

# Erectile Dysfunction



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## **Objective: Be able to**

- Explain pathway of penile erection and erectile dysfunction
- Conduct simple assessment of erectile dysfunction
- Explain drug therapy for erectile dysfunction

## **Scope**

- ☐ Definition and prevalence of erectile dysfunction
- ☐ Physiology and pathway of penile erection
- ☐ Etiology of erectile dysfunction
- ☐ Assessment of erectile dysfunction
- ☐ Management for erectile dysfunction
- ☐ Drug therapy for erectile dysfunction

Erectile Dysfunction is a persistent or recurrent inability to attain an adequate penile erection until completion of sexual activity. It must, exclusively, not due to pharmacological effects of substance (addicted drug or medication) or general medical condition. (Am Psychiatric Association, 2000)

### **Prevalence**

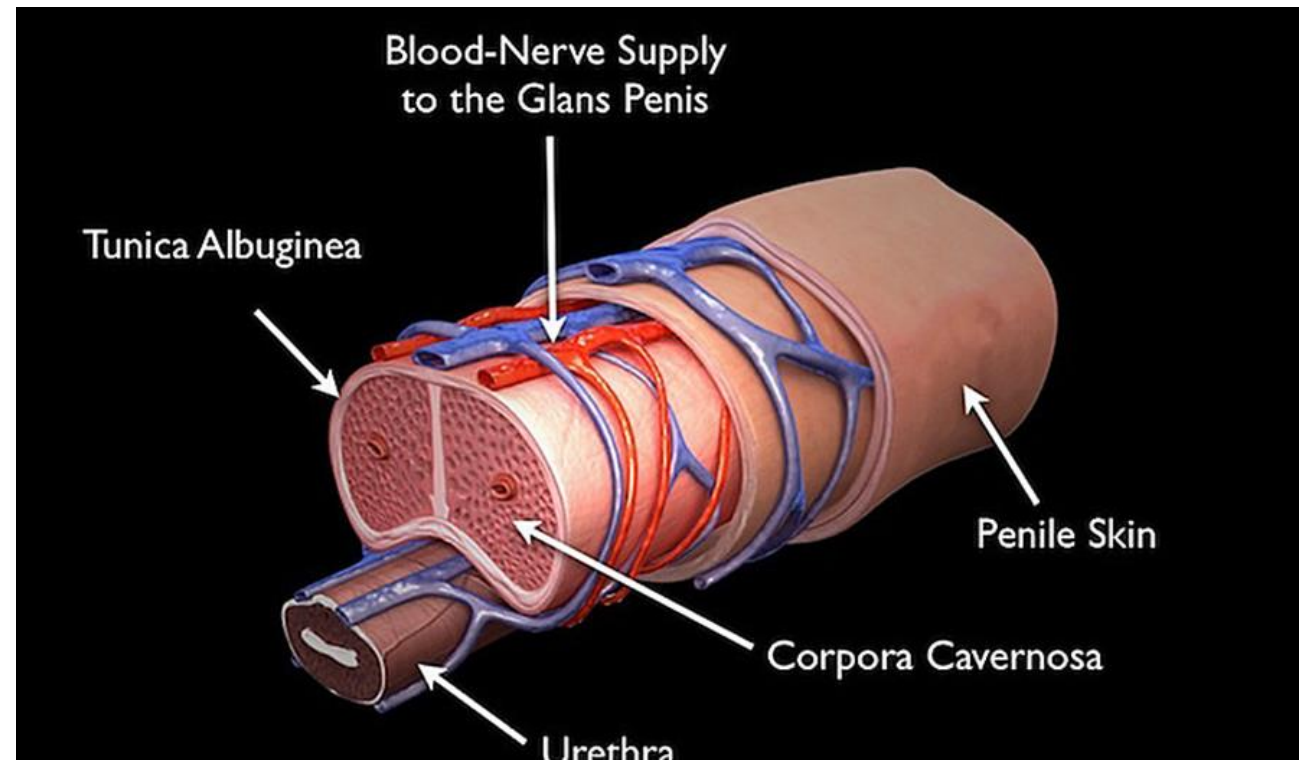
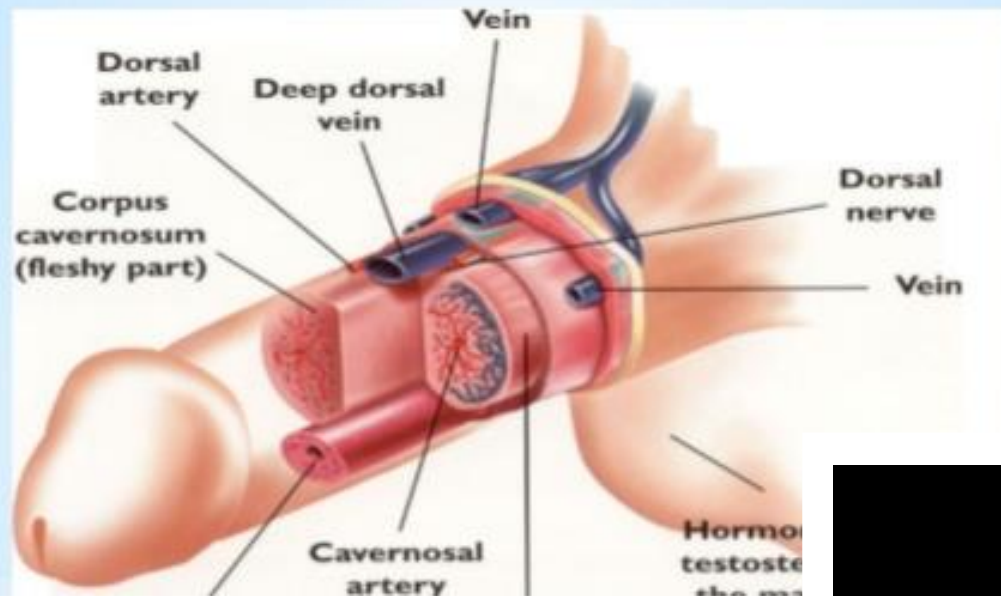
2% in men age < 40

25% in men age 65

75% in men age > 75

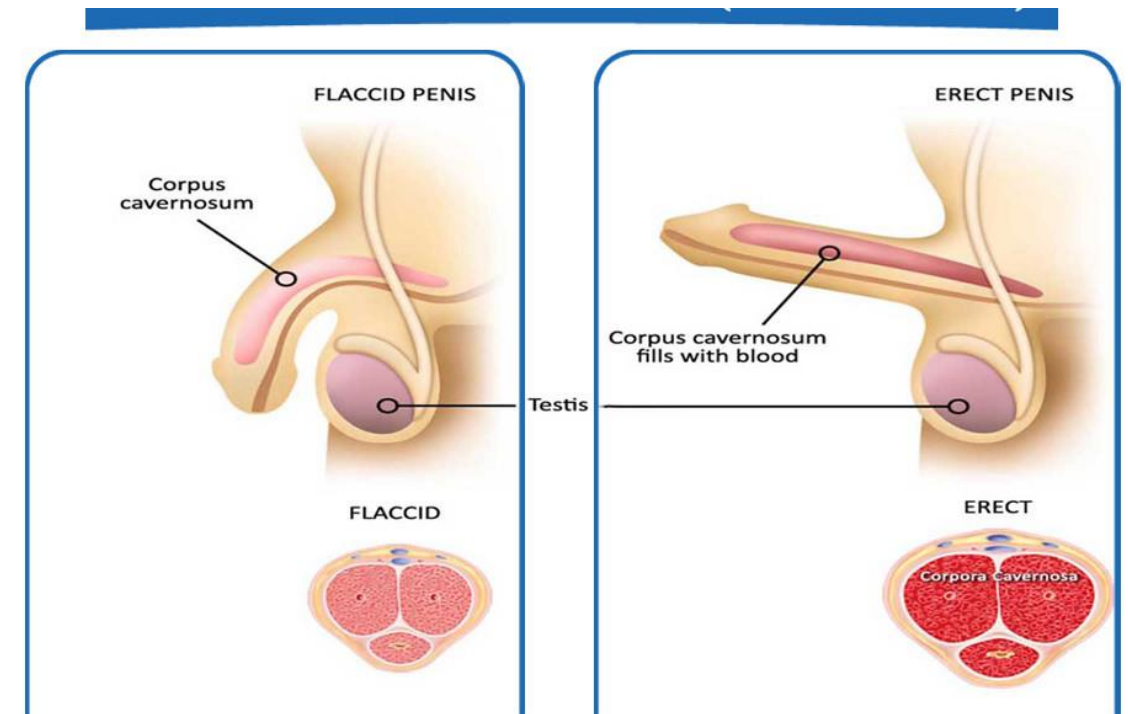
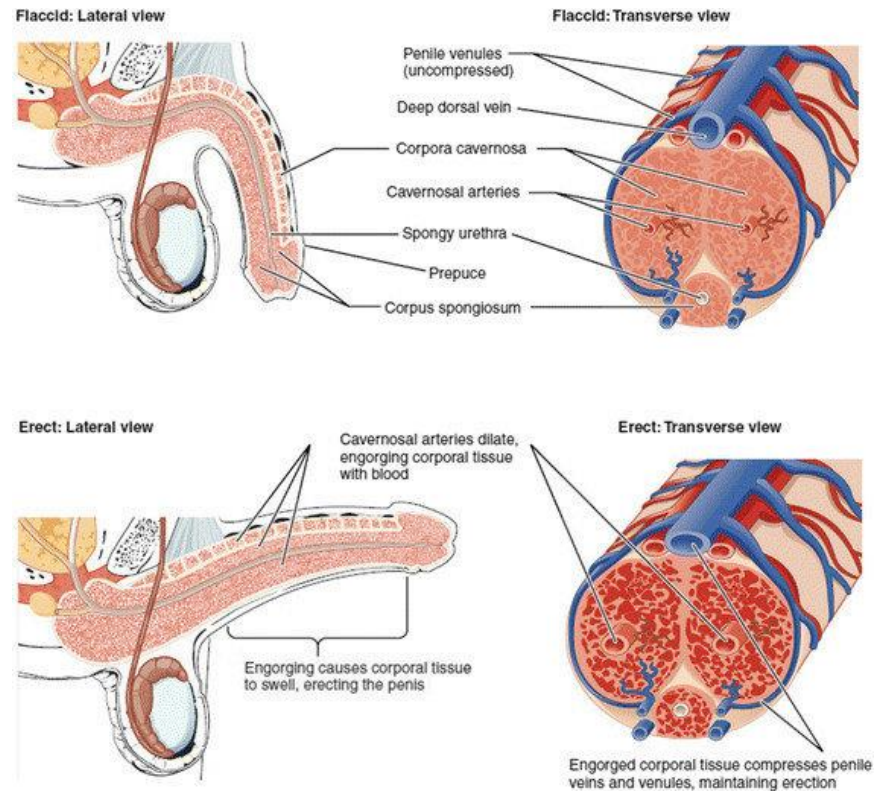
ED is more prevalent in patients with atherosclerosis, hypertension, DM, hypercholesterolemia, heart disease, smoker

# Anatomy of Penis



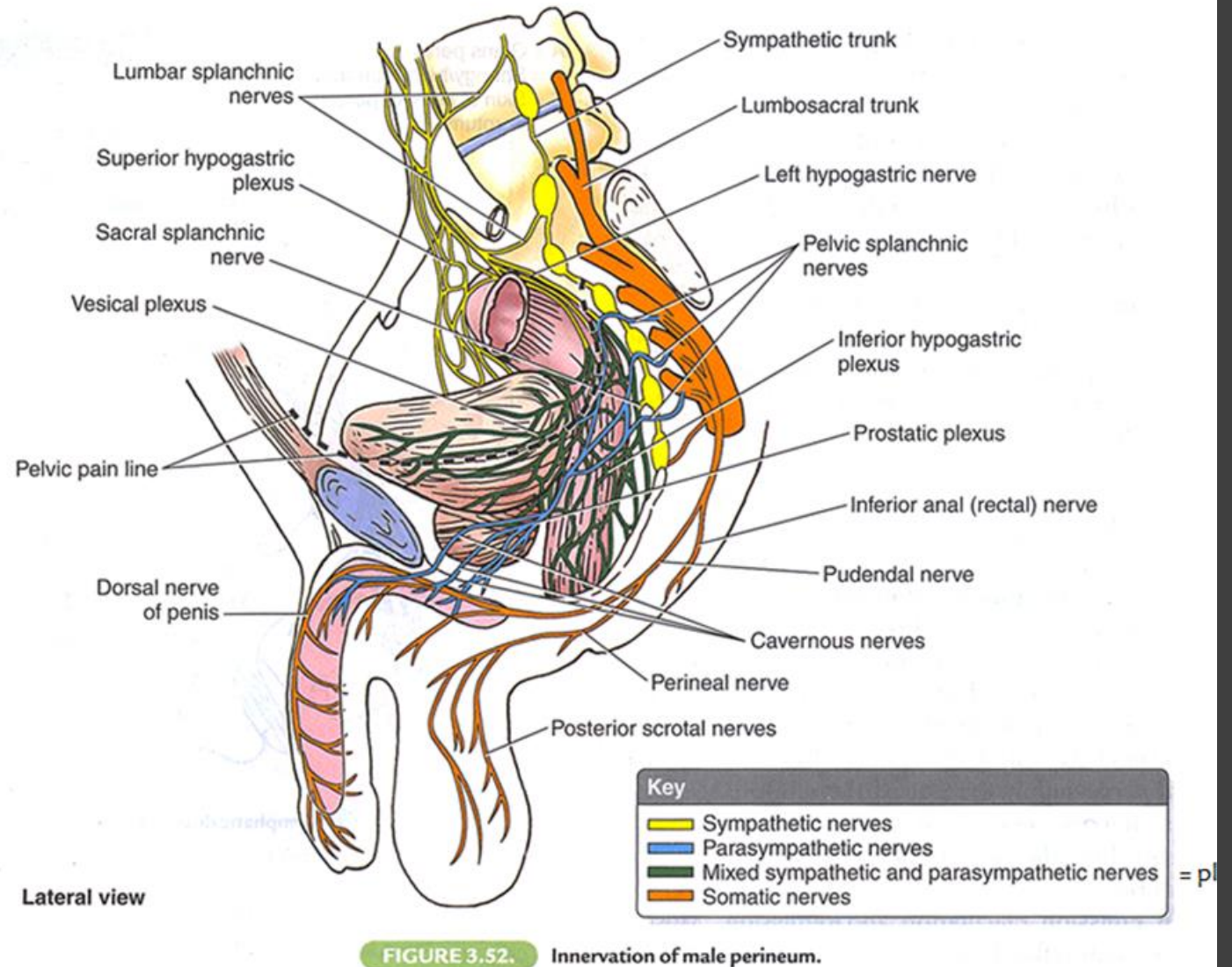
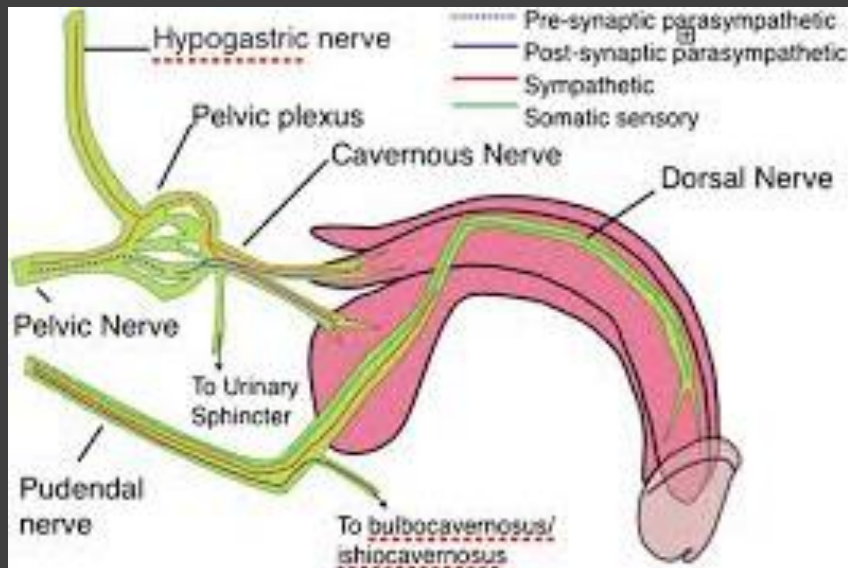


# Flaccid penis and Erect penis



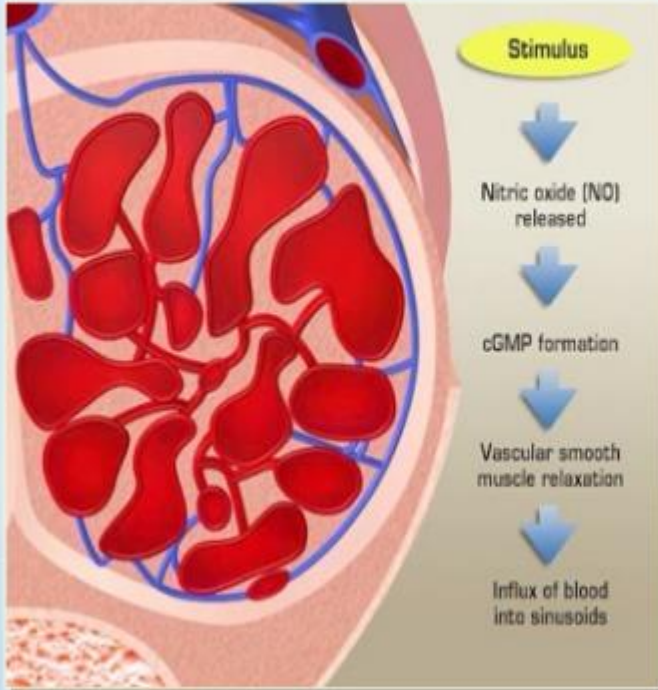
## What is innervation of erection and ejaculation?

- Autonomic
  - Sympathetic nerves from T11-L2
  - Parasympathetic from S2-4, form the pelvic plexus
  - The cavernosal nerves are branches of pelvic plexus (i.e. parasympathetic) that innervate the penis
  - Parasympathetic stimulation causes erection
  - Sympathetic activity causes ejaculation and detumescence (loss of erection)

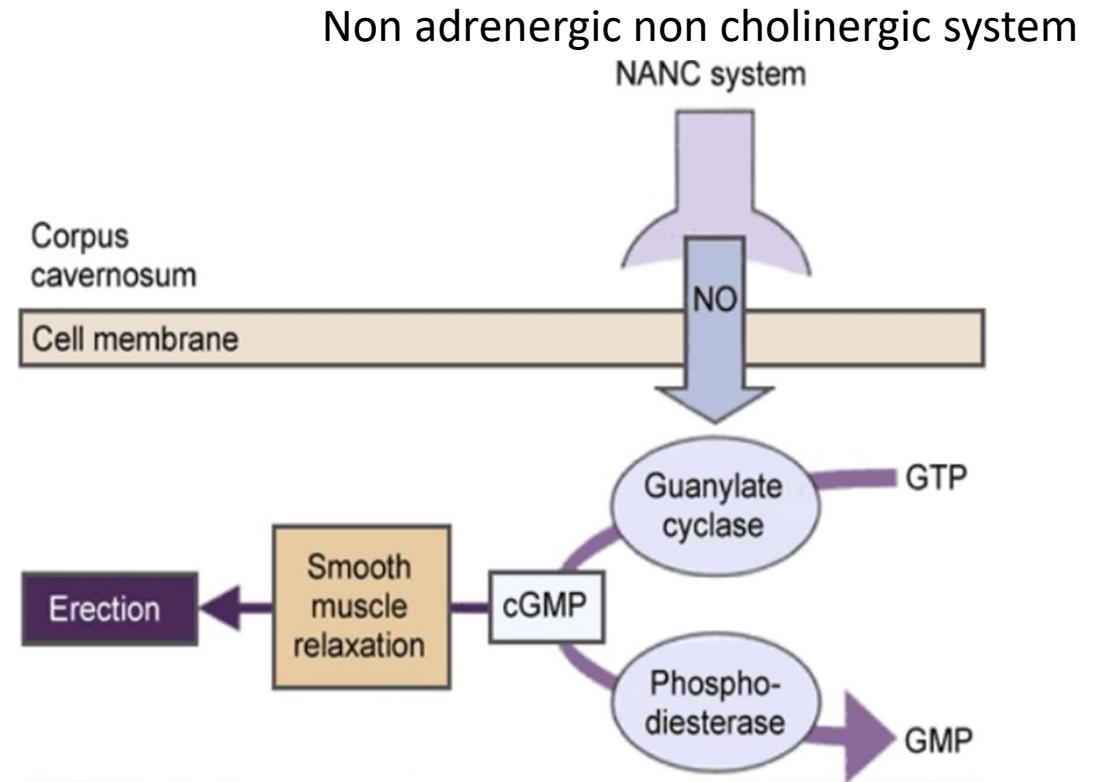


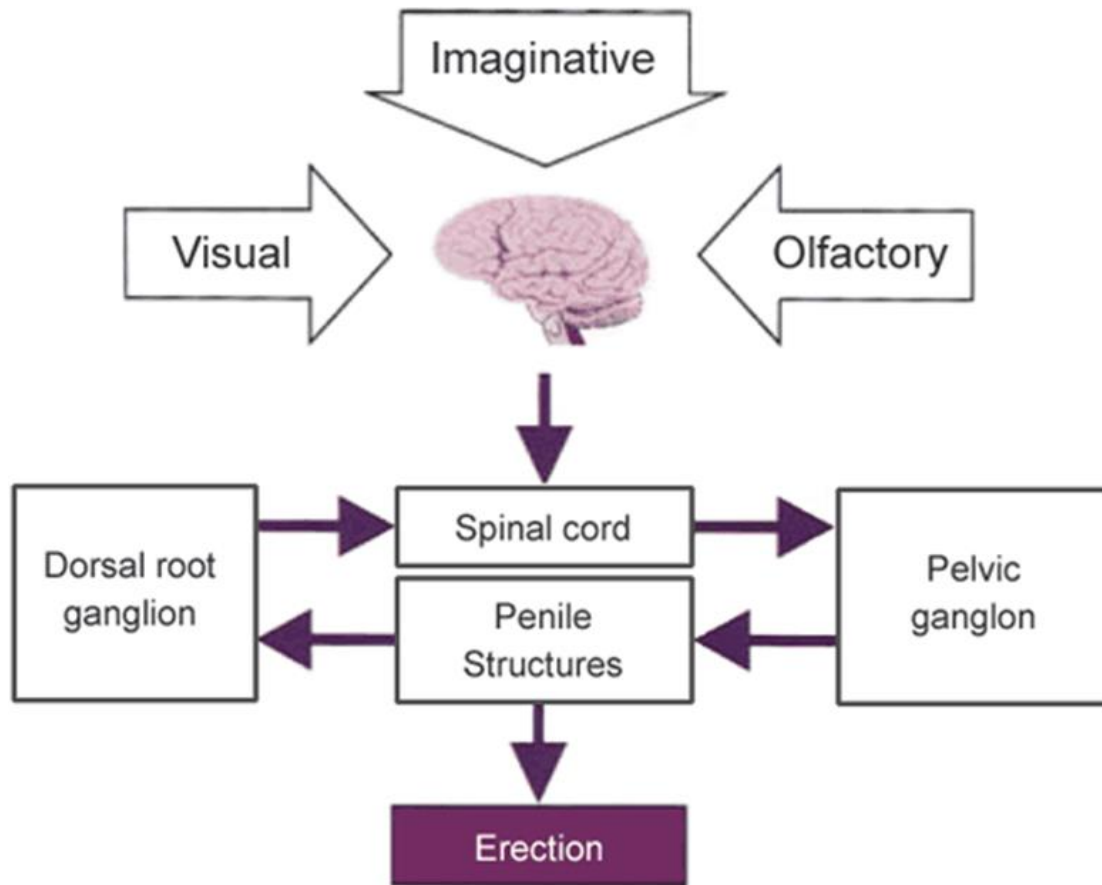


# Pathway of penile erection

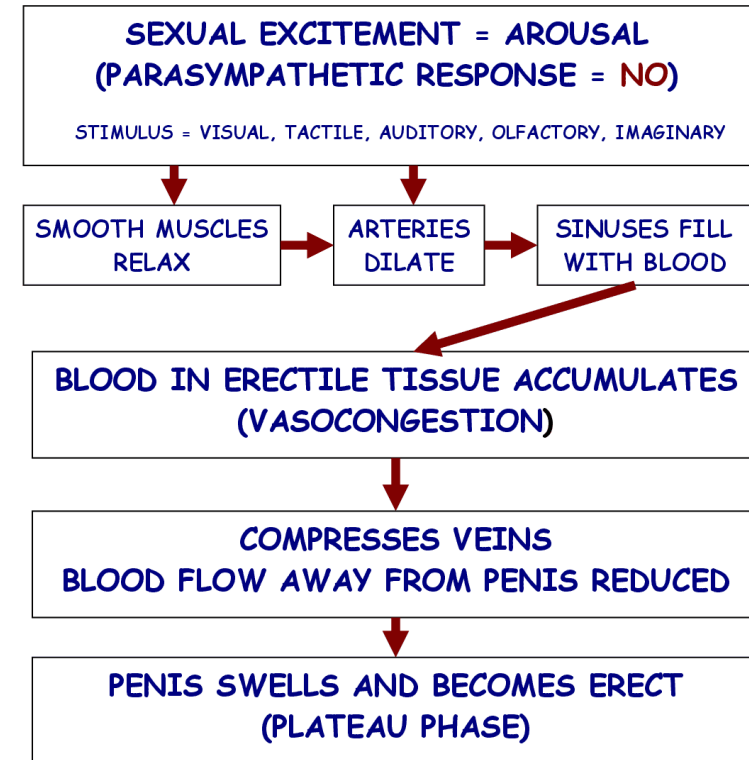


Nerve impulses cause the release of neurotransmitters (NO) from the cavernous nerve terminals. Nitric oxide diffuses into cavernosal smooth muscle cells, activates Guanylate cyclase, which converts GTP to cGMP resulting in **smooth muscle relaxation** in the arteries and arterioles supplying the erectile tissue and a several fold increase in penile blood flow.





## ERECTION: HOW DOES IT WORK?





# Etiology of erectile dysfunction

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## ETIOLOGY

- 1) **Psychogenic.**
- 2) **Vasculogenic :**
  - Cardiovascular disease
  - Hypertension
  - Diabetes mellitus
  - Major surgery or radiotherapy (pelvis or retroperitoneum).

## ETIOLOGY

- 3) **Neurogenic**
  - Central causes**
    - Multiple sclerosis
    - Parkinson's disease
    - Tumors
    - Stroke
    - Spinal cord disorders( disc disease )
  - Peripheral causes**
    - Diabetes mellitus
    - Alcoholism
    - Polyneuropathy
    - Surgery (pelvis or retroperitoneum).

# Etiology of erectile dysfunction

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## ETIOLOGY

- 4) **Anatomical / structural**
  - Peyronie's disease
  - Penile fracture
  - Congenital curvature of the penis
- 5) **Hormonal**
  - Hypogonadism
  - Hyperprolactinemia
  - Hyper- and hypothyroidism
  - Cushing's disease.

## ETIOLOGY

- 6) **Drug-induced**
  - Antihypertensives (beta-blocker, thiazide and clonidine .less with ACE inhibitors )
  - Antidepressants (tricyclic antidepressants and MAO inhibitor)
  - Antipsychotics
  - Antiandrogens
  - Antihistamines
  - Recreational drugs (Heroin and cocaine)

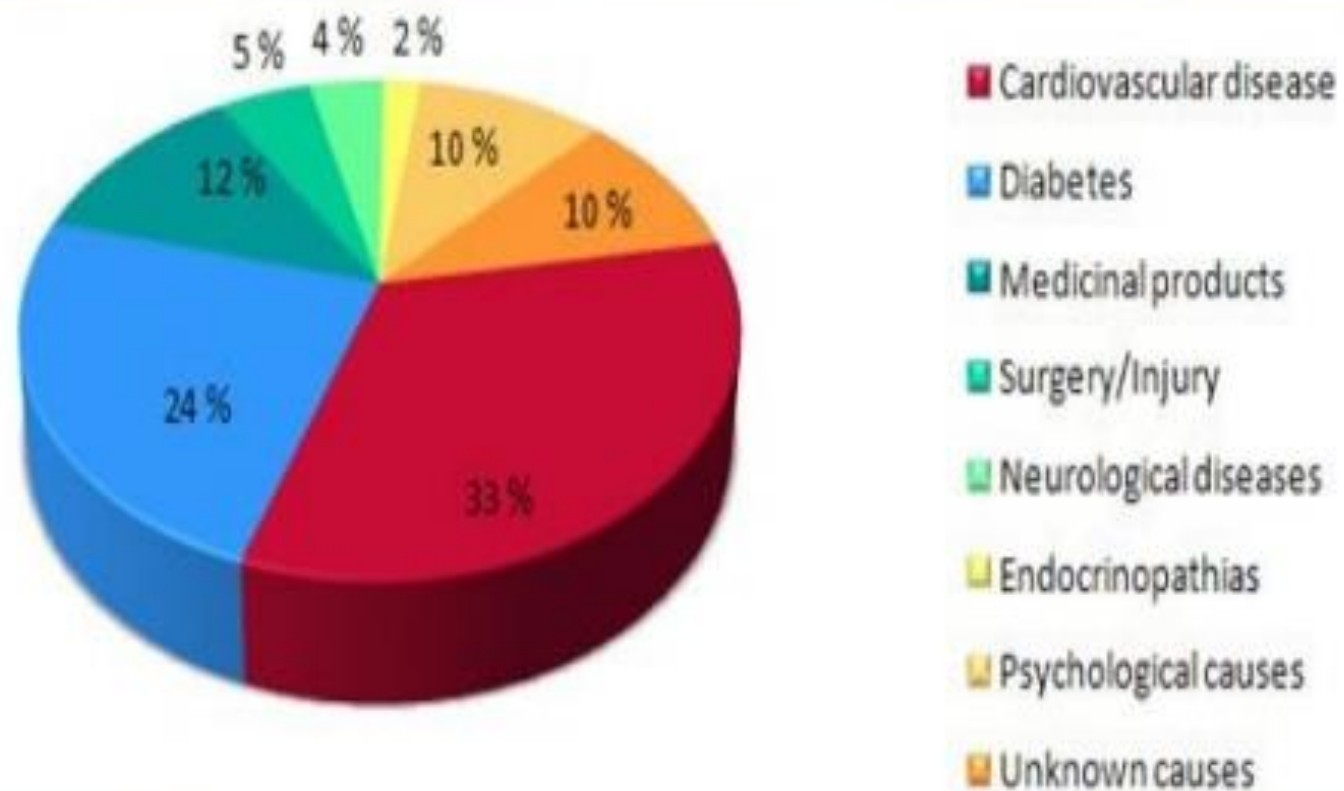
# Psychogenic

- Performance anxiety
- Relationship problems/difficulties
- Loss of attraction to partner
- Depression and anxiety disorders
  - Anxiety
  - Depression
  - Fatigue
  - Guilt
  - Stress
  - Marital Discord
  - Excessive alcohol consumption





# Causes of ED



# Assessment for Erectile Dysfunction

## The simplified International Index of Erectile Function (IIEF-5)

Please encircle the response that best describes you for the following five questions:

<b>Over the past 6 months:</b>					
1. How do you rate your confidence that you could get and keep an erection?	Very low 1	Low 2	Moderate 3	High 4	Very high 5
2. When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	Almost never or never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always or always 5
3. During sexual intercourse, how often were you able to maintain your erection after you had penetrated your partner?	Almost never or never 1	A few times (much less than half the time) 2	Sometimes (about half the time) 3	Most times (much more than half the time) 4	Almost always or always 5

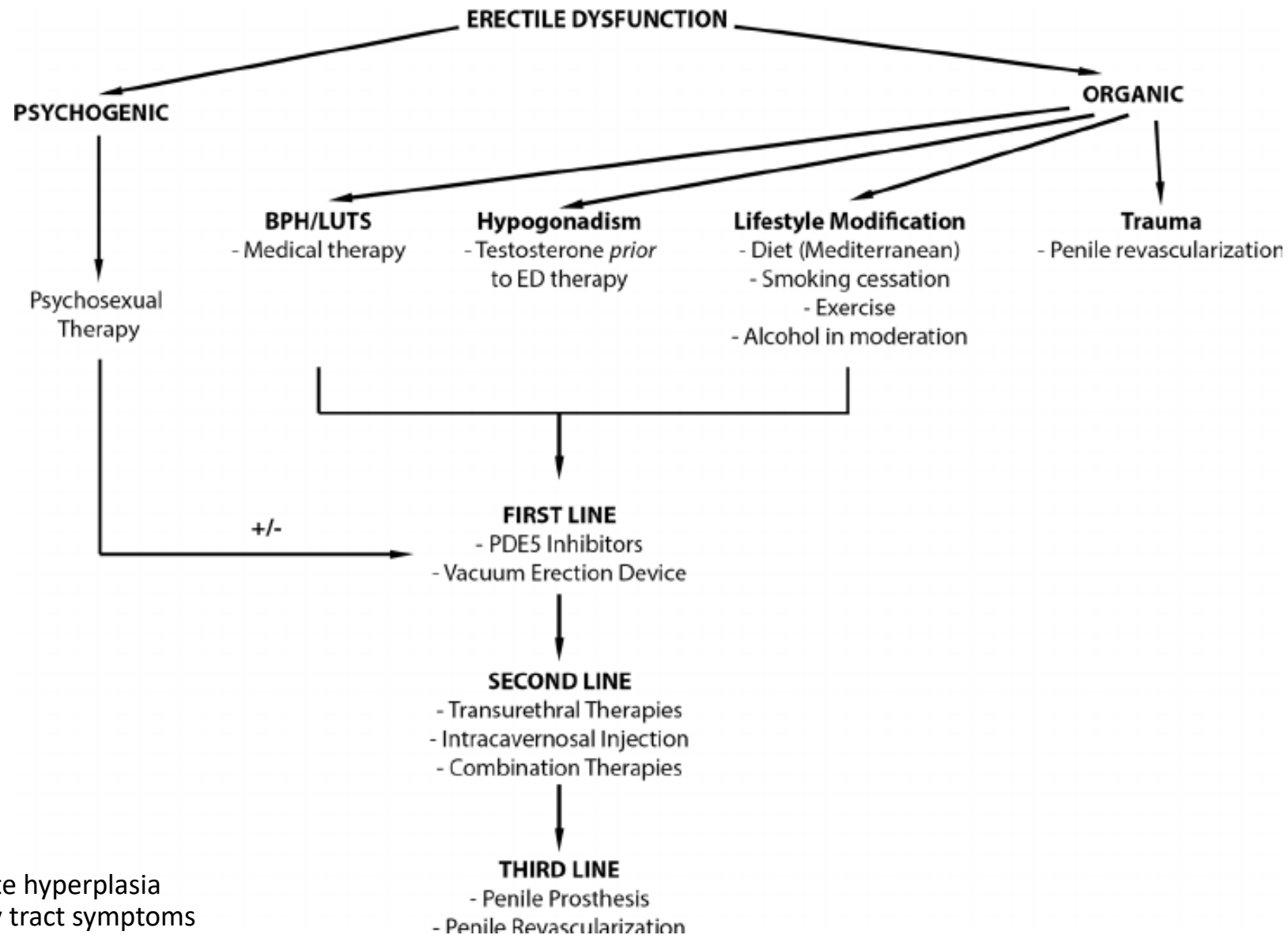
# Assessment for Erectile Dysfunction

4. During sexual intercourse, how difficult was it to maintain your erection to completion of intercourse?	Extremely difficult	Very difficult	Difficult	Slightly difficult	Not difficult
	1	2	3	4	5
5. When you attempted sexual intercourse, how often was it satisfactory for you?	Almost never or never	A few times (much less than half the time)	Sometimes (about half the time)	Most times (much more than half the time)	Almost always or always
	1	2	3	4	5

**Total Score:** \_\_\_\_\_

1-7: Severe ED    8-11: Moderate ED    12-16: Mild-moderate ED    17-21: Mild ED    22-25: No ED





BPH= Benign prostate hyperplasia  
LUTS= Lower urinary tract symptoms

# Management for Erectile Dysfunction

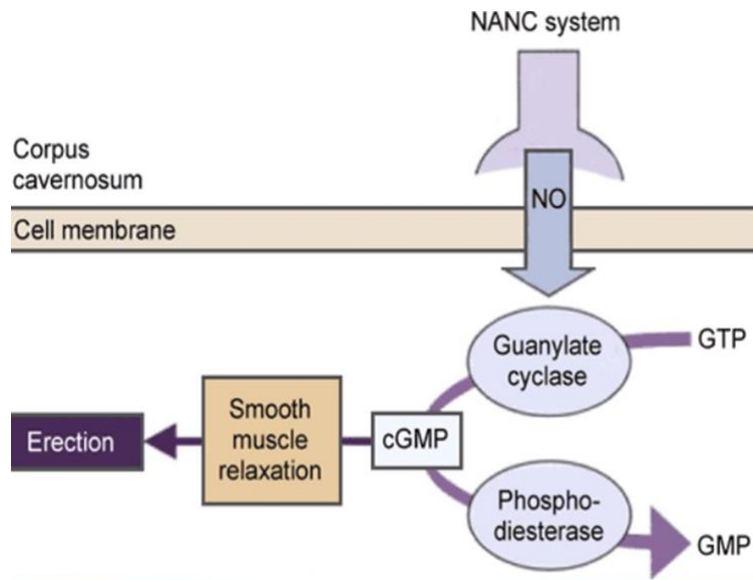
- General assessment
- Psychosexual therapy
- Drug therapy
- Vacuum treatment
- Surgical treatment
- Patient counseling: smoking cessation, reduce alcohol, weight control, exercise, dietary component, adherence to drug therapy

# Drug Therapy for Erectile Dysfunction

- ☐ Oral drugs
  - Phosphodiesterase 5 inhibitors
  - Apomorphine
  - Yohimbine
  - Tazodone
- ☐ Intra cavernosa injection
  - PGE1 : Alprostadil
  - Papaverine
- ☐ Intraurethral drug: Alprostadil



# Phosphodiesterase 5 inhibitors: Mechanism



- PDE 5 inhibitor inhibits enzyme phosphodiesterase → increase cGMP conc in glans penis, corpus cavernosum and corpus spongiosum → smooth muscle relaxation → blood infiltration → penile erection
- PDE 5 inh has no effect if there is no sexual arousal when NO and cGMP are low
- PDE 5 inh: Sildenafil, Tadalafil, Vardenafil

# Phosphodiesterase 5 inhibitors: Regimen

- Sildenafil ( $t_{1/2}$  3-4 h)
  - 25, 50, 100mg 1 h before sexual activity
  - 4-6 h window
  - Absorption delayed by fatty food
- Tadalafil ( $t_{1/2}$  17 h)
  - 5, 10, 20mg 30 min before sexual activity
  - 36 h window
  - Absorption is not affected by food
- Vardenafil ( $t_{1/2}$  4-5 h)
  - 5, 10, 20mg 30-60 min before sexual activity
  - 4-6 h window
  - Absorption delayed by fatty food



# Phosphodiesterase 5 inhibitors: ADR

- **Adverse Effects**

- Facial flushing
- Headache
- Nasal congestion
- Dizziness
- Dyspepsia
- Visual disturbance (Blue halo)
- Priapism
- Non arteritic anterior ischaemic optic neuropathy

# Phosphodiesterase 5 inhibitors: DI

## Drug interactions

- Nitrate: Glyceryl trinitrate, Isosorbide mono/di nitrate
  - Chest pain
  - Do not take together within 24 h for sildenafil / vardenafil and within 48 h for tadalafil
- Cytochrome P450 inhibitors (Protease inhibitors, cimetidine, ketoconazole, erythromycin)
- Cytochrome P450 inducers (Rifampin, phenobarb, phenytoin, carbamazepine)
- Alpha blockers

## Dosage adjustment

- If concomitant use with CYP3 A4 inhibitor, blood level of PDE 5 inh will increase. Lower dose is required.
- If concomitant use with CYP3 A4 inducer, blood level of PDE 5 inh will decrease. Higher dose is required.

# Phosphodiesterase 5 inhibitors: CI

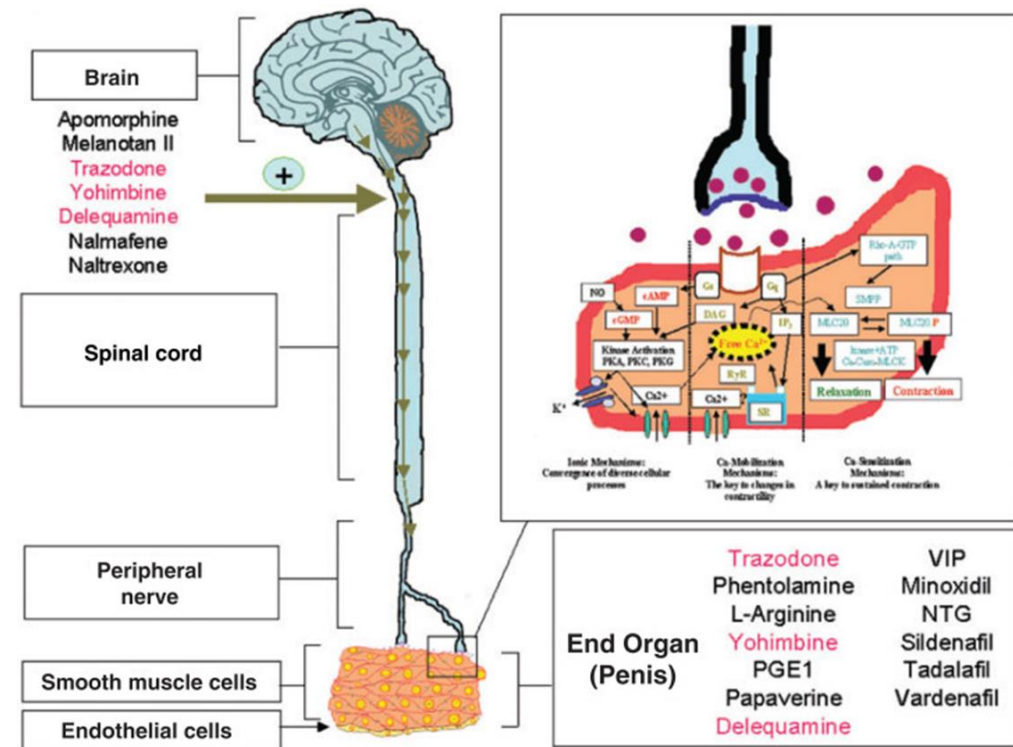
- **Contraindications**

- Recent cardiovascular event
- Patient using nitrate
- Hypotension patient
- Predisposition to prolonged erection : Sickle cell disease, Multiple myeloma, Leukemia
- Anatomical deformity: Cavernosal fibrosis, Peyronie's disease



# Other oral medications (Not FDA approved)

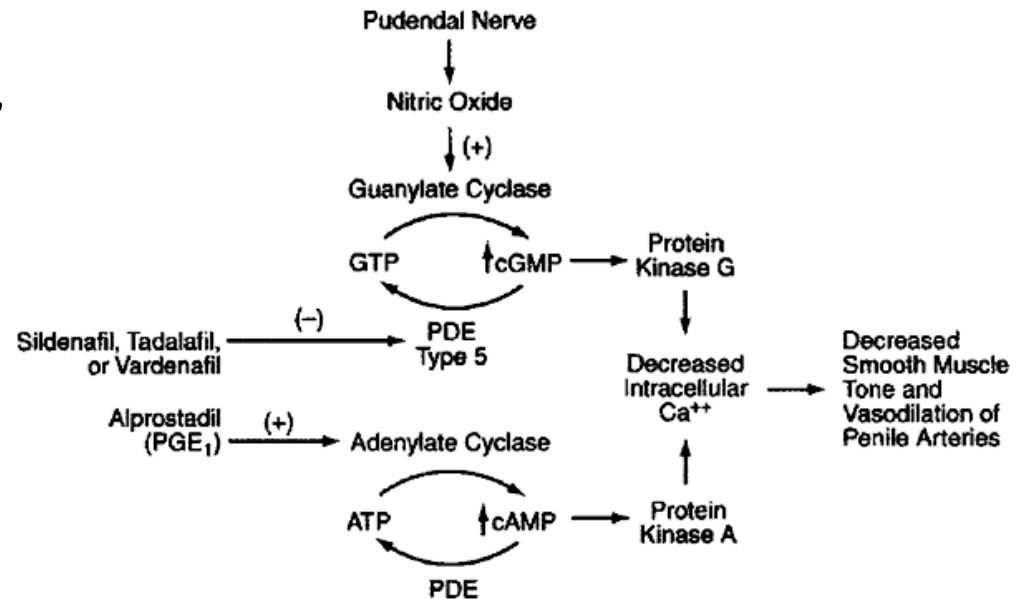
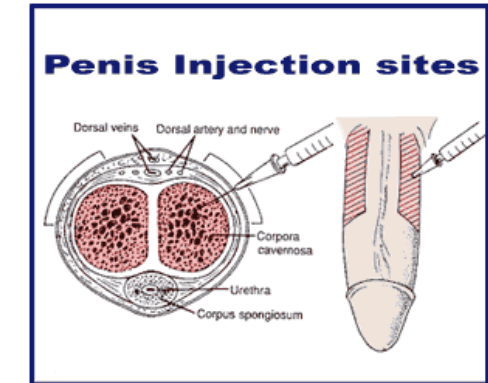
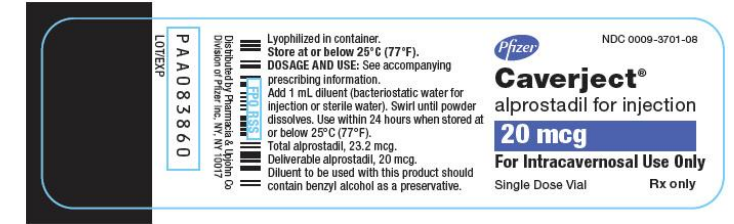
- Apomorphine S/L
  - Centrally acting dopamine agonist
  - Acts on paraventricular nucleus (sexual drive center)
- Yohimbine HCl
  - Centrally and peripherally alpha 2 adrenergic antagonist
  - ADR: high BP, anxiety, tachycardia, headache
- Phentolamine: alpha blocker
- Trazodone



# Intracavernosal injection

## Alprostadil

- PGE<sub>1</sub>
- 5-40 mcg inject directly to corporeal body of the penis
- ADR: peno scrotal pain, haematoma, fibrosis at injection site, priapism

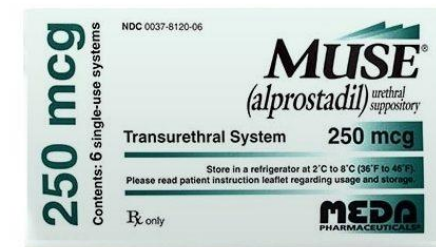
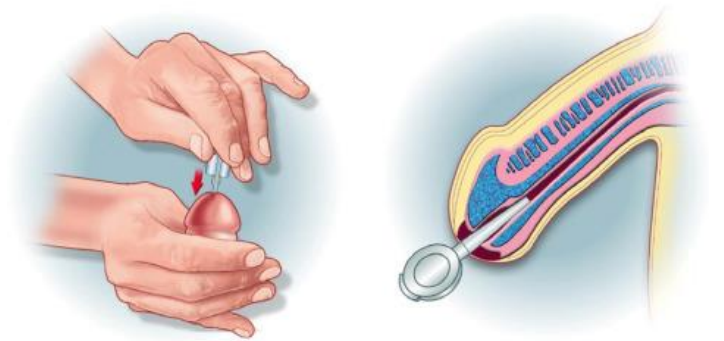


# Intraurethral administration

## Alprostadil intraurethral pellet

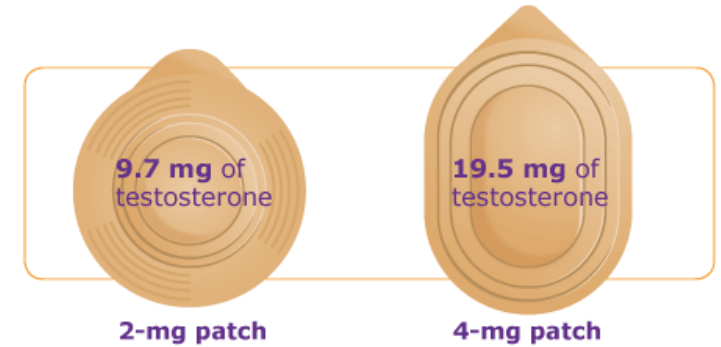
- PGE1
- 125 mg – 1000 mg through applicator
- Erection starts 5-20 min after administration and last for 30-45 min
- ADR: pain, bleeding, priapism

**MUSE** (= Medical Urethral System for Erection):  
Einmalsystem zur Verabreichung von Alprostadil (PGE1) in die Harnröhre



# Androgen replacement therapy

- For hypogonadism
- Injection: 200 mg testosterone cypionate or testosterone enanthate or testosterone propionate q 2-3 wks
- Transdermal patch
- Transdermal gel
- Contraindicated in prostate cancer and BPH

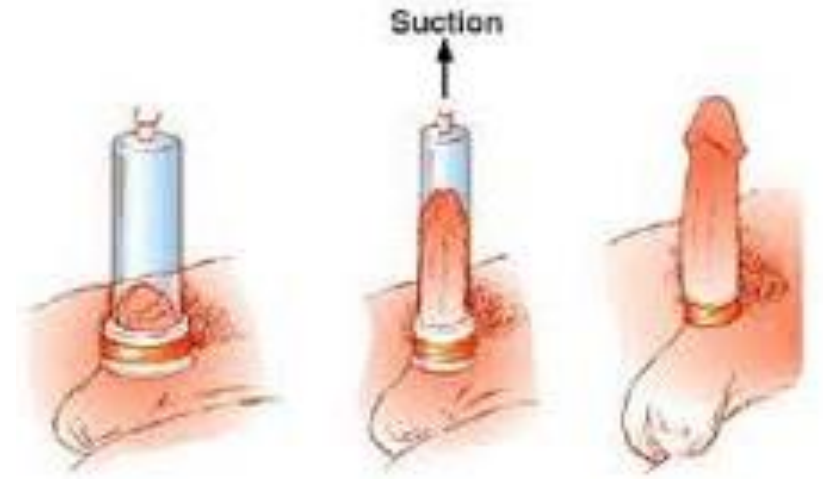


# Vacuum Device for ED

- Blood trapped in intracorporal and extracorporal compartments of penis
- May cause cyanosis, edema and cold



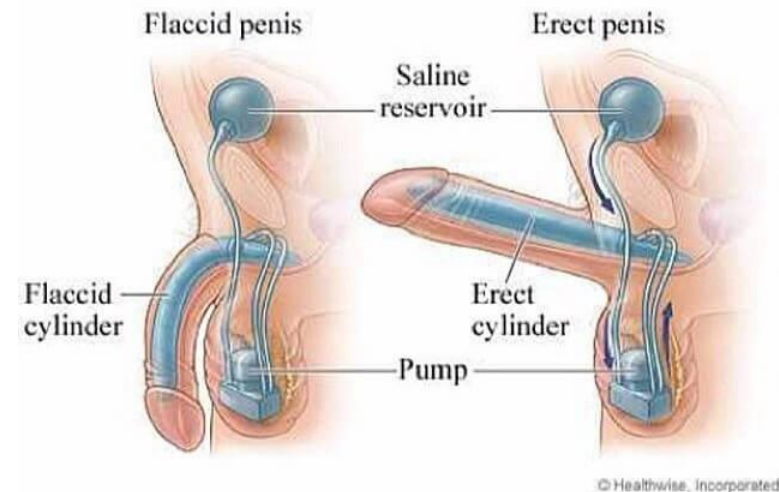
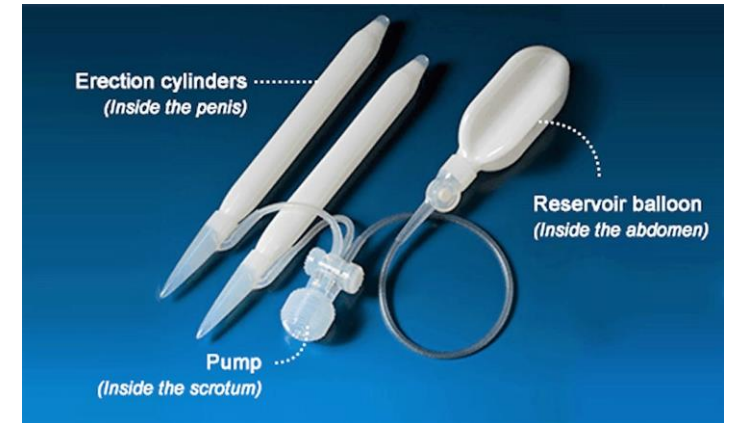
## Treatment for Erectile Disorder





# Surgical Treatment: Penile Prosthesis

- The third line therapy after failure of other treatments
- Complication: mechanical failure, infection





# Discussion Questions