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- An astute clinician, a keen academician and a popular teacher. Several Publications in Indexed journals
- Associate Editor of API Medicine Update 2009 and Clinical Medicine Update 2013
- Editor, Journal of Indian Association of Clinical Medicine
- Chairman, API Delhi State Chapter
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ERECTILE DYSFUNCTION

- “Man survives earthquakes, experiences the horrors of illness, and all of the tortures of the soul. But the most tormenting tragedy of all time is, and will be, the tragedy of the bedroom.”
- Tolstoy

DEFINITION

Erection- complex neurovascular process involving synchronised action of vascular endothelium, smooth muscle and psychological, neuronal and harmonal systems

Erectile Dysfunction is defined as the persistent inability to attain and maintain an erection sufficient to permit satisfactory sexual performance.

WHY IS IT IMPORTANT TO DIAGNOSE AND TREAT?

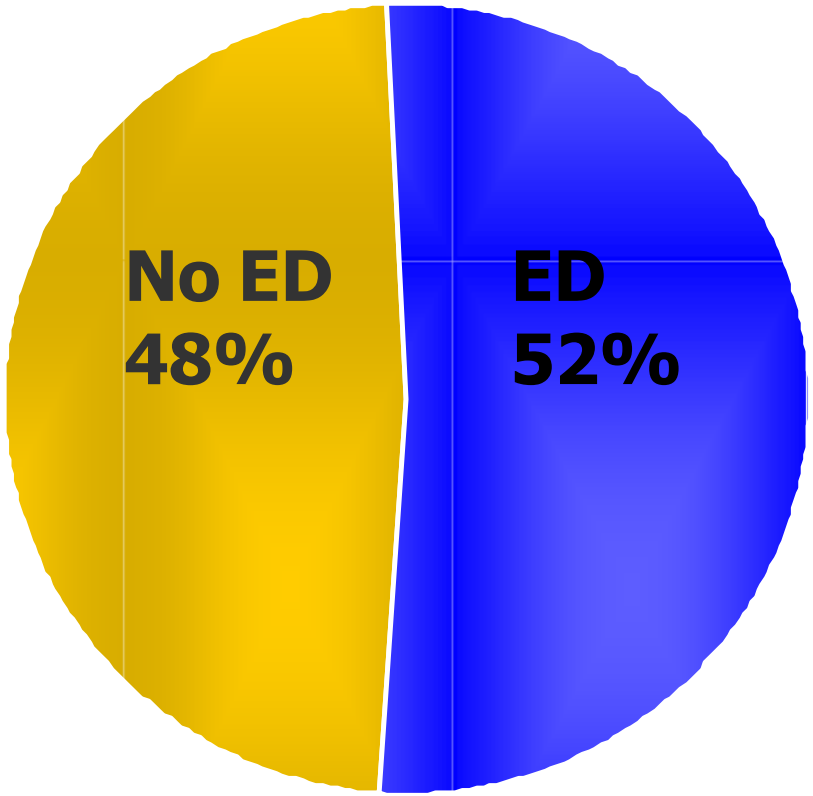
- ED may affect physical and psychosocial health and may have a significant impact on the quality of life (QoL) of sufferers and their partner's.

- Early manifestation of CAD, PVD and Diabetes.

- a potential warning sign of cardiovascular disease (CVD) especially in younger patients

Massachusetts Male Aging Study (US): Key Prevalence Study of ED

Men aged 40 to 70 years (N=1290)



Minimal ED, "usually able to get or keep an erection."
Moderate ED, "sometimes able to get and maintain an erection."
Complete ED, "unable to get and keep an erection."

Feldman HA et al. J Urol. 1994;151:54-61.

CLASSIFICATION OF ED

- organic,
- psychogenic and
- mixed ED.

most cases are actually of mixed aetiology.

It is therefore suggested to use the terms **primary organic or primary psychogenic**.

Covid- 6 times likely to develop ED (endothelial dysfunction)

Etiologies of erectile dysfunction[1-3]

Vascular	Cardiovascular disease, hypertension, diabetes mellitus, hyperlipidemia, smoking, major surgery (radical prostatectomy) or radiotherapy (pelvis or retroperitoneum)
Neurologic	Spinal cord and brain injuries, Parkinson disease, Alzheimer disease, multiple sclerosis, stroke, major surgery (radical prostatectomy) or radiotherapy of the prostate
Local penile (cavernous) factors	Peyronie's disease, cavernous fibrosis, penile fracture
Hormonal	Hypogonadism, hyperprolactinemia, hyper- and hypothyroidism, hyper- and hypocortisolism
Drug induced	Antihypertensives, antidepressants, antipsychotics, antiandrogens, recreational drugs, alcohol
Psychogenic	Performance-related anxiety, traumatic past experiences, relationship problems, anxiety, depression, stress

DRUGS ASSOCIATED WITH ED

Post Finasteride Syndrome

TYPE OF DRUG	EXAMPLES
Acid suppression	ranitidine, cimetidine
Anticonvulsants	carbamazepine, gabapentin, phenytoin, phenobarbital, pregabalin,[11] topiramate
Antidepressants	SSRIs, TCAs, lithium, MAOIs
Antipsychotics	haloperidol, phenothiazines
Antihypertensives	BBs, methyldopa, clonidine; CCBs (less likely)
Cardiac-related	digoxin, fibrates, statins
Diuretics	spironolactone, thiazides (especially higher doses than are now used for hypertension, eg, hydrochlorothiazide ≥50 mg)
Hormonal	progesterone, estrogen, corticosteroids, 5α-reductase inhibitors, cyproterone acetate
Immunomodulators	interferon α
NSAIDs	indomethacin[12]

CLUES TO DIFFERENTIATE

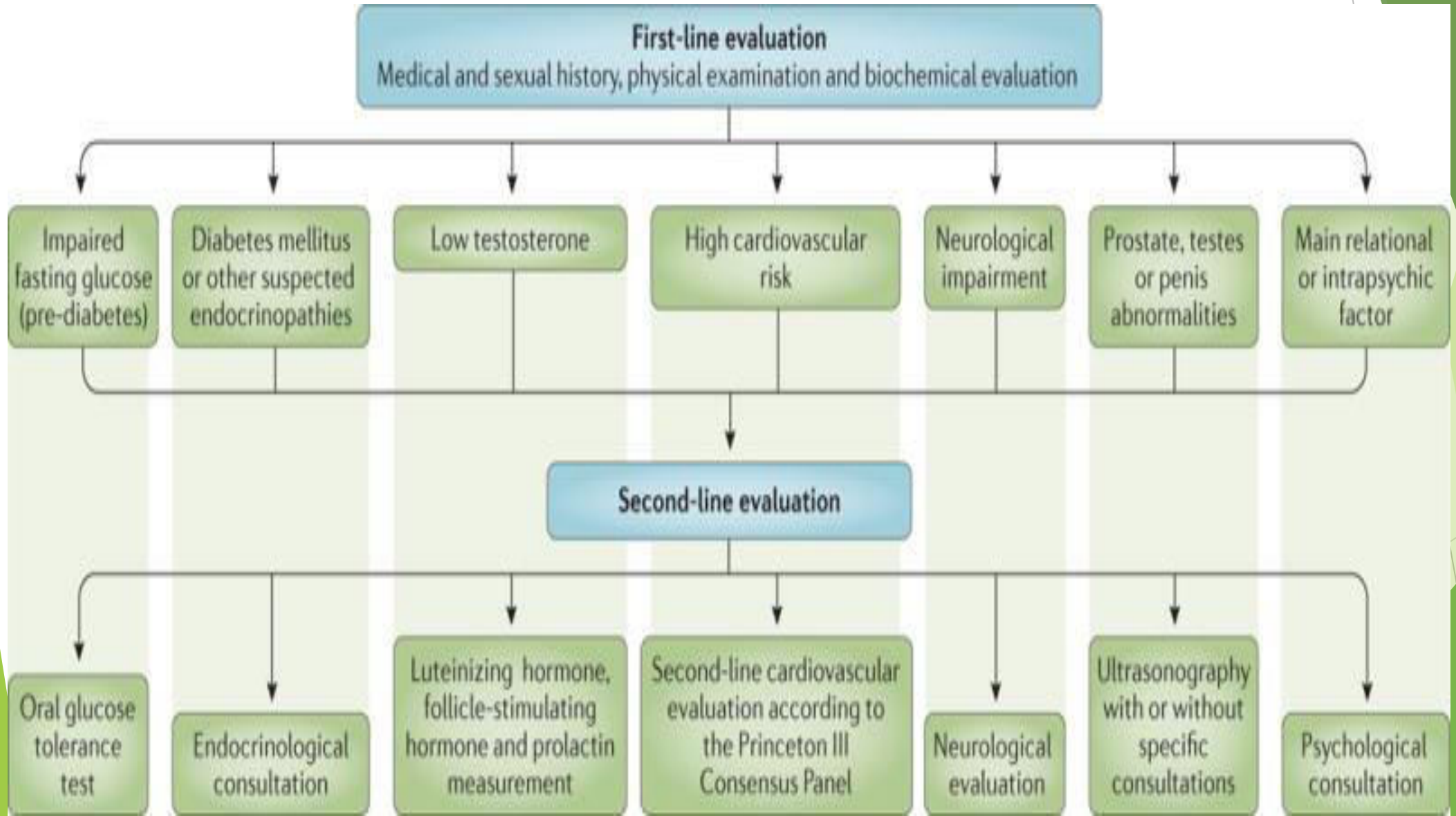
Psychogenic

- Sudden onset
- Situational
- Normal waking and nocturnal erections
- Normal erection with masturbation
- Tumescence present
- Relationship problems
- Major Life event
- Anxiety, fear, depression

Organic

- Gradual onset
- All situations
- Reduced or absent waking and nocturnal erections
- No erection with masturbation
- Lack of tumescence
- Normal libido, normal ejaculation
- Known Cardiovascular, endocrinal,, neurological conditions
- Operations, radiotherapy, trauma to testes/scrotum
- Medications, smoking, alcohol

DIAGNOSTIC WORKUP



IIEF-5 SCORE

Over the Past 6 Months:	1	2	3	4	5
How do you rate your confidence that you could get and keep an erection?	Very low	Low	Moderate	High	Very high
When you had erections with sexual stimulation, how often were your erections hard enough for penetration?	Almost never or never	Much less than half the time	About half the time	Much more than half the time	Almost always or always
During sexual intercourse, how often were you able to maintain your erection after you had penetrated (entered) your partner?	Almost never or never	Much less than half the time	About half the time	Much more than half the time	Almost always or always
During sexual intercourse how difficult was it to maintain your erection to the completion of intercourse?	Extremely difficult	Very difficult	Difficult	Slightly difficult	Not difficult
When you attempted sexual intercourse, how often was it satisfactory for you?	Almost never or never	Much less than half the time	About half the time	Much more than half the time	Almost always or always

NOTE: The IIEF-5 score is the sum of questions 1 to 5. The lowest score is 5 and the highest score 25. Lower scores indicate higher perceived erectile dysfunction (Rosen, Cappelleri, Smith, Lipsky, & Pena, 1999).

5- ITEM INTERNATIONAL INDEX OF ED

- ED Classification according IIEF-5 Score:
  - Severe (5-7),
  - Moderate (8-11),
  - Mild – Moderate (12-16),
  - Mild (17-21),
  - No ED (22-25).

INDICATIONS FOR SPECIFIC DIAGNOSTIC TESTS

- Primary ED (not caused by organic disease or psychogenic disorder).
- Young patients with a history of pelvic or perineal trauma, who could benefit from potentially curative revascularisation surgery or angioplasty.
- Patients with penile deformities which might require surgical correction (e.g., Peyronie's disease, congenital penile curvature).
- Patients with complex psychiatric or psychosexual disorders.
- Patients with complex endocrine disorders.
- Medico-legal reasons (e.g., implantation of penile prosthesis to document end stage ED, sexual abuse)

SPECIFIC DIAGNOSTIC TESTS

Nocturnal Penile Tumescence and Rigidity (NTPR) using Rigiscan®
Vascular studies: - Intracavernous vasoactive drug injection - Penile Dynamic Duplex Ultrasonography - Penile Dynamic Infusion Cavernosometry and Cavernosography - Internal pudendal arteriography
Neurological studies (e.g., bulbocavernosus reflex latency, nerve conduction studies)
Endocrinological studies
Specialised psychodiagnostic evaluation

CARDIAC RISK STRATIFICATION (2ND AND 3RD PRINCETON CONSENSUS)

Cardiac risk stratification (2nd & 3rd Princeton Consensus)

Low-risk category	Intermediate-risk category	High-risk category
Asymptomatic, < 3 risk factors for CAD (excluding sex)	≥ 3 risk factors for CAD (excluding sex)	High-risk arrhythmias
Mild, stable angina (evaluated and/or being treated)	Moderate, stable angina	Unstable or refractory angina
Uncomplicated previous MI	Recent MI (> 2, < 6 weeks)	Recent MI (< 2 weeks)
LVD/CHF (NYHA class I or II)	LVD/CHF (NYHA class III)	LVD/CHF (NYHA class IV)
Post-successful coronary revascularisation	Non-cardiac sequelae of atherosclerotic disease (e.g., stroke, peripheral vascular disease)	Hypertrophic obstructive and other cardiomyopathies
Controlled hypertension		Uncontrolled hypertension
Mild valvular disease		Moderate-to-severe valvular disease

CAD = coronary artery disease; CHF = congestive heart failure; LVD = left ventricular dysfunction; MI = myocardial infarction; NYHA = New York Heart Association.

TREATMENT ---GENERAL MEASURES

- Smoking cessation
- Reduce Alcohol intake
- Weight loss
- Exercise
- Treating comorbidities – hypertension, diabetes, hypercholesterolemia, BPH, CVD, evaluation of drugs/medicines

PSYCHOSEXUAL THERAPY

- Even if the cause is physical, the patient develops psychosexual issues.
- Address Performance anxiety
- Sensate focus exercises
- Relationship counselling

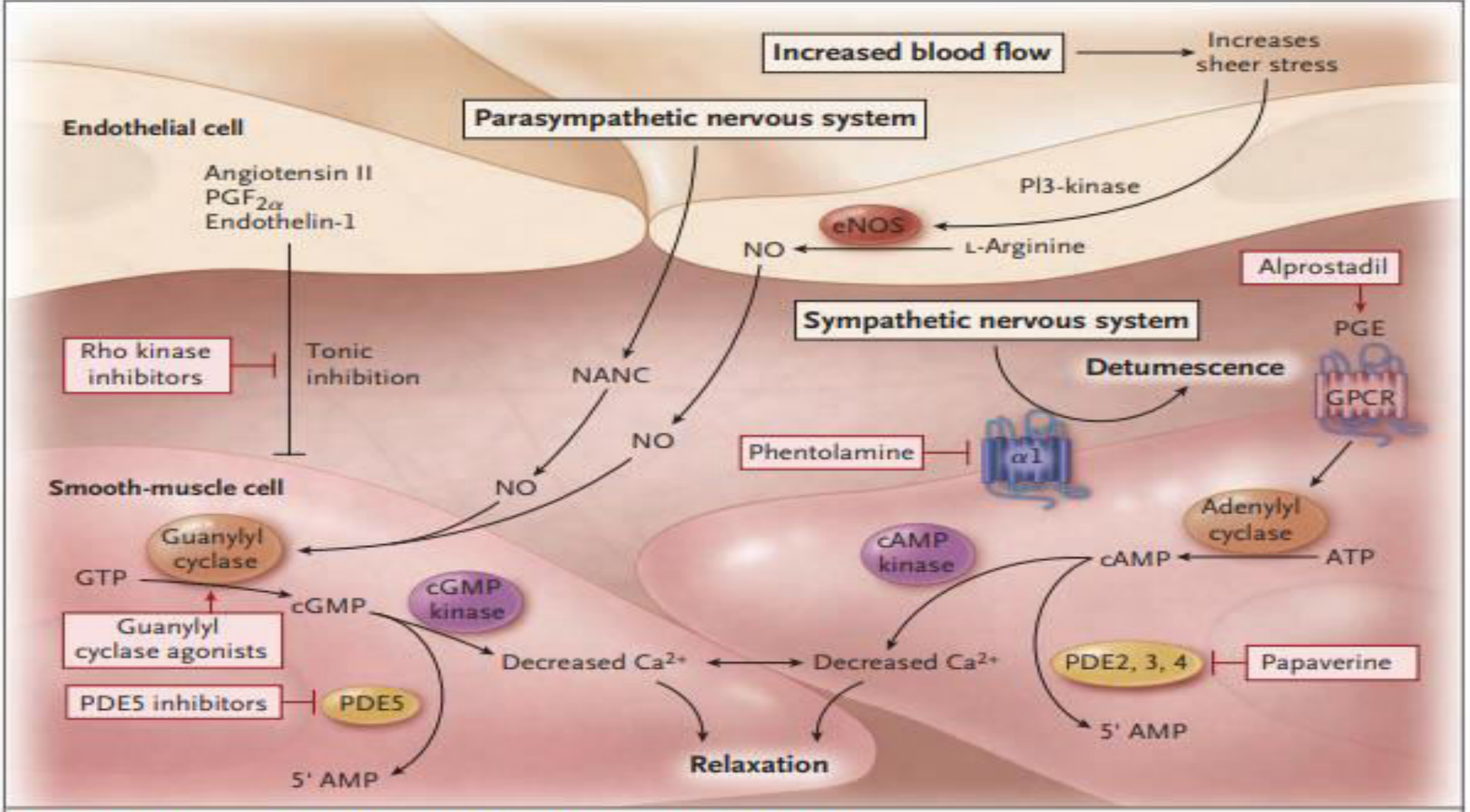


Figure 2. Molecular Mechanism of Penile Smooth-Muscle Relaxation.

PDE-5 INHIBITORS

- Oral Pharmacotherapy
  - PDE5-I drug
    - Sildenafil
    - Tadalafil
    - Valdenafil
    - Avanafil
    - Please be advised, PDE5I is not an initiator of erection, patient still need sexual stimulation to facilitate erection.

EAU Guidelines 2019

PDE5 INHIBITORS

Key Characteristics of PDE5 Inhibitors

Characteristic	Sildenafil	Tadalafil	Vardenafil	Avanafil
Year of FDA approval	1998	2003	2003	2012
Usual dosage	25-100 mg/day	5-20 mg/day prn; 2.5-5 mg/day once daily	5-20 mg/day	50-200 mg/day
Administration time before sexual activity	1 h	0.5 h	1 h	0.5 h
Time frame of efficacy	0.5-4 h post dose	Up to 36 h post dose	5-7 h post dose	As early as 0.25 h post dose
Effect of fatty meals	↑ C_{max} 29%; ↓ t_{max} by 1 h; avoid	Not affected	↓ C_{max} 18%-50%; may use per manufacturer	↓ C_{max} 24%-39%; ↑ t_{max} by 1.12-1.25 h; may use per manufacturer
Renal dose adjustments	CrCl <30 mL/min: starting dose 25 mg/day	prn—CrCl 30-50 mL/min: Starting dose 5 mg/day, max 10 mg/48 h. CrCl <30 mL/min or if hemodialysis: Max 5 mg/72 h. Once daily—CrCl <30 mL/min: Do not use	Do not use in hemodialysis patients	Do not use if CrCl <30 mL/min or in hemodialysis patients
Cost (AWP/unit)	$66.46 (all doses)	$13.68 (2.5 mg, 5 mg); $80.16 (10 mg, 20 mg)	$61.80 (all doses)	$74.50 (all doses)
Generic availability	Yes (authorized generic)	No	No	No

AWP: average wholesale price; C_{max}: maximum concentration of drug; CrCl: creatinine clearance; max: maximum; min: minute; PDE5: phosphodiesterase type 5; t_{max}: time of occurrence for maximum drug concentration.
Source: References 21-26.

SIDE EFFECTS OF PDE-5I

Adverse event	Sildenafil	Tadalafil	Vardenafil	Avanafil, 200mg
Headache	12.8%	14.5%	16%	9.3%
Flushing	10.4%	4.1%	12%	3.7%
Dyspepsia	4.6%	12.3%	4%	uncommon
Nasal congestion	1.1%	4.3%	10%	1.9%
Dizziness	1.2%	2.3%	2%	0.6%
Abnormal vision	1.9%		< 2%	none
Back pain		6.5%		< 2%
Myalgia		5.7%		< 2%

- It is **CONTRAINDICATED** in
  - Patient suffered from myocardial infarction, stroke, life threatening arrythmia within the LAST 6 MONTHS
  - Resting hypotension < 90/50 mmHg or hypertension >170/100 mmHg
  - Unstable angina, Angina with sexual intercourse or CHF NYHA IV
  - Nitrates → result in cGMP accumulation and unpredictable blood pressure drop. If patient taken PDE5I, develop angina, nitrate should be postponed base of PDE5I drugs half-life.
- Co-administrative with other anti hypertensive agent, considered safe
- Interaction with alpha-blocker →orthostatic hypotension

Side Effects of PDE 5 i

- NAION
- Unilateral hearing loss
- Drug interactions (CYP 450)
- Contraindicated with nitrates, Guanyl Cyclase inhibitors, precaution with alpha blockers
- QTc prolongation- avanafil, verdanafil
- Priapism- Sickle Cell Disease, multiple myeloma, leukemia
- Retinal Detachment, Central Vein Occlusion
- Melanoma
- Cancer prostrate

ISSUES TO CONSIDER IN CASE OF FAILURE OF PDE5I

- A trial of medication on at least 6 different days at the maximal dose should be performed before declaring patient nonresponsive to PDE5I.
- Confirm that the patient didn’t partake in a high fat meal prior to medication.
- Failure to include physical and psychic stimulation at the time of foreplay to induce endogenous NO.
- Unrecognized hypogonadism.

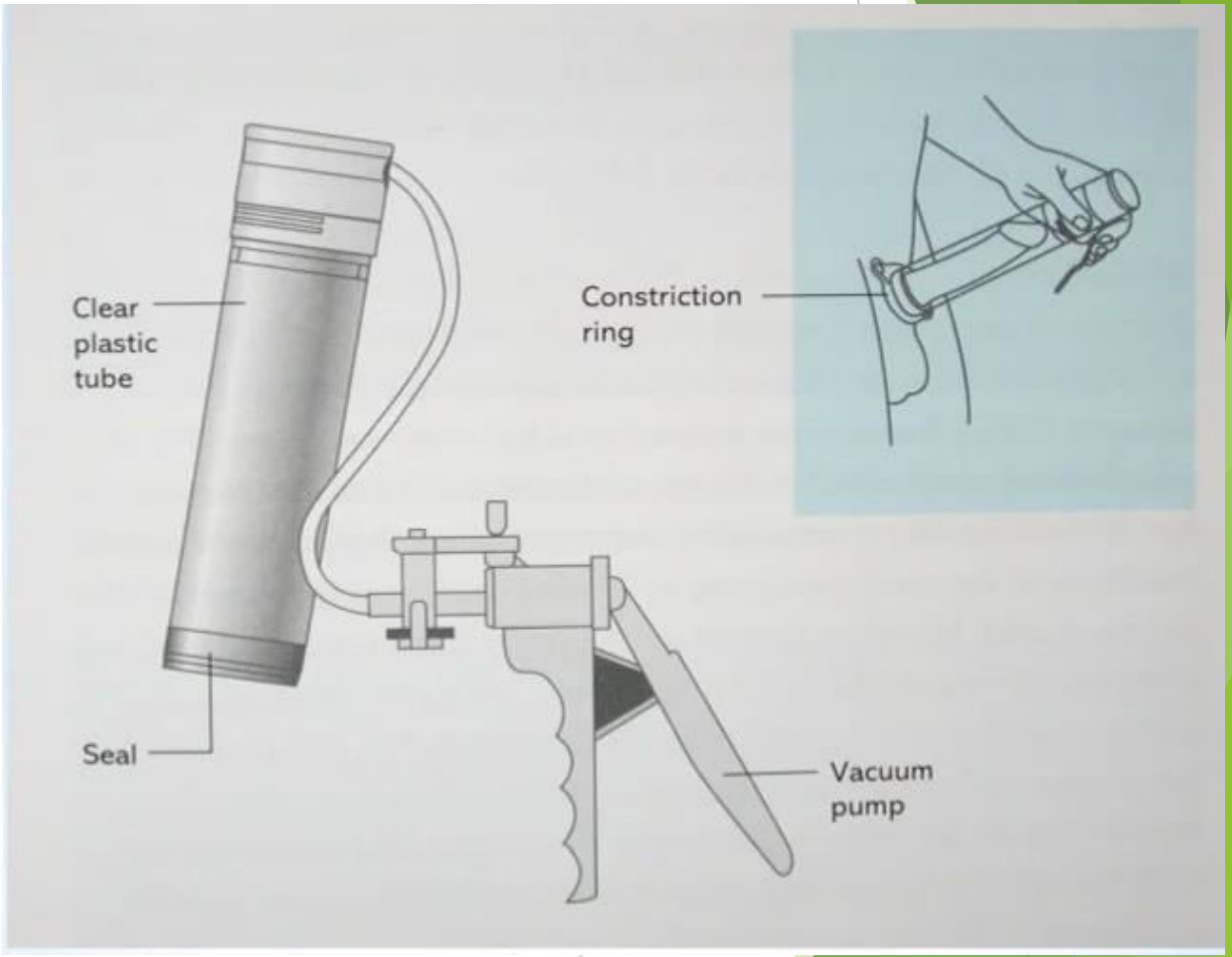
VACUUM ERECTION DEVICES

For patients without bleeding disorder or on anticoagulant therapy.

ADVERSE EVENTS:

- Pain
- Unable to ejaculate
- Petechiae, bruising
- Numbness

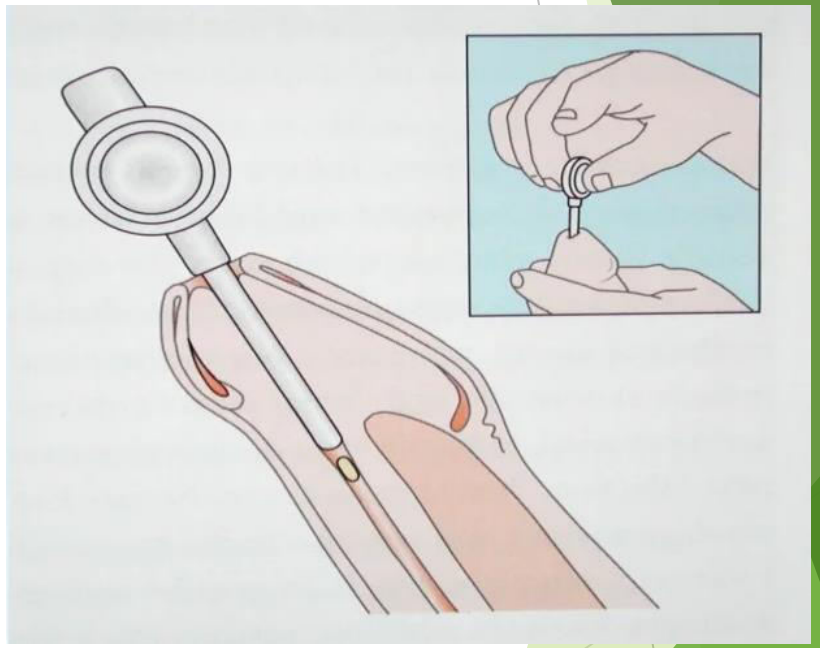
Remove ring before 30 min after intercourse.



INTRAURETHRAL ALPROSTADIL MUSE

- Vasoactive agent, topical route(300mcg) or medicated pellet(500mcg) via urethral meatus.
- Massage penis for better absorption.

- Adverse effects: local pain, erythema, dizziness/hypotension,UTI

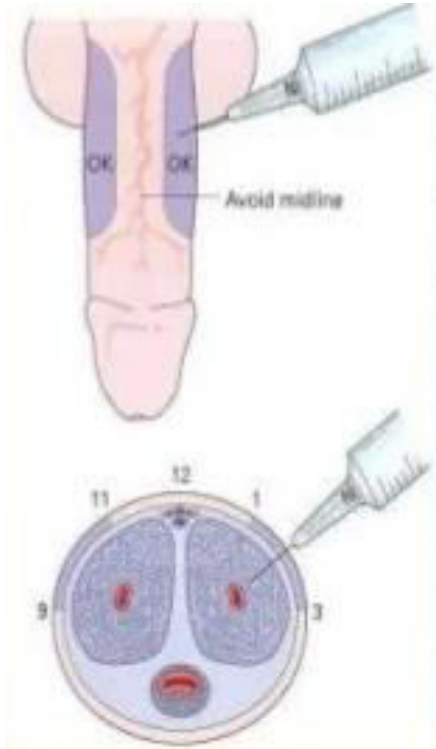


SHOCK WAVE THERAPY

- Low intensity extracorporeal shock wave therapy
- Can improve IIEF and Erection hardness score of mild ED patients

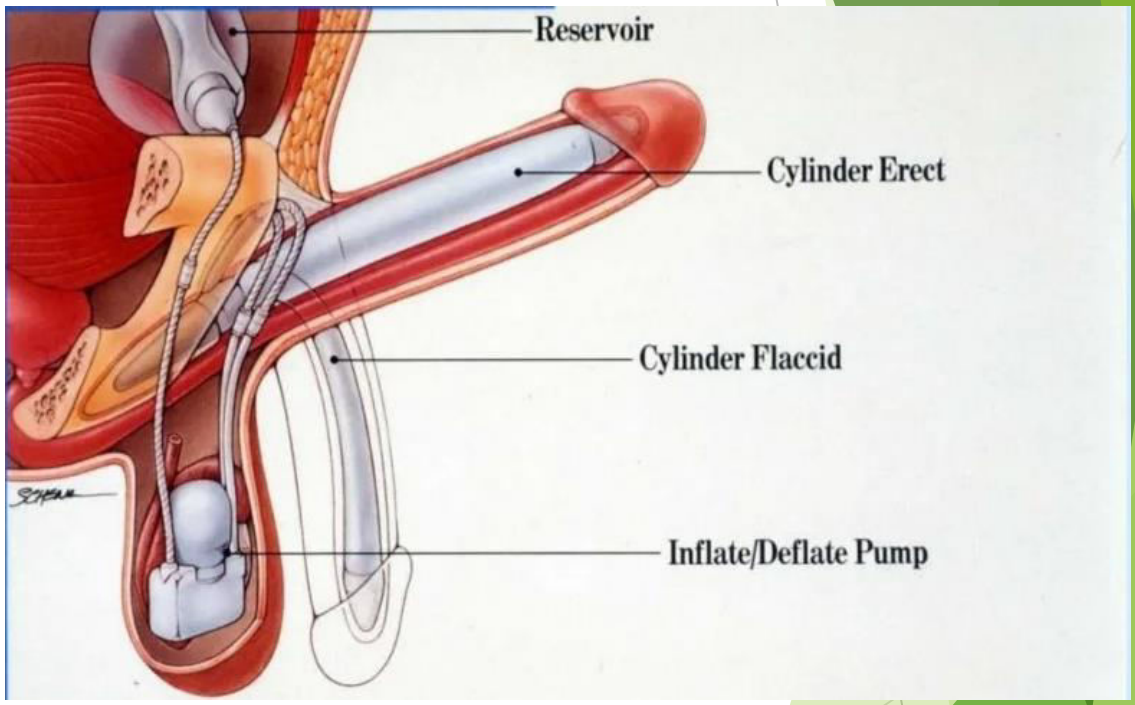
INTRACAVERNOUS ALPROSTADIL(SECOND LINE)

- Intracavernous dose- 5-40mcg.
- Erection appears after 5-15 min(no need for manual stimulation)
- Complications: penile pain, prolonged erection, priapism, fibrosis.



PENILE PROSTHESIS (Third line)

- Patients with failed pharmacotherapy and those who prefer a permanent solution.
- 2 classes:
  - Inflatable and semi- rigid
- Complications : mechanical failure and infection



What's New

- Soluble Guanylate Cyclase stimulators
- ROCK Inhibitors
- SLx 2101
- Maxi K channel activators and Gene Therapy
- Topical preparations, ODF
- Mirabegron
- Bremelanotide
- PRP
- NO donors
- Stem Cell Therapy- Bone Marrow/ Adipose derived

THANK YOU