MEDICAL TREATMENTS OF BPH

BY

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- Introduction
- Medical treatment
- Surgical treatment

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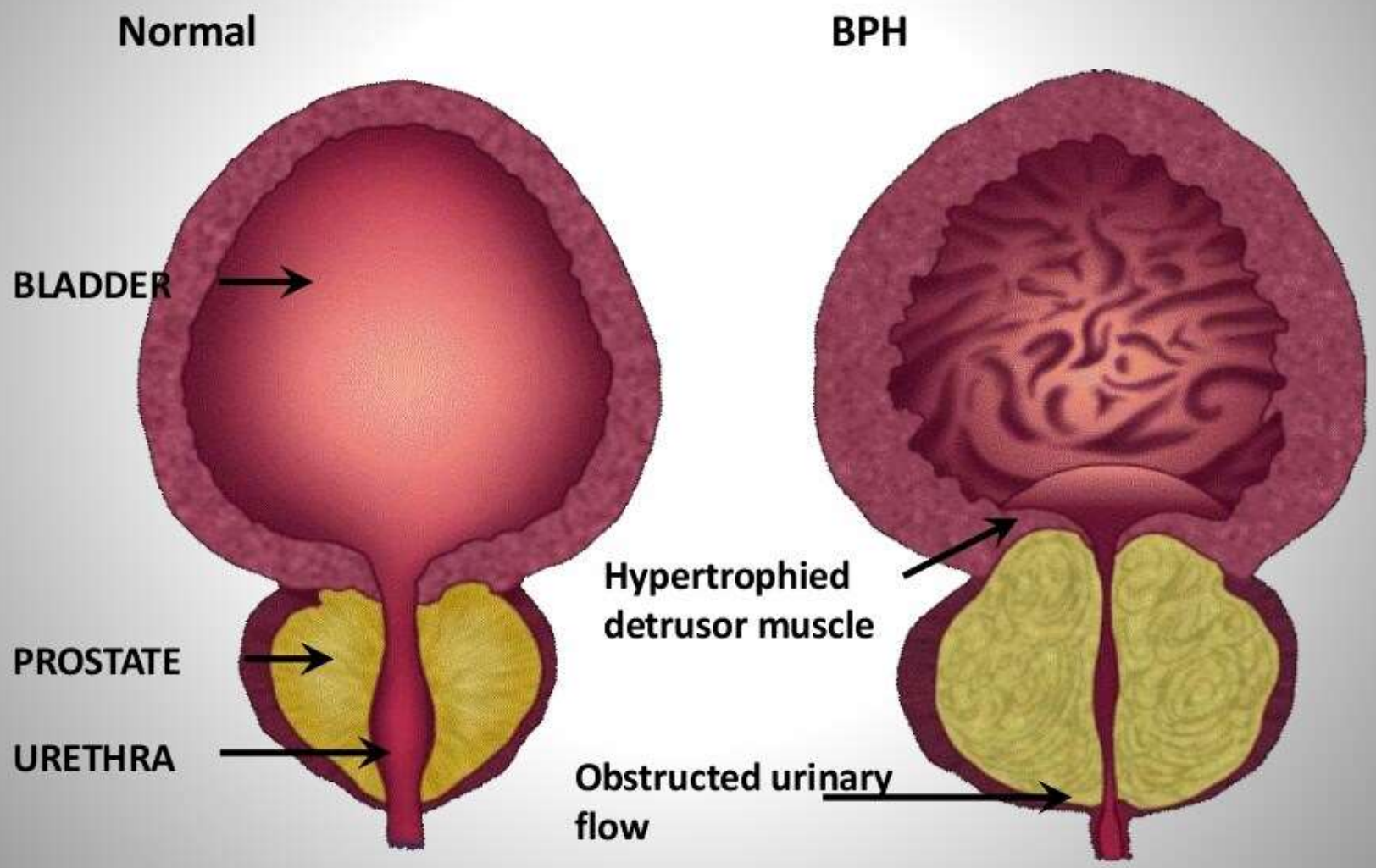
Introduction

- Benign Prostatic Hyperplasia
- Most common condition in elderly men
- >50% men demonstrate histopathologic BPH by age 60 yrs
- 90% by age 80 yrs



Roehrborn CG, McConnell JD. In: Walsh PC et al, eds. Campbell's Urology. 8th ed. **Philadelphia, Pa: Saunders; 2002:1297-1336.**

pathophysiology

- Hypertrophy of bladder neck, smooth muscle of the prostate, prostatic capsule, proximal urethra
- On contraction causes obstructive voiding symptoms- dynamic component of BPH
- Increased prostatic mass mechanically blocks the urethra – static component of BPH

Symptoms

Obstructive Symptoms

- Hesitancy
- Weak stream
- Straining to pass urine
- Prolonged micturition
- Feeling of incomplete bladder emptying
- Urinary retention

Irritative Symptoms

- Urgency
- Frequency
- Nocturia
- Urge incontinence

Treatment

- Watchful waiting
- Pharmacological treatment
- Surgical treatment

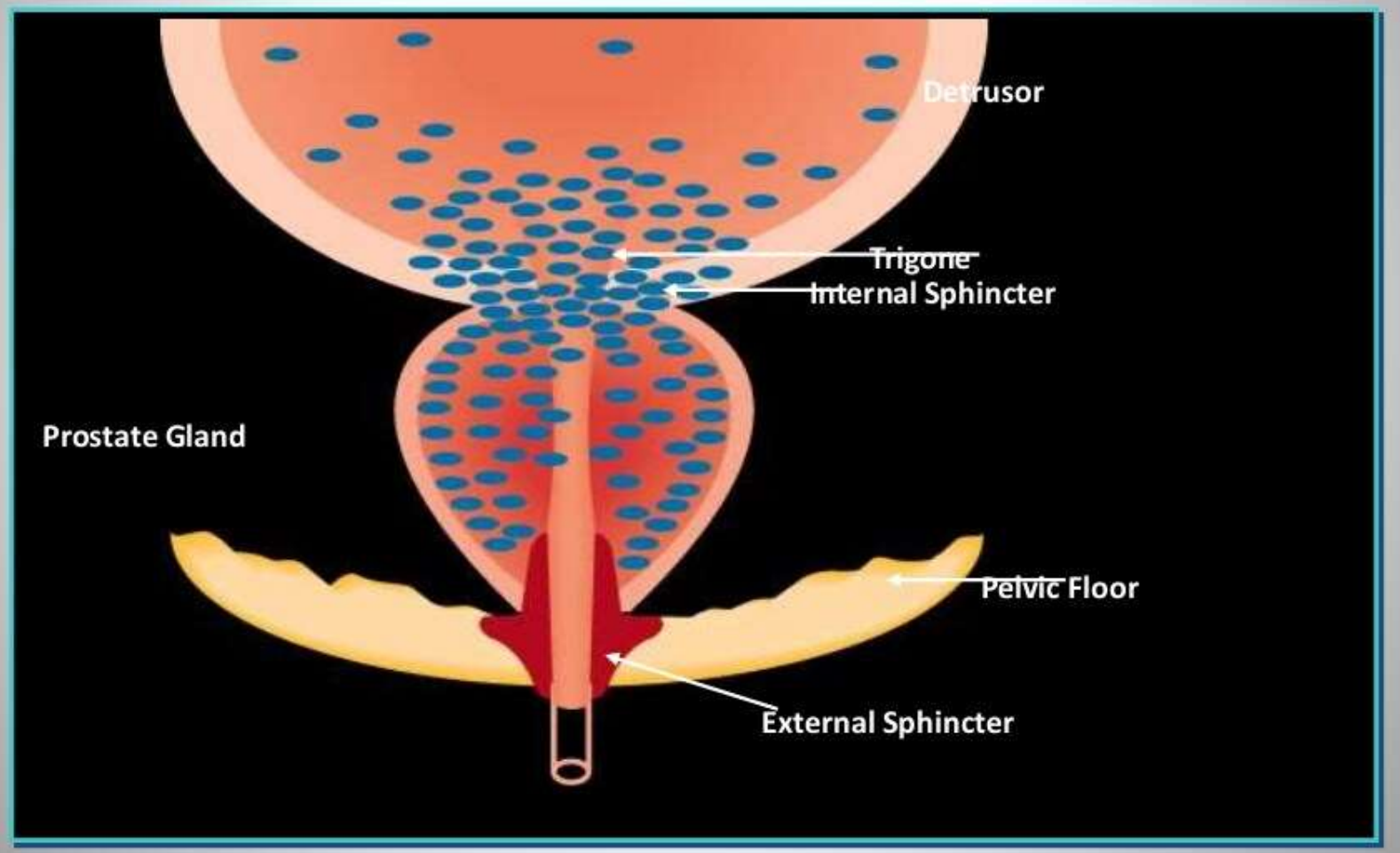
Watchful waiting

- Regular follow ups
- In patients with mild symptoms
- Patients with moderate symptoms who are not bothered by their symptoms

Medical management

- **Non selective alpha 1 antagonists**
  a) short acting: Prazosin, Alfuzosin
  b) long acting: Terazosin, Doxazosin
- **Selective alpha 1 A antagonists**
  Tamsulosin, Silodosin
- **5- alpha reductase inhibitors**
  Finasteride, Dutasteride
- **Miscellaneous**
  PDE 5 inhibitor – Tadalafil
  GnRH agonists – Naferelin acetate, Leuprolide

Distribution of Alpha Receptors in the Prostate and Bladder



Alpha 1 blockers

- Relaxation of both bladder neck and prostatic smooth muscle, thus decreasing pressure in the bladder and urethra improve the urinary flow
- Improve the obstructive symptoms than irritative symptoms
- Drugs are- Prazosin
  Terazosin
  Doxazosin
  Alfuzosin
  Tamsulosin
  Silodosin

PRAZOSIN

- $\alpha 1 > \alpha 2$
- Potent inhibitor of cyclic nucleotide phosphodiesterases
- Well absorbed orally
- Bioavailability 50 – 70 %
- Tightly bound to plasma proteins
- Metabolized in liver
- Duration of action 7 to 10 hrs
- Initial dose 1mg at bed time
- Off label use in BPH, 1-5mg, twice daily

Terazosin

- Structural analog of prazosin
- More soluble in water than prazosin
- More effective than finasteride in treatment of BPH
- Bioavailability is 90%, highly protein bound
- $t_{1/2}$ is 12 hrs, duration of action more than 18 hrs, once daily dosing
- Metabolized in by demethylation, dealkylation in liver
- 40% excreted in urine

- Contraindicated in patients with known sensitivity to quinazolines
- Side effects – first dose hypotension, dizziness, fatigue
- Used with caution in patients taking diuretics, other antihypertensive agents, phosphodiesterase 5 inhibitors
- Dosage: initially 1 mg daily at bed time,

  10 mg/day for maximal effect in BPH

Doxazosin

- Structural analog of prazosin
- Bioavailability 65%, highly protein bound
- $t_{1/2}$ is 20 hrs, duration of action around 36hr
- Metabolized in by demethylation, dealkylation in liver
- Most of the metabolites are excreted in feces
- Contraindicated in patients with known with sensitivity to quinazolines

- Used with caution in patients taking diuretics, other antihypertensive agents, phosphodiesterase 5 inhibitors, in hepatic dysfunction
- Side effects – first dose hypotension, dizziness, fatigue, headache
- Dosage: intially 1 mg, maintainace dose is

  1 – 8mgdaily
- Extended release formulations are also available

Alfuzosin

- Used extensively for treatment of BPH, not approved for treatment of HTN
- Bioavailability 64%
- $t_{1/2}$ is 3-5 hrs
- Substrate for CYP3A4
- Contraindicated in patients with moderate to severe hepatic impairment, known hypersensitivity, in patients taking other CYP3A4 inhibitors
- Avoided in patients with prolonged QT syndrome
- Dosage: 10 mg extended release tablet daily

Tamsulosin

- Benzene sulfonamide
- More effective in treatment of BPH, little effect on BP
- Well absorbed
- $t_{1/2}$ is 5 – 10 hrs
- Extensively metabolized by CYPs
- Contraindicated in patients with sulfa allergy, in patients taking CYP inhibitors
- Side effect is retrograde ejaculation, intra operative floppy syndrome
- Dosage: 0.4mg starting dose, maintain with 0.4-0.8mg

Silodosin

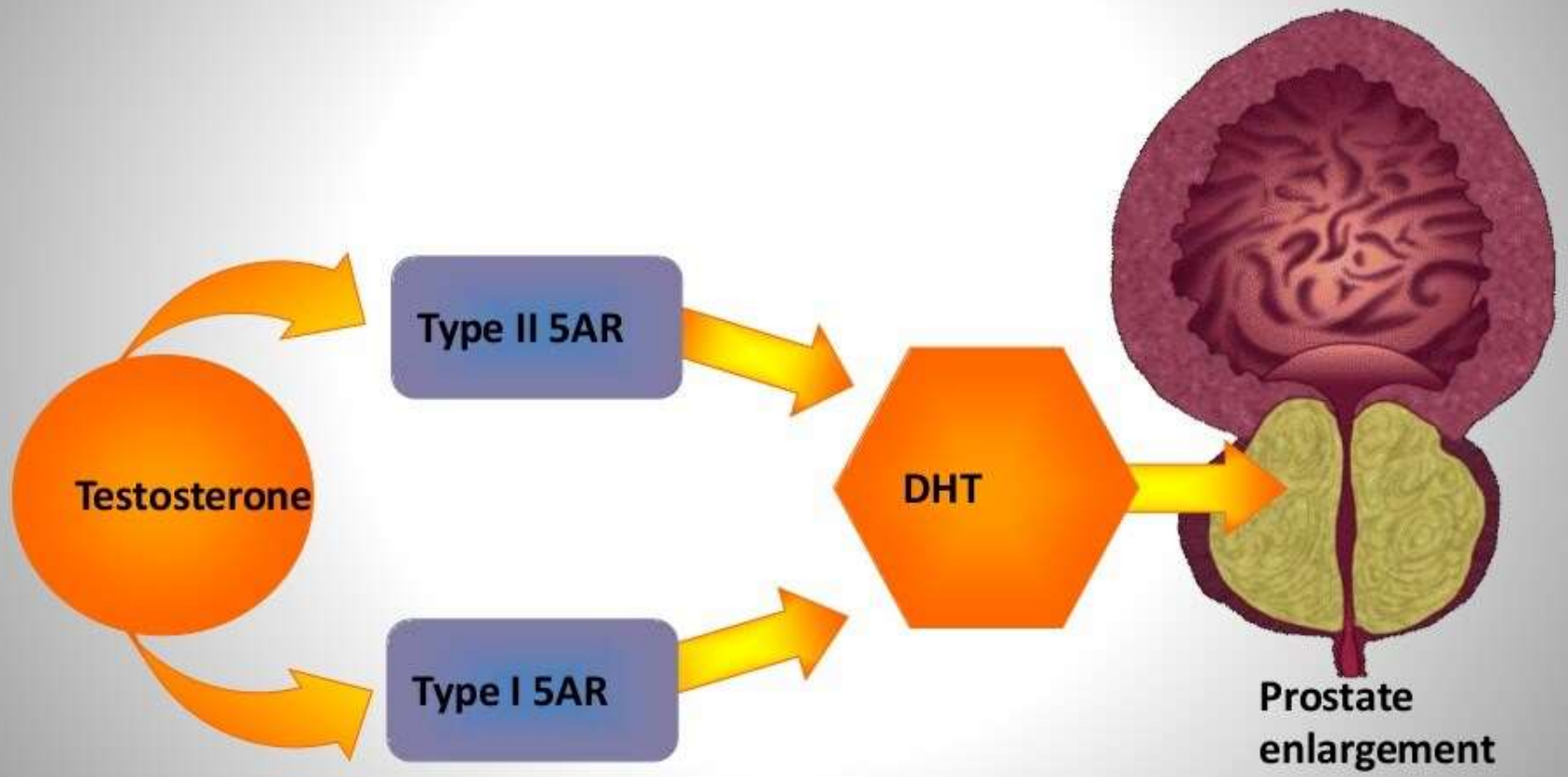
- Selective for α1A receptors
- $t_{1/2}$ is 13-14 hrs
- Metabolized by glucuronidation
- Dosage: 8 mg daily
- Side effects: retrograde ejaculation
- Contraindicated in patients with renal impairment, severe hepatic impairment

5 alpha reductase inhibitors

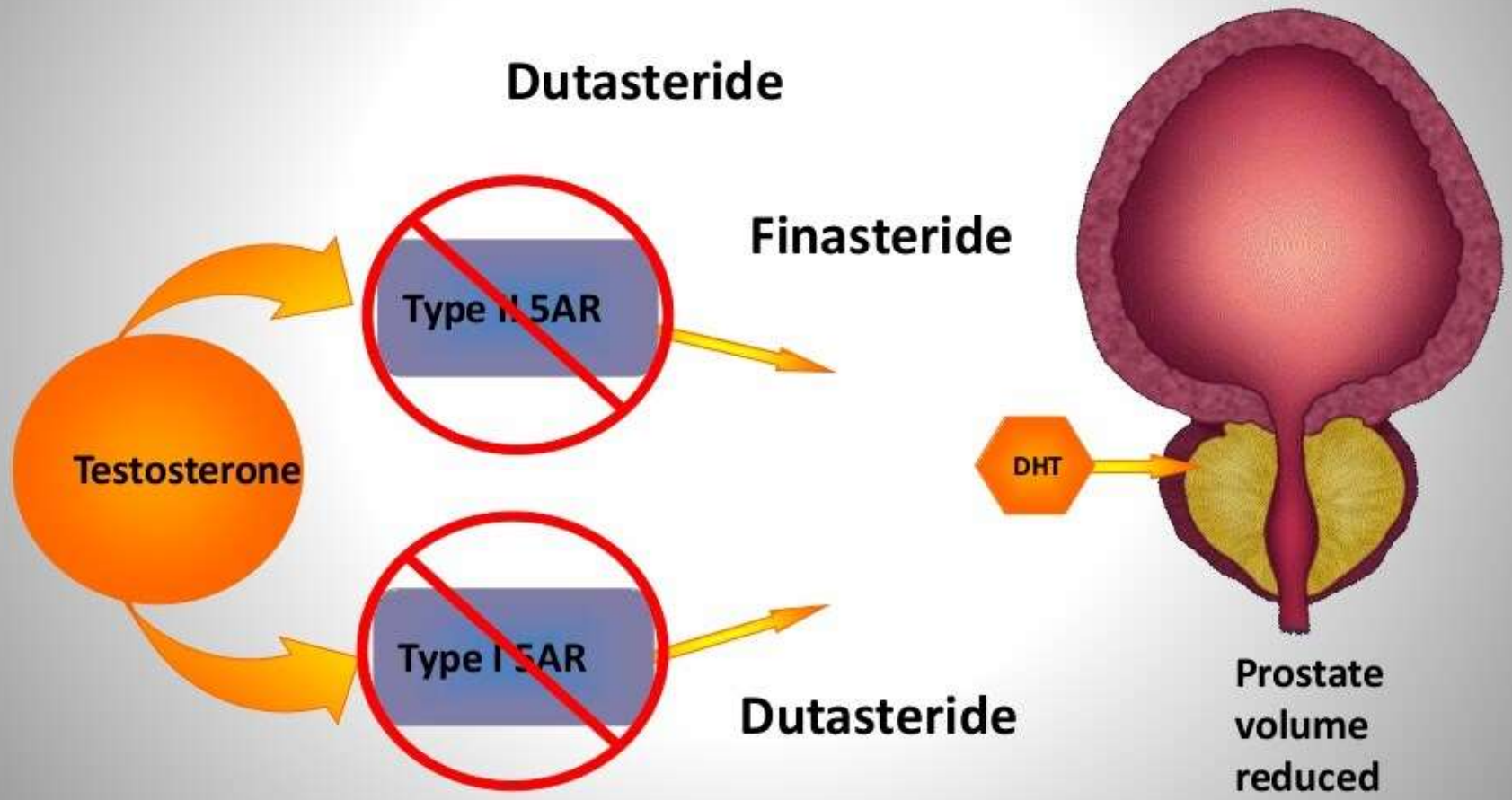
- In prostate, testosterone converted to dihydroxy testosterone (DHT) by 5 alpha reductase enzyme.
- DHT increases the growth in prostate
- Drugs: Finasteride

  Dutasteride

Two 5α-Reductase (5AR) Isoenzymes Convert Testosterone to DHT



Near Complete DHT Suppression Requires Inhibiting Both 5AR Isoenzymes



Bartsch G et al. Eur Urol. 2000;37:367–380.

Finasteride

- Inhibits type 2 isoform of 5 alpha reductase
- Bioavailability 63%
- $t_{1/2}$ is 6-8 hrs
- Dosage 5 mg daily
- Excreted in urine, semen
- Effective only in patients with palpably enlarged prostate
- Contraindicated in patients with obstructive uropathy or prostate cancer

Dutasteride

- Inhibits both isoforms of 5 alpha reductase
- Bioavailability 60%
- Half life is 5 wks
- Metabolized by cytochrome p 450
- Dosage: 0.5mg daily
- Side effects: decreased libido, ejaculatory dysfunction, impotence, gynaecomastia

5 alpha reductase inhibitors and alpha blocker combination

- 0.5mg Dutasteride & 0.4 mg Tamsulosin combination
- Used in treatment of symptomatic BPH in men with enlarged prostate

PDE 5 INHIBITORS

- MAO: Selective inhibitor of cGMP specific PDE5
- Decreases cGMP conc. in corpus cavernosa & pulmonary arteries, in smooth muscles of prostrate, bladder & blood vessels.

TADALAFIL

- Half life – 17 hrs. Metabolized by CYP 450
- Dosage: 5 mg daily
- C/ I: patients using nitrates. Not combined with alpha blockers due to risk of bp lowering

- Also used in pulmonary hypertension, erectile dysfunction
- If erection lasting for more than 4 hrs- requires emergency treatment.
- Stop- if sudden loss of vision in one or both eyes, if sudden decrease or loss of hearing
- Drug Interactions: CYP inhibitors increase Tadalafil exposure, and CYP inducers decrease exposure

Phytochemical Agents

- Plant derived non nutritive compounds.
- Active ingredients & dosage of active medication not known
- Mechanism of action is not clear
- Pumpkin

- Flavonoids

- Hypoxia rooperi

- Saw palmetto- berry extracts

-African plum

thank you