ED

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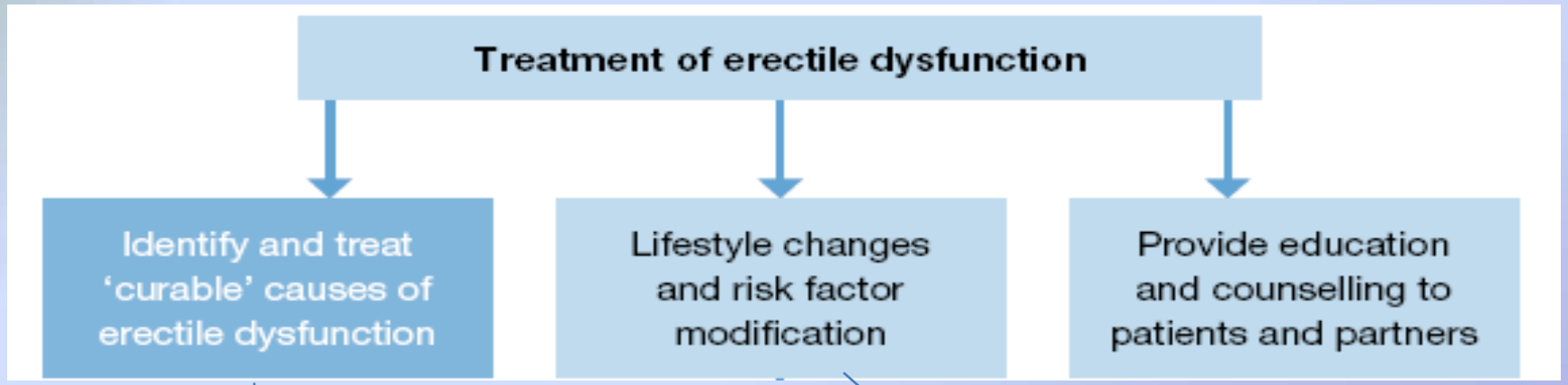
KUMS

treatment

Step 1



As a rule, ED can be treated successfully with current treatment options, but cannot be cured.

The only exceptions :
1-psychogenic ED
2-post-traumatic arteriogenic ED in young patients
3- hormonal causes (e.g. hypogonadism and hyperprolactinaemia)

-Exercise-W.Loss

-Mediterranean-style diets

-Drug adjustment-alcohol

-smoking -bicycle

-DM-M.S-CVD

- **Psychosexual Therapy:**

All patient

In younger patients (< 40 years) with long-term primary ED

Androgen:

-tes<300ng/dl

-Before initiating TS, digital rectal examination, serum PSA test, haematocrit, liver function tests and lipid profile should be performed(306 month-every year)

-3 month→ re evaluation

Oral?

TS is controversial in men with a history of Pca

TS is contraindicated in patients with untreated PCa (LE: 4).

TS is contraindicated in patients with unstable cardiac disease.

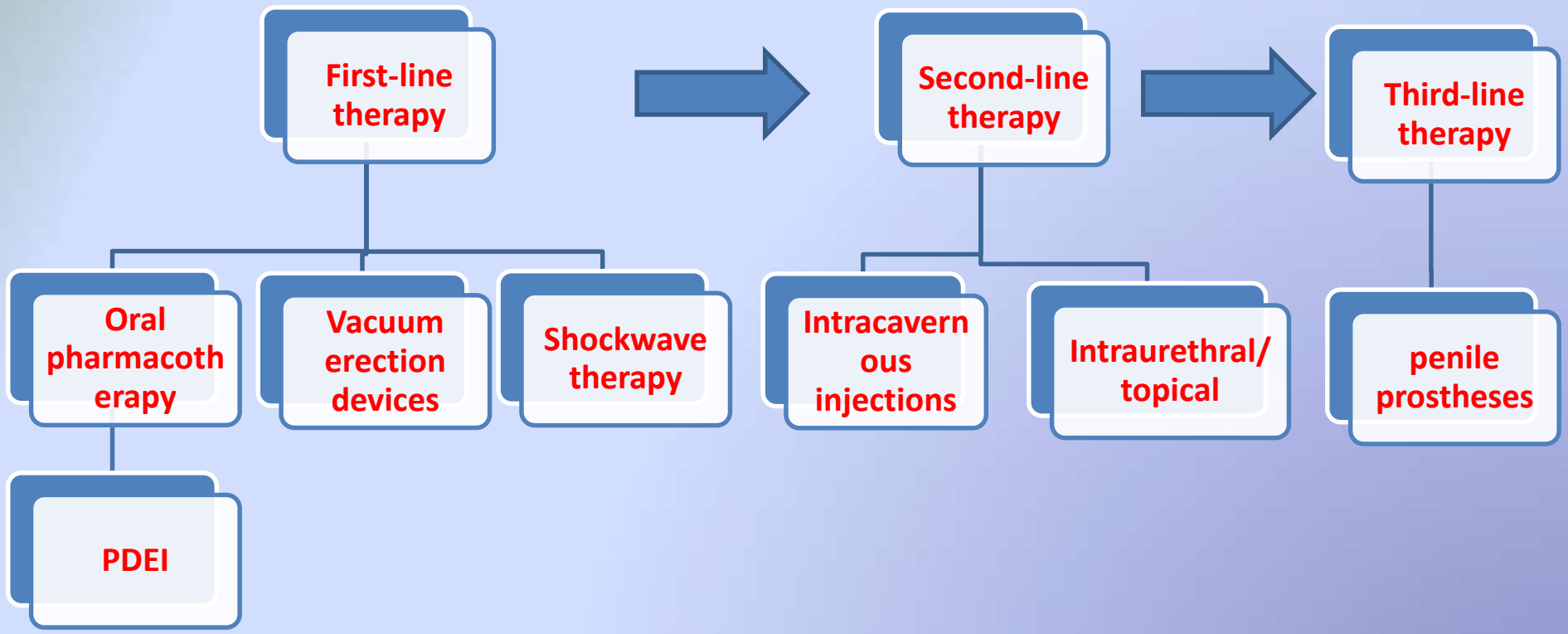
hyperprolactinemia

- Drug adjustment: morphine-estrogen-neuroleptic
- Bromocryptine-cabergoline→surgery
- Max effect→prl>40ng/dl

Drug adjustment:

- **Antipsychotic:** bupropion, nefazodone, buspirone, mirtazapine
- **Antihypertensive:** **ca-blocker-ACEI-** angiotensin receptor blockers
- **SSRI:** drug holidays- SSRI dosage reduction-watchful waiting- PDE5 inhibitors

Step 2:


First-line therapy
Second-line therapy
Third-line therapy
Oral pharmacotherapy
Vacuum erection devices
Shockwave therapy
PDEI
Intracavernous injections
Intraurethral/ topical
penile prostheses

MEDICAL THERAPY

- PDE5I
- Alfa-blocker:phentolamine-yohimbine
- Dopaminergic agonist:Apomorphine
- Melanocortine agonist:melanothane
- Serotonine agonist: trazodon

PDEI

- They are not initiators of erection and require sexual stimulation to facilitate an erection
- Sildenafil 60MIN
- Tadalafil 120MIN
- Vardenafil 60MIN
- Avanafil 30MIN

70%
DM:40-50%
NSRP:60-70%

Sildenafil

- It is administered in doses of 25, 50 and 100 mg.
- The recommended starting dose is 50 mg and should be adapted according to the patient's response and side-effects.
- Sildenafil is effective from 30-60 min after administration.
- Its efficacy is reduced after a heavy, fatty meal due to prolonged absorption.
- Efficacy may be maintained for up to 12 h
- The efficacy of sildenafil in almost every subgroup of patients with ED has been successfully established.

Tadalafil

- effective from 30 min after administration, with peak efficacy after about 2 h.
- Efficacy is maintained for up to 36 h and is not affected by food.
- It is administered in on-demand doses of 10 and 20mg and also an alternative daily dose of 5mg. (Continuous dosing may also be used in the comorbid patient with LUTS and ED.)
- The efficacy of tadalafil in almost every subgroup of patients with ED, thus including difficult-to-treat subgroups (e.g. diabetes mellitus), has been successfully established.

Vardenafil

- It is effective from 30 min after administration
- Its effect is reduced by a heavy, fatty meal (> 57% fat).
- Five, 10 and 20 mg doses have been approved for on-demand treatment of ED.

-The recommended starting dose is 10 mg

-The efficacy of vardenafil in almost every subgroup of patients with ED, thus including difficult-to-treat subgroups (e.g. diabetes mellitus), has been successfully established.

-More recently, an ODT of vardenafil has been released .

-Orodispersable tablet formulations offer improved convenience over film-coated formulations and may bepreferred by patients.

-Absorption is unrelated to food intake and they exhibit better bioavailability compared to film-coated tablets .

- The efficacy of vardenafil ODT has been demonstrated in several randomised controlled trials and did not seem to differ from the regular formulation

Avanafil

- It is a highly-selective PDE5I that recently became commercially available
- Avanafil has a high ratio of inhibiting PDE5 as compared with other PDE subtypes allowing for the drug to be used for ED while minimising adverse effects [108].
- Fifty, 100, and 200 mg doses have been approved for on-demand treatment of ED .
- The recommended starting dose is 100 mg taken orally as needed approximately 30 min before sexual

- The maximum recommended dosing frequency is once per day.
- Dosage adjustments are not warranted based on renal function, hepatic function, age or gender
- Administration with food may delay the onset of effect compared with administration in the fasted state but avanafil can be taken with or without food.
- The efficacy of avanafil in many subgroup of patients with ED, including difficult-to-treat
- subgroups (e.g diabetes mellitus), has been successfully established

TABLE 27-7 Comparison of Four Phosphodiesterase Type 5 Inhibitors Currently Available in the United States

	SILDENAFIL	VARDENAFIL	TADALAFIL	AVANAFIL
Cmax (ng/mL)	450	20.9	378	2153
Tmax (hr)	0.8	0.7-0.9	2	0.3-0.5
Onset of action (min)	15-60	15-60	15-120	15-60
Half-life (hr)	3-5	4-5	17.5	3-5
Bioavailability	40%	15%	Not tested	30%
Fatty food	Reduced absorption	Reduced absorption	No effect	Reduced absorption
Recommended dosage	25, 50, 100 mg	5, 10, 20 mg	5, 10, 20 mg	50, 100, 200 mg
Side effects:				
Headache, dyspepsia, facial flushing	Yes	Yes	Yes	Yes
Backache, myalgia	Rare	Rare	Yes	Rare
Blurred/blue vision	Yes	Rare	Rare	No
Precaution with antiarrhythmics	No	Yes	No	No
Contraindication with nitrates	Yes	Yes	Yes	Yes

All PDE5Is are contraindicated in:

-Myocardial infarction, stroke, or life-threatening arrhythmia within the previous 6 mo

- **New York Heart Association class II or greater heart failure or coronary artery disease causing unstable angina or** angina with sexual intercourse
- **Resting hypotension (<90/50 mm Hg) or hypertension (>170/100 mm Hg)**
- **Known hereditary degenerative retinal disorders including retinitis pigmentosa**
- **Severe hepatic impairment (Child-Pugh C) or end-stage renal disease requiring dialysis**

Interaction:

1-Absolute contraindication to PDE5Is is represented by patients who are using any form of organic nitrate

If a PDE5I is taken and the patient develops chest pain, nitroglycerine must be withheld for at least 24 h if sildenafil(and probably also vardenafil) is used (half-life, 4 h), or at least 48 h if tadalafil is used (half-life, 17.5 h), and for no less than 12 h if avanafil is used (half-life, 6-17 h)

PDEI→ممنوع تا ۲ هفته پس از نیترات

2- ketoconazole and itraconazole and protease inhibitors such as ritonavir → impair the metabolic breakdown of PDE5 inhibitors by blocking the CYP3A4 pathway.

3- rifampin phenobarbital, phenytoin and carbamazepine **may induce CYP3A4→ enhancing the breakdown of inhibitors and requiring higher PDE5 dose**

4- Kidney or hepatic dysfunction may require dose adjustments or warnings.

5-Sildenafil labelling advises that 50 or 100 mg sildenafil should be used with caution in patients taking an α-blocker (especially doxazosin).

Tadalafil is not recommended in patients taking doxazosin, but this is not the case for tamsulosin

phentolamine

- Alfa 1-2 antagonist
- 40mg
- 40%
- Headach-flushing

Yohimbine

- Alfa2 blocker
- Organic ED→no
- erectogenic

Apomorphine

- D1-D2 Agonist
- Psychologic ED
- Sublingual 2-4-8mg
- 12min→2h
- Oral→no

trazodon

- 5HT2c agonist
- 5HT2A antagonist
- HTN-AUR-periapism

Vaccum device

- Ind:1- medicl therapy failure
  2- maintenance of erection
  3-glanular insufficiency
  4- VEDs may be the treatment of choice in wellinformed older patients with infrequent sexual intercourse and comorbidity requiring non-invasive, drug-free management

Vacuum Device

- **Externally applied device mechanically effects penile blood engorgement**
- **Cylinder/pump placed over penis creates closed chamber; pump creates vacuum, drawing blood into corpora cavernosa**
- **Constrictive elastic ring then placed at base of penis to restrict flow of suctioned blood**

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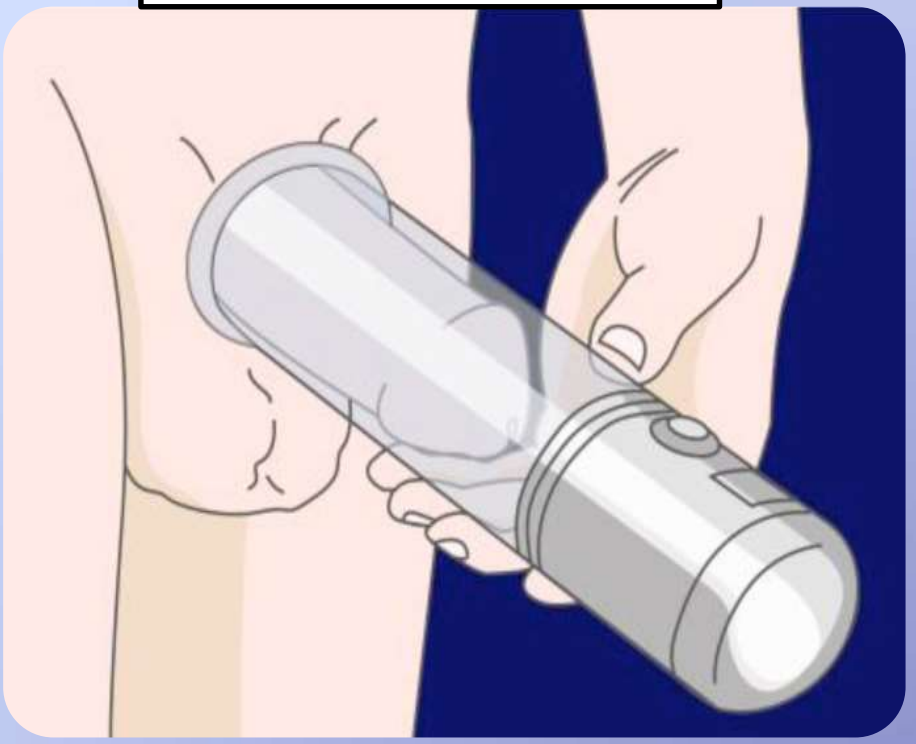


- The commonest adverse events include pain, inability to ejaculate, petechiae, bruising, and numbness, which occur in < 30% of patients
- Serious adverse events (skin necrosis) and fornnier can be avoided if patients remove the constriction ring within 30 min.(no metalic ring)
- VEDs are contraindicated in patients with bleeding disorders or on anticoagulant therapy.

Shockwave therapy

- Recently, the use of low-intensity extracorporeal shock wave therapy (LI-SWT) was proposed as a novel treatment for ED
- Current data are still limited and clear recommendations cannot be given.

Intracavernous injections

- Success rate is high (85%)
- Alprostadil is the first and only drug approved for intracavernous treatment of ED
- most efficacious as monotherapy at a dose of 5-40 µg
- The erection appears after 5-15 min and lasts according to the dose injected

- Perceived advantages of alprostadil for intracavernosalpharmacotherapy relative to other agents are lower incidencesof prolonged erection, systemic side effects, and penile fibrosis.

- Disadvantages include a higher incidence of painfulerection and higher cost, and, after reconstitution into liquidfrom powder, alprostadil has a shortened half-life if not refrigerated.

- COMPLICATION:
- penile pain (50% of patients reported pain but pain reported only after 11% of total injections),
- prolonged erections (5%)
- priapism (1%)
- fibrosis (2%)
- Systemic side-effects are uncommon. The most common is mild hypotension, especially when using higher doses

Contraindications

- history of hypersensitivity to alprostadil
- men at risk of priapism
- men with bleeding disorders

Combination therapy

- Papaverine (20-80 mg) was the first oral drug used for intracavernous injections.

  It is most commonly used in combination therapy due to its high incidence of side-effects as monotherapy.
- Phentolamine has been used in combination therapy to increase efficacy. As monotherapy, it produces a poor erectile response
- vasoactive intestinal peptide (VIP), NO donors (linsidomine),

BIMIX-TRIMIX-INVICORP

Intraurethral Suppositories

- **alprostadil** (125, 250, 500, and 1000 µg dosages) into the distal urethra (3 cm from the external urethral meatus).

A calculated final responder rate to MUSE is approximately 50%, and among responders approximately 70% of administrations result in sexual intercourse

1-The main indications for this therapy are patients who are nonresponsive to PDE5 inhibitors resulting from damage of the autonomic penile nerve supply (e.g., radical prostatectomy, cystectomy, and trauma

2-soft (cold) glans syndrome, which may occur after penile prosthesis implantation

MUSE:

1-local urogenital pain (approximately one third of patients)

2-minor urethral bleeding (5%)

3-hypotension (3%)

3-dizziness (4%)

4- priapism (0.1%)

MUSE is contraindicated in patients with known hypersensitivity to alprostadil, abnormal penile anatomy, and conditions that increase the risk of priapism

Transdermal/Topical Pharmacotherapy

Nitroglycerin→nitric oxide donor formulated as a 2% paste- produce tumescence but rarely penile rigidity sufficient for sexual intercourse

Papaverine→ formulated as a gel

Alprostadil

Further clinical trials will be useful to define and establish their place in the treatment of ED.

Vascular surgery

Inf epigastric

Revascularization or arterialization

Venous leakage: considered investigational

inclusion criteria :age less than 55 years, nonsmoker, nondiabetic, absence of venous leakage, and radiographic confirmation of stenosis of the internal pudendal artery

The highest success rates are reported in young men (less than 30 years of age) with isolated arterial stenosis following perineal or pelvic trauma

Corporeal veno-occlusive dysfunction is a contraindication to revascularisation and must be excluded by dynamicinfusion cavernosometry or cavernosography.

comlication

- Hyperemia of glans 13%
- Thrombosis of shunt 8%
- Ing .hernia 6%

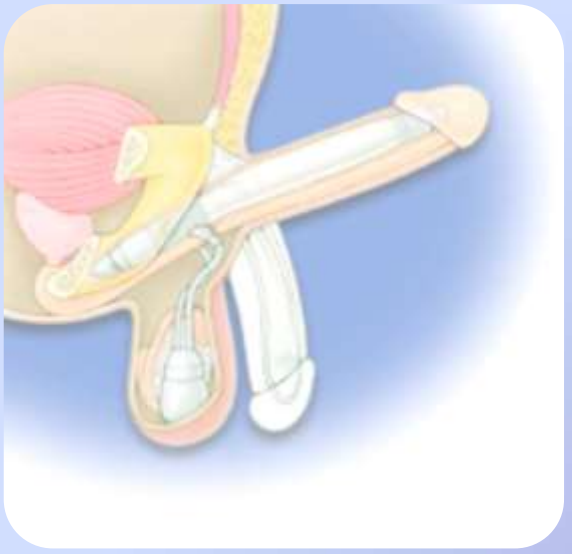
Penile Implants

- An Option For men who have tried other option without success
  - 40 year history
  - High patient and partner satisfaction

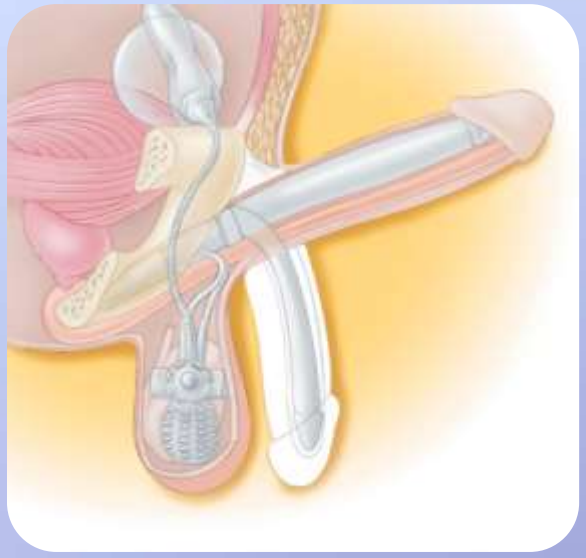
- Penile implants are an attractive solution for patients who do not respond to more conservative therapies.
- There is sufficient evidence to recommend this approach in patients not responding to less-invasive treatments due to its high efficacy, safety and satisfaction rates

Types Penile Prosthesis

One-Piece Non-Inflatable



Two-Piece Inflatable



Three-Piece Inflatable

- Most patients prefer the 3-piece inflatable devices due to the more “natural” erections obtained.
- Likewise, 3-piece inflatable devices provide the best rigidity and the best flaccidity because they will fill every part of the corporal bodies.
- However, the 2-piece inflatable prosthesis can be a viable option among patients who are deemed high-risk of complications with reservoir placements

Possible Risks

- If an infection occurs, the prosthesis may have to be removed
- May cause the penis to become shorter, curved or scarred
- There may be mechanical failures of the prosthesis
- Urogenital pain (typically associated with healing process)

THANK YOU