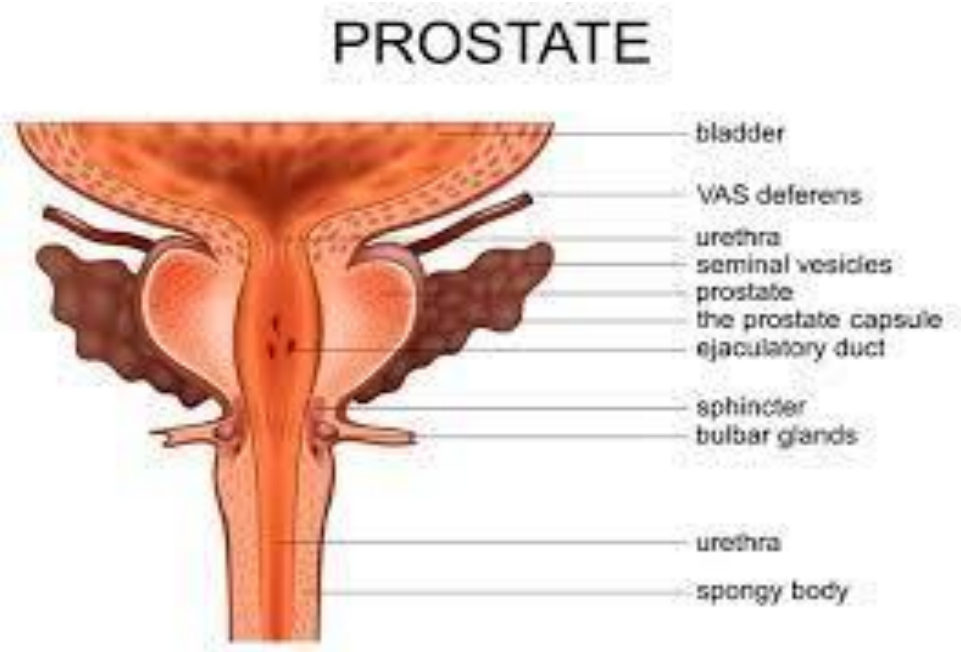
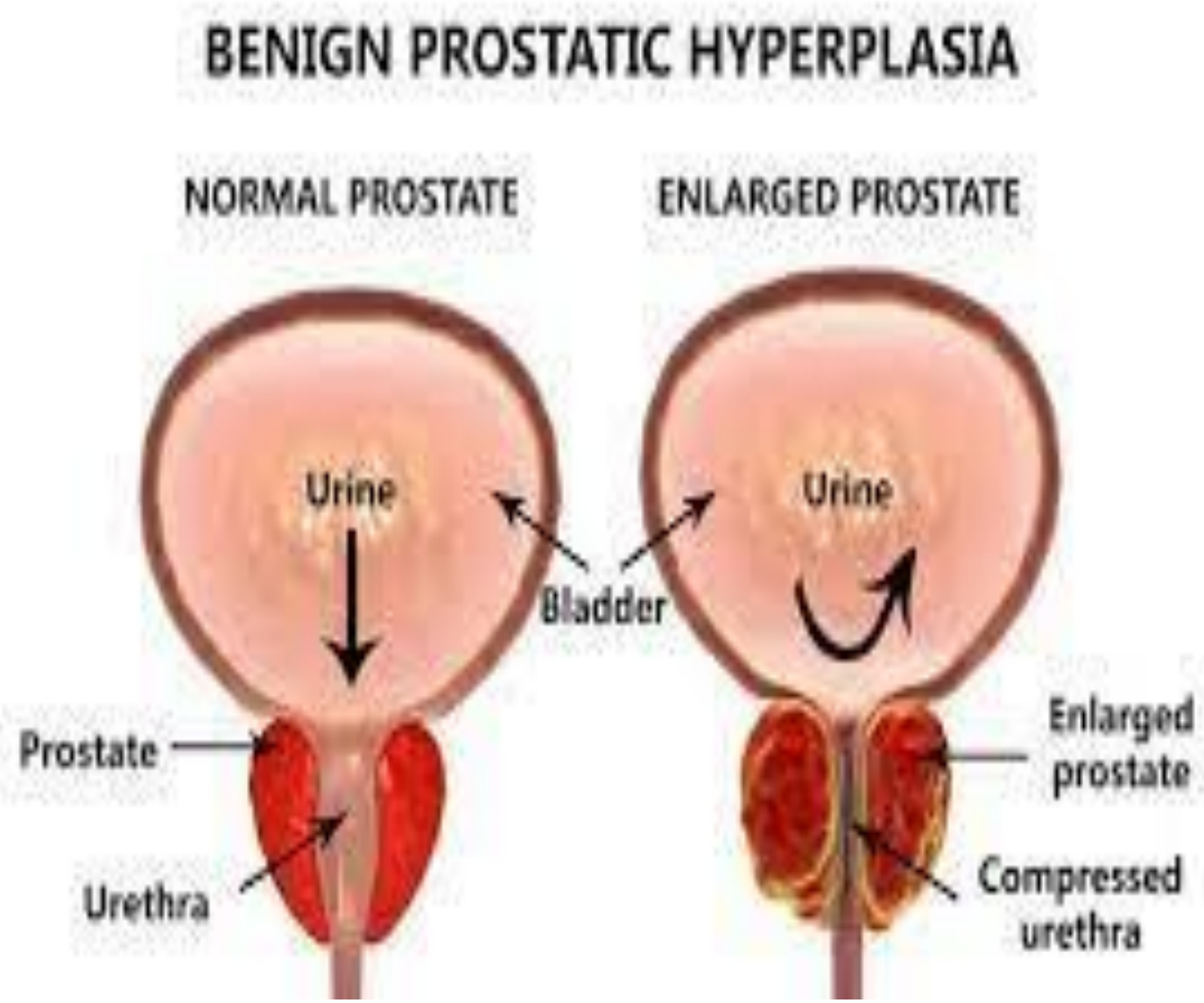
د.احمد جاسم العراك

UROLOGIC DISORDERS

Benign Prostatic Hyperplasia(BPH)




BENIGN PROSTATIC HYPERPLASIA
NORMAL PROSTATE
ENLARGED PROSTATE
Urine
Urine
Bladder
Prostate
Urethra
Enlarged prostate
Compressed urethra

PATHOPHYSIOLOGY

- Three types of prostate gland tissue: epithelial or glandular, stromal or smooth muscle, and capsule. Both stromal tissue and capsule are embedded with α1-adrenergic receptors.
- • The precise pathophysiologic mechanisms that cause BPH are not clear. Both intraprostatic

dihydrotestosterone (DHT) and type II 5α-reductase are thought to be involved.

- BPH commonly results from both **static** (gradual enlargement of the prostate) and **dynamic** (agents or situations that increase α-adrenergic tone and constrict the gland's smooth muscle) factors. Examples of drugs that can exacerbate symptoms include testosterone, α-adrenergic agonists (eg, decongestants), and those with significant anticholinergic effects (eg, antihistamines, phenothiazines, tricyclic anti- depressants, antispasmodics, and antiparkinsonian agents).

CLINICAL PRESENTATION

- **Obstructive signs and symptoms** result when dynamic and/or static factors reduce bladder emptying. Patients experience urinary hesitancy, urine dribbling and the bladder feels full even after voiding.
- **Irritative signs and symptoms** are common and result from long-standing obstruction at the bladder neck. Patients experience urinary frequency, urgency, and nocturia.
- BPH progression may produce complications including chronic kidney disease, gross hematuria, urinary incontinence, recurrent urinary tract infection, bladder diverticula, and bladder stones.

DIAGNOSIS

- • Includes careful medical history, physical examination, objective measures of bladder

emptying (eg, peak and average urinary flow rate and postvoid residual [PVR] urine volume), and laboratory tests (eg, urinalysis and prostate-specific antigen [PSA]).

- • On digital rectal examination, the prostate is usually but not always enlarged (>20 g),
- soft, smooth, and symmetric.

TREATMENT

- Pharmacologic therapy interferes with the stimulatory effect of testosterone on prostate

gland enlargement (reduces the static factor), relaxes prostatic smooth muscle (reduces the dynamic factor), or relaxes bladder detrusor muscle

- Initiate therapy with an α1-adrenergic antagonist for faster onset of symptom relief.
- Select a 5α-reductase inhibitor in patients with a prostate gland more than 40 g.
- Consider combination therapy for symptomatic patients with a prostate gland more than 40 g and PSA of 1.4 ng/mL or more.
- Consider monotherapy with a phosphodiesterase inhibitor or use in combination with an α-adrenergic antagonist when erectile dysfunction and BPH are present.

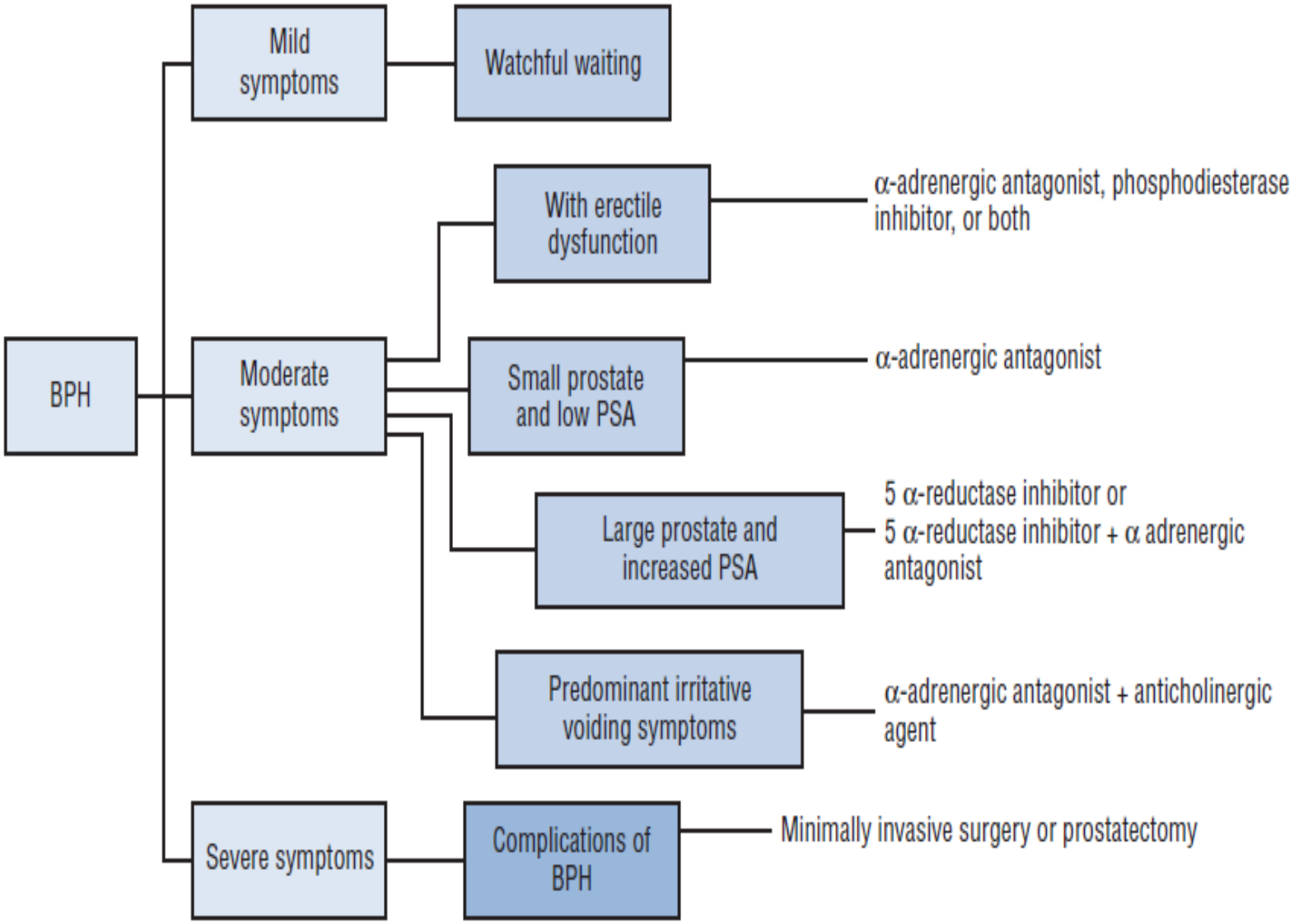


FIGURE 79–1. Management algorithm for benign prostatic hyperplasia (BPH).

- **α-Adrenergic Antagonists:**

- α-Adrenergic antagonists relax smooth muscle in the prostate and bladder neck, increasing urinary flow rates by 2 to 3 mL/sec in 60% to 70% of patients and reducing PVR urine volumes.
- α1-Adrenergic antagonists **do not decrease prostate volume or PSA levels.**
- **Prazosin, terazosin, doxazosin**, and **alfuzosin** are second-generation α1-adrenergic antagonists. They antagonize peripheral vascular α1-adrenergic receptors in addition to those in the prostate. Adverse effects include first-dose syncope, orthostatic hypotension, and dizziness. Alfuzosin is less likely to cause cardiovascular adverse effects than other second-generation agents.

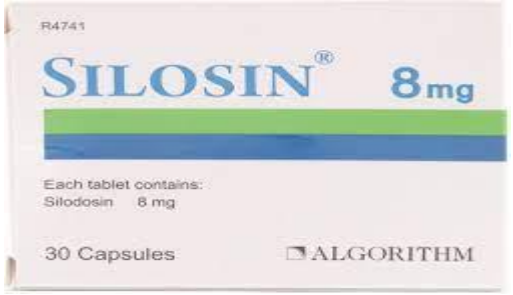
- Slowly titrate to a maintenance dose at bedtime to minimize orthostatic hypotension and first-dose syncope with immediate-release formulations of terazosin and doxazosin.
- **Tamsulosin** and **silodosin**, third-generation α1-adrenergic antagonists, are selective for prostatic α1A-receptors. Therefore, they do not cause peripheral vascular smooth muscle relaxation and associated hypotension.
- **Tamsulosin** is a good choice for patients who cannot tolerate hypotension; has severe coronary artery disease, volume depletion, cardiac arrhythmias, severe orthostasis, or liver failure; or are taking multiple antihypertensives. Tamsulosin is also suitable for patients who want to avoid the delay of dose titration.

- Potential drug interactions include decreased metabolism of α1-adrenergic antagonists

with CYP 3A4 inhibitors **(**eg, **cimetidine** and **diltiazem)** and increased catabolism

of α1-adrenergic antagonists with concurrent use of CYP 3A4 stimulators (eg, **carbamazepine** and **phenytoin).**

- Reduce the dose of silodosin in patients with moderate renal impairment or hepatic dysfunction.



- **5α-Reductase Inhibitors**
- • 5α-Reductase inhibitors interfere with the stimulatory effect of testosterone.These agents slow disease progression and decrease the risk of complications.
- Compared with α1-adrenergic antagonists,

disadvantages of 5α-reductase inhibitors

include 6 months of use to maximally shrink prostate, less likely to induce objective improvement and more sexual dysfunction.

- **Dutasteride inhibits types I and II 5α-reductase, whereas finasteride inhibits only type II**. Dutasteride more quickly and completely suppresses intraprostatic DHT (vs 80%–90% for finasteride) and decreases serum DHT by 90% (vs 70%).
- 5α-Reductase inhibitors may be preferred in patients with uncontrolled arrhythmias, poorly controlled angina, use multiple antihypertensives, or cannot tolerate hypotensive effects of α1-adrenergic antagonists.

- Measure PSA at baseline and again after 6 months of therapy. If PSA does not decrease by 50% after 6 months of therapy in a compliant patient, evaluate the patient for prostate cancer.
- 5α-Reductase inhibitors are in FDA pregnancy category X and are therefore contraindicated in pregnant women. Pregnant and potentially pregnant women should not handle the tablets or have contact with semen from men taking 5α-reductase inhibitors.

- **Phosphodiesterase Inhibitors**

- Increase in cyclic GMP by phosphodiesterase inhibitors (PI) may relax smooth muscle in prostate and bladder neck. Effectiveness may be result of direct relaxation of detrusor muscle of bladder.

- **Tadalafil** 5 mg daily improves voiding symptoms but does not increase urinary flow rate or reduce PVR urine volume. Combination therapy with α-adrenergic antagonist results in significant improvement in lower urinary tract symptoms, increased urinary flow rates, and decreased PVR volume.

Anticholinergic Agents

- Addition of **oxybutynin** and **tolterodine** to α-adrenergic antagonists relieves irritative voiding symptoms including urinary frequency, urgency, and nocturia. Start with lowest effective dose to determine tolerance of CNS adverse effects and dry mouth.
- Measure PVR urine volume before initiating treatment (should be less than 250 mL).
- If systemic anticholinergic adverse effects are poorly tolerated, consider transdermal or extended-release formulations or uroselective agents (eg, **darifenacin** or **solifenacin**).

- **SURGICAL INTERVENTION**
- • Prostatectomy, performed transurethrally or suprapubically, is the gold standard for treatment of patients with moderate or severe symptoms of BPH and for all patients with complications.
- • Retrograde ejaculation complicates up to 75% of transurethral prostatectomy procedures.
- Other complications seen in 2% to 15% of patients are bleeding, urinary incontinence, and erectile dysfunction.

Thanks