterization immediately before EEJ (remove the catheter)
- Rectoscopy prior to EEJ
- Wave-like pattern stimulation; 10-20 stimulations

Spinal innervation of eiaculation



PAST AND FUTURE SESSIONS

- Session One: Clinical investigation of the infertile male
- Session Two: Genetic causes of male infertility and their impact on future generations
- Session Three: Medical Treatments for Male Infertility
- Session Four: Surgical Treatments and Assisted Reproductive Technology (ART) for Male Infertility
- Session Five: Ejaculatory disorders, diagnosis, and management
- **Session Six: Clinical investigation and laboratory analyses in male hypogonadism**
- **Session Seven: Testosterone deficiency syndrome, , Androgen replacement—indications and principles**
- **Session Eight: Female-to-Male Transsexualism**


Q&A
answers
questions
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problem