

Update on Benign Prostatic conditions

1 BPH

2 BPH management



Introduction

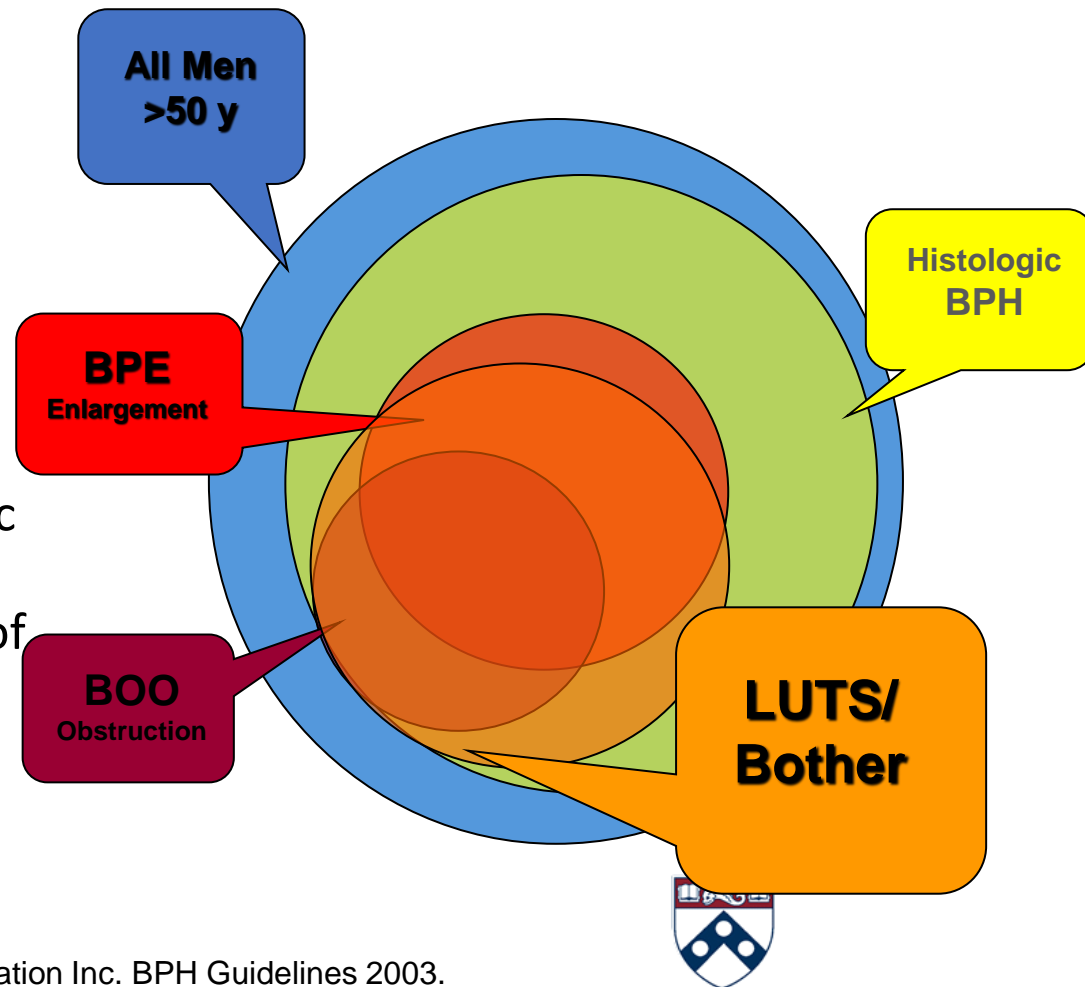
- Epidemiology
- Changes in Terminology
- Evaluation
- Medical Therapy
- Surgical Therapy
- BPH and Sex!



A Modern View of BPH

Clinical, Anatomic, and Pathophysiologic Changes

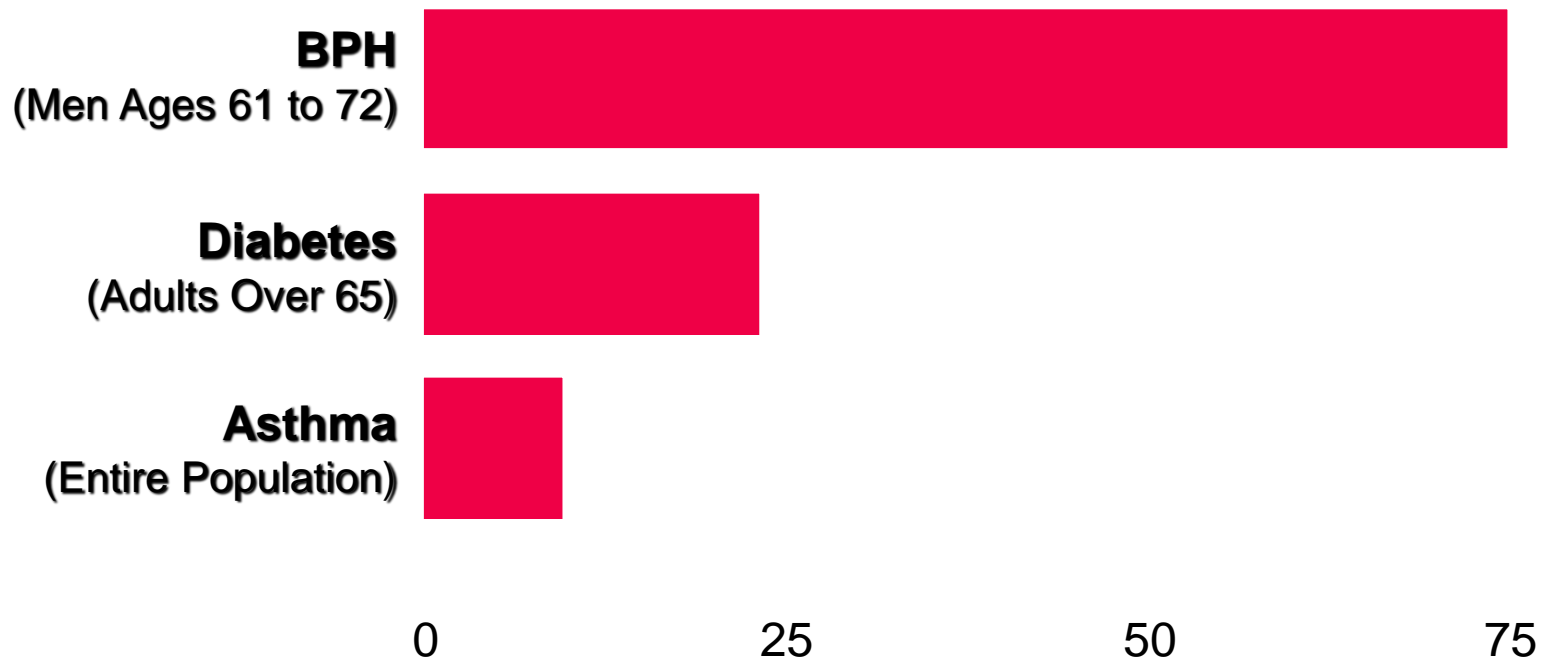
- BPH = Benign Prostatic Hyperplasia
 - Histologic: stromoglandular hyperplasia¹
- May be associated with
 - Clinical: presence of bothersome LUTS²
 - Anatomic: enlargement of the gland (BPE = Benign Prostatic Enlargement)²
 - Pathophysiologic: compression of urethra and compromise of urinary flow (BOO = Bladder Outlet Obstruction)²



1. American Urological Association Research and Education Inc. BPH Guidelines 2003.

2. Nordling J et al. In: Chatelain C et al, eds. *Benign Prostatic Hyperplasia*. Plymouth, UK: Health Publication Ltd; 2001:107166.

Prevalence of BPH Versus Other Common Conditions



Berry SJ, et al. *J Urol*. 1984;132:474-479.

CDC. 2003 National Diabetes Fact Sheet.

Available at <http://www.cdc.gov/diabetes/pubs/estimates.htm>. Accessed May 16, 2003.

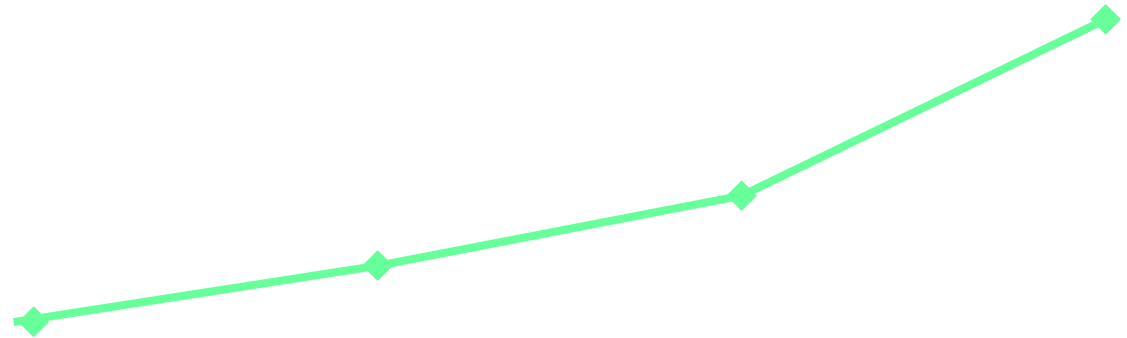
CDC. 1998 Forecasted State-Specific Estimates of Self-Reported Asthma Prevalence.

Available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/00055803.htm>. Accessed January 8, 2003.



Prevalence of Symptomatic BPH

**Male Medicare
patients (>65 y)
with LUTS/BPH**

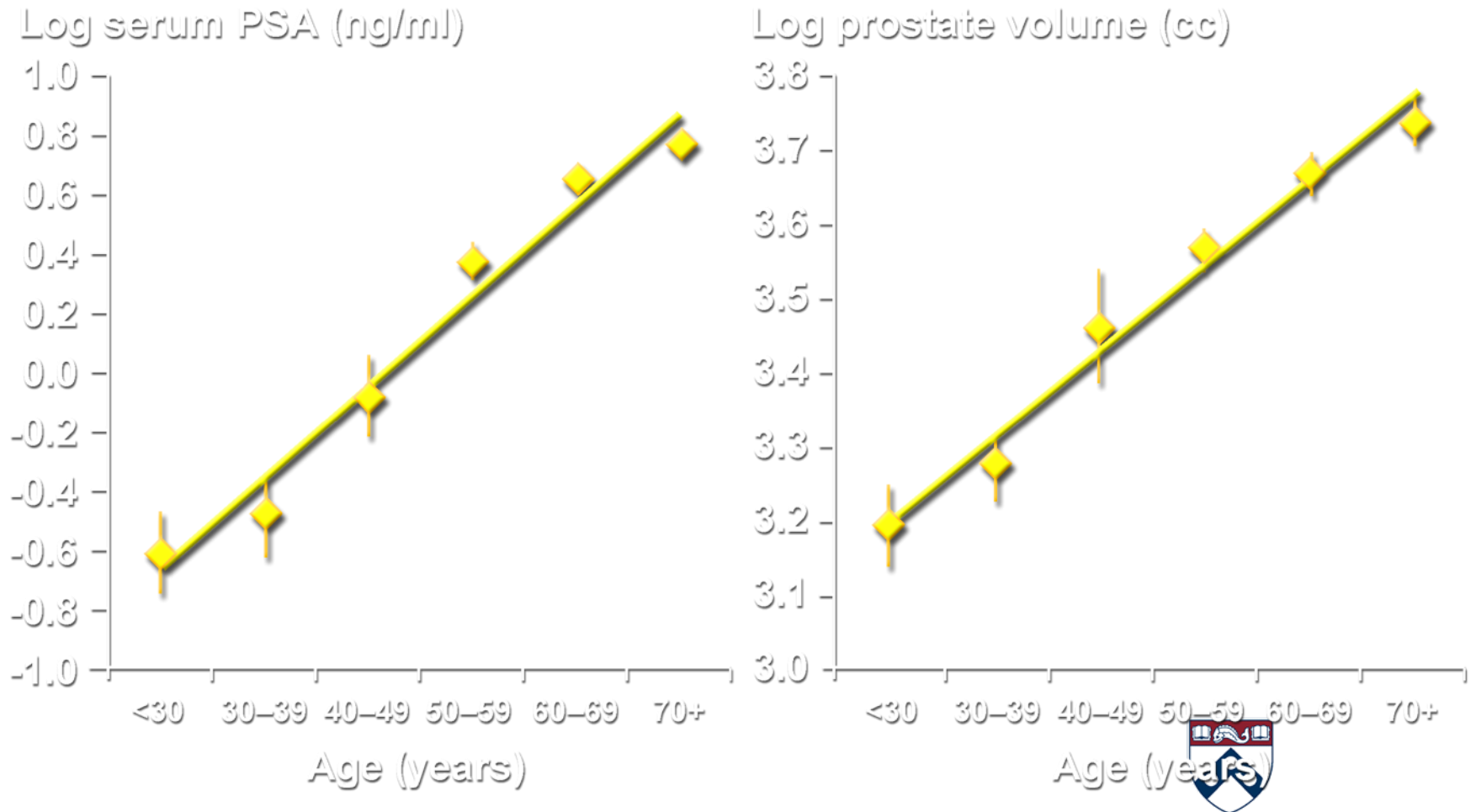


PSA... It's not just for cancer

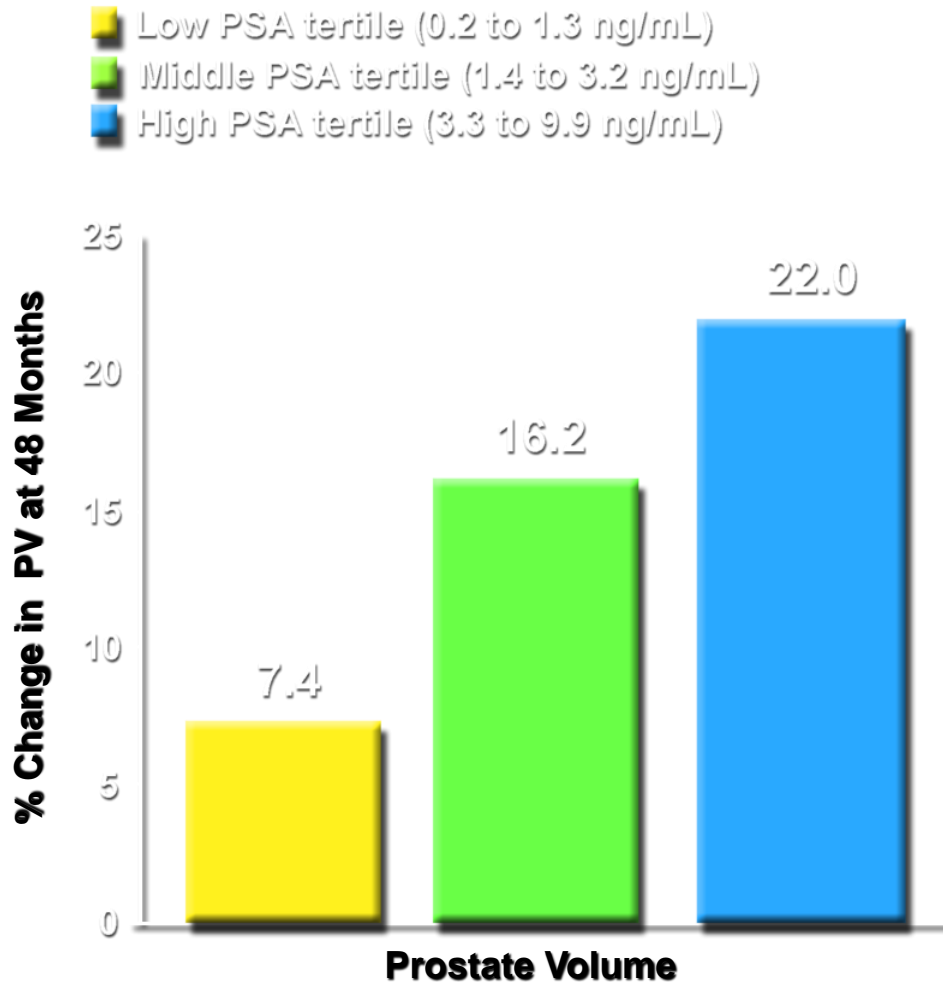
- Serine protease produced by epithelial cells
- Dissolves semen coagulum
- Most bound to antiproteases ACT
- Increased with-
 - Malignancy
 - Hyperplasia
 - Infection/Inflammation



Serum PSA and Prostate Volume Increases Correlate with Age



PSA as a Predictor of Future Prostate Growth



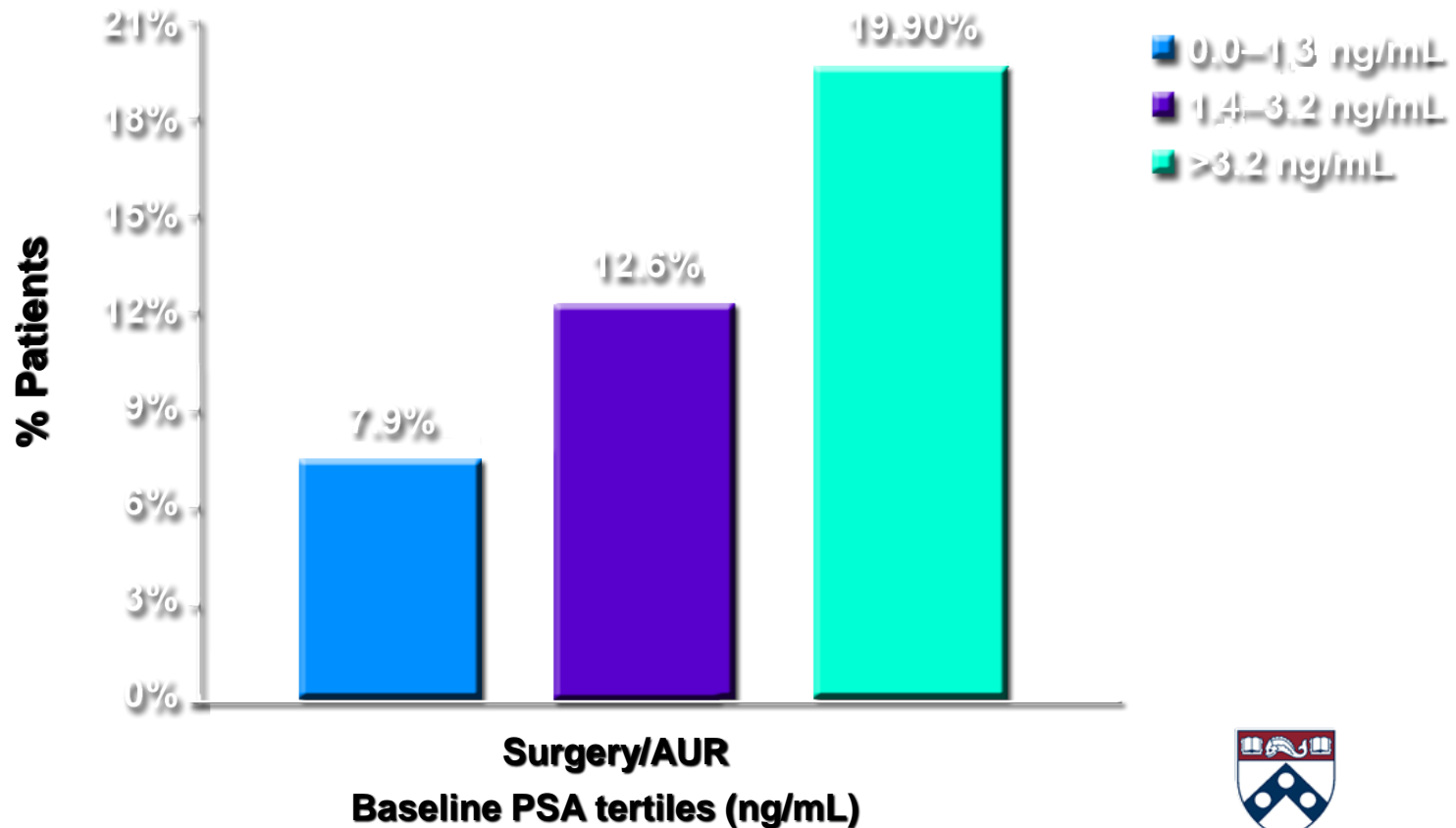
Annualized Growth Rates

- Low PSA tertile:
0.7 mL/year
- Middle PSA tertile:
2.1 mL/year
- High PSA tertile:
3.3 mL/year



Incidence of AUR and/or Surgery Over 4 Years by PSA Tertiles

Left untreated 1 in 6 patients with a PSA of >1.4 ng/mL will experience AUR or BPH-related surgery over a 4-year time period



What is “BPH”?

- “Prostatism” and “BPH”
- Benign Prostatic Hyperplasia is a histological diagnosis
- New Urological Lexicon



Terminology

BPH

**Histologic
diagnosis**

BPE

**Enlargement due
to benign growth
(can be without
obstruction)**

BPO

**Urodynamically
proven BOO
(static/dynamic
components)**



BPH = benign prostatic hyperplasia; BPE = benign prostatic enlargement; BPO = benign prostatic obstruction; BOO = bladder outlet obstruction

LUTS

- **Symptoms attributable to lower urinary tract dysfunction**
 - **storage (irritative) symptoms**
 - **emptying (obstructive) symptoms**
 - **may be associated with BPH, BPE, and BPO, but not exclusive to these**



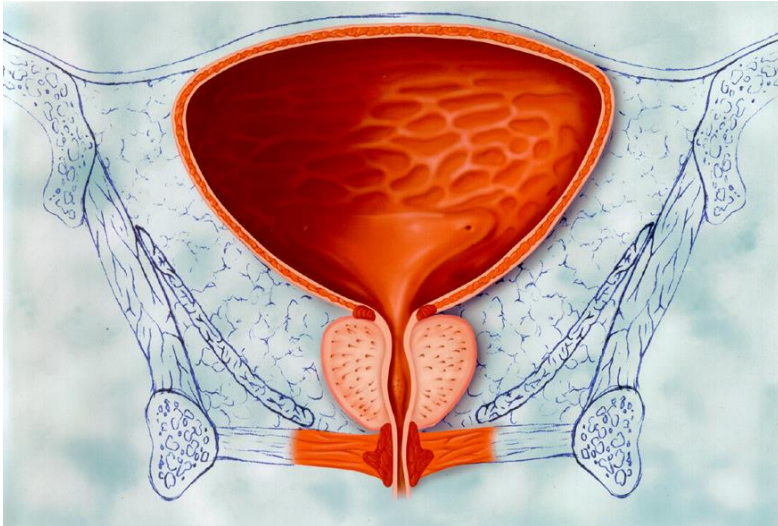
Differential Diagnosis

- **Urethral stricture**
- **Bladder neck contracture**
- **Bladder stones**
- **Urinary tract infection**
- **Interstitial cystitis**
- **Neurogenic bladder**
- **Inflammatory prostatitis**
- **Medications**
- **Carcinoma of the prostate**
- **Carcinoma in situ of the bladder**

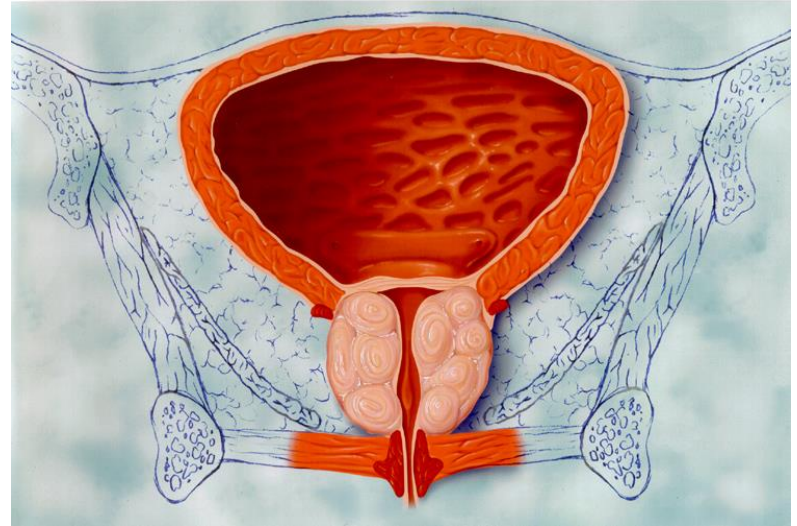


Old Paradigm

***Small prostate,
thin bladder wall***

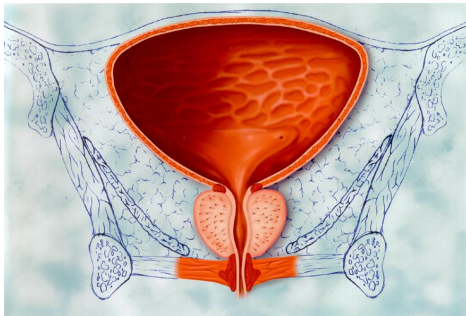


***Enlarged prostate,
thick bladder wall***

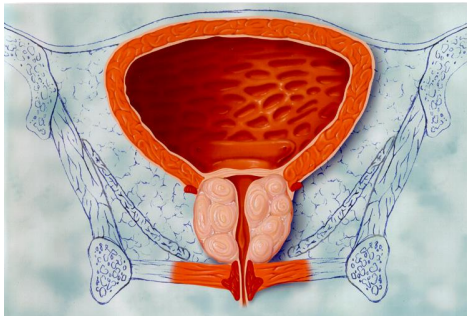


Subsequent Paradigm

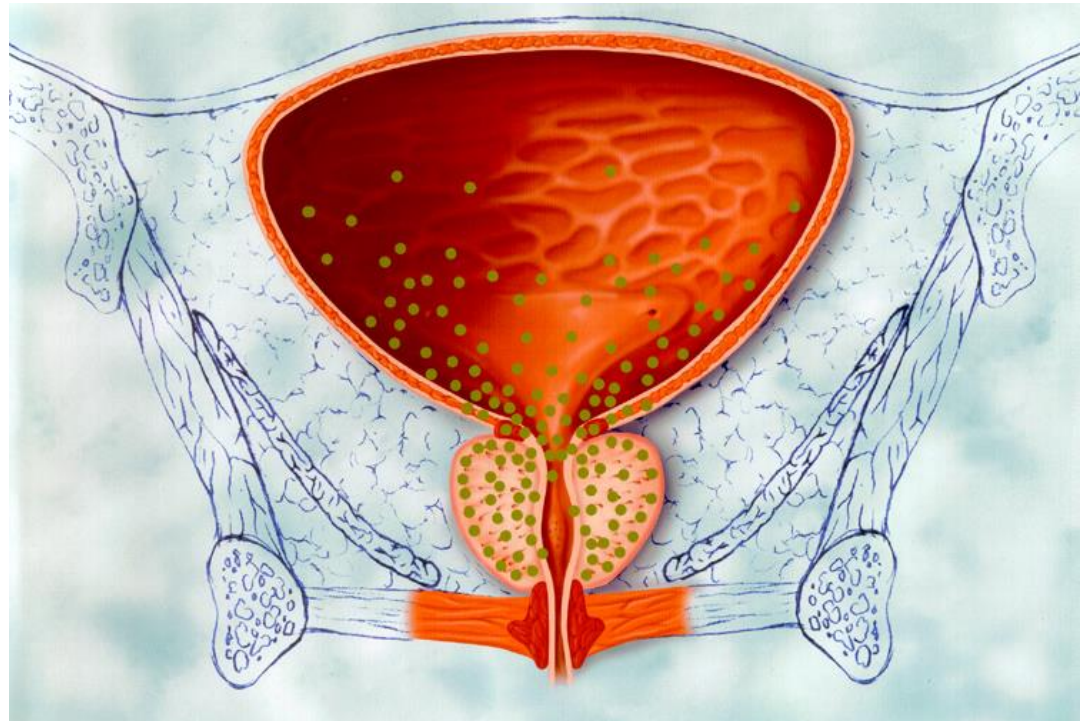
Normal prostate



Enlarged prostate

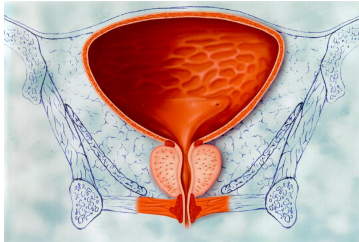


Small prostate with α -receptors

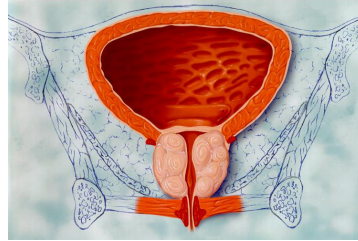


Current Paradigm

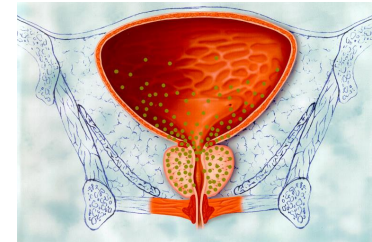
Normal



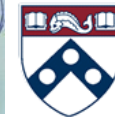
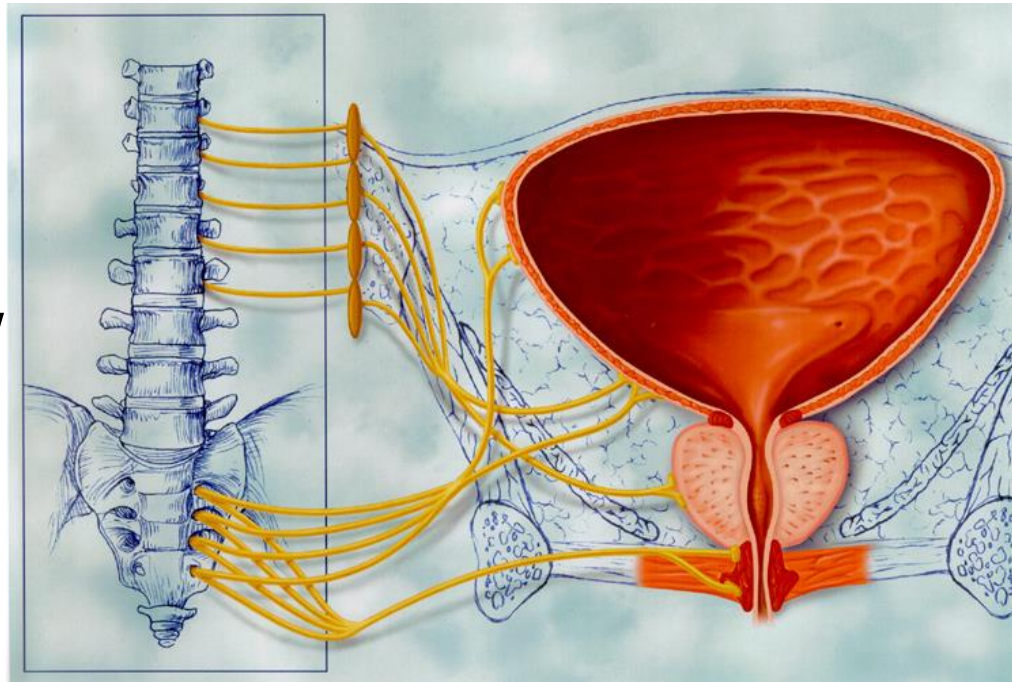
Enlarged



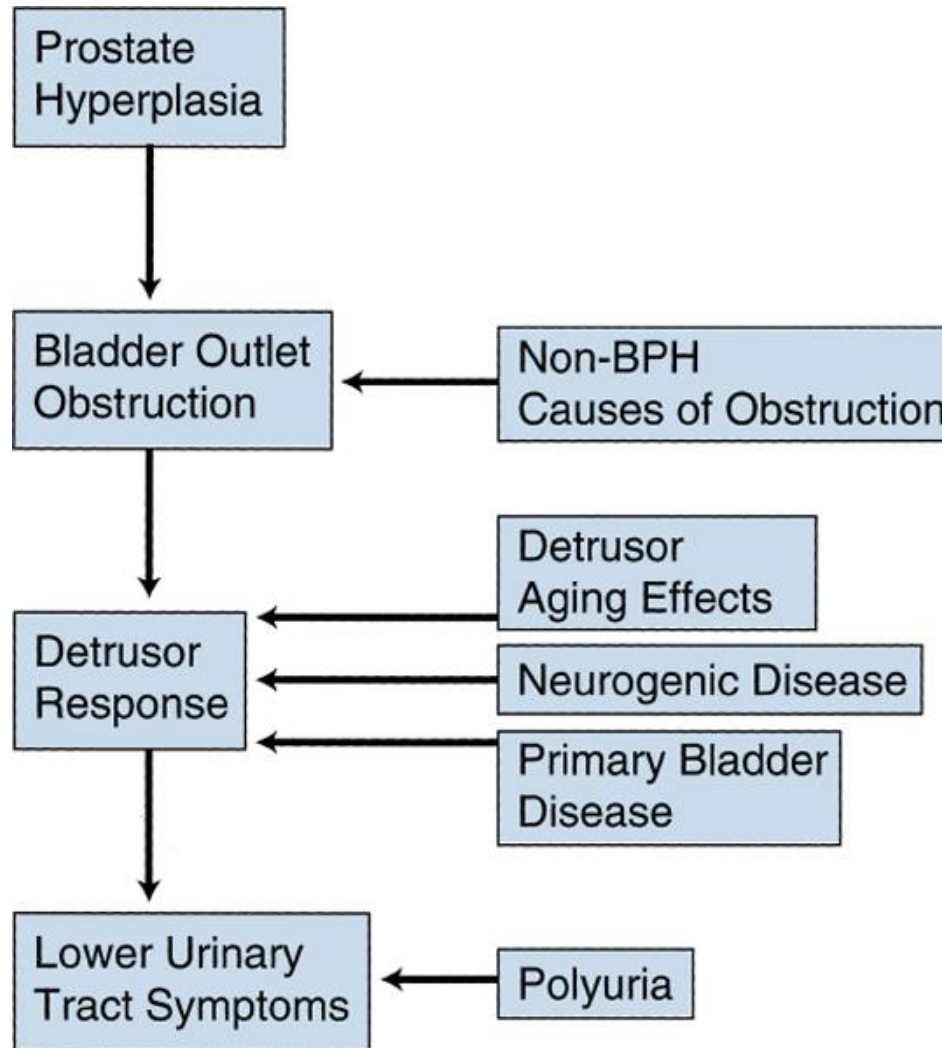
α -receptors



**Brain/
Spinal column/
Prostate**



BPH/LUTS Pathophysiology



Initial Evaluation

- **Detailed medical history**
- **Physical exam**
 - including DRE and neurologic exam
- **Urinalysis**
- **Serum creatinine no longer mandatory**
- **PSA***
- **Symptom assessment (AUA-SS)**

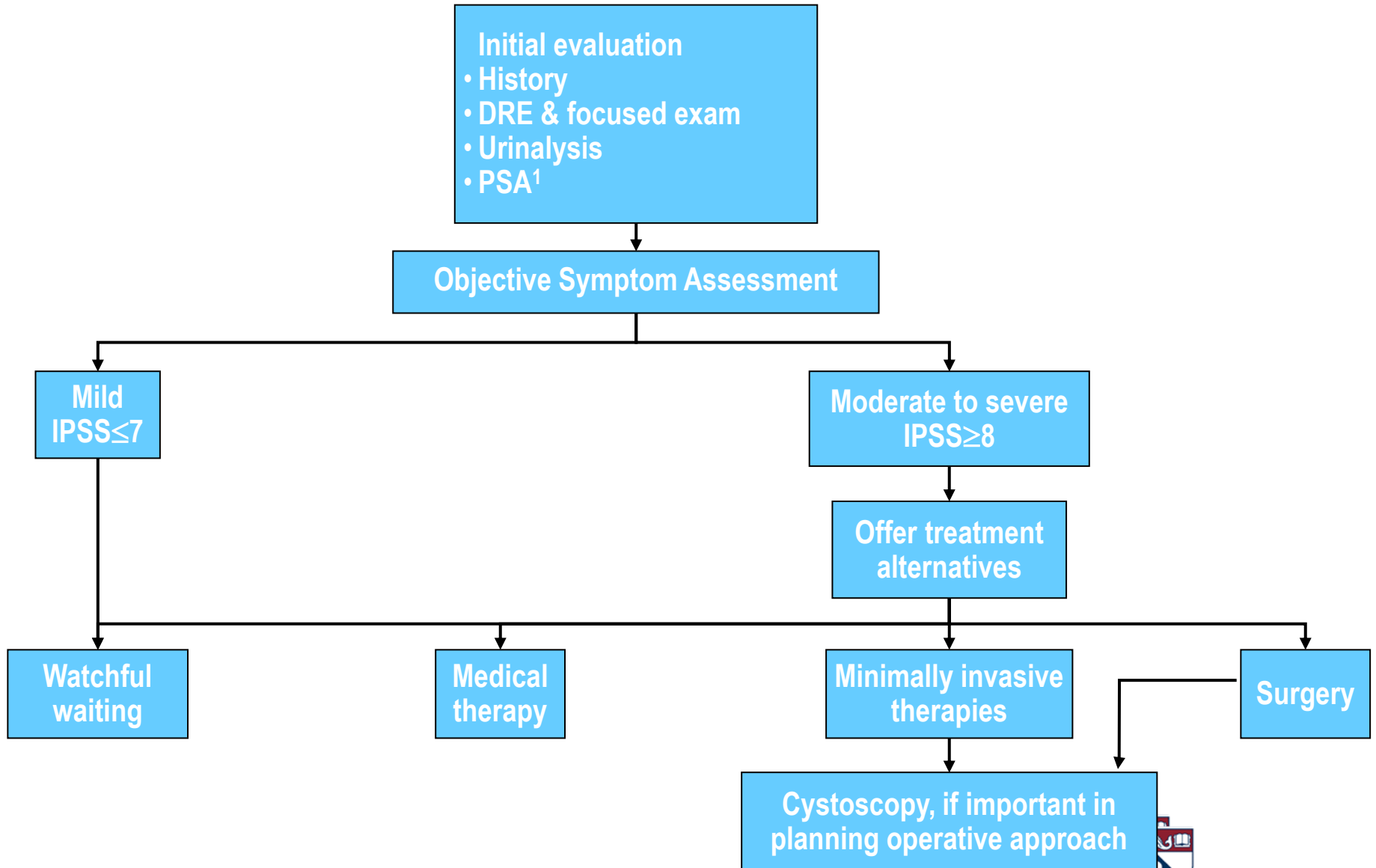
PSA = prostate-specific antigen

*Per physician's clinical judgment

AUA BPH Guidelines 2003



Evaluation (Part 1)



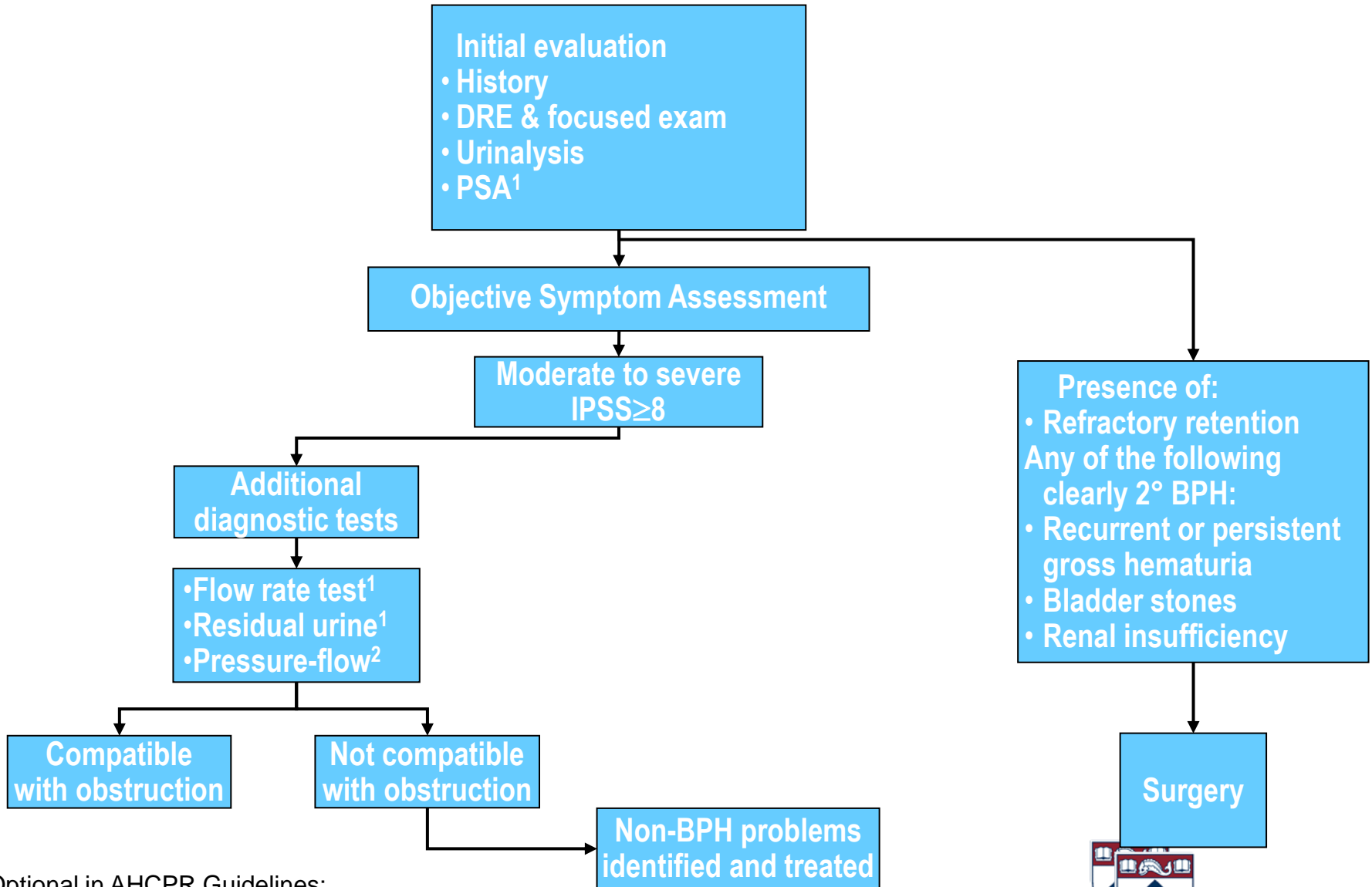
¹Optional in AHCPR Guidelines;
Recommended by International Consensus Committee

4.2

Clinical Practice Guideline, Number 8.
AHCPR Publication No. 94-0582.



Evaluation (Part 2)



¹Optional in AHCPR Guidelines;
Recommended by International Consensus Committee

²Optional in both AHCPR and International Consensus recommendations



Goals of Therapy for BPH

BPH Treatment Success measured by:

- ↓ symptoms (IPSS/AUA)
- ↓ bother (bother score) and ↑ QOL
- ↓ prostate size or arrest further growth
- ↑ Increase in peak flow rate / Relieve obstruction
- Prevention of long-term outcomes/complications
- Acceptable adverse events profile



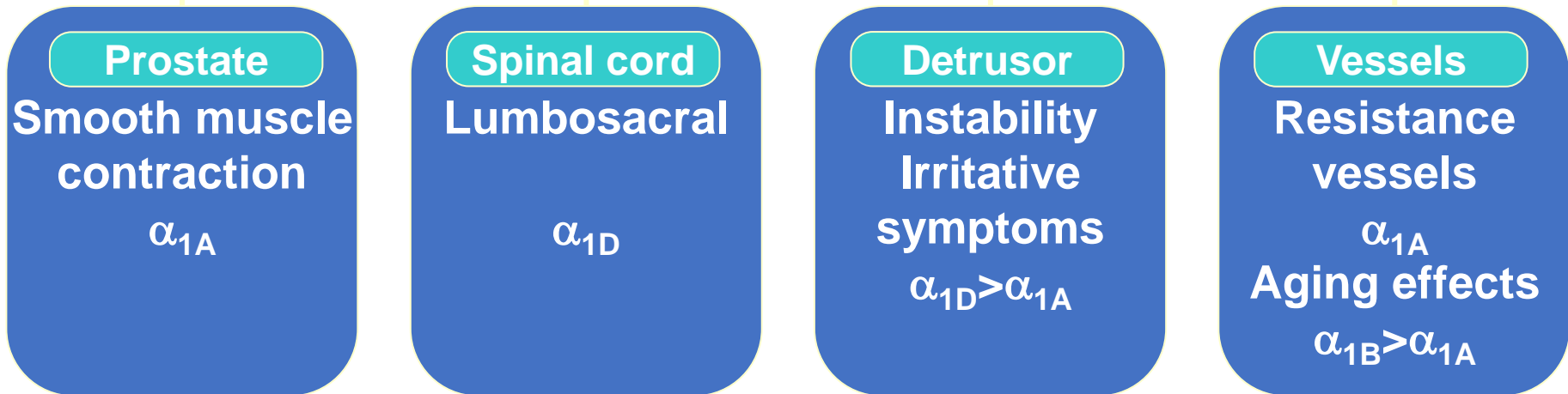
Medical Treatments for BPH, LUTS, BOO

- α -adrenergic blockers
 - Dynamic component
- 5 α -reductase inhibitors
 - Anatomic component
- Anticholinergic Therapy
 - Storage Sx's



Role of α_1 -Adrenoreceptors

α_1 -ARs and Human LUTS




Schwinn DA. *BJU Int.* 2000;86:11-22.

Jardin A et al. *Benign Prostatic Hyperplasia. 5th International Consultation on Benign Prostatic Hyperplasia.* Paris, France. June 25-28, 2000:459-477.

Rudner XL et al. *Circ.* 1999;100:2336-2343.



Comparison of α -Adrenergic Blockers

Agent	Dosing	Titration	Uroselective
Terazosin (Hytrin [®])	1 mg, 2 mg, 5 mg, 10 mg, 20 mg	+	NO
Doxazosin (Cardura [®])	1 mg, 2 mg, 4 mg, 8 mg, 16 mg	+	NO
Tamsulosin (Flomax [®])	0.4 mg, 0.8 mg	+/- (for improved efficacy)	YES (Relative affinity for α_{1A} receptors over α_{1B})
Alfuzosin	10 mg	-	YES (Highly diffused in prostatic tissue )

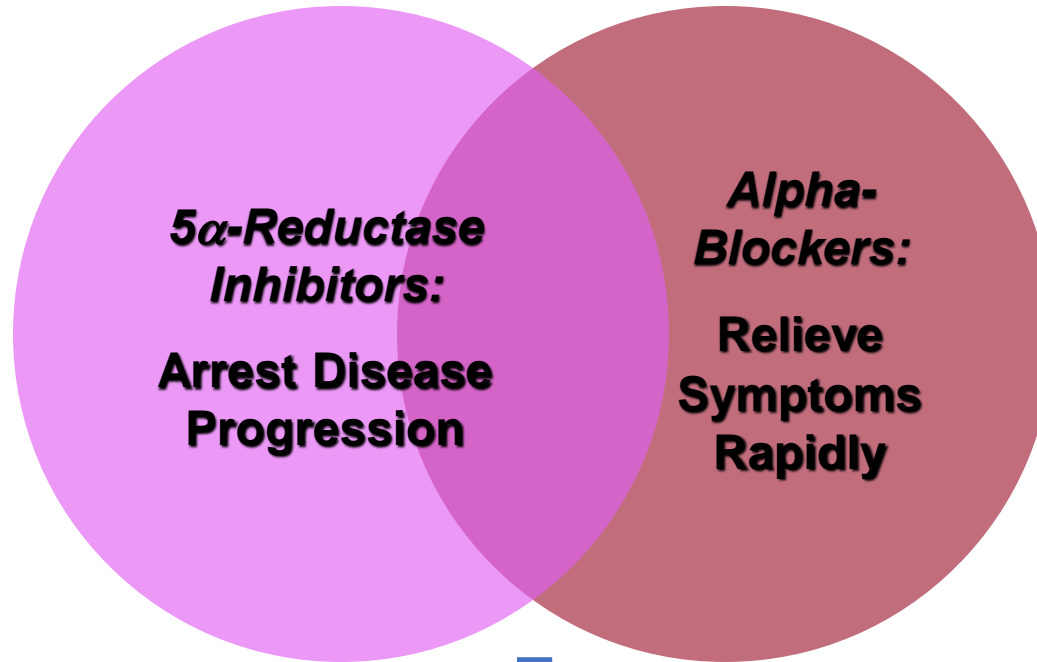
1. Hytrin[®] (terazosin hydrochloride) Prescribing Information, Abbott Laboratories.
 2. Cardura[®] (doxazosin mesylate tablets) Prescribing Information, Pfizer Inc.
 3. Flomax[®] (tamsulosin hydrochloride) Prescribing Information, Boehringer Ingelheim Pharmaceuticals Inc.
 4. Uroxatral[®] (alfuzosin HCl extended release tablets) Prescribing Information, Sanofi-Synthelabo Inc.

Dihydrotestosterone (DHT) Action

- Testosterone is converted to DHT by two 5α -reductase isoenzymes
- The target for DHT is the androgen receptor
- DHT has approximately 5 times greater affinity for the androgen receptor than testosterone
- The greater affinity makes DHT a more potent androgenic steroid at physiologic concentrations
- The DHT/androgen receptor complex alters gene expression



Rationale for Combination Therapy



**Combination Therapy: Arrest Disease Progression
and Rapidly Relieve Symptoms**



Surgical Therapy



Indications for Surgery

Absolute

- None

Relative

- Symptoms
- Pt. Choice
- AUR
- Bleeding
- Bladder Calculus
- UTI
- Renal Insufficiency



Transurethral Resection of the Prostate (TURP): Overview

Advantages

- **Availability of long-term outcomes data**
- **Good clinical results**
- **Treats prostates <150 g**
- **Low retreatment rate**
- **Low mortality**

Disadvantages

- **Retrograde ejaculation**
- **Bleeding**
- **TUR Syndrome**
- **Catheter time**
- **Hospital Stay**

Borth CS et al. *Urology*. 2001;57:1082-1086.

Mebust WK et al. *J Urol*. 1989;141:243-247.

Wagner JR et al. *Semin Surg Oncol*. 2000;18:216-228.



Alphabet Soup

Electrosurgical

TURP

TUVP

Gyrus

TUIP

Open

Suprapubic

Retropubic

Perineal

Laser

PVP

HoLAP

HoLEP

ILC

CLAP

VLAP

Minimally-Invasive

TUMT

TUNA

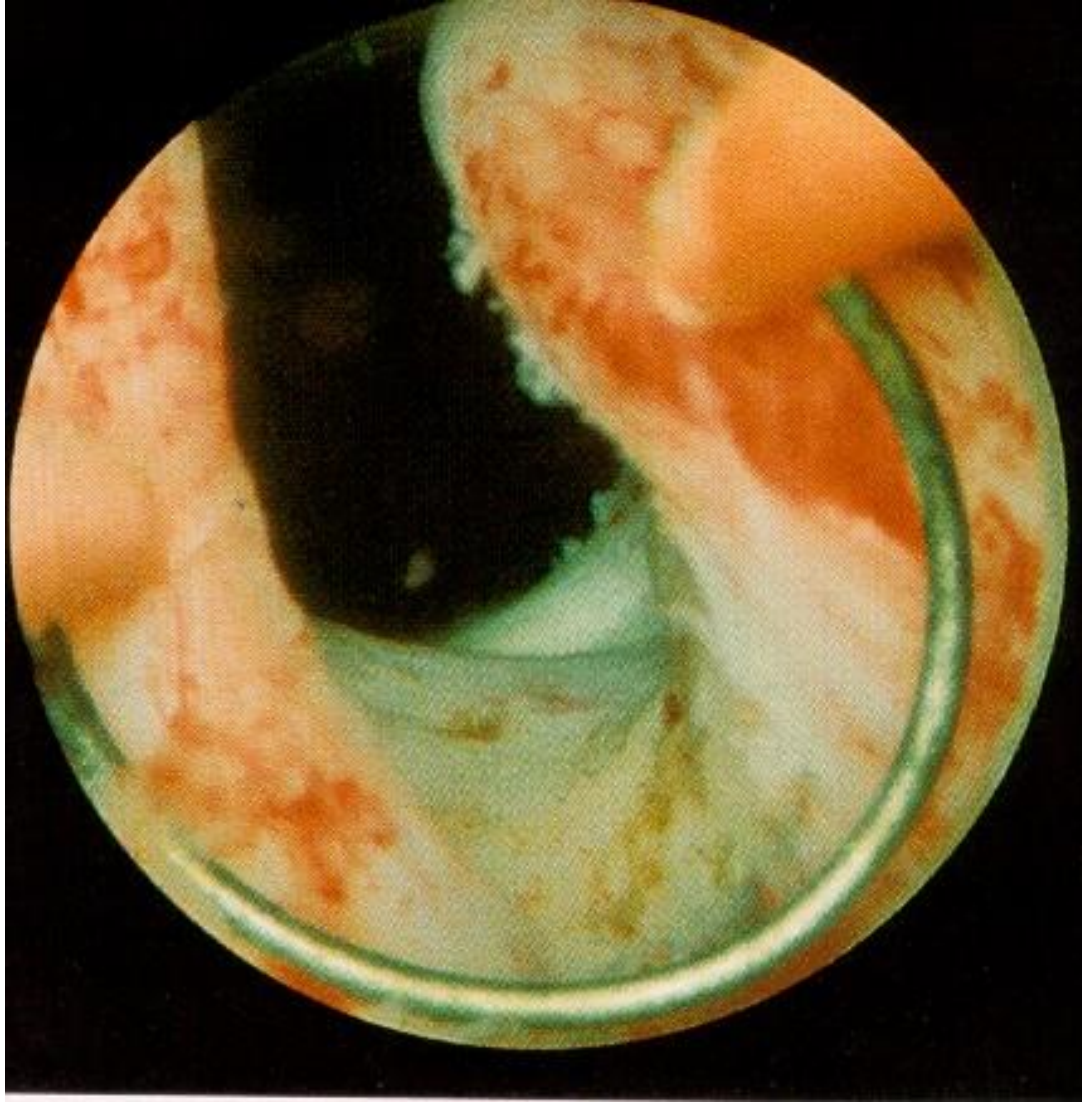
WIT

TEAP

Botox

ILC





TURP: Efficacy

- **Symptom improvement in 88% of patients**
- **82% decrease in AUA Symptom Score**
- **125% improvement in peak flow rate (Q_{\max})**
- **Re-op rate approx. 1.5%/yr**

Jepsen JV et al. *Urology*. 1998;51(suppl 4A):23-31.



TURP: Complications

Clot Retention	16%
Urethral Stricture	8.4%
Transfusions	7.0%
TUR Syndrome	0.9%
Incontinence	1.3%



Sildenafil Citrate Improves LUTS

Mulhall et al, 2002

- **Men (n=30) presenting with ED and LUTS (IPSS \geq 10)**
- **No prior or current alpha-blocker therapy**
- **Treated with Viagra (standard fashion)**
- **Sequential assessment of IIEF and IPSS**
- **Statistically significant improvement in IPSS on Viagra**



Take-Home Messages

- Aging Population= More BPH
- Not all Male LUTS=BPH
- Not all BPH=LUTS
- Consider Combination Therapy
- Quality of life issues

