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Orgasmic Disorder in the Male*

Learning Objective: At the conclusion of this continuing medical education activity, the participant will be able to differentiate orgasmic disorders in general from anorgasmia, describe the limitations in the diagnostic capabilities for addressing these issues and identify the various therapies that have been tried in previously reported uncontrolled studies.

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INTRODUCTION

Male orgasmic dysfunction, including delayed orgasm and anorgasmia, remains among the most challenging disorders of sexual function to manage. Operative definitions for these disease processes are varied. A consensus statement from the Fourth International Consultation on Sexual Medicine in 2015 defined anorgasmia as "the inability to reach orgasm despite adequate and prolonged sexual stimulation leading to adequate sexual arousal. Anorgasmia might or might not lead to personal distress."[1] **The International Consultation on Sexual Medicine does not provide a definition for delayed orgasm, but instead offers definitions for primary and acquired delayed ejaculation, described to occur in 75%-100% of coital activity and >50% of coital activity, respectively.** In the most recently updated ICD-11 published by the World Health Organization anorgasmia is defined as either lifelong or acquired, and within these classifications is further specified as situational or generalized.[2] Additional ICD-11 codes associate anorgasmia with medical or psychological conditions, use of medications or substances, lack of knowledge, or relationship or cultural factors. However, there is no specific ICD-11 code for delayed orgasm.

This Update summarizes the reported data on evaluation of and available therapies for orgasmic disorder in general and anorgasmia in particular. Much of the problem in reaching meaningful conclusions is a lack of established objective diagnostic criteria. Orgasmic dysfunction is poorly studied and currently has no FDA (U.S. Food and Drug Administration) approved treatment strategies. The majority of past research efforts seeking effective treatment strategies have focused on erectile dysfunction and premature ejaculation, given that these 2 entities represent the most commonly reported sexual dysfunctions.[1] Physical examination, laboratory testing and other adjunctive diagnostic maneuvers may identify correctible causes of orgasmic dysfunction.

The standard operating procedures in disorders of orgasm and ejaculation published by the International Society for Sexual Medicine address evaluation and treatment of men with anorgasmia, although delayed orgasm and delayed ejaculation are discussed under the umbrella term "delayed ejaculation."[3] In addition, DSM-5 (Diagnostic and Statistical Manual of Mental Disorders, 5th edition) eliminated the term "male orgasmic disorder" and replaced it with "delayed ejaculation."[4] DSM-5 defines delayed ejaculation as "marked delay, infrequency or absence of ejaculation on almost all or all occasions (75%–100% of the time) of partnered sexual activity without the individual desiring delay." **However, when discussing orgasmic dysfunction, it is important to define it separately from ejaculatory dysfunction, as orgasm may occur in the absence of ejaculation in some men due to medical or postsurgical reasons.**[5] Regarding delayed orgasm, DSM-5 states, "It is important in the history to ascertain whether the complaint concerns delayed ejaculation or the sensation of orgasm or both. Ejaculation and orgasm usually occur together but not always."[4] Future definitions of orgasmic and ejaculatory dysfunction should focus on providing specific, separate definitions for these disorders as they are separate entities.[6]

The prevalence of anorgasmia and delayed orgasm in the general population is not well studied, but is estimated at 3%.[7,8] Causes of orgasmic dysfunction vary and include medication use, previous surgeries, endocrinopathies, hormonal abnormalities, psychosexual factors and changes in penile sensation. A grasp of the various etiologies leading to orgasmic dysfunction is essential to diagnose and treat this challenging condition.

MEDICATION RELATED ORGASMIC DYSFUNCTION

Medications represent the most common cause of orgasmic dysfunction. **Medications known to affect orgasmic function include antidepressants, antipsychotics, tranquilizers, 5-alpha-reductase inhibitors and opiates.** A Micromedex® search revealed that 16 medications list orgasmic dysfunction as a potential side effect, with risk of orgasmic dysfunction ranging between <1% and 10% as a function of the medication.[6] All medications identified were antidepressants or antipsychotics. In a study of more than 2000 men treated with selective serotonin reuptake inhibitors use of these agents led to a sevenfold increased risk of delayed orgasm.[9] Methadone has also been associated with decreased orgasmic function in patients on maintenance therapy.[10–12] 5-alpha-reductase inhibitors such as finasteride have been associated with a myriad of sexual side effects, including orgasmic dysfunction.[13] Finasteride blocks the type 2 isoform of the 5-alpha-reductase enzyme, the predominant form found in the prostate and hair follicles. Studies have shown that side effects of finasteride, including erectile dysfunction, loss of libido and ejaculatory changes, occur in up to 15% of patients after a year of treatment. **Orgasmic and sexual side effects of finasteride may extend beyond cessation of treatment.** In an analysis of men with persistent sexual dysfunction following finasteride use 68% reported persistent orgasmic dysfunction after stopping the drug.[14]

Previous surgeries and injuries can also lead to orgasmic dysfunction. **Prior pelvic surgery is a major cause of orgasmic dysfunction in men, especially those with a history of prostate or colon cancer.** In a questionnaire based study of men who had undergone robot-assisted laparoscopic radical prostatectomy 73% of respondents reported a "poor ability to reach an orgasm."[15] Improved orgasmic function after robot-assisted laparoscopic prostatectomy can be observed in the context of nerve sparing procedures.[16] In the general surgery literature the impact of pelvic surgery on sexual function is well documented.[17–19] However, studies have not specifically examined subsequent orgasmic dysfunction. Similarly a history of spinal cord injury can lead to significant rates of anorgasmia. In an analysis of 23 studies describing 604 men with previous spinal cord injury only 40% of all males and 45% of sexually active males reported achieving orgasm.[20]

HORMONAL ETIOLOGIES OF ORGASMIC DYSFUNCTION

Variations in hormone levels, specifically prolactin, thyroid-

ABBREVIATIONS: DE (delayed ejaculation), IIEF (International Index of Erectile Function), PRL (prolactin), SSRI (selective serotonin reuptake inhibitor), T (testosterone), TSH (thyroid-stimulating hormone)

stimulating hormone and testosterone, have a significant impact on normal orgasm. In a cohort of 194 men presenting with delayed ejaculation Corona et al correlated worsening symptom severity from delayed ejaculation to anorgasmia with PRL, TSH and T levels, showing that the severity of the endocrinopathy correlated with severity of ejaculatory disorer.[21] PRL levels have been demonstrated to rise following orgasm and ejaculation, and are likely responsible for the refractory period.[22] Furthermore, pharmacologically elevating PRL levels may significantly increase ejaculatory latency times in healthy patients.[23] Data on the correlation between PRL levels and DE or orgasmic dysfunction are conflicting. In a study of approximately 80 men hyperprolactinemia was associated with DE on univariate analysis but not on multivariate analysis.[24] Similarly in a cohort of 51 men with anejaculation Buvat et al reported normal serum PRL levels in all patients.[25] In contrast, a large European cohort of more than 2000 men demonstrated that lower PRL levels were correlated with diminished orgasmic enjoyment on multivariate analysis.[26] **While the role of prolactin in orgasmic dysfunction is unclear, it remains a target for therapy.**

Thyroid dysfunction, specifically hypothyroidism, has been suggested as a cause of persistent DE in some patients. In a multicenter study of 48 men with thyroid related endocrinopathies Carani et al described a significant improvement in ejaculatory latency in men with hypothyroidism suffering from DE after hormone balancing.[27] This result is in contrast to the findings of Corona et al, who correlated worsening DE with increasing TSH levels.[21] **Although data regarding the role of TSH specifically in orgasmic dysfunction may be conflicting, it is widely accepted that thyroid disorders can impact sexual function.**

T levels have a key role in male sexual health and overall sexual function.[21, 28–31] In a meta-analysis of 14 studies on the impact of testosterone therapy on male sexual dysfunction significant improvement in the orgasm domain of the International Index of Erectile Function was observed among 1300 men.[29] Similar improvements were noted in men receiving topical testosterone gel in a large multicenter registry study.[32] After 12 months of treatment there was significant improvement in ejaculatory function domain scores on the Brief Male Sexual Function Inventory, and these scores positively correlated with changes in T level.

PSYCHOSEXUAL AND BEHAVIORAL CAUSES OF ORGASMIC DYSFUNCTION

Psychosexual etiologies for orgasmic and ejaculatory dysfunction have been suggested as possible explanations for development of orgasmic dysfunction. These factors include unexpressed anger, fear of failure, concerns regarding pregnancy, aggression, personal beliefs and even religious constructs.[33–36] Although these concepts are discussed in the literature, no studies have fully examined their role in orgasmic dysfunction. Idiosyncratic masturbation techniques are associated with men suffering from delayed orgasm. Perelman and Rowland describe these self-stimulation techniques as difficult to replicate with partnered sexual activity.[35] Furthermore, the authors suggest that men suffering from delayed orgasm related to idiosyncratic masturbation are unlikely to discuss their preferences with their partners or physicians due to embarrassment, which is supported by research showing that **men suffering from primary delayed orgasm had more masturbatory activity, higher anxiety, and lower satisfaction scores with orgasm and intercourse.**[37] This increased masturbatory activity can also lead to worsened delayed orgasm due to disparity between sexual fantasy used for sexual arousal and the reality of sexual activity with a partner.[35]

PENILE SENSATION

Penile sensation and stimulation are essential to orgasm. Penile sensation decreases with age, leading to a higher incidence of orgasmic dysfunction. In a cohort of more than 1800 men ejaculatory and orgasmic dysfunction increased from 3% among men in their 40s to 43% among men in their 70s.[38] **Similarly data collected from more than 1600 Dutch men showed an increase in complete absence of ejaculation/orgasm with advanced age.**[39] The incidence of anorgasmia among men younger than 65 years was less than 4% but rose to 16% in those older than 65 years. Penile sensation changes can also occur in men with diabetes.[40] Vibrotactile thresholds of men with diabetes with vs without erectile dysfunction show a marginal difference, suggesting a decline of penile sensation with advanced disease.

CLINICAL EVALUATION OF ORGASMIC DYSFUNCTION

Similar to other medical conditions, the clinical evaluation of orgasmic disorders begins with a detailed medical history and physical examination. First, it is important to determine if the patient's experience truly represents an abnormality of orgasm. Symptoms should be differentiated from anejaculation, in which the patient experiences orgasm but does not exhibit expulsion of semen. The clinician must then seek to determine the onset of the condition (lifelong or acquired), timing of symptoms (situational or generalized), consistency (sometimes or always), setting (with masturbation, with some or all forms of sexual activity with a partner, with all partners or with one/some partners), comorbidities, and prior behavioral strategies and medical treatments used for the condition.

Psychological/psychiatric history is particularly relevant, as SSRIs and other psychotropic medications may be a contributing factor. History of retroperitoneal or pelvic surgery must be elucidated as well. It is also important to discern the nature of prior sexual relationships, current relationship status, satisfaction with current relationship, social history and habits (alcohol, marijuana, illicit substances), religious history, trauma, external stressors, ability to achieve and sustain an erection, and emotional or physical abuse. Investigating the duration of the sexual encounter may reveal diminished ability to sustain relations sufficiently to achieve orgasm due to diminished exercise tolerance or physical strength. Given the interplay between medical, social and psychological factors, a multidisciplinary approach with a treatment team consisting of a medical doctor, psychologist/psychiatrist and/or sexual therapist may be useful.

Loss of penile sensation and/or psychological factors are often contributory in the male who has difficulty achieving orgasm with a partner but not with masturbation. This phenomenon may occur in the aging male with degeneration of penile afferent nerves. Decreased penile sensitivity can be overcome with vigorous masturbation, and thus a detailed masturbatory history may be informative. Men with diabetes or neurological disorders impacting sensation are at increased risk for diminished penile sensation. **Any medical, surgical or psychological**

process that compromises central control of orgasm, peripheral sympathetic input to the vasa deferentia and bladder neck, somatic afferent nerve supply to the penis, and/or somatic efferent input to the pelvic floor can result in disorders of orgasm.

Physical examination should include the standard genitourinary evaluation. **Assessment of anal sphincter tone and quality of bulbocavernosus reflex should be considered in most individuals, particularly those in whom neurosensory deficits are suspected.** The clinician should also evaluate for signs and symptoms of endocrine disorders such as diabetes, hypothyroidism, testosterone deficiency and hyperprolactinemia.

LABORATORY AND ADJUNCTIVE TESTING

If the history or physical examination is suggestive of endocrine dysfunction, laboratory testing including assessment of thyroid function, T and/or PRL levels should be performed. Identified endocrinopathies should be corrected, and a collaborative approach with a primary care provider or endocrinologist should be used in the setting of thyroid dysfunction or hyperprolactinemia. Elevated prolactin levels should prompt magnetic resonance imaging of the brain to assess for pituitary adenoma. Other evaluations include tests of nerve function if physical examination suggests potential neurological insult. In patients with subjective reduction of penile sensitivity biothesiometry or pudendal somatosensory evoked potentials may be considered.[41] The former examines the sensory threshold of vibratory tactile stimulation and compares these values to age matched reference range standards, while the latter assesses afferent activity from the dorsal nerve of the penis toward higher control centers. Sacral reflex arc testing evaluates the motor and sensory branches of the pudendal nerve and S2-S4 nerve roots.[42] The final diagnostic maneuver is sympathetic skin testing, which assesses sympathetic outflow to the skin on the genitalia.[41] The value of these adjunctive neurological tests has been questioned, and none is used routinely by urologists in clinical practice. An algorithmic approach to orgasmic dysfunction is presented in the figure.[5]

TREATMENT

Treatment of orgasmic dysfunction should be tailored to the suspected etiology on an individual basis. **Treatment may include a combination of patient/couple counseling, behavioral modification, psychosexual therapy and/or pharmacological agents.** In couples attempting to achieve pregnancy options for sperm retrieval must be discussed if anejaculation is also present.

If thorough evaluation for organic or pharmacological causes is negative, referral to a psychosexual or couples therapist is usually indicated to identify and rectify behavioral issues or provide counseling/psychotherapy. Behavioral changes may include practicing methods to maximize genital stimulation, minimizing alcohol and illicit substance consumption, and improving intimacy between patient and partner. Other therapeutic strategies may include modification of arousal methods,

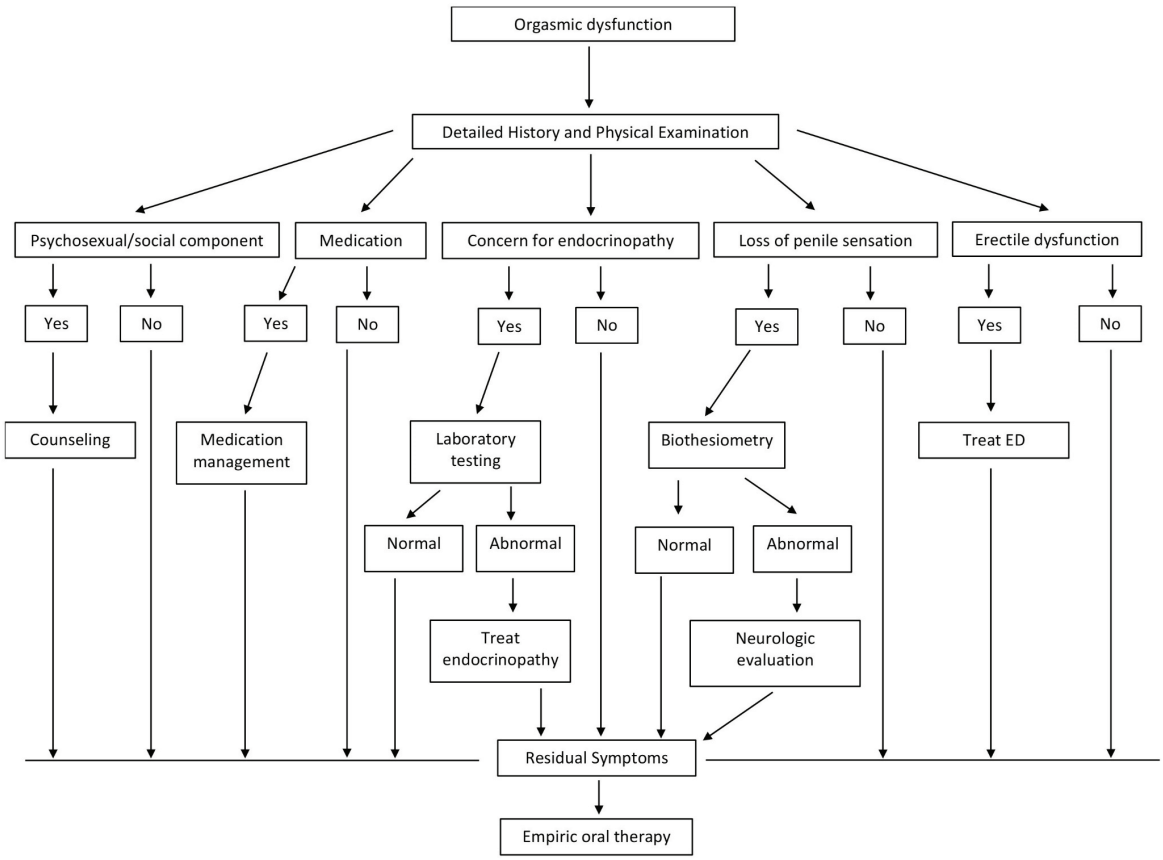

Figure. Diagnostic evaluation of orgasmic dysfunction. *ED*, erectile dysfunction.

masturbation retraining, reducing anxiety related to sexual activity and adjustment of sexual fantasies.[3, 33, 43]

Medical therapy. There are no FDA approved therapies for orgasmic disorders, and pharmacological agents for orgasmic dysfunction are largely experimental with limited efficacy and often undesirable side effect profiles. There have been no randomized controlled trials assessing medical treatments for orgasmic dysfunction. Pharmacotherapy includes medications with central effects on oxytocin, serotonin and/or dopamine. A summary of options is presented in the table.

SSRI induced orgasmic dysfunction. **Drug substitution, decreasing the dosage or cessation of the offending agent can be considered in the setting of SSRI induced orgasmic dysfunction but must be discussed with the prescribing provider.** This condition has also been treated with cyproheptadine, amantadine, yohimbine, bupropion and buspirone (minimal data available).

Cyproheptadine is an antihistamine with antiserotonergic properties. Based on small case series and anecdotal evidence, the suggested dosage is 4-16 mg 3-4 hours before intercourse on a regular or on demand basis. Approximately 50% of men report some or much improvement in SSRI induced orgasmic dysfunction with cyproheptadine.[44, 45] Dose related sedation and weight gain may occur and can limit overall efficacy. In addition, cyproheptadine is used as an antidote in serotonin syndrome and thus will reverse SSRI effects in the treatment of depression.

Amantadine has been used historically for prophylaxis and treatment of the flu as well as parkinsonian symptoms. The mechanism of action is poorly defined but the drug likely stimulates dopaminergic neurons indirectly by antagonizing the N-methyl-D-aspartate receptor. A small case series indicated improvement in SSRI induced orgasmic dysfunction in 8 of 19 men (42%).[44] Amantadine may be administered on demand (100-400 mg 2 days before sexual activity) or chronically (100-200 mg twice daily).[46]

Yohimbine is an indole alkaloid derived from the bark of the African tree Pausinystalia johimbe. This agent is an alpha-2 adrenergic antagonist that has been traditionally used as an aphrodisiac and may have some benefit in treatment of erectile dysfunction. However, studies to date on orgasmic dysfunction have been poorly designed with conflicting results. In a small case series administration of yohimbine resulted in improvement in SSRI induced orgasmic dysfunction to a greater degree than treatment with cyproheptadine or amantadine (17 of 21 patients, 81%).[44] Another small study showed that 19 of 29 men with anorgasmia (66%) were able to achieve orgasm at a mean yohimbine dose of 38 mg.[47]

Bupropion is a norepinephrine-dopamine reuptake inhibitor that is used to treat depression and seasonal affective disorder, and to aid in smoking cessation. A small study describing administration of 150 mg sustained-release bupropion daily in men with reported lifelong delayed orgasm revealed a 25% decrease in mean intravaginal ejaculatory latency time, significant increase in orgasm and intercourse satisfaction domain scores on the IIEF, and improvement in patient reported ejaculatory control from "fair" to "good" in 21% of men.[37] Another case series of 10 men with delayed orgasm corroborated these findings.[48]

Generalized anorgasmia or delayed orgasm. Oxytocin is an amino acid peptide released by the posterior pituitary gland linked to sexual function and orgasm, bonding and lactation/uterine contractions in females.[49] In males there is a physiological increase in oxytocin level followed by an immediate decrease to baseline at the time of orgasm, and administration of oxytocin has demonstrated decreased ejaculation latency in animal models.[50, 51] Individual case reports and a case series have indicated improved ability to achieve orgasm, improved intensity of orgasm and restoration of orgasm in anorgasmic males.[52–54]

Cabergoline is a dopamine agonist prescribed for hyperprolactinemia of pituitary or idiopathic origin. **A recent retrospective review of men treated with 0.5 mg cabergoline twice weekly for delayed orgasm or anorgasmia found that two-thirds (87 of 131) reported subjective improvement in ability to orgasm.[55]** Duration of therapy and concomitant testosterone

Table. Medical therapy for orgasmic dysfunction

Medication	Approved Indications	Common Side Effects	As Needed Dosage	Continuous Dosage
Cabergoline	Hyperprolactinemia	Nausea, headache, dizziness	-	0.5 mg 2 times weekly
Bupropion	Depression, seasonal affective disorder, smoking cessation	Headache, dry mouth, nausea, weight loss, insomnia, agitation, dizziness	-	150-300 mg per day
Cyproheptadine	Hypersensitivity reaction	Drowsiness, dizziness, disturbed coordination	4-16 mg	4-16 mg
Amantadine	Parkinson disease, dyskinesia associated with Parkinson disease, drug induced extrapyramidal symptoms	Hallucinations, dizziness, dry mouth, peripheral edema, constipation, orthostatic hypotension	100-400 mg	100-200 mg 2 times daily
Oxytocin	Postpartum hemorrhage, labor induction, incomplete or inevitable abortion	Changes to heart rate, excessive bleeding, hyponatremia, hypertension, effects on fetus	20-24 IU	-
Yohimbine	None	Anxiety, headache, sweating, nausea, tachycardia, priapism	-	20-40 mg per day

therapy were associated with a significant positive response to cabergoline in multivariate analysis.

Testosterone therapy significantly improves erectile function and other sexual parameters in hypogonadal men. **Multiple meta-analyses of hundreds to thousands of men have shown statistically significant improvements in IIEF orgasm function domain with treatment of hypogonadism.**[29, 56] The relative efficacy of testosterone gels, injections and subcutaneous pellets in the setting of orgasmic dysfunction is currently unclear.

Penile vibratory stimulation. In men with delayed orgasm secondary to loss of penile sensation penile vibratory stimulation may provide a suitable treatment option. This therapy involves mechanical stimulation of the frenulum of the penis with an external vibrator. Approximately 70% of treated patients report restored orgasm at least some of the time, and those who respond to this treatment have significant increases in IIEF orgasm satisfaction domain scores.[57]

Fertility. **Electroejaculation for obtaining semen may be offered to couples attempting to conceive in the setting of refractory orgasmic dysfunction.** Electroejaculation is performed under general anesthesia and involves placement of a transrectal probe that delivers manually controlled cyclic, progressively higher electrical current to the seminal vesicles and prostate gland, leading to ejaculation. Depending on the concentration of sperm within the ejaculate, couples may proceed with intrauterine insemination or in vitro fertilization.[58, 59] Other options include testicular or epididymal sperm aspiration or extraction for in vitro fertilization in men with refractory anorgasmia.

CONCLUSIONS

Orgasmic dysfunction remains insufficiently defined and characterized, leading to limitations in the ability to diagnose, classify and treat this condition. There remains a substantial need for further investigation of orgasmic dysfunction, particularly regarding the timing of orgasm, the neurophysiology of ejaculation and orgasm, and factors that influence ejaculatory latency. Currently there are no large, randomized, controlled trials of pharmacotherapies for DE. Although a number of potentially effective therapies exist, they lack the evidence base for more definitive conclusions regarding efficacy. These therapies should be subjected to clinical trial evaluation pending or preceding the development of other treatment approaches.

The current definition of delayed ejaculation is limited by the paucity of data on what constitutes "delayed" to the point of being pathological. In fact, the 25-minute latency time defining DE was assigned based on population level data and statistical assumptions rather than objective evaluation of affected men. Many men with DE or orgasmic dysfunction that is troublesome are likely to have ejaculatory latency times shorter than 25 minutes. Additional studies to better define the factors that constitute troublesome DE for the man and his partner will facilitate improved diagnosis and management of DE and orgasmic dysfunction.

Mental health approaches to the management of delayed ejaculation and orgasmic dysfunction, particularly in the absence of effective pharmacotherapies, will continue to evolve and be an integral part of management, along with tighter integration of mental health and biomedical approaches. These methods, as well as future therapies, will be further guided by a more complete understanding of the pathophysiology of orgasmic dysfunction. Thus, as our understanding of orgasmic dysfunction evolves, and as we continue to develop the evidence base for effective therapies, our ability to manage these conditions will continue to improve.

DID YOU KNOW?

- Male orgasmic dysfunction is best discussed in terms of delayed orgasm and anorgasmia. Unfortunately operative diagnoses are varied and without consensus.
- Medications represent the most frequent identifiable causes of orgasmic dysfunction. These medications include antidepressants, antipsychotics, tranquilizers, 5-alpha-reductase inhibitors and opiates.
- Previous pelvic surgery, as experienced by men with prostate and colon cancer, is an important cause of orgasmic dysfunction.
- Abnormalities in hormonal homeostasis may result in orgasmic dysfunction. Specific endocrine disorders involving prolactin, thyroid function and testosterone are most commonly cited. Manipulation of these hormones may also serve as a direction for targeted therapy.
- Aging is an important factor in orgasmic dysfunction, affecting penile sensation and development of associated comorbidities such as hypogonadism and diabetes mellitus.
- Behavioral causes of orgasmic dysfunction must always be identified and addressed. Working with a knowledgeable mental health specialist is essential in treating these disorders.
- Accurate diagnosis must include identifying endocrinopathies, evaluating neuropathic disorders and assessing sympathetic outflow integrity.
- Treatment of the symptoms of anejaculation and orgasmic disorders must be clearly differentiated. The judicious use of cyproheptadine, amantadine, yohimbine, bupropion, oxytocin or cabergoline can be considered.

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Study Questions Volume 39 Lesson 18

1. A 38-year-old man is anorgasmic. His physical examination and endocrine evaluation are normal. The next step is consultation with a urologist and a
   a. pelvic floor physical therapist
   b. interventional radiologist
   c. acupuncturist
   d. psychologist or psychiatrist

2. A reduced incidence of post-prostatectomy orgasmic dysfunction is associated with
   a. Retzius sparing approach
   b. nerve sparing techniques
   c. use of robotic surgery
   d. anterior approach

3. A 68-year-old man with a history of hypertension and diabetes has been unable to achieve orgasm for 3 years. He achieves erections sufficient for penetrative intercourse with 100 mg sildenafil as needed. He also describes increasing fatigue and low libido. Physical examination is unremarkable. The next step is
   a. psychological evaluation
   b. testosterone and thyroid function tests
   c. biothesiometry
   d. penile duplex ultrasound

4. The mechanism of action of cabergoline in treating hyperprolactinemia induced orgasmic dysfunction is
   a. dopamine agonist
   b. stimulates testosterone production
   c. norepinephrine-dopamine reuptake inhibitor
   d. alpha-2 adrenergic antagonist

5. The proposed action and appropriate dosage of oxytocin in the treatment of delayed orgasm are
   a. increased penile sensation, 20-24 IU daily
   b. decreased latency time, 20-24 IU as needed
   c. decreased refractory period, 10-14 IU daily
   d. increased penile sensation, 10-14 IU as needed

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