Management of Sexual Dysfunction in Men

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Objectives

1. Explain the etiology, including pathophysiology and contributing factors, of male sexual dysfunction
2. Given a male patient, classify the type of sexual dysfunction he is experiencing
3. Discuss the adverse effects, role in therapy and significant drug-drug interactions associated with sexual dysfunction treatment options
4. Describe appropriate strategies to utilize in the male patient with erectile dysfunction who is not responding to traditional therapy recommendations

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Objectives, cont'd

5. Explain characteristics that would make various sexual dysfunction treatment modalities inappropriate in men (i.e. contraindications)
6. Provide appropriate non-pharmacologic and pharmacologic recommendations for a given male patient with sexual dysfunction based on patient-specific parameters
7. Counsel a given patient on the appropriate administration and potential adverse effects of various sexual dysfunction treatment modalities
8. Discuss healthcare disparities related to erectile dysfunction and strategies to reduce them in clinical practice

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What is Sexual Dysfunction?[1]

"A heterogeneous group of disorders that are typically characterized by a clinically significant disturbance in a person's ability to respond sexually or to experience sexual pleasure"

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Epidemiology[2]

- National Health and Social Life Survey (1999)
  - Prevalence of sexual dysfunction in U.S. men – 31%
    - Sexual dysfunction included:
      - Unpleasurable sexual activities
      - Lack of interest in sexual activities
      - Erectile dysfunction
      - Inability to achieve orgasm
      - Premature ejaculation
      - Anxiety about sexual performance

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Epidemiology[3]

- National Health and Nutrition Examination Survey (NHANES 2001-2002)
  - Overall prevalence of ED in US men ≥ 20 yo - 18.4%
    - ~18 million American men
  - Prevalence ↑ with age, diabetes, BPH, HTN, CVD
    - Prevalence of ED in men with diabetes was found to be 51.3%
    - Prevalence of ED in men with CVD was found to be 50.0%

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Physiology of an Erection[4]

- Erections involve the vascular, nervous and hormonal systems
- Penis contains 2 corpora cavernosae (CC)
  - Sponge-like erectile tissue connected by sinuses which engorge with blood when stimulated
  - Surrounded by tunica albuginea
- Penis contains 1 corpus spongiosum (CS)
  - Surrounds the urethra

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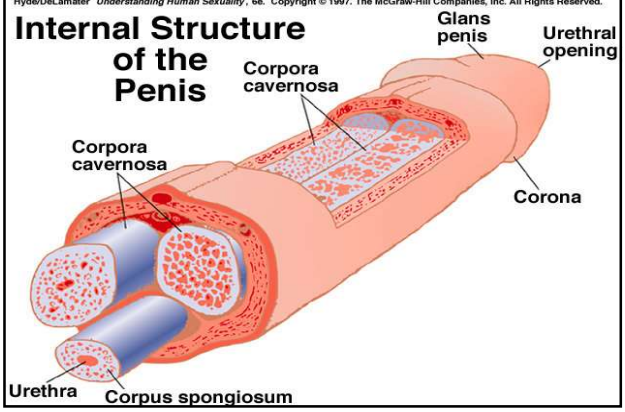
Structure of the Penis



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Physiology of an Erection, cont'd[4]

- Flaccidity: Arterial blood flow in = venous outflow

Sexual Stimulation → Activation of parasympathetic system → Smooth muscle relaxation → ↑ arterial blood flow into corpora cavernosae → Penile elongation & swelling = ERECTION

- Erection maintained by ↓ venous outflow due to compression of subtunical venules

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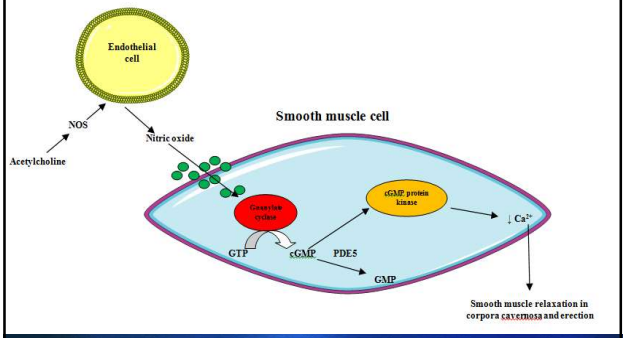
Physiology of an Erection[4,5]



Adapted from References 4,5; Designed by presenter

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Physiology of an Erection, cont'd[4]

- **Detumescence**
  - NE is released following ejaculation (sympathetic nervous system)
    - ↑ in smooth muscle tone
    - Leads to smooth muscle contractions
    - ↓ blood flow into the corpora → FLACCIDITY
  - Catabolism of cGMP by Type 5 phosphodiesterase contributes to flaccidity

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Physiology of an Erection, cont'd[4,6]

- **Hormonal Influences**

Testosterone —(5-alpha reductase)→ Dihydrotestosterone

- Testosterone's effects on sexual function
  - Helps maintain libido
  - May help with vasodilation of arterioles through its effects on PDE5 and NO synthase
- Estrogen's role is less clear

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Contributing Factors – *Lifestyle*[4,7,8]

- **Physical inactivity**
  - ↑ exercise has been linked to greater improvements in sexual activities, orgasms, and EF
- **Obesity**
  - Higher risk for ED (RR 1.3; 95% CI 1.2-1.4) for BMI > 28.7 kg/m^2
- **Smoking**
  - Causes atherogenic changes and endothelial injury
- **Acute and chronic alcohol ingestion**
  - Can lead to ↓ sexual performance
  - May ↓ testosterone production

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Contributing Factors – *Medications*[4,9]

- **↓ Libido**
  - Beta blockers
  - Thiazide diuretics
  - Spironolactone
  - Clonidine
  - Selective serotonin reuptake inhibitors (SSRIs)
  - Tricyclic antidepressants
  - Benzodiazepines
  - Niacin
  - Phenobarbital
  - Phenytoin
  - Antipsychotics
    - Greater with typicals
- **ED**
  - Beta blockers
  - Thiazide diuretics
  - Spironolactone
  - Clonidine
  - Alpha blockers
  - Reserpine
  - SSRIs
  - Phenobarbital
  - Phenytoin
  - 5-alpha reductase inhibitors

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Contributing Factors – *CVD*[10]

- **Both ED and CVD are indicators of the SAME disease state process**
  - Impaired endothelial function leading to the inhibition of vasodilation
- **ED often precedes the development of heart disease by 2-5 years**
- **Patients with ED who do not have a history of CVD or symptoms of CVD should be considered at risk for CVD until it can be ruled out**

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Contributing Factors – *CVD*, cont'd[11]

E D

Represents Erectile Dysfunction
AND
Endothelial Dysfunction

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Contributing Factors – *Other Diseases*[4,7,12,13]

- Diabetes
- Benign prostatic hyperplasia
- Hypogonadism
- Chronic kidney disease
- Sleep apnea
- Neurogenic conditions
  - Stroke
  - Multiple sclerosis
  - Parkinson's disease
  - Dementias
  - Spinal cord injury
- Psychological conditions
  - Depression
  - Anxiety
  - Stress

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Quiz Question #1

Activation of the sympathetic nervous system ultimately leads to the occurrence of an erection.

A. True
B. False

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Quiz Question #2

Catabolism of cGMP by _____ is responsible for promoting flaccidity once ejaculation has occurred?

A. 5-α-reductase
B. Alpha antagonism
C. Dihydrotestosterone
D. Type 5 phosphodiesterase

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Classifications of Sexual Dysfunction[1]

- 4 types in men are recognized
  - Erectile disorder (or dysfunction)
  - Male hypoactive sexual desire disorder
  - Premature ejaculation
  - Delayed ejaculation

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Subtypes of Sexual Dysfunction[1]

- Provide insight on the TIMING of symptoms
- ACQUIRED
  - Appears after a period of normal sexual function
- LIFELONG
  - Has been present since first sexual attempt
- GENERALIZED
  - Difficulties occurring despite the stimulation, situation or partner
- SITUATIONAL
  - Difficulties occurring and are dependent on the stimulation, situation and/or partner

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Other Qualifiers[1]

- Symptoms MUST be present for at least 6 months
- Symptoms MUST cause significant patient distress and cannot be explained by any nonsexual mental condition or stressors
- Premature ejaculation, delayed ejaculation and ED must occur 75-100% of the time with sexual attempts

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Clinical Assessment[4,7,14,15]

1. Physical exam, sexual history, and medical history
2. Medication list
3. Lab Values
   - -Blood glucose/hemoglobin A1c
   - -Lipid profile
   - -Thyroxine level
   - -Testosterone level in men >50yo or ≤ 50 with complaints of ↓ libido
     - -Total testosterone then free testosterone , prolactin and LH

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Erectile Disorder or Dysfunction (ED)[1,14]

- AUA
  - *"The inability to achieve or maintain an erection sufficient for satisfactory sexual performance"*
- DSM-V (any or all of the following criteria)
  - Difficulty achieving an erection for sexual activities
  - Difficulty maintaining an erection for the completion of sexual activities
  - Reduction in penile rigidity

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Types of ED[4,7,14,15]

- Organic
  - ED resulting from a *physical* cause
    - Lifestyle factors
    - Diseases
    - Medications
  - Gradual onset
- Psychogenic
  - ED resulting from high-stress situations
  - Sudden onset
  - Often manifests episodically
- Mixed
  - Organic + psychogenic factors

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ED Management Options[4,14,15,16]

1. Non-pharmacologic options
2. Pharmacotherapy
   -First & second generation PDE5 inhibitors
   -Prostaglandin agents
3. Medical devices
   -Vacuum erection devices
4. Surgery
   -Penile prosthesis

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Non-Pharmacologic Options[4,16]

- Reduce stress or anxiety
- Lose weight
  - Mediterranean diet?
- Increase physical activity
- Stop smoking
- Moderate alcohol intake

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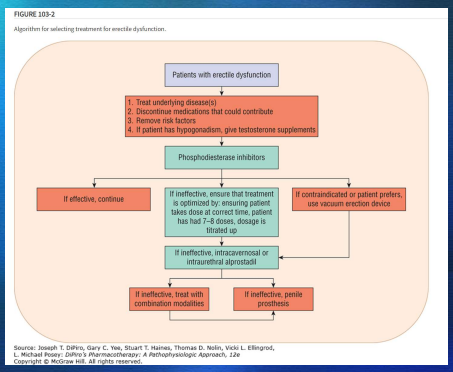
ED Algorithm[4]



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ED Treatment Algorithm – AUA 2018[14]

"…All men should be informed of all treatment options that are not medically contraindicated to determine the appropriate treatment. Although many men may choose to begin with the least invasive option, the Panel notes that it is valid for men to begin with any type of treatment, regardless of invasiveness or reversibility. Men also may choose to forgo treatment."

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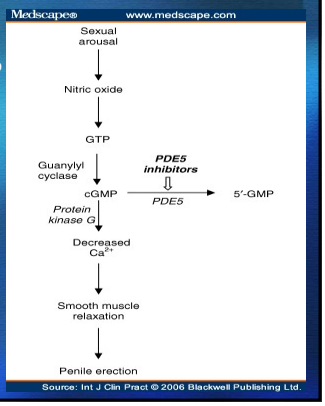
PDE5 Inhibitors[4,14,15,17]

- **MOA:** Inhibit Type 5 phosphodiesterase to ↓ catabolism of cGMP yielding NO-induced vasodilation
- **Examples:**
  - ***First generation:***
    - Sildenafil (Viagra®)
  - ***Second generation:***
    - Tadalafil (Cialis®)
    - Vardenafil (Levitra®)
    - Avanafil (Stendra®)



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PDE5 Inhibitors, cont'd[4,14,15,17,18]

- First Generation: Sildenafil
  - Dose: 50mg (25-100mg)
  - Take 1 hr before sexual activity
  - Fatty meals ↓ absorption – Do not take within 2 hrs of meals
  - No more than 1 dose/day
  - t1/2 ~ 4 hours
  - Effects last ~ 4-5 hrs

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PDE5 Inhibitors, cont'd[4,14,15,17,19]

- Second Generation: Vardenafil
  - MOA same as sildenafil
  - Dose: 10mg (2.5-20mg) 25-60 min before sexual activity
  - No more than 1 dose per day
  - Fatty meals ↓ absorption –Do not take within 3 hrs of meals
  - t1/2 ~ 4 hours
  - Effects last ~ 4-5 hrs

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PDE5 Inhibitors, cont'd[4,14,15,17,20]

- Second Generation: Tadalafil
  - MOA same as sildenafil
  - Dose: 10mg (2.5-20mg) ~30 min before sexual activity
  - No more than 1 dose per day
  - Begins working in ~30 minutes
  - Food does NOT affect absorption
  - t1/2 ~ 17.5 hours
  - Effects last ~ 36hrs ("Weekend Viagra")

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PDE5 Inhibitors, cont'd[4,14,15,17,21]

- Second Generation: Avanafil
  - MOA same as sildenafil
  - Dose:
    - PRN: 100mg (50-200mg) ~30 min before sexual activity
    - Do not use with strong CYP 3A4 inhibitors
    - 50 mg dose with moderate CYP 3A4 inhibitors
  - No more than 1 dose per day
  - Effects last ~ 6 hours
  - Food does NOT affect absorption

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Adverse Effects[18,19,20,21,22]

- Headache
- Facial flushing
- Nasal congestion
- Dyspepsia
- Dizziness
- Priapism > 4 hours
- Sensitivity to light, blurred vision, loss of blue-green color discrimination (sildenafil only)
- Back & muscle pain (tadalafil only)
- CV effects: Ventricular arrhythmia, cerebrovascular hemorrhage, TIA, MI, hypotension, sudden cardiac death

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Adverse Effects, cont'd[18,19,20,21,22]

- Vision loss in 1 or both eyes
  - Non-arteritic anterior ischemic optic neuropathy (NAION)
  - Potentially linked to ↓blood flow to optic nerve
  - Risk ↑ in patients with glaucoma, macular degeneration, diabetic retinopathy
- Hearing loss in 1 or both ears
  - Accompanied by tinnitus, vertigo
  - ~1/3 of cases had temporary hearing loss

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Precautions & Contraindications[18,19,20,21,22]

- CV history
  - Recent MI/stroke
  - Life-threatening arrhythmia
  - Uncontrolled HTN
  - Hypotension
  - Hx of unstable angina
  - Cardiac failure
  - Multiple antihypertensives
- Retinitis pigmentosa (sildenafil only)
- Severe liver impairment
- ESRD requiring dialysis

MAYBE

DEFINITELY NOT

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CV Risk Stratification[23]

Risk Category	Patient Condition	Management Approach
Low risk	• Asymptomatic CVD with < 3 risk factors for CVD • Well-controlled HTN • Mild CHF (NYHA I/II) • Mild valvular heart disease • MI > 8 weeks ago	Patient can be initiated on PDE5 inhibitor
Intermediate risk	• 3+ risk factors for CVD • Mild-moderate angina • Recent MI or stroke within the past 2-8 weeks • Moderate CHF (NYHA III) • Hx of stroke, TIA, or PAD	Patient requires CV workup and evaluation, including treadmill test, to determine tolerance to increased myocardial energy consumption associated with increased sexual activity. They would then be reclassified as low or high risk following testing.
High risk	• Unstable or refractory angina despite treatment • Uncontrolled HTN • Severe CHF (NYHA IV) • Recent MI or stroke within past 2 weeks • Moderate-severe valvular heart disease • High risk cardiac arrythmias • Obstructive hypertrophic cardiomyopathy	PDE5 inhibitor therapy is contraindicated. Sexual intercourse should also be deferred.

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Drug Interactions[18,19,20,21,22,23]

- Nitrates
  - Causes severe hypotension
  - Avoid this combination!!!
- α-adrenergic antagonists
  - Produce systemic hypotension
  - Ensure stable dose of α-adrenergic antagonist before initiation of low dose PDE5 inhibitor (vice versa)

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Patient Counseling[18,19,20,21,22,23]

- PDE5 inhibitors do NOT prevent STD transmission
- Appropriate counseling regarding fatty food ingestion & administration of drug
- Alcohol can impair sexual activities, especially if the patient is dehydrated
- Seek medical assistance with an erection lasting longer than 4 hours
- Don't forget ADRs!

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Treatment Strategies for Non-Responders[24,25]

1. Patient education
   - Follow-up
   - Adjustment of administration time
   - Sexual stimulation
   - Titration to the maximum tolerated dose
2. Improvement in disease state management and other lifestyle factors

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Treatment Strategies for Non-Responders, cont'd[24,25]

3. Normalization of testosterone levels
4. Switch PDE5 inhibitors
5. Daily use of PDE5 inhibitor
   - Tadalafil 2.5 mg (up to 5 mg) PO Qdaily
   - Concerns about tachyphylaxis
6. Psychosexual counseling
   - In combination with PDE5 inhibitor therapy

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Comparison Between PDE5 Inhibitors[26]

- All three agents are efficacious
- A systematic review and meta-analysis found:
  - PDE5 inhibitors were more effective than placebo
    - 69% vs 35%, respectively
  - Improved erections were greater with PDE5 inhibitors (range 67-89%) vs placebo (27-35%)
  - High placebo responses

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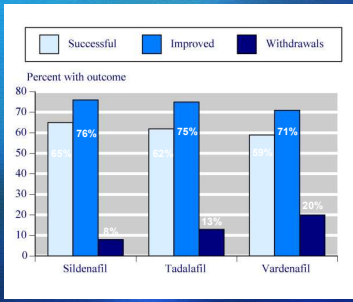
Comparison Between PDE5 Inhibitors, cont'd[27]

- Findings from another systematic review



Moore RA, et al. *BMC Urol* 2005;5:18.

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Comparison Between PDE5 Inhibitors, cont'd[28]

- Open-label, randomized, crossover study

  Sildenafil X 12 weeks → Tadalafil X 12 weeks

  OR

  Tadalafil X 12 weeks → Sildenafil X 12 weeks

  THEN

  Patient selection of drug X 8 weeks

- Efficacy measured with IIEF & SEP diaries

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Comparison Between PDE5 Inhibitors, cont'd[28]

- **Results**
  - 291 of 367 men completed both treatments
  - 29% chose sildenafil and 71% chose tadalafil (p<0.001)

	Baseline	Sildenafil	Tadalafil	p-value*
IIEF Score	14.2	23.9	24.3	0.08
SEP2 (penetration)	46%	82%	85%	0.06
SEP3 (successful sex)	19%	72%	77%	0.003

*sildenafil vs. tadalafil

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Quiz Question #3

Blue-green color discrimination is a potential side effect to counsel a patient receiving avanafil (Stendra®).

A. True
B. False

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Quiz Question #4

Which patient listed below can safely receive treatment with sildenafil (Viagra®)?

A. 61yo male on dialysis
B. 51yo male who had a MI 1 mo ago
C. 67yo male with Type 2 DM
D. 70yo male with uncontrolled HTN

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Quiz Question #5

KK is receiving atenolol, isosorbide dinitrate, aspirin, tamsulosin, and simvastatin. His physician asks you about starting vardenafil. Which medication that KK is receiving is a contraindication to treatment with vardenafil?

A. Atenolol
B. Isosorbide dinitrate
C. Simvastatin
D. Tamsulosin

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Quiz Question #6

Johnny is a 67 yo male receiving sildenafil 100 mg PO 60 minutes prior to sexual activities. He shares with you today that his sildenafil does not seem to be working anymore. He has a history of type 2 diabetes, hypertension and dyslipidemia. Which of the following is/are a/an appropriate recommendation(s) for Johnny?

A. Switch Johnny from sildenafil to tadalafil
B. Ensure Johnny's blood pressure, cholesterol, and diabetes are at guideline targeted goals
C. Consider administering sildenafil daily
D. All of the above

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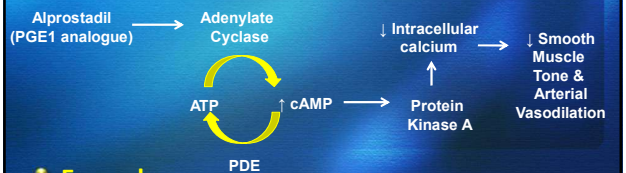
Prostaglandin Analogs[14,15,29,30]

- **MOA:** Acts like prostaglandin E_1 to ↑ cAMP which ↑ blood flow into the corpora



- **Example:**
  - Alprostadil (MUSE®, Caverject Impulse®)

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Prostaglandin Analogs[14,15,29]

Medication **U**rethral **S**ystem for **E**rections

- Urethral insert
- Used via insertion of a pellet into the urethra
- Dose: 125-1000mcg IU 5-10 minutes before sexual activities (no more than 2 systems/24hrs)
  - Urinate before insertion

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Proper use of MUSE®[29]

- Hold penis with 1 hand and insert drug with other hand into urethra
- Push drug into urethra using plunger and rock back and forth gently
- Massage penis to ↑ absorption

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MUSE®, cont'd[14,15,29]

- Effects last for ~30-60 minutes
- Efficacy rate is 43-60%
- Adverse effects:
  - Urethral bleeding
  - Urethral pain
  - Priapism > 4-6 hours
  - Dizziness & syncope

******Female partners can experience vaginal burning, irritation, itching or pain******

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Caverject Impulse®[14,15,30]

- Intracavernosal injection
- Used via injection into the corpora
- Dose: 2.5-60mcg IC given 5-10 min before sexual activities (no more than 1 dose/24hrs AND 3 doses/week)
  - SLOWLY titrate dose to effect
- Effects last no more than 1 hour
- Efficacy rate is 70%-90%

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Proper Use of Caverject Impulse®[30]

- MULTIPLE steps to use properly
- Must select dose on injection device
- Inject into SPONGY tissue on 1 side of penis
- Never inject into dorsal or ventral surfaces
- Avoid injecting into visible veins
- Apply pressure to injection site X 5 min

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Caverject Impulse Adverse Effects®[30]

- Corporal fibrosis
- Penile pain
- Priapism > 4-6 hours
- Injection site hematoma
- Dizziness & hypotension

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Contraindications to Prostaglandin Analogs[29,30]

- Sickle cell anemia
- Multiple myeloma
- Thrombocythemia
- Penile abnormalities
- Not for use in intercourse with a pregnant female unless condom is used (MUSE® only)

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Quiz Question #7

Patients receiving Caverject Impulse® should be counseled to inject on both sides of the penis to increase efficacy.

A. True
B. False

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Quiz Question #8

A potential adverse effect associated with alprostadil is:

A. Dizziness
B. Dyspepsia
C. Hearing loss
D. NAION

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Vacuum Erection Devices (VEDs)[4,14,15]

- Creates a vacuum-like chamber around the penis which draws blood in →ERECTION
  - Contains 3 parts: Cylinder where the penis is place
  - Pump to generate negative pressure
  - Elastic band to maintain erection
- Caution in patients on anticoagulant therapy

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Surgery[4,14,15]

- Penile prostheses
  - Most invasive treatment for ED
  - Malleable vs inflatable
  - Inserted under anesthesia
  - >90% patient satisfaction
  - Adverse effects:
    - Infection
    - Mechanical failure

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Male Hypoactive Sexual Desire Disorder[1]

- DSM-V criteria
  - Deficient or absent sexual or erotic thoughts or fantasies
  - Deficient or absent desire for sexual activity
    - Clinical judgment takes into consideration age, general, socio-cultural contexts of a patient's life
- Can be somewhat subjective
- The association between mood and sexual desire is not always linear

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Male Hypoactive Sexual Desire Disorder, cont'd[31]

- Study involved 919 heterosexual, white men
  - 9.4% reported an ↑ and 42% reported a ↓ in sexual interest when depressed
  - 20.6% reported an ↑ and 28.3% reported a ↓ in sexual interest when stressed/anxious
- From this cohort, 43 participants were asked why interest would ↑ when stressed/depressed
  - Sex could serve as means of self-validation
  - Sex provides a calming effect
  - Sex allows for an "excitation transfer"

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Male Hypoactive Sexual Desire Disorder Management Options[1]

1. Disease State/Lifestyle/Medication Management
2. Pharmacotherapy
   -Testosterone
   -Antidepressants
3. Behavioral/Sex Therapy

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Disease/Lifestyle/Medication Management[32]

- Consider changing therapies or using lowest possible doses of medications that can ↓ libido
- Work to control diseases such as diabetes, depression, and anxiety
- Healthy eating and physical activity to improve body image and self-esteem

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Testosterone[4,14,15,33]

- Indicated for men with hypogonadism
  - Do NOT use in eugonadal men
- Goal – normalize testosterone levels
- Several formulations available
- Screen for prostate cancer and BPH
- Adverse effects: Weight gain, exacerbation of HTN, gynecomastia, CHF, edema

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Antidepressants[32]

- Most SSRIs and TCAs cause sexual dysfunction
- SOME can be used in men with ↓ libido AND depression

Antidepressant	Effect on Libido
Fluoxetine, paroxetine, citalopram, sertraline	↓
Imipramine	↓
Bupropion	↑
Trazodone	↑
Nefazodone	Neutral

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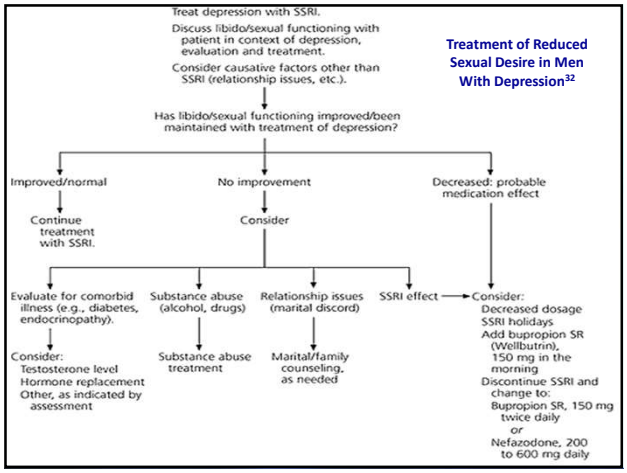

Treatment of Reduced Sexual Desire in Men With Depression[32]

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Antidepressants, cont'd[32]

- Adverse Effects
  - Specific for each antidepressant
    - Bupropion – seizures
    - Nefazodone – hepatotoxicity
  - Serotonin syndrome
- Drug-Drug Interactions
  - Specific for each antidepressant
  - Numerous interactions through the CYP450 system

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Behavioral/Sex Therapy[34]

- Can be beneficial for men with depression to discuss their concerns
- Sex therapy includes both the patient and his partner to help improve
  - Communication
  - Comfort with physical intimacy
  - Concerns about sexual activities
  - Familiarity with the body via sensate focus activities

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Premature (Early) Ejaculation[1]

- DSM-V criteria
  - Ejaculation occurring within ~ 1 minute after vaginal penetration BEFORE the male wishes to do so
    - Mild – occurring within 30 sec to 1 minute
    - Moderate – occurring within 15 to 30 seconds
    - Severe – occurring at the start of sexual activities up to 15 seconds
  - May be applied to early ejaculation occurring with nonvaginal sexual activities
    - Specific duration of time has not been established

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Premature Ejaculation, cont'd[35]

- International Society for Sexual Medicine criteria
  - Ejaculation occurring within 1 minute of vaginal penetration on almost or all occasions

OR

  - ↓ time to ejaculation, usually < 3 minutes

AND

  - Patient is unable to delay ejaculation upon penetration

AND

  - Produces negative consequences for the patient (i.e. frustration, distress, avoidance)

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Premature Ejaculation Management Options[36,37]

- Desensitizing creams
  - Example – lidocaine/prilocaine cream
  - Applied topically 20-30 minutes before sexual activities
  - Use of product for prolong periods of time (i.e. 30-45 min) has been associated with loss of erection
  - Can be used with or without a condom
  - Female partner may experience vaginal numbness and dulling of sensation

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Premature Ejaculation Management Options[36,37]

- SSRIs/TCAs
  - Situational versus continuous dosing

Antidepressant	Dosing Regimen
Clomipramine	25-50 mg/day OR 25 mg 4-24 hours before sex
Fluoxetine	5-20 mg/day
Paroxetine	10-40 mg/day OR 20 mg 3-4 hours before sex
Sertraline	25-200 mg/day OR 50 mg 4-8 hours before sex

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Premature Ejaculation Management Options[36,37,38]

- SSRI + PDE5 inhibitor
  - Exact reason for efficacy is unknown
  - Possibly effective due to improved erection from PDE5 inhibitor which ultimately down regulates receptors involved with latency
- Tramadol
  - 50 mg PO PRN
  - Poorly understood but may be a link between central opioid receptors and control of ejaculation

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Delayed Ejaculation[1]

- DSM-V criteria
  - Ejaculation that is:
    - Markedly delayed
      OR
    - Infrequent or absent
  - Occurs when the individual does not desire a delay
  - Subjectivity involved with the term *delayed*
  - Patient and partner may report fatigue and genital pain which cause them to avoid sexual activities

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Delayed Ejaculation Management Options[39,40]

- Delayed ejaculation is difficult to treat
- Pharmacotherapy for delayed ejaculation has
  - Limited efficacy
  - Numerous, unwanted side effects
  - Typically been used experimentally
- Drugs used to treat delayed ejaculation do so through the following effects:
  - Dopaminergic
  - Anti-serotinergic
  - Oxytocinergic

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Delayed Ejaculation Management Options[39,40]

Medication	Dosing Regimen
Cabergoline	0.25 – 2 mg twice weekly
Amantadine	100-400 mg/day for 2 days prior to sex OR 100-200 mg BID
Bupropion	150 mg Qdaily or BID
Buspirone	5-15 mg BID
Cyproheptadine	4-12 mg given 3-4 hours prior to sex

Most reports focus on use in men with SSRI-induced delayed ejaculation

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Delayed Ejaculation Management Options[39,40]

- Behavioral/Non-pharmacologic interventions
  - Use of vibrators to stimulate sexual arousal
  - Encourage fantasizing to help with stimulation
  - Encourage to focus on genital stimulation
  - Use of male-superior position during sexual activities
  - Sex therapy to manage any underlying self or partner issues
  - Adjust medications that might be contributing to sexual dysfunction

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Quiz Question #9

Testosterone replacement therapy is recommended in first line in all men with ED because it is an endogenously produced hormone.

A. True
B. False

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Quiz Question #10

Bob is a 51 yo male who shares with you that he is unable to ejaculate with almost every attempt at sexual activities. This is very frustrating for both him and his wife as it often leads to painful, tiring intercourse. He maintains his libido and does not have difficulty achieving or maintaining an erection. Which type of sexual dysfunction is Bob likely experiencing?

A. Delayed ejaculation
B. Erectile disorder
C. Male Hypoactive Sexual Desire Disorder
D. Premature ejaculation

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Quiz Question #11

Thomas is a 44 yo male reporting ejaculation occurring within about a minute following vaginal penetration in which he does not desire. He has a history of hypertension, GERD, and depression. His current medications include:

Bupropion SR 150 mg PO BID
Lisinopril 10 mg PO Qdaily
Ranitidine 150 mg PO BID

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Quiz Question #11, cont'd

Which of the following treatment options should be recommended to manage Thomas' premature ejaculation?

A. Initiate lidocaine/prilocaine cream applied an hour before sexual activities
B. D/C bupropion and initiate sertraline
C. Add cyprohepatadine 4 mg PO 3-4 hours prior to sexual activities
D. All of the above are plausible options

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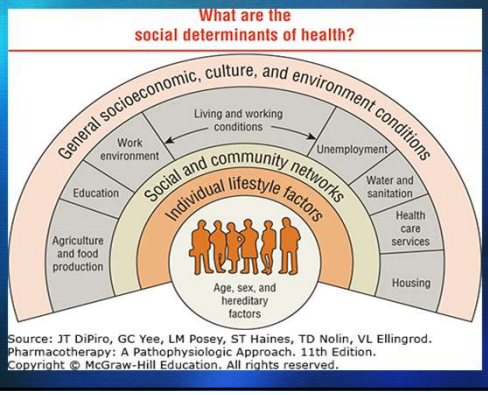
Social Determinants of Health



Source: JT DiPiro, GC Yee, LM Posey, ST Haines, TD Nolin, VL Ellingrod. Pharmacotherapy: A Pathophysiologic Approach. 11th Edition.

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ED & Healthcare Disparities[41,42]

- Not much is documented about healthcare disparities and ED.
- What we know:
  - ED impacts quality of life including well-being, self-esteem, relationships, and self-worth.
  - ED is being discussed more with healthcare providers.
  - Medications for ED can be costly and are not often not considered a necessity.
  - Treatment for ED is widely considered "medically necessary" by health-care insurers but there are more challenges with employer-sponsored health insurance.

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Race & ED Treatment[43]

- 2022 study was the first study on the association between ED treatment and race in the US
- Data from a database that utilizes commercial and Medicare claims
- Over 800,000 claims from men in the US between 2003 and 2018
  - 3.1% Asian
  - 10.5% African American
  - 11.5% Hispanic
  - 74.9% Caucasian

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Race & ED Treatment[43]

- Results
  - Compared to Caucasians:
    - Asian and Hispanic men had a lower probability of receiving any ED treatment (HR 0.92, 95% CI 0.87-0.96 and HR 0.89, 95% CI 0.85 to 0.94).
    - African-American men had a higher probability of receiving ED treatment (HR 1.10, 95% CI 1.05-1.16).
- Comments
  - Cultural and healthcare infrastructure may influence how men seek care
  - Hispanic patients frequently use herbal medications or traditional healers
  - Differing perspectives of a serious health problem vs natural part of the aging process

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References

1. American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders (5th edition). Arlington, VA: American Psychiatric Publishing.
2. Laumman EO, Paik A, Rosen RC. Sexual dysfunction in the United States: Prevalence and predictors. *JAMA*. 1999;281(6):537-544.
3. Selvin E. Burnett AL, Platz EA. Prevalence and risk factors for erectile dysfunction in the US. *Am J Med*. 2007;120:151-157.
4. Lee M, Sharifi R. Erectile Dysfunction. In: DiPiro JT, Yee GC, Haines ST, Nolin TD, Ellingrod VL, Posey M, eds. *Pharmacotherapy: A Pathophysiologic Approach, 12e* New York, NY: McGraw-Hill; Accessed on December 14, 2023.
5. Ferguson III JE, Carson III CC. Phosphodiesterase type 5 inhibitors as a treatment for erectile dysfunction: Current information and new horizons. *Arab J Urol*.2013;11:222-229.
6. Mikhail N. Does testosterone have a role in erectile function? *Am J Med*. 2006;119(5):373-382.
7. Mobley DF, Khera M, Baum N. Recent advances in the treatment of erectile dysfunction. *Postgrad Med J*. 2017;93:679-685.
8. Bacon CG, Mittleman MA, Kawachi I, Giovannucci E, Glasser DB, Rimm EB. Sexual function in men older than 50 years of age: Results from the Health Professionals Follow-up Study. *Ann Int Med*. 2003;139:161-168.

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References, cont'd

9. Park YW, Kim Y, Lee JH. Antipsychotic-induced sexual dysfunction and its management. *World J Mens Health*. 2012;30(3):153-159.
10. Ibrahim A, Ali M, Kiernan TJ, Stack AG. Erectile dysfunction and ischaemic heart disease. *Eur Cardiol*. 2018;13(2):98-103.
11. Life Extension Web site. Available at: http://www.lifeextension.com/protocols/male-reproductive/erectile-dysfunction/Page-03. Accessed January 8, 2024.
12. Palmer BF. Sexual dysfunction in men and women with chronic kidney disease and end-stage kidney disease. *Adv Ren Replace Ther*. 2003;10(1):48-60.
13. Budweiser S, Enderlein S, Jörres RA, et al. Sleep apnea is an independent correlate of erectile and sexual dysfunction. *J Sex Med*. 2009;6:3147-3157.
14. Burnett AL, Nehra A, Breau RH, et al. Erectile dysfunction: AUA guideline. *J Urol*. 2018;200:633-641.
15. American Association of Clinical Endocrinologists. Medical guidelines for clinical practice for the evaluation and treatment of male sexual dysfunction: A couple's problem – 2003 update. *Endocr Pract*. 2003. 9:79-95.
16. Montague DK. Nonpharmacologic treatment of erectile dysfunction. *Reviews in Urology*. 2002; 4:S9-S16.

90

References, cont'd

17. Setter SM, Iltz JL, Fincham JE, et al. Phosphodiesterase 5 inhibitors for erectile dysfunction. *Ann Pharmacother.* 2005;39:1286-1295.
18. Viagra® [package insert]. New York, NY: Pfizer Labs; 2017.
19. Levitra® [package insert]. West Haven, CT: Bayer HealthCare; 2022.
20. Cialis® [package insert]. Indianapolis, IN: Eli Lilly and Company; 2020.
21. Stendra® [package insert]. Freehold, NJ: Metuchen Pharmaceuticals, LLC; 2019.
22. Yafi FA, Sharlip ID, Becher EF. Update on the safety of phosphodiesterase type 5 inhibitors for the treatment of erectile dysfunction. *Sex Med Rev.* 2018;6(2):242-252.
23. Nehra A, Jackson G, Miner M, et al. The Princeton III Consensus Recommendations for the Management of Erectile Dysfunction and Cardiovascular Disease. *Mayo Clin Proc.* 2012;87(8): 766-778.
24. Park NC, Kim TN, Park HJ. Treatment strategy for non-responders to PDE5 inhibitors. *World J Mens Health.* 2013;31(1):31-35.
25. Lowe G, Bahnson R. Non-invasive management of primary phosphodiesterase type 5 inhibitor failure in patients with erectile dysfunction. *Ther Adv Urol.* 2010;1(5):235-242.
26. Tsertsvadze A, Fink HA, Yazdi F, et al. Oral phosphodiesterase-5 inhibitors and hormonal treatments for erectile dysfunction: A systematic review and meta-analysis. *Ann Intern Med.* 2009;151:650-661.

91

References, cont'd

27. Moore RA, Derry S, McQuay HJ. Indirect comparison of interventions using published randomised trials: systematic review of PDE-5 inhibitors for erectile dysfunction. *BMC Urol.* 2005:5:18.
28. Eardley I, Fourcroy J, Glina S, et al. An open-label, multicentre, randomized, crossover study comparing sildenafil citrate and tadalafil for treating erectile dysfunction in men naïve to phosphodiesterase 5 inhibitor therapy. *BJU Int.* 2005;96:1323-1332.
29. MUSE® [package insert]. Somerset, NJ: Meda Pharmaceuticals; 2018.
30. Caverject Impulse® [package insert]. Kalamazoo, MI: Pharmacia & Upjohn Company; 2023.
31. Bancroft J, Janssen E, Strong D, Carnes L, Vukadinovic Z, Long JS. The relation between mood and sexuality in heterosexual men. *Arch Sex Behav.* 2003;32(3):217-230.
32. Phillips Jr, RL, Slaughter JR. Depression and sexual desire. *Am Fam Physician.* 2000;62(4):782-786.
33. Rastrelli G, Corona G, Maggi M. Testosterone and sexual function in men. *Maturitas.* 2018;112:46-52.
34. Montgomery KA. Sexual desire disorders. *Psychiatry (Edgmont).*2008;5(6):50-55.
35. Althof SE, McMahon CV, Waldinger MD, et al. An update of the International Society of Sexual Medicine's guidelines for the diagnosis and treatment of premature ejaculation (PE). *J Sex Med.* 2014;11(6):1392-1422.

92

References, cont'd

36. Montague DK, Jarow J, Broderick GA, Dmochowski RR, Heaton JP, Lue TF, et al. Premature ejaculation: Guideline on the pharmacologic management of ejaculation. *J Urol.*2004;172:290-294.
37. Mohee A, Eardley I. Medical therapy for premature ejaculation. *Ther Adv Urol.*2011;3(5):211-222.
38. Yang L, Qian S, Liu H, Liu L, Pu C, Han P, et al. Role of tramadol in premature ejaculation: A systematic review and meta-analysis. *Urol Int*. 2013;91(2):197-205.
39. McMahon CG. Management of ejaculatory dysfunction. *Int Med J.* 2014;44:124-131.
40. Abdel-Hamid IA, Elsaied MA, Mostafa T. The drug treatment of delayed ejaculation. *Transl Androl Urol*. 2016;5(4):576-591.
41. Burnett AL, Rojanasarot S, Amorosi SL. An analysis of a commercial database on the use of erectile dysfunction treatments for men with employer-sponsored health insurance. *Urol.* 2021;149:140-145.
42. Burnett AL, Edwards NC, Barrett TM, Nitschelm KD, Bhattacharyya SK. Addressing health-care system inequities in the management of erectile dysfunction: A call to action. *Am J Mens Health.* 2020Sep-Oct;14(5):1557988320965078. doi: 10.1177/1557988320965078. PMID: 33045918; PMCID: PMC7557698.
43. Chen T, Li S, Eisenberg ML. Associations between race and erectile dysfunction treatment patterns. *Urol Pract.* 2022; 9: 423-430.

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