



Medical management of BPH

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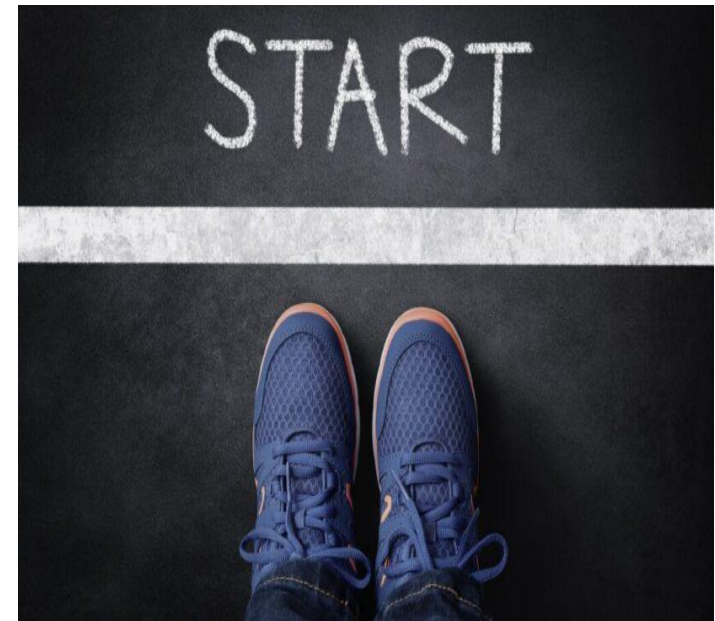
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Disclosure

No conflict of interest related to this presentation

Introduction

- Medical management of (BPH) has progressed gradually in recent years
- But **remains the starting point** for most symptomatic patients seeking treatment.
- Beyond well-known **alpha-blockers and 5-alpha reductase inhibitors**,
- there is growing evidence
- for the use of **phosphodiesterase-5 inhibitors and beta-3 agonists** in managing the condition, which may afford additional relief of “bothersome” **symptoms** in some patients.



The goal of medical treatment for lower urinary tract symptoms associated with BPH

has long been to

- **maximize quality of life**

and

- **minimize “bothersome” symptoms.**

More recently, focus on

- **preventing side effects**

My history with medical management

Residency : before 2000

pygeum africanum

military service

Doxazosine 4 mg

After military service 2002

Alpha blokera surgery --

Retention = surgery

Alfuzosine 10 mg for urinary retention :2006

- no side effects
- But No effectiveness
- Surgery +++

- effectiveness
- But Side effects
- surgery -



First Revolution



Last big Revolution

What is the mechanism of development of BPH ?

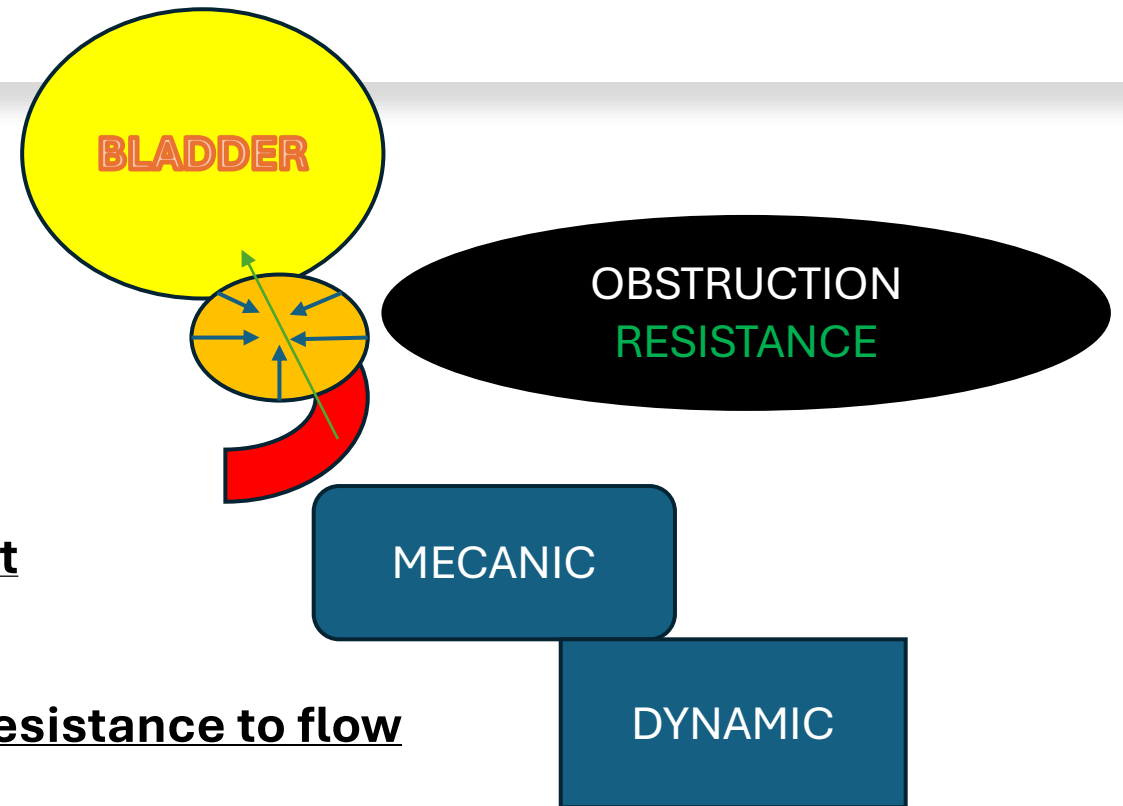
The mechanism is unknown

- But we know
 - that the prevalence of BPH increases with age
 - reaching 60% at age 60 and 80% at age 80
 - **Age** related changes causing
 - metabolic disturbances,
 - changes in **hormone balance**
 - and chronic inflammation.
-

What's are the consequences of prostate enlargement ?

An enlarged prostate gland, while not in itself pathologic, but

- It can result in
- **lower urinary tract symptoms**
- either
- by directly obstructing the bladder outlet
- or
- **by increasing smooth muscle tone** and resistance to flow



How to characterize lower urinary symptoms ?

Lower urinary tract symptoms associated with BPH are characterized

storage symptoms

- frequency
- nocturia
- urgency

Voiding symptoms

- feelings of incomplete emptying
- weak stream
- Intermittency
- straining

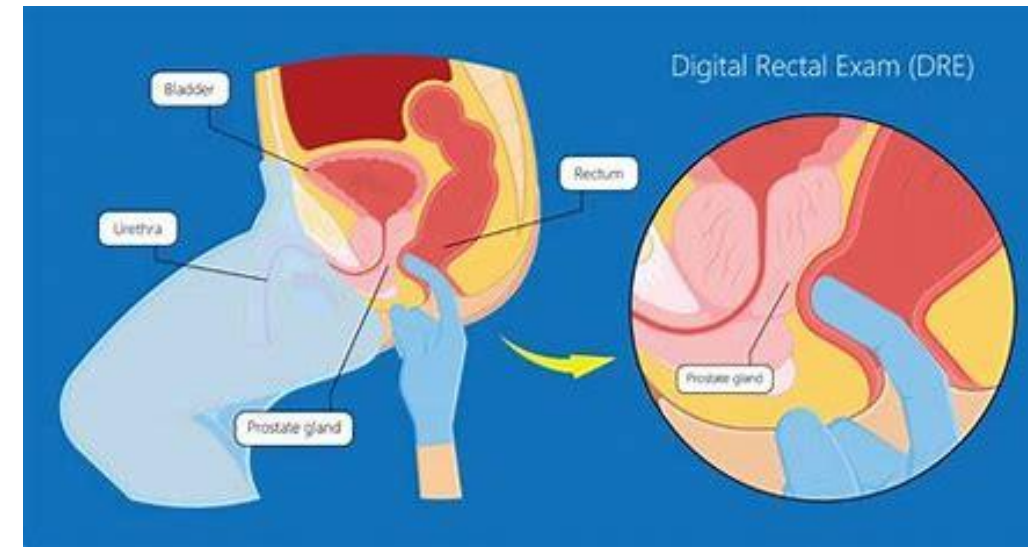


DIAGNOSTIC EVALUATION

Before treating
Every patient will need

It is recommended to obtain a **detailed medical history** including an **assessment of**

- fluid intake (volume and type),
- voiding patterns
- bowel habits
- surgical history
- **DRE**
- **PSA**
- **International Prostate Symptom Score**
- **sexual history**
- **medications** (including supplements and complementary therapies),
- mental health, and physical activity levels can be helpful.



Over the past month....	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	Your score
Incomplete Emptying How often have you had a sensation of not emptying your bladder completely after you finish urinating?	0	1	2	3	4	5	
Frequency How often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
Intermittency How often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
Urgency How difficult you found it to postpone urination?	0	1	2	3	4	5	
Weak stream How often have you had a weak urinary stream?	0	1	2	3	4	5	
Straining How often have you had to push or strain to begin urination?	0	1	2	3	4	5	
Over the past month....	No	1 time	2 times	3 times	4 times	5 times	Your score
Nocturia How many times did you most typically get up to urinate from the time you went to bed until the time you got up in the morning?	0	1	2	3	4	5	
Total Score							



A urinalysis should be obtained

- to **rule out alternate causes for the lower urinary tract symptoms,**
 - FOCUSING on the presence or absence of **glucose, protein, inflammation, or blood** (microhematuria: ≥ 3 red blood cells per high-power field on microscopic evaluation of a single specimen).
-



AFTER EVALUATION



Patients with symptoms considered
mild by the IPSS (0–7)
can opt for **lifestyle modifications**

Conservative management

lifestyle modifications

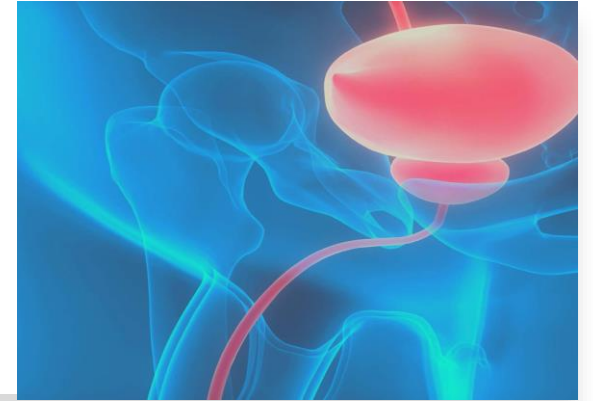
bladder management

lifestyle modifications



- losing **weight**
 - decreasing **evening fluid intake**
 - decreasing the quantity of substances with **bladder-irritating** or **diuretic properties** such as
 - **caffeinated beverages** (coffee, tea, energy drinks, cola),
 - **sugary beverages** (soft drinks, juices),
 - **alcoholic beverages**,
 - fluids containing **artificial sweeteners**, **artificial colorings**, or **artificial flavorings** (often these substances exert diuretic and bladder irritating effects).
-

bladder management



- **timed voiding** (every 2–3 hours) and **double-voiding**.
 - **Doing pelvic floor stretches or relaxation exercises** not strengthening or Kegel exercises
 - **maintaining a regular bowel regimen to** avoid constipation.
-

For patients with
moderate to severe lower urinary tract
symptoms

or

symptoms refractory to conservative
management

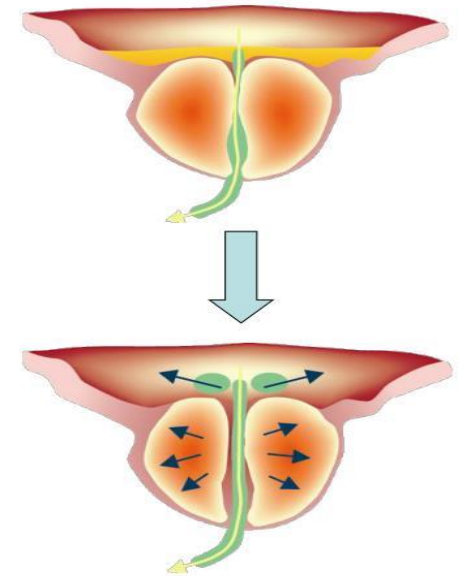
pharmacotherapy

Alpha-blockers

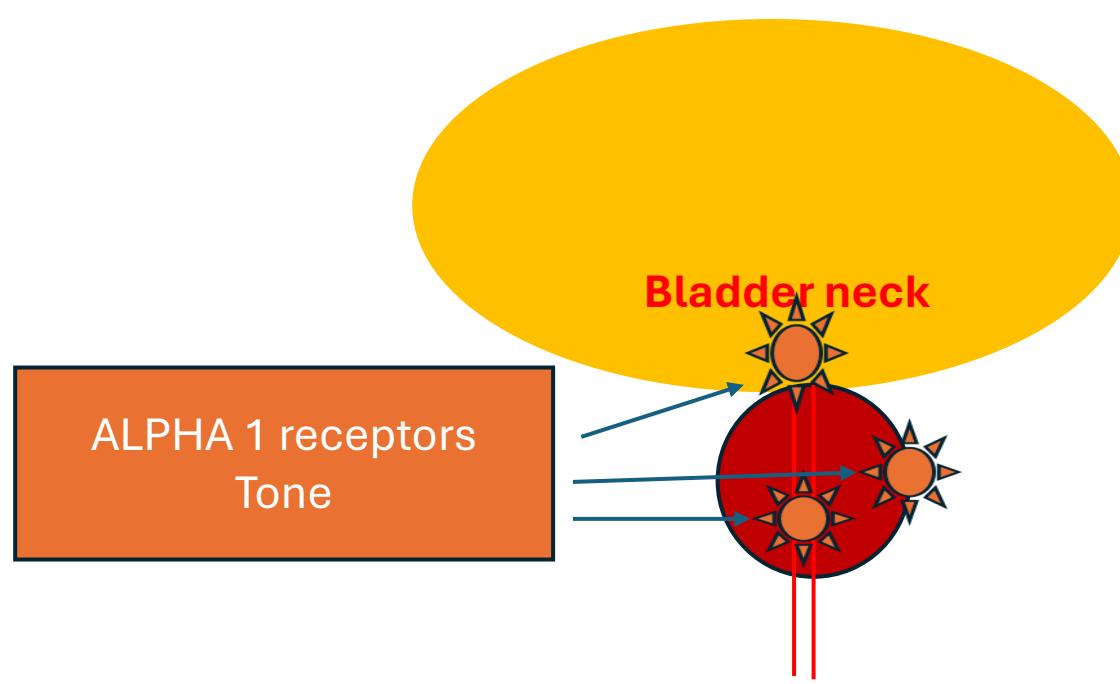
Alpha blockers

Alpha blockers

- Act by relaxing smooth muscle within the prostate and the bladder neck



- They work by
- **antagonizing alpha-1 receptors** in the **bladder neck and prostate**, which results in the **relaxation** of smooth muscle in these areas
- and in turn
- **reduced constriction** of the urinary channel and **lower resistance** to urinary flow.
- expected IPSS improvement from baseline of **4 to 7** points.



ALPHA BLOKERS

The **5 main alpha-blocker** medications include :

second-generation drugs (TERAZOSIN, DOXAZOSIN)

third-generation drugs (*TAMSULOSIN, ALFUZOSIN, SILODOSIN*).

The **third-generation** drugs are generally well tolerated

How effective are they?

- 60% of patients benefit
- 40% improvement in symptoms
- 30% improvement in urine flow

The therapeutic effect starts within hours to days,
it takes 3 to 7 days to reach **maximum effect**.

- Best taken at bedtime

what are the Side Effects ?

- dizziness, headache, nasal congestion, and **ejaculatory dysfunction (tamsulozine)**
- **generally dose-dependent,**
- **resolve** with medication discontinuation
- **changing alpha-blockers** from a *second- to a third-generation* can be **beneficial to avoid orthostatic symptoms and hypotension.**
- among third-generation alpha-blockers **can be beneficial** over **nasal congestion,** or **ejaculatory changes.**

Four types of dizziness



Vertigo
strong sense
of motion or
spinning



Disequilibrium
feeling off-balance,
unsteady or
wobbly



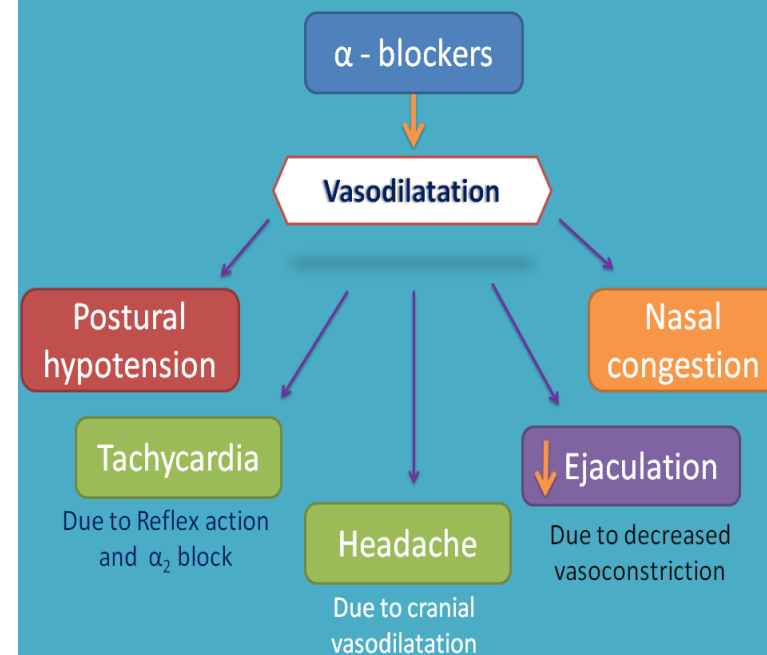
Lightheadedness
woozy
or disconnected from
environment



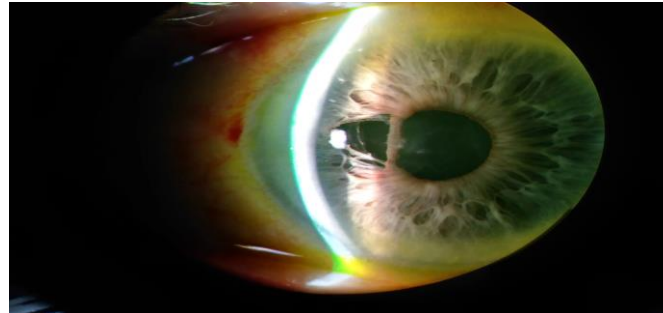
Presyncope
a feeling of losing
consciousness or
about to faint

Hearing Directory

Non-selective α blockers – Side effects



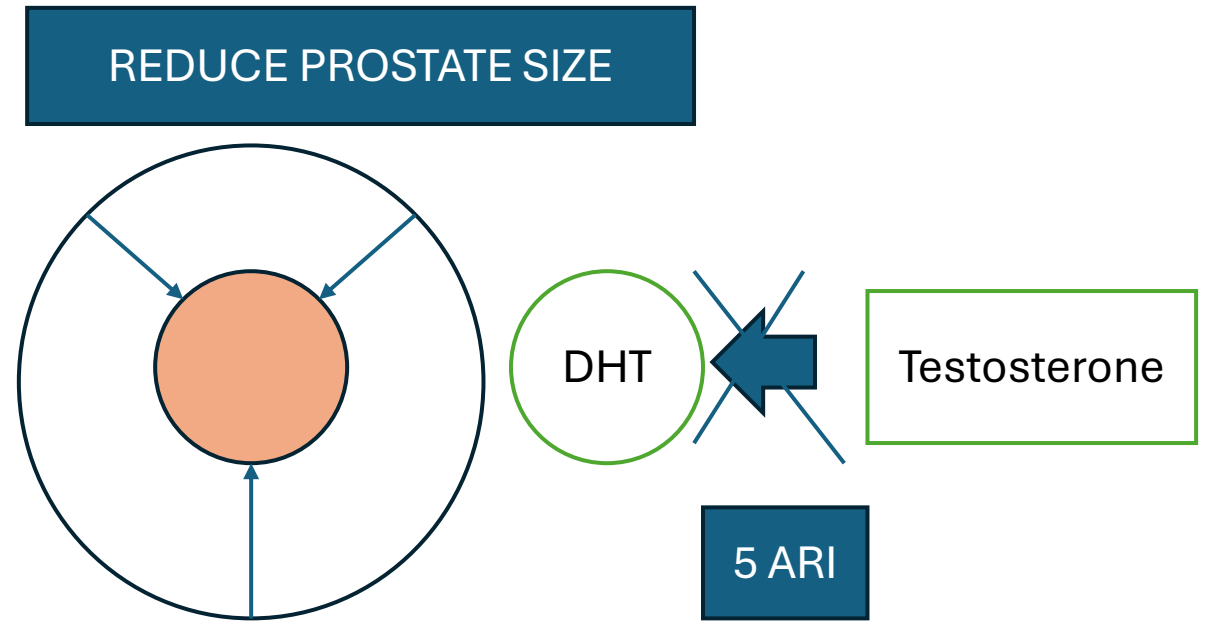
SIDE EFFECTS

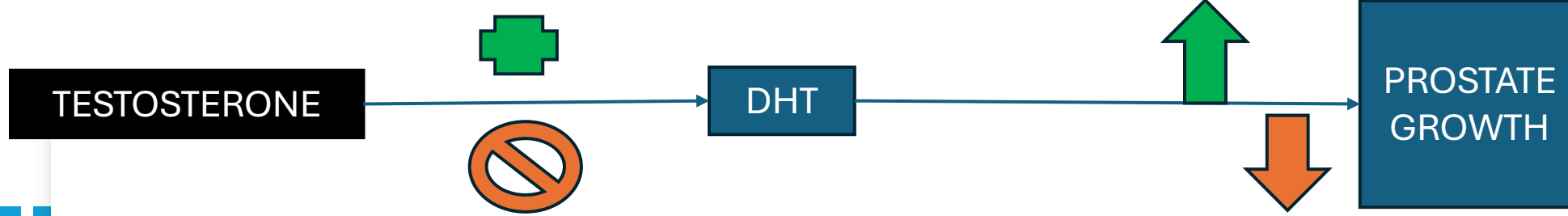


- **Patients taking alpha-blockers, specifically TAMSULOSIN, who plan to undergo cataract surgery should be informed of the possible associated risk of intraoperative floppy iris syndrome.**



5 ARI



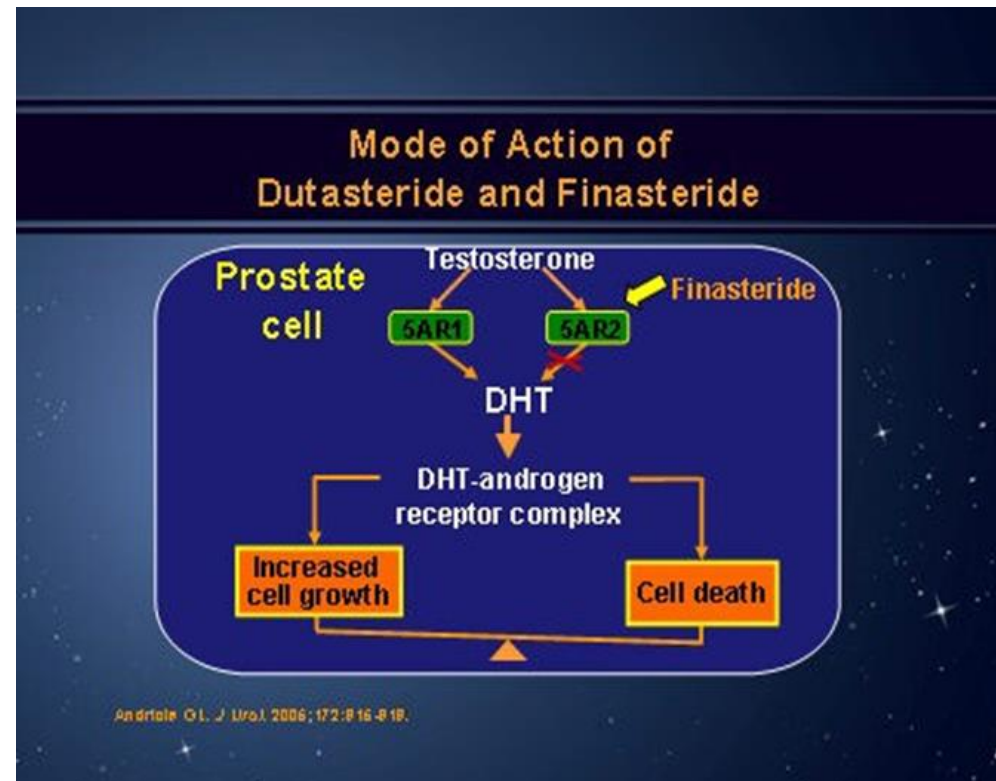


5-alpha reductase inhibitors

- Inhibiting the conversion of testosterone to DHT reduce prostate growth
- The impact on the glandular cells results in a decrease in PSA of approximately 50% after 6 to 12 months of treatment.
- measurement of baseline PSA is recommended
- reserved for symptomatic BPH with **prostate glands 30 cc or larger.**

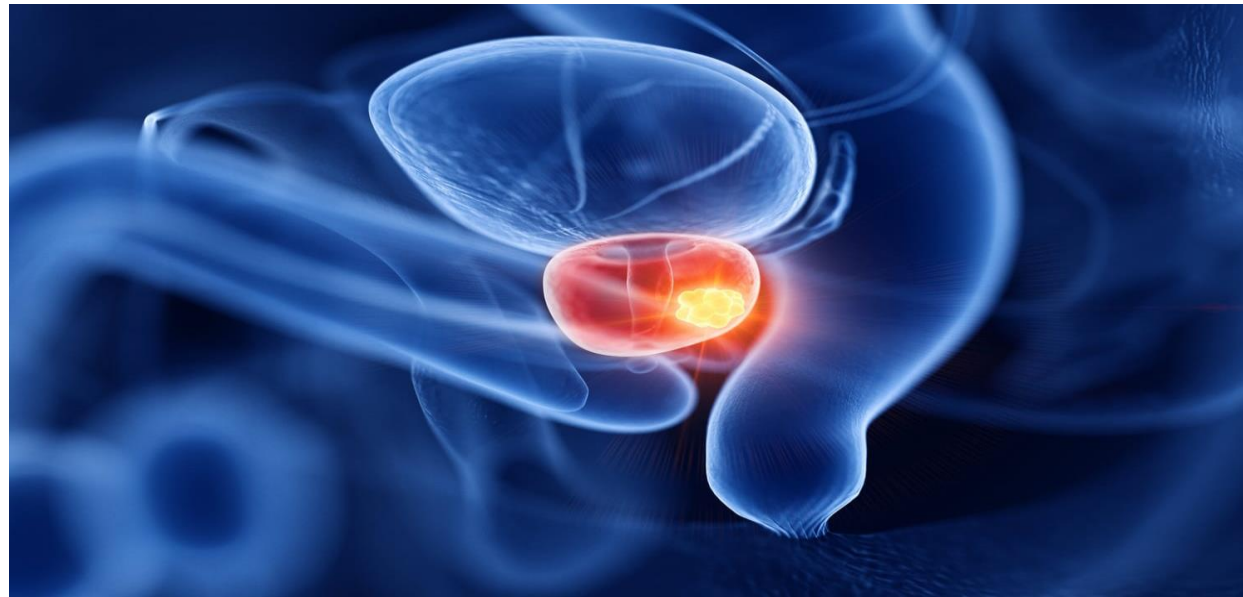
Finastéride and Dutasteride

- **Finasteride** inhibits the 5AR type II isoenzyme
- **Dutasteride** inhibits **type I and II** isoenzymes
- It is important to explain to patients the expected **time frame(3-6 months)** to ensure medication adherence.



5ARI and prostate cancer

- **5ARIs reduce overall prostate cancer rates, particularly low-grade cancers.**
- **because of its selective inhibition of low-grade cancers**
- **finasteride reduces prostate volume, resulting in improved detection of cancer on prostate biopsy**





How well do they work ?

- Reduce prostate size by 20%
 - Improve symptoms by 30 %
 - Improve urine flow rate
 - Reduce risk of retention
-

Side effects of 5ARIs include

- **erectile dysfunction 10%**
- **ejaculatory dysfunction 5%**
(reduced semen volume)
- **decreased libido**
- **gynecomastia and breast tenderness 1%**
- **Side effects are mild and decrease with time**

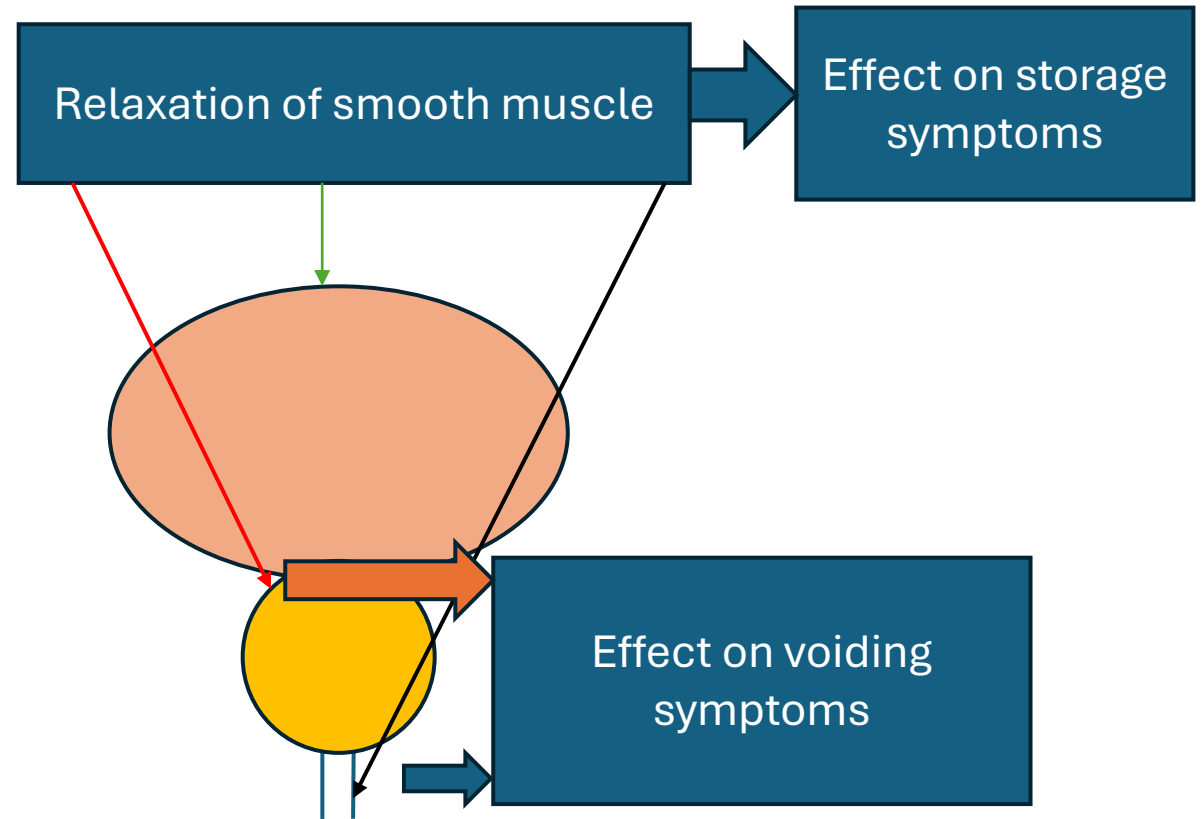


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PDE 5



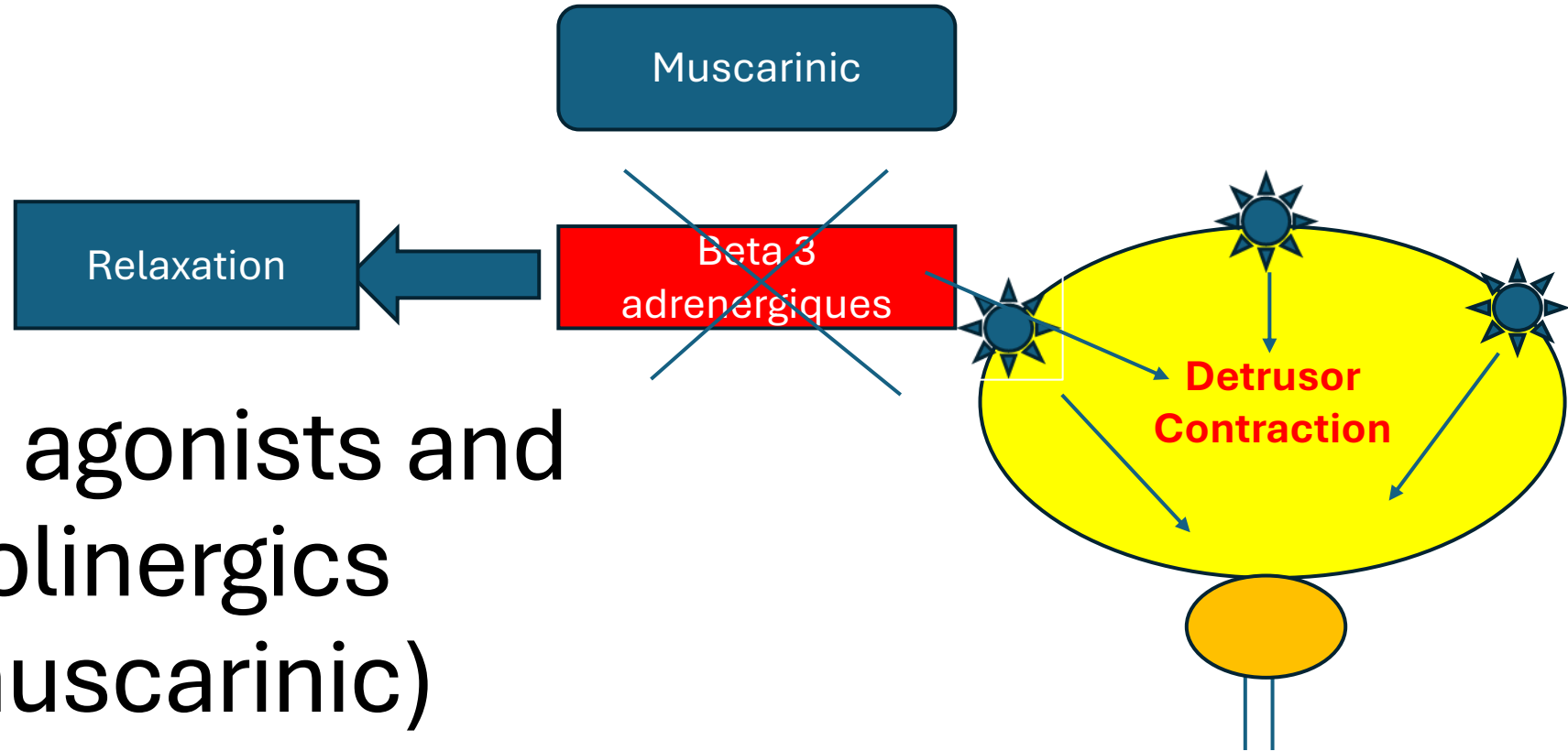
Phosphodiesterase-5 inhibitors PDE5

- **relaxation of smooth muscle** throughout the prostate, detrusor muscle (bladder), and urethra.
 - an **average improvement in IPSS of 3 or more.**
 - Onset of effect is **usually within hours.**
 - **PDE5 inhibitors offer an alternative therapy** for patients who **cannot tolerate or prefer not to use alpha-blockers or 5ARIs.**
 - a **decrease in urinary urgency and frequency**, has been noted in patients taking PDE5 inhibitors.
-

Side effects of PDE5 inhibitors include

- facial flushing
- headache
- back pain
- dyspepsia
- and the potential for blue-tinted vision
- however, **most of these side effects are minimal or absent at low daily doses** for BPH.
- Well-known **contraindications** to PDE5 inhibitors include the **use of nitrates**.

Beta-3 agonists and anticholinergics (anti muscarinic)



Beta-3 agonists

- Beta-3 agonists work **via the sympathetic pathway** to cause relaxation of the detrusor muscle and increase bladder capacity.
- They can benefit patients with predominantly irritative lower urinary tract symptoms, including urgency, frequency, and incontinence.
- Onset of maximum effect is generally at 3 weeks

side effect

- The most common for mirabegron is **hypertension**.
- both **mirabegron and vibegron** are contraindicated in patients with poorly controlled hypertension
- although **vibegron** has been found to pose a negligible risk of **blood pressure change**.

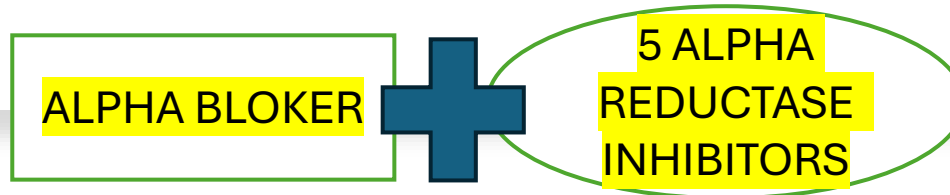


anticholinergic

- were used to treat **bothersome symptoms**.
 - are **associated with cognitive impairment and dementia**, in addition **mental confusion**.
 - **have undesired side effects, including dry mouth, dry eyes, constipation, and potential vision changes**
 - exert therapeutic effect within hours to days
-

Combination therapy

MTOPS trial



- has been shown to be **more effective than monotherapy** or placebo
 - This follows findings from the 2003 **MTOPS** (Medical Therapy of Prostatic Symptoms) study of combination **doxazosin + finasteride** vs **monotherapy** or placebo
 - that demonstrated **decreased rates** of **symptom progression, urinary retention, and invasive BPH surgery.**
 - Side effects are additives
-



CombAT trial

- Combination of **Avodart and Tamsulosin** trial found **significant reduction**
 - In the relative **risk of acute urinary retention** or bph related surgery
 - **compared to monotherapy** ($P < .001$).
-

Other Combinations

- **tadalafil + finasteride** is **helpful**, and avoid alpha-blocker side effects.
 - **anticholinergic + alpha-blocker** for patients experiencing **predominantly** irritative symptoms. (potential cognitive effects of anticholinergics)
 - **alpha-blockers + beta-3 agonists** presents a **safer** and **well-tolerated alternative** to improve symptoms with **fewer side effects**.
 - use of **PDE5 inhibitors + alpha-blockers** remains an option, albeit with **close monitoring** (risk of **orthostatic hypotension**).
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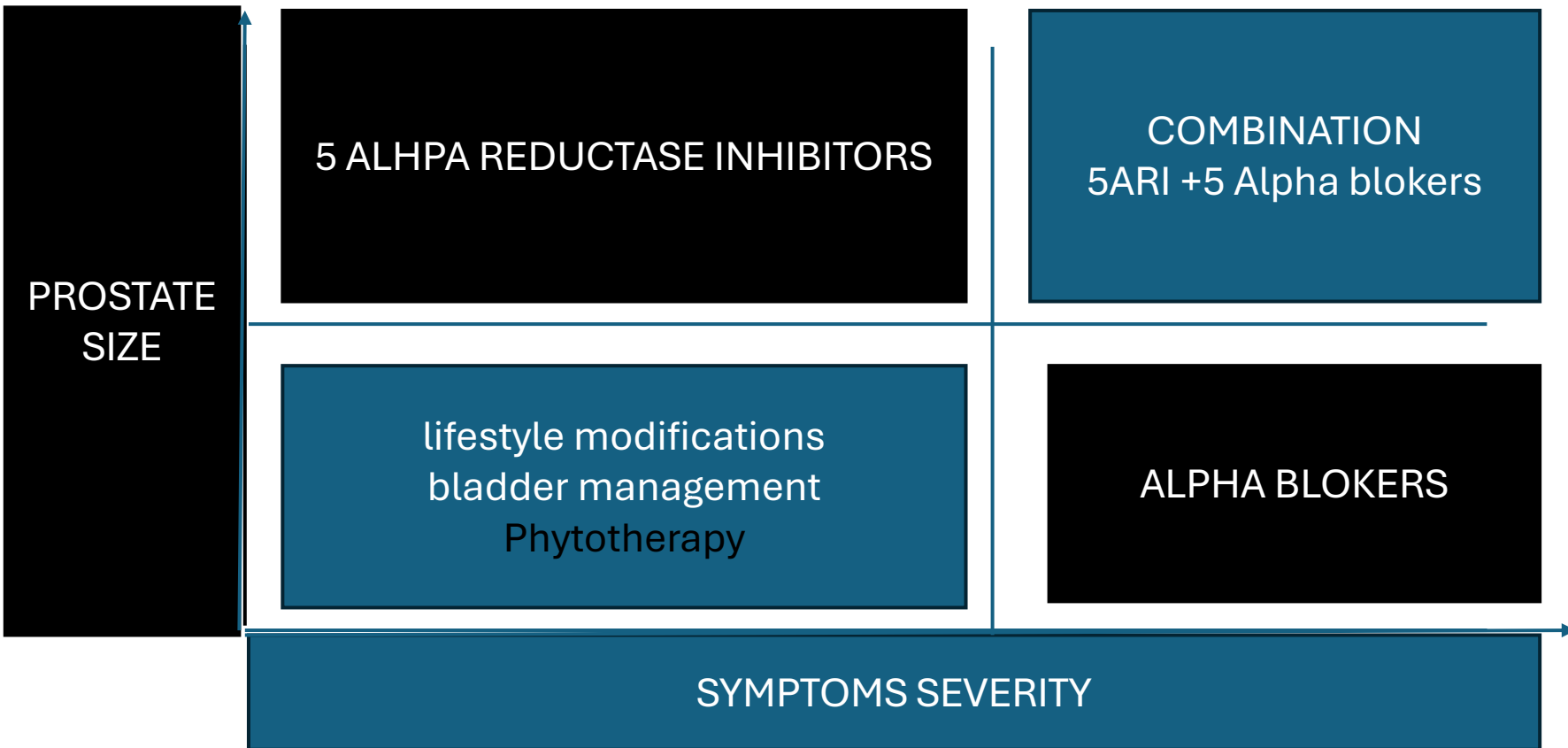
MEDICINAL PLANTS

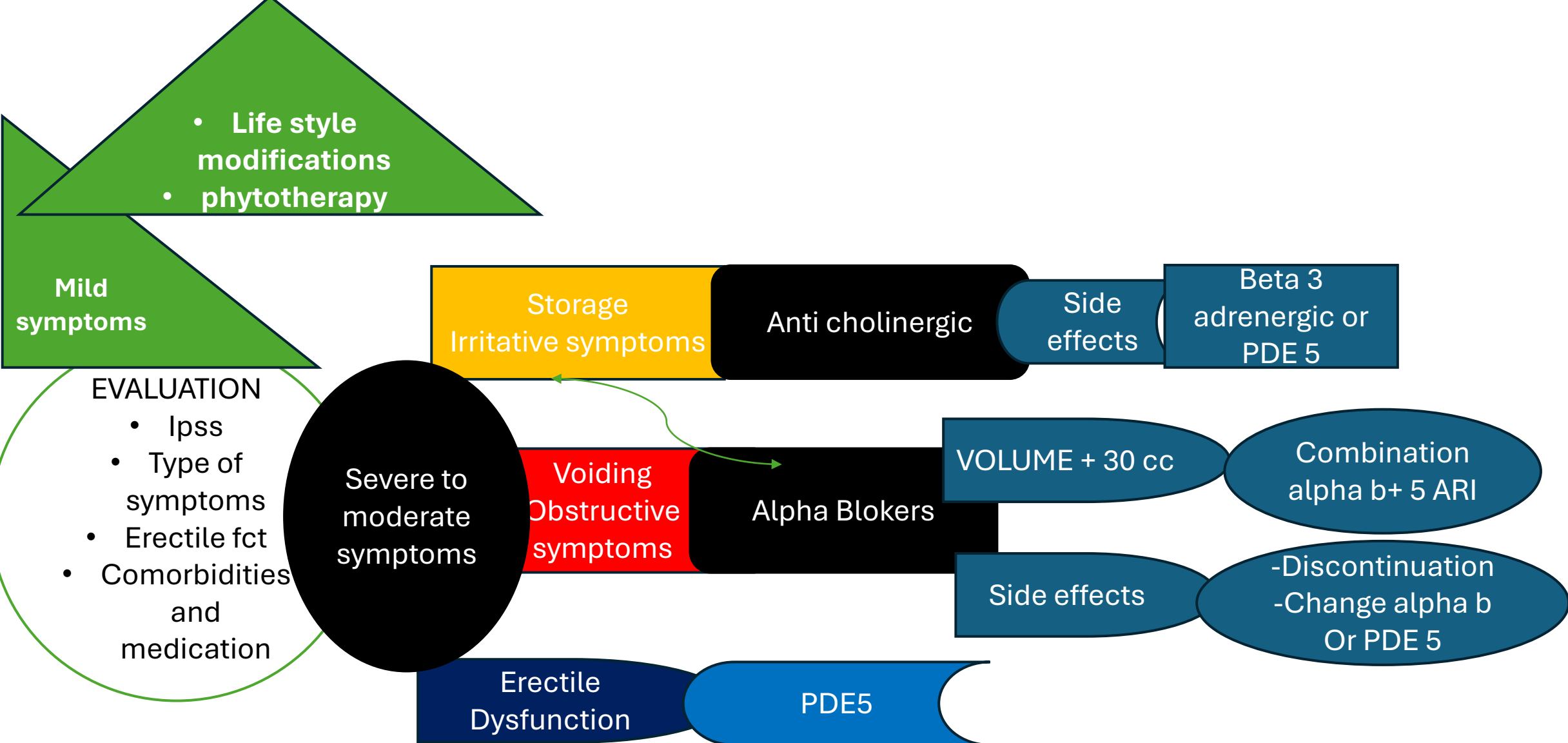


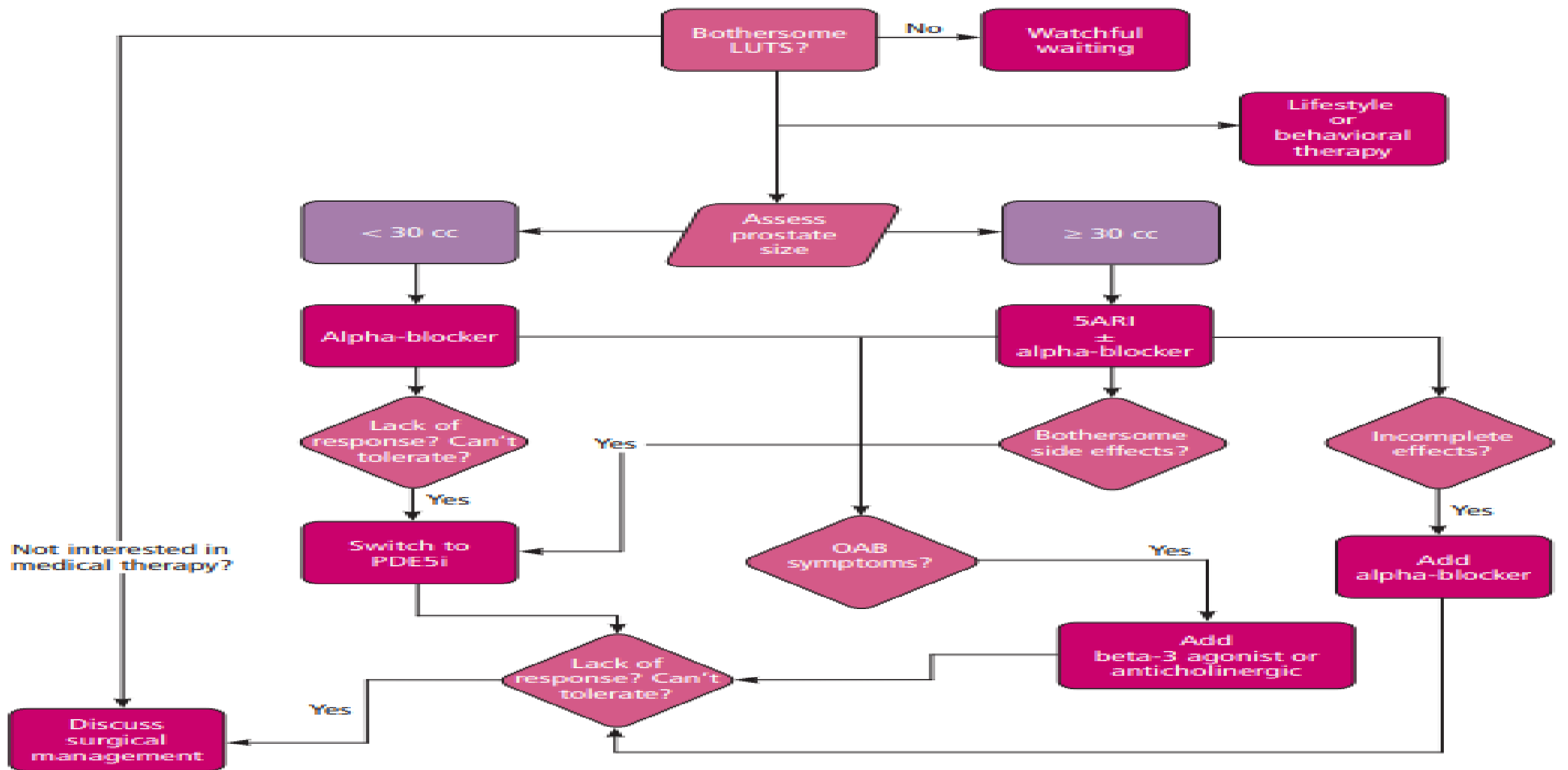
- **Pumpkin seed (*Cucurbita pepo*)** contains a variety of biologically active compounds thought to **inhibit 5-alpha reductase**
- can cause **gastrointestinal symptoms (indigestion and diarrhea)**.
- the fruit extract of the saw palmetto plant (***Serenoa repens***),
- **mechanisms of action** :include 5-alpha reductase inhibition and inhibition of dihydrotestosterone binding to androgen receptors.



SUMMARY







Algorithmic approach to medical management of benign prostatic hyperplasia.

5ARI = 5-alpha reductase inhibitors; LUTS = lower urinary tract symptoms; OAB = overactive bladder; PDE5i = phosphodiesterase-5 inhibitor

Adapted from the American Urological Association guideline

CONCLUSION

- Alpha blockers usually used first line
 - Relax muscle urethra prostate
- 5 alpha reductase inhibitors added when prostate is large
 - Shrink prostate size (+ 30 cc)
- Combination alpha b and 5 ARI are superior to monotherapy
- Anti cholinergic and Beta 3 adrenergic
- PDE 5 (erectile dysfunction or alternative)
- Alpha blockers are used also for urinary retention
- (self catheterisation)