Benign Prostate Disorders

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Objectives

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

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

Benign Prostate Disorders

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

BPH/BPE

- Epidemiology
- Etiology
- Symptoms
- Objective Data
- Nonsurgical/Medical Management
- Surgical Management

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

- Exact molecular etiology is unknown
- Androgens and estrogens
- Growth factors
- Cell-cell interactions
- Impaired programmed cell death (apoptosis)
- Neurotransmitters

BPH
Role of Androgens

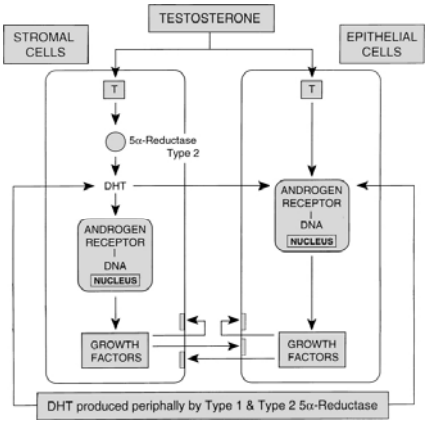
- Prostate retains ability to respond to androgens throughout ones life
- Concentration of androgens does not increase with age
- Stromal cell – 5 alpha reductase Type 2 interaction seems to be key event in the development of BPH
- Role of estrogens is unclear

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



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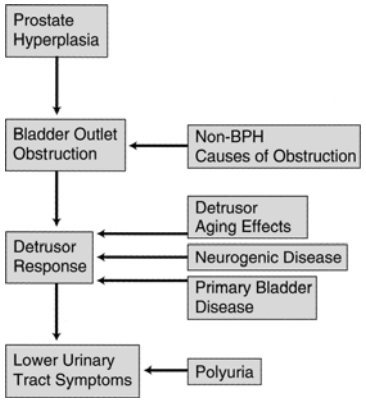
Pathophysiology of Obstruction

- 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

BPH

- Obstructive uropathy/Urinary obstruction
- Bladder outlet obstruction (BOO)
- Lower Urinary Tract Sx (LUTS)
- Prostatism

- BPH ≠ Urinary obstruction
- Urinary obstruction ≠ BPH



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BPE

- Explanation of increased urethral resistance due to BPE is too simplistic
- Must factor in age related detrussor and bladder neck dysfunction
- Static and dynamic factors

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

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)

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

Clinical Manifestations of BPH

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

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

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

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 detrussor hypocontractility

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

Urinary Obstruction

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

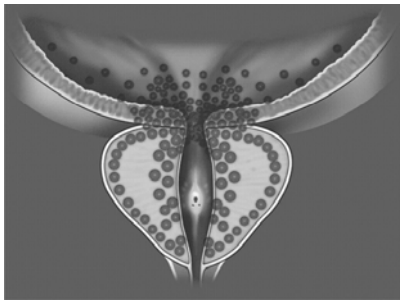
Medical Management

- 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

Nonsurgical Management of BPH

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

Alpha Adrenergic Receptors



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Alpha Blocker Therapy Side Effects

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

Alpha Blocker Therapy

- Selective α1 Adrenergic receptor blockade
- Several medications available:
  - Doxazosin (Cardura)
  - Terazosin (Hytrin)
  - Tamsulosin (Flomax)
  - Alfuzosin (Uroxatrol)

Androgen Ablation

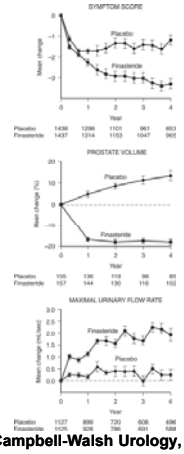
- Agents causing a loss of Testosterone or DHT action result in a decrease in the volume of the prostate.
- Primarily an epithelial regression.
- Maximum results occur within 6 months
- Treats static component of BPH
- 5 alpha reductase inhibitors

Androgen Ablation

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

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



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Combination Therapy

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

Phytotherapy

- ***Serenoa repens*** **Saw palmetto berry**
- *Sabal serrulata* American dwarf palm
- *Hypoxis rooperi* South African star grass
- *Pygeum africanum* African plum tree
- *Urtica dioica* Stinging nettle
- *Secale cereale* Rye pollen
- *Cucurbita pepo* Pumpkin seed
- *Opuntia* Cactus flower
- *Pinus* Pine flower
- *Picea* Spruce

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.**

Phytotherapy

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

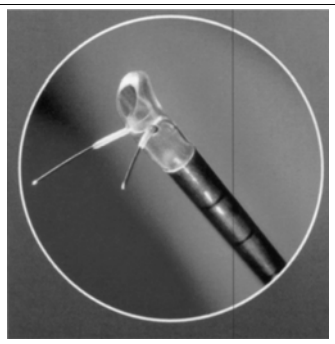
Surgical Treatment Options

- **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



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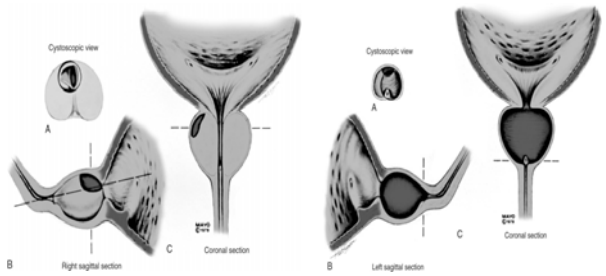
TUNA

- 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

Transurethral Laser Therapy

- Greenlight Laser
- Holmium Laser (HoLEP)

TURP



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Benign Prostate Disorders

- Prostatitis
- Chronic Pelvic Pain Syndrome (CPPS)

Transurethral Vaporization

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

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

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

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

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

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

Prostatitis Other Organisms

- Corynebacterium
- Chlamydia
- Ureaplasma
- Candida
- Trichamonas

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

CPPS

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

CPPS

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

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