Objectives/Goals

- To understand the causes of BPH
- To review the symptoms related to BPH
- To gain knowledge of the different forms of treatment for bladder outlet obstruction due to BPH
  - Medical management
  - Surgical options
  - Other treatments
Objectives

- To review the causes and symptoms of prostatitis
- To understand the diagnosis and management of prostatitis and Pelvic Pain Syndrome

Benign Prostate Disorders

- Benign Prostatic Hyperplasia (BPH)
- Prostatitis
- Pelvic Pain Syndrome (PPS)
Epidemiology

Etiology

Symptoms

Objective Data

Nonsurgical/Medical Management

Surgical Management

BPH

Exact molecular etiology is unknown

Androgens and estrogens

Growth factors

Cell-cell interactions

Impaired programmed cell death (apoptosis)

Neurotransmitters
### BPH
**Role of Androgens**

- Post natal androgen surges are critical
- Imprinting of prostate cells
- Affects maturation process and cell death
- Necessary during puberty and aging
- Prostatic levels of dihydrotestosterone (DHT) and androgen receptors play a key role

### BPH
**Role of Androgens**

- Prostate retains ability to respond to androgens throughout ones life
- Concentration of androgens does not increase with age
- Stromal cell – 5 alpha reductase Type 2 interaction seems to be key event in the development of BPH
- Role of estrogens is unclear
BPH

- Stromal events induce glandular proliferation
- Interaction between growth factors, GF receptors, and steroid hormones
- Programmed cell death/apoptosis
BPH
Other Factors

- Inheritable component: earlier onset, larger gland size, autosomal dominant
- Sympathetic nerve pathways
- Inflammation
- Reflux
- Environmental

Pathophysiology of Obstruction

- BPH develops in the Transition and Periurethral Zones: central prostate
- Prostate Cancer develops in the Peripheral Zone: posterior prostate
- Static component of obstruction
- Dynamic component of obstruction
<table>
<thead>
<tr>
<th><strong>BPH</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Obstructive uropathy/Urinary obstruction</td>
</tr>
<tr>
<td>▪ Bladder outlet obstruction (BOO)</td>
</tr>
<tr>
<td>▪ Lower Urinary Tract Sx (LUTS)</td>
</tr>
<tr>
<td>▪ Prostatism</td>
</tr>
<tr>
<td>▪ BPH ≠ Urinary obstruction</td>
</tr>
<tr>
<td>▪ Urinary obstruction ≠ BPH</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>BPE</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Explanation of increased urethral resistance due to BPE is too simplistic</td>
</tr>
<tr>
<td>▪ Must factor in age related detrusor and bladder neck dysfunction</td>
</tr>
<tr>
<td>▪ Static and dynamic factors</td>
</tr>
</tbody>
</table>
Size Doesn’t Matter

- Not critical when deciding whether or not to Rx
- Not well correlated with Sx severity, degree of obstruction, or Rx outcome
- Important wrt deciding mode of Rx
- However, size does correlate with disease progression and risk of acute retention

From: Campbell-Walsh Urology, 9th edition
# BPH

- Microscopic BPH: stromal and epithelial cellular proliferation
- Macroscopic BPH: increase in the size of the prostate as a result of microscopic BPH (BPE)
- Clinical BPH: signs and Sx of obstruction due to BPE (LUTS, BOO, Prostatism)

## Clinical Manifestations of BPH

- Hematuria
  - Microscopic
  - Gross
- LUTS
- UTI
- Urinary retention
- Hydronephrosis
- Renal Insufficiency
### Evaluation

- History
- AUA/IPSS Symptom Score
- DRE
- Urinalysis (r/o UTI)
- Uroflow and Post Void Residual (PVR)
- Imaging: Transrectal U/S (TRUS) with volume measurement
- Urodynamic Testing

### International Prostate Symptom Score (IPSS)

- 7 questions + QOL assessment
- Considered “Gold Standard”
- Not intended to establish the Dx of BPE
- Initial assessment of severity of Sx
- Determinant of Rx response
- Determinant of Sx progression
### IPSS

- **0-7 Mild Sx**
  - 8-19 Moderate Sx
  - 20-35 Severe Sx
- **Degree of “bothersomeness”**
- **Need to consider patient’s lifestyle, performance status**

### Uroflow

- **Non invasive**
- **Inaccurate for voided volumes <150mL**
- **Max flow rate (Qmax)**
- **No definite cutoff as a determinant for Rx**
- **No age or voided volume adjustment**
- **Low flow does not differentiate BOO from detrusor hypocontractility**
Post Void Residual (PVR)

- High intra-individual variability
- Poor correlation with other signs and Sx
- Measured by U/S or catheterization
- ? Predictor of Rx outcome
- Increasing PVRs may be an indicator of the need for intervention

Cystoscopy

- Not indicated to determine the need for treatment
- Poor correlation between visual appearance and treatment outcome
- Indicated to determine the most appropriate type of treatment for those who have opted for surgical management
### Surgical Rx: Indications

- Patient preference
- Recurrent urinary retention
- Recurrent UTI’s
- Recurrent gross hematuria
- Bladder calculus
- Large bladder diverticula
- Renal insufficiency due to BPE

### Medical Management

- Preferred treatment for those men lacking absolute indications for surgical intervention.
- US Medicare Database:
  - 250,000 prostate surgeries in 1987
  - 116,000 in 1996
  - 88,000 in 2000
# Urinary Obstruction

- Static Component: BPH/mechanical obstruction
- Dynamic Component: smooth muscle function at bladder outlet

## Nonsurgical Management of BPH

- Alpha Adrenergic Blockers
- Androgen Suppression/Ablation
- Combination Therapy
- Aromatase Inhibitors
- Phytotherapy
Alpha Adrenergic Receptors

From: Campbell-Walsh Urology, 9th edition

Alpha Blocker Therapy

- Selective $\alpha_1$ Adrenergic receptor blockade
- Several medications available:
  - Doxazosin (Cardura)
  - Terazosin (Hytrin)
  - Tamsulosin (Flomax)
  - Alfuzosin (Uroxatrol)
### Alpha Blocker Therapy Side Effects

- Dizziness
- Orthostatic hypotension
- Fatigue/somnolence
- Headache
- Rhinitis
- Nausea
- Retrograde ejaculation

### Androgen Ablation

- Agents causing a loss of Testosterone or DHT action result in a decrease in the volume of the prostate.
- Primarily an epithelial regression.
- Maximum results occur within 6 months
- Treats static component of BPH
- 5 alpha reductase inhibitors
Androgen Ablation

- 5 alpha reductase converts T $\rightarrow$ DHT
- DHT is predominant intraprostatic androgen
- Finasteride (Proscar) Type 1
- Dutasteride (Avodart) Type 1 and 2
- $\sim$30% volume reduction

From: Campbell-Walsh Urology, 9th edition
Androgen Ablation

- Decreased risk of urinary retention
- Decreased need for prostate surgery
- Volume reduction of prostate
- Can lower PSA – effect on cancer detection
- Side effects: impotence

Combination Therapy

- Theory: synergistic effects of alpha blocker and antiandrogen
- Treats both components of prostate obstruction: static and dynamic
- VA Coop Study
### Phytotherapy

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serenoa repens (Permixon)</td>
<td>Saw palmetto berry</td>
</tr>
<tr>
<td>Sabal serrulata</td>
<td>American dwarf palm</td>
</tr>
<tr>
<td>Hypoxis rooperi</td>
<td>South African star grass</td>
</tr>
<tr>
<td>Pygeum africanum</td>
<td>African plum tree</td>
</tr>
<tr>
<td>Urtica dioica</td>
<td>Stinging nettle</td>
</tr>
<tr>
<td>Secale cereale</td>
<td>Rye pollen</td>
</tr>
<tr>
<td>Cucurbita pepo</td>
<td>Pumpkin seed</td>
</tr>
<tr>
<td>Opuntia</td>
<td>Cactus flower</td>
</tr>
<tr>
<td>Pinus</td>
<td>Pine flower</td>
</tr>
<tr>
<td>Picea</td>
<td>Spruce</td>
</tr>
</tbody>
</table>

### Dosages of Common Phytotherapeutic Preparations

- Serenoa repens (Permixon) 160 mg bid
- Pygeum africanum (Tadenan) 50 mg bid
- Secale cereale (Cernilton) 6 capsules
- β-Sitosterol (Harzol) 20 mg tid
- β-Sitosterol (Azuprostat) 65 mg tid
Phytotherapy

- Little is know about active compounds
- Little is know about dosage
- Little is know about mechanism of action
- Paucity of double blinded prospective comparative studies
- Almost all data is anecdotal.

**Surgical Treatment Options**

- Intraprostatic Stents
- Transurethral Needle Ablation (TUNA)
- Transurethral Microwave (TUMT)
- Transurethral Laser Therapy
- TURP : Gold Standard
- Transurethral Incision (TUIP)
- Transurethral Vaporization
- Open Prostatectomy
Intraprostatic Stents

- Primary indication is in patients who are unfit for surgery
- Temporary vs. Permanent
- Complications: migration, pain
- May be useful as a temporary measure after Laser Rx or TUMT

TUNA

- Heats prostate tissue to >60°C
- Uses radiofrequency (RF) energy
- Results in deep tissue necrosis
- Spares the prostatic urethra
- Doesn’t require anesthesia, therefore, office procedure
TUNA

Transurethral Laser Therapy

- Greenlight Laser

- Holmium Laser (HoLEP)
Transurethral Vaporization

- Principle similar to TURP
- Removal of central prostate tissue
- No specimen for path analysis
- Less blood loss

From: Campbell-Walsh Urology, 9th edition
Benign Prostate Disorders

- Prostatitis
- Chronic Pelvic Pain Syndrome (CPPS)

Prostatitis

- Most common GU Dx in men <50 yrs old
- 3rd most common GU Dx in men >50 yrs
- (BPH, prostate cancer)
- 2-10% of men have prostatitis-like Sx
- 9-16% have had the Dx of prostatitis
- Accounts for 3-12% of male GU office visits
Prostatitis Classification

- Acute Bacterial
- Chronic Bacterial
- Non-bacterial
- Prostatodynia

Prostatitis Classification
NIH System

- Category I : Acute bacterial
- Category II : Chronic bacterial
- Category III : Chronic Pelvic Pain Syndrome (CPPS)
  - IIIA : Inflammatory CPPS
  - IIIB : Non-inflammatory CPPS
- Category IV : Asymptomatic
Bacterial Prostatitis

- Gold Standard for Dx is the Meares Stamey “4 Glass” collection technique
- 1st described in 1968
- Can use pre and post massage “2 Glass” collection

Acute Bacterial Prostatitis/UTI

- E coli accounts for 65-80% of infections
- Pseudomonas, Klebsiella, Serratia, Enterobacter account for another 10-15%
- Enterococci 5-10%

- Urovirulence : p-fimbri, biofilms
- Reflux of urine into the intraprostatic ducts
### Bacterial Prostatitis Etiologies

- UTI
- Transurethral surgery
- Indwelling catheter
- Dysfunctional voiding/neurogenic bladder
- Phimosis
- Altered host immune response
- Idiopathic

### Prostatitis Other Organisms

- Corynebacterium
- Chlamydia
- Ureaplasma
- Candida
- Trichomonas
## Bacterial Prostatitis Treatment

- Most antibiotics achieve poor intraprostatic concentrations and yet antibiotics are the mainstay of treatment
  - Fluoroquinolones
  - Trimethoprim-sulfa
  - Macrolides: erythromycin, azithromycin
  - Tetracycline/doxycycline
  - No standard treatment durations

## Chronic Bacterial Prostatitis Treatment

- Duration of optimal Rx is unknown
- Sulfa-trimethoprim remains primary agent
- 30-50% efficacy rates
- Fluoroquinolones also useful
- 1 month vs. 3 month Rx
- Differential Dx = CPPS
**CPPS**

- Absence of bacteria in prostatic secretions
- Common presenting Sx is pain
- Perineal, suprapubic, penile
- Can also be groin, testicular, low back
- Pain during and after ejaculation (50%)
- Irritative or obstructive voiding Sx

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**CPPS**

- >3 months Sx = CPPS
- Sx tend to wax and wane
- Up to 33% will resolve over 1 year’s time
### CPPS

- Intraductile reflux
  - Chemical prostatitis
- Immunological Alterations
- Neurological
- Pelvic floor muscle dysfunction
- Psychological factors

### CPPS Treatment

- 40% achieve benefit from antibiotic Rx
- Long duration Rx not recommended
- Alpha blocker Rx
- Anti-inflammatory Rx
- Biofeedback
- Pelvic muscle relaxation
- Antidepressants
- Psych