DISORDERS OF PROSTATE

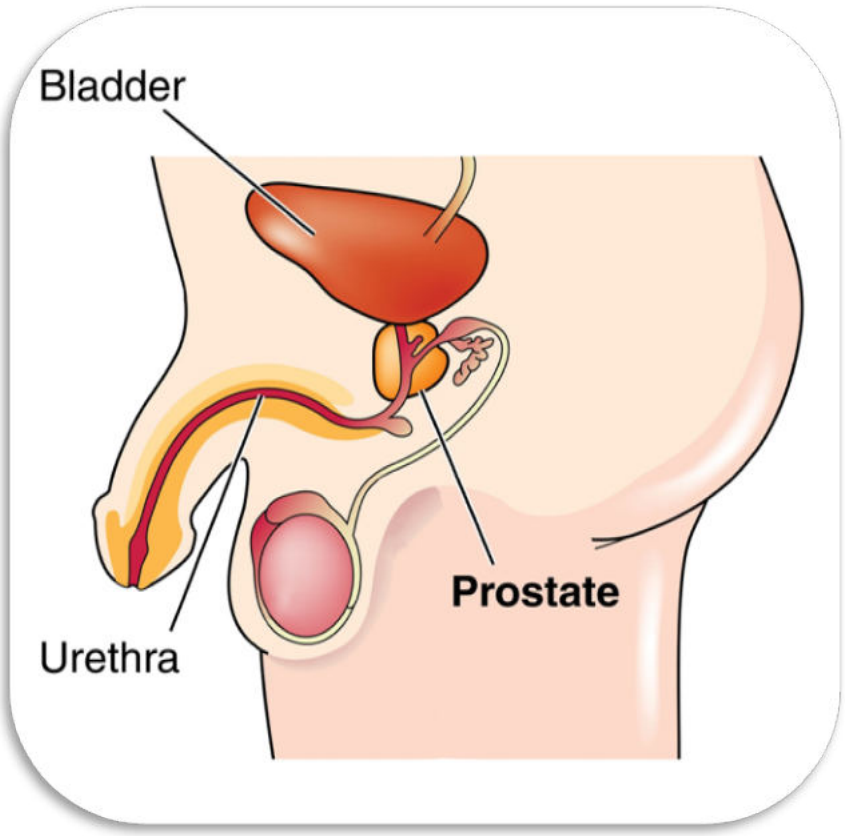
Outline

- Introduction
- BPH
- Prostate cancer
- Prostatitis
  - Acute bacterial
  - Chronic bacterial prostatitis
  - Chronic pelvic pain (CPP) syndrome (inflammatory/non-inflammatory)

Prostate Overview

What is the Prostate?[1]

- Walnut sized gland at base of male bladder
- Surrounds the urethra
- Produces fluid that transports sperm during ejaculation
- Prostate grows to its normal adult size in a man's early 20s; it begins to grow again during the mid-40s



- the normal prostate measures between 3-4cm at its widest portion; it is 4-6cm in length & 2-3cm in thickness.
- Weight 17-25 gm
- In the early 1970's McNeal proposed a concept of zonal anatomy.
- According to this concept, the glandular portion of the prostate is composed of a large peripheral & a Small central zone, which together constitute about 95% of the gland.

Benign Prostate Hyperplasia

Incidence & Epidemiology

- The term BPH is a misnomer because the actual change is a hyperplasia & not hypertrophy.
- The initiation of BPH may not be environmental or genetically influenced.
- It is also suggested that the prevalence of BPH increases with age in all male populations.

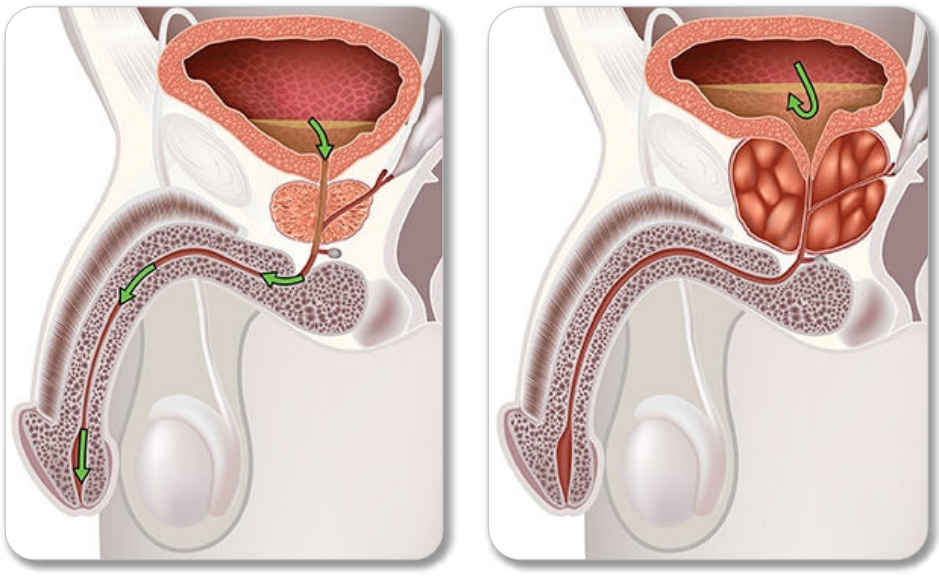
Etiology

- Two factors are necessary for BPH
  1)Endocrine control(DHT)
  2) Aging

Relative role of testosterone estrogen, DHT is complex

Normal vs. Enlarged Prostate

- As the prostate enlarges, pressure can be put on the urethra causing urinary problems (LUTS)[1]
- Prostate size does not correlate with degree of obstruction or severity of symptoms.[3]



Normal Prostate Enlarged Prostate

Pathophysiology Of Symptoms

Symptoms of BPH:

1) obstructive

- decrease in force & caliber of the stream: due to urethral compression is one of the early & constant features of BPH.

  Hesitancy: occurs because the detrusor takes a longer time to generate the initial increased pressure to overcome the urethral

  resistance.
- Intermittency: occurs because the detrusor is unable to sustain the increased pressure until the end of voiding.
- Terminal dribbling of urine & incomplete sense of bladder

  emptying

Pathophysiology Of Symptoms

2) Irritative symptoms:

- Frequency:

  Incomplete emptying during each void results in shorter intervals between voids.

  The presence of enlarged prostate provokes the bladder to trigger a voiding response more frequently than in normal individuals, especially if the prostate is growing intravesically.

- Nocturia: normal cortical inhibitors are lessened and also because the normal urethral and sphincteric tone is reduced during sleep.

- urgency & dysuria: uncommon.

Symptoms

- Systemic symptoms related to the UT:
  - Vesicoureteral reflux
  - Dilatation & hydronephrosis
  - Renal failure & symptoms of uremia

- Symptoms unrelated to the UT:
  - hernias, hemorrhoids and vesical calculus
  - change in the caliber of bowl movements

- Symptoms related to complications:
  - cystitis
  - pyelonephritis
  - bladder calculi
  - micro or gross hematuria.

Signs of BPH

- If the disease is advanced & has resulted in renal failure.

Signs of renal failure include elevated BP, rapid puse & respiration, uremic fetor, pericarditis & pallor of nail beds.

- Abdominal examination may reveal palpable kidney or flank tenderness if there is hydronephrosis or pyelonephritis.

- A distended bladder may be noted on palpation or percussion.
- DRE: Enlarged prostate. Median sulcus always present

How is an Enlarged Prostate Diagnosed?[12]

- Medical History
- Physical Exam*
  - Prostate Exam
    - Digital rectal exam (DRE)
  - Urinary Output Testing
    - Peak urinary flow (Qmax) testing
    - Post-void urine volume testing
- Self Evaluation of Symptoms
  - American Urological Association Symptom Index (AUA-SI)
  - International Prostate Symptom Score (IPSS)
  - Quality of Life (QoL) Questions
  - Bladder Impact Index (BII)

**Additional testing is optional and may be done at physician's discretion and/or depending on patient symptoms*

Laboratory Findings

- **Urinalysis & microscopic examination:** to R O infection

- **serum U/E & creatinine:** to provide baseline information

- **Uroflowmetry:** At a volume of 125-150ml, normal individuals have average flow rates of 12ml/sec & peak flow close to 20ml/sec.

- **Residual Urine:** estimated by U S or catheterizations. Volumes >150 ml are considered significant since they constitute approximately one-third of normal bladder volume.

IMAGING

- Ultrasound KUB-

Document :

✓size of prostate

✓Post void residual urine

✓Hydronephrosis

Treatment

- Because BPH is not invariably progressive, the timing of intervention is variable

- Absolute indications for treatment include severe obstructive symptoms & renal insufficiency.
  - Relative indications - moderate symptoms of prostatism, recurrent UTI,vesical calculus and hematuria.

- Until recently, surgery was the mainstay of therapy for BPH. In the last decade or so , there has been a tremendous resurgence of interest in non surgical therapies.

Treatment Options Overview

WATCHFUL WAITING/ MEDICAL THERAPIES	MINIMALLY INVASIVE SURGERY	INVASIVE SURGERY
Alpha Blockers	Microwave Therapy (TUMT)	Open Prostatectomy
5 Alpha-Reductase Inhibitors	Laser	
	TURP (Monopolar, Bipolar, Button)	

Treatment Options

Watchful Waiting/Medical Therapies

- **Characteristics**[12]
  - Best for men with mild symptoms
  - Consists of yearly exams and no active intervention
  - No surgery
  - No drugs
  - May involve lifestyle modification such as adjusting diet, evening fluid intake, medication use and exercise patterns
- **Side Effects**
  - Symptoms may worsen or remain unchanged without lifestyle modification[1]

Medical Treatment

- Obstruction secondary to BPH occurs because of 2 factors:

Dynamic component: a result of contraction of smooth muscles of the prostate & prostatic urethra mediated mostly by adrenergic receptors.

Mechanical component: related to the presence of a mass which compresses & narrows the urethral lumen.

Alpha adrenergic agonist

- Ideally suited for the treatment of the without impairing detrusor contractility dynamic component of BOO because they can selectively reduce resistance along the bladder outlet
- Example:

  Tamsulosin 0.4mg OD, Silodosin 8 mg
  Alfuzosin XL 10mg OD, Terazosin
  Doxazosin 4mgTID

alpha- reductase inhibitor 5

- Agents that selectively blockade androgens at the prostate cellular level are termed anti-androgens.
- the prostate normally requires conversion of testosterone to dihydrotestosterone by the enzyme 5 alpha-reductase.
- In long term clinical trials, proscar has been shown to decrease prostatic size & improve urine flow rates & symptoms of BPH.
- Dutasteride and finasteride

MINIMALLY INVASIVE SURGERY(Conventional)

- TURP
- TUIP
- Laser Prostatectomy
- TUNA(Trans urethral needle ablation of prostate)

Conventional Surgical Therapy

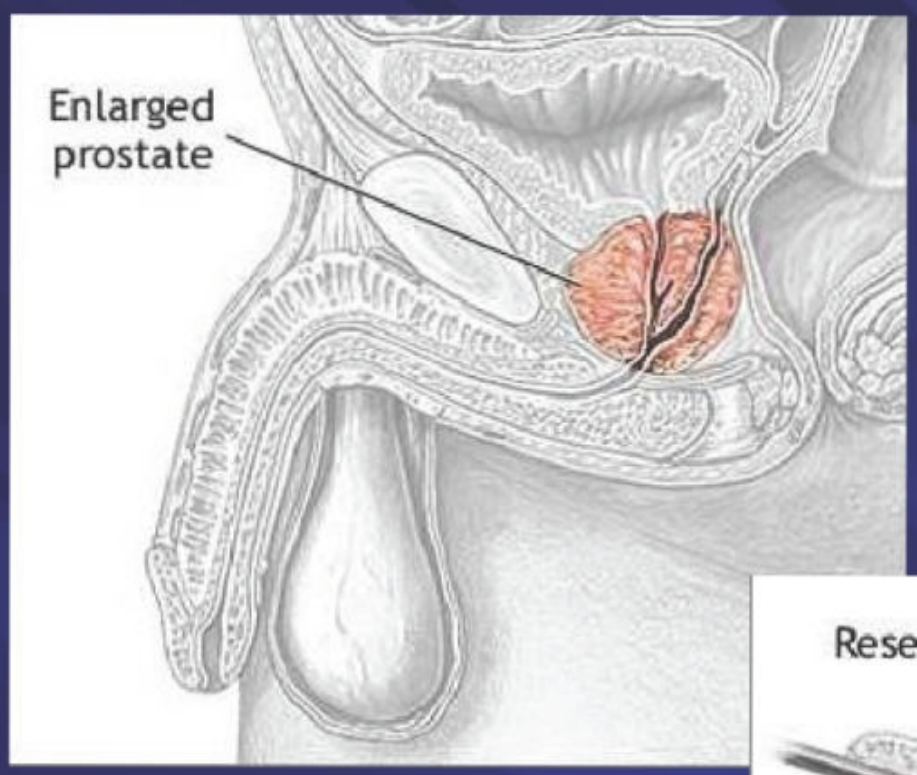
TURP

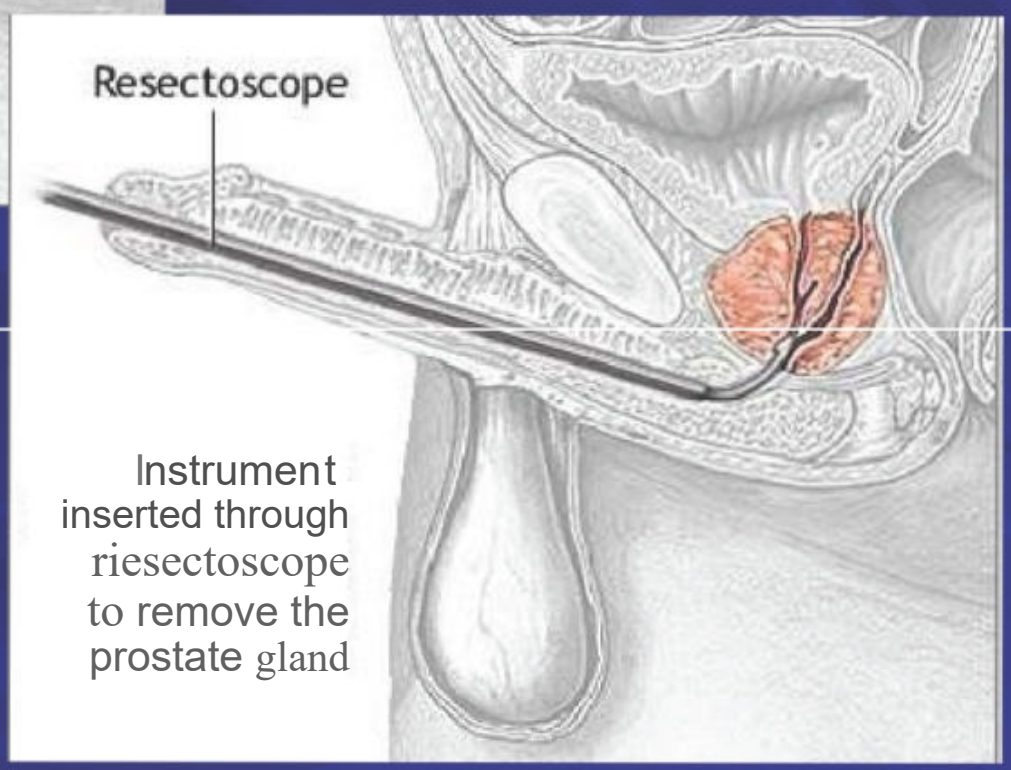
The principles of TURP are to remove the obstructing adenomatous portion of the prostate via the urethra.

- Overall morbidity: 18%.
- Current mortality: 0.2%.

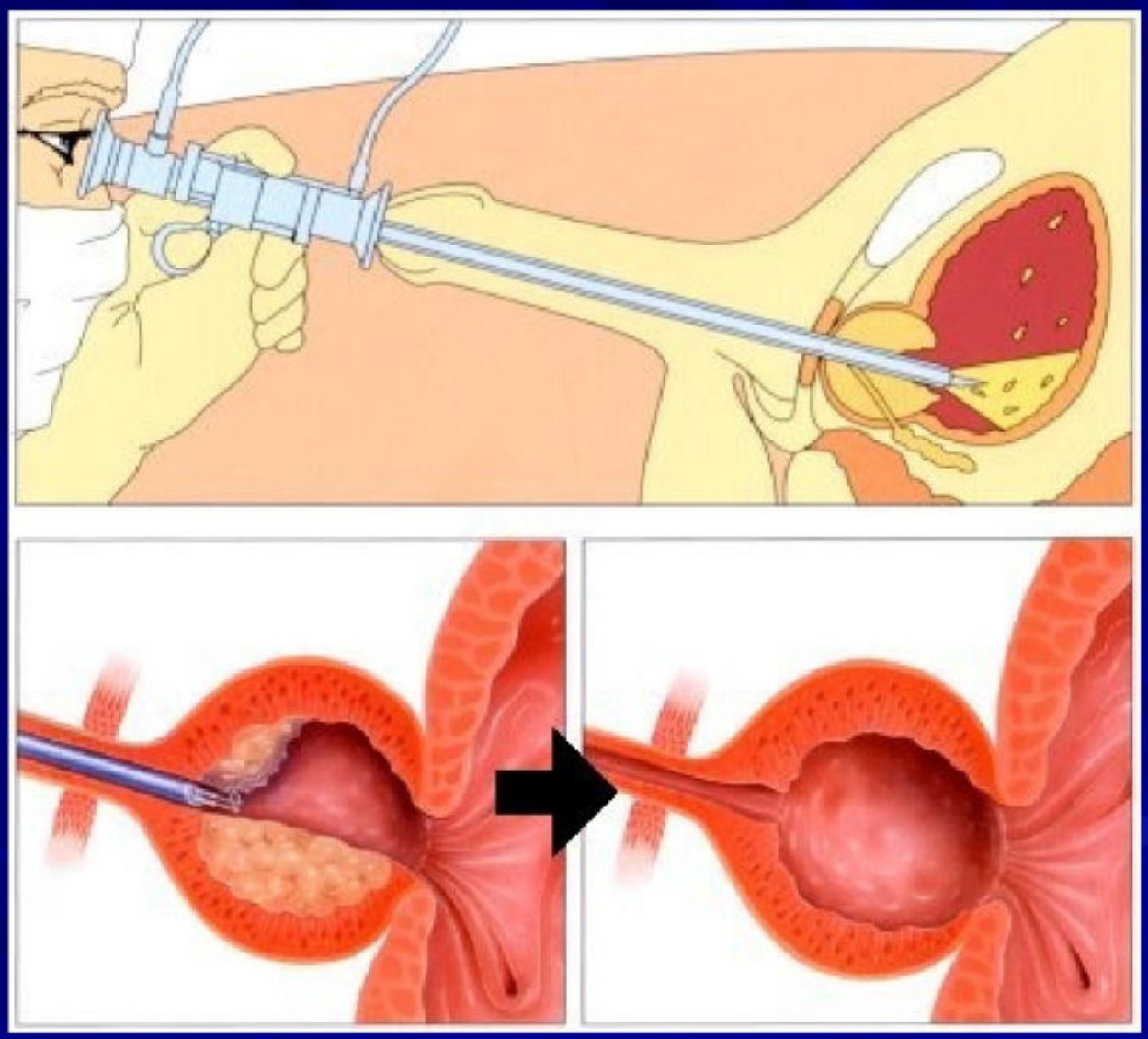
One preventable complication is TUR syndrome

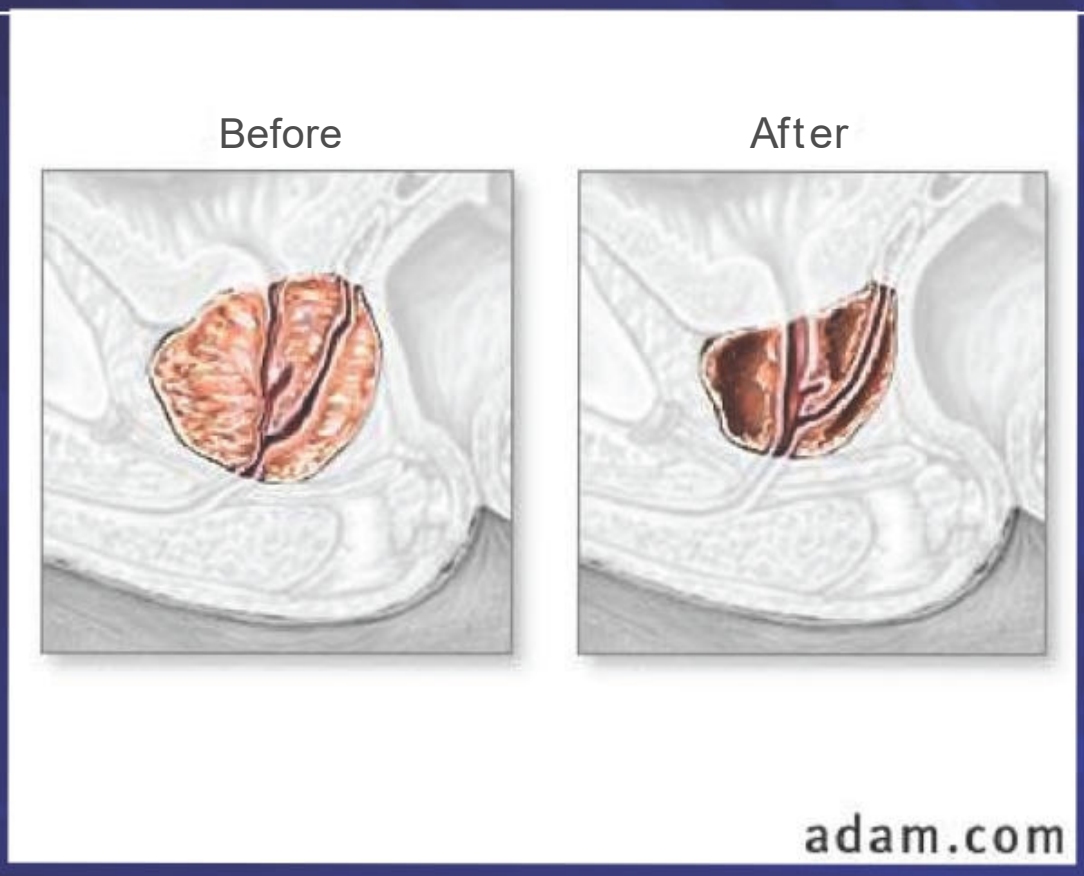
- Immediate complications: failure to void, post op haemorrhage, clot retention, & UTI.
- Late complications: impotence, incontinence, uretheral stricture and retrograde ejaculation.

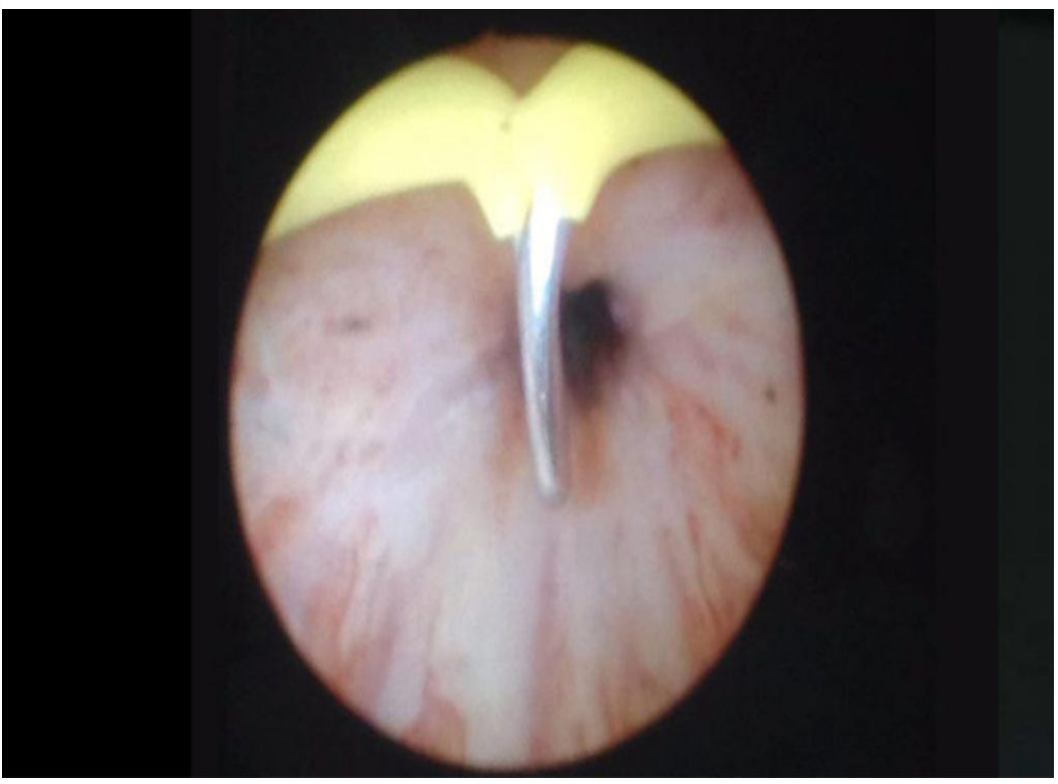




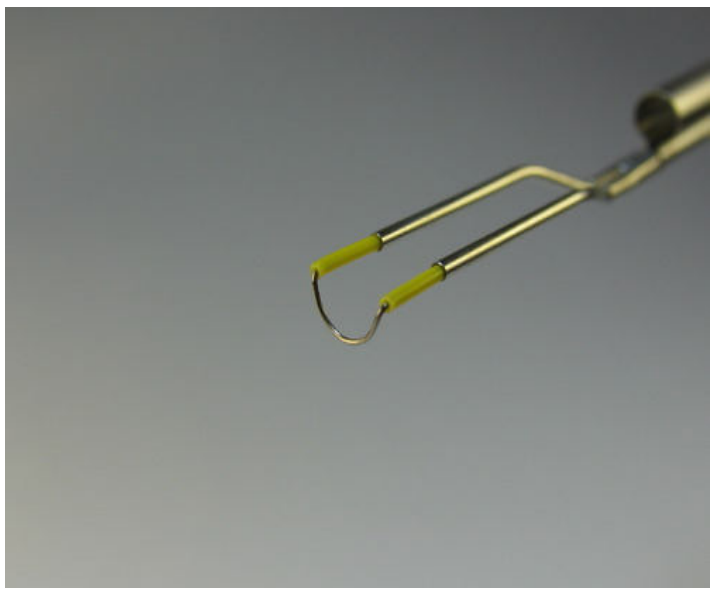
Instrument inserted through riesectoscope to remove the prostate gland





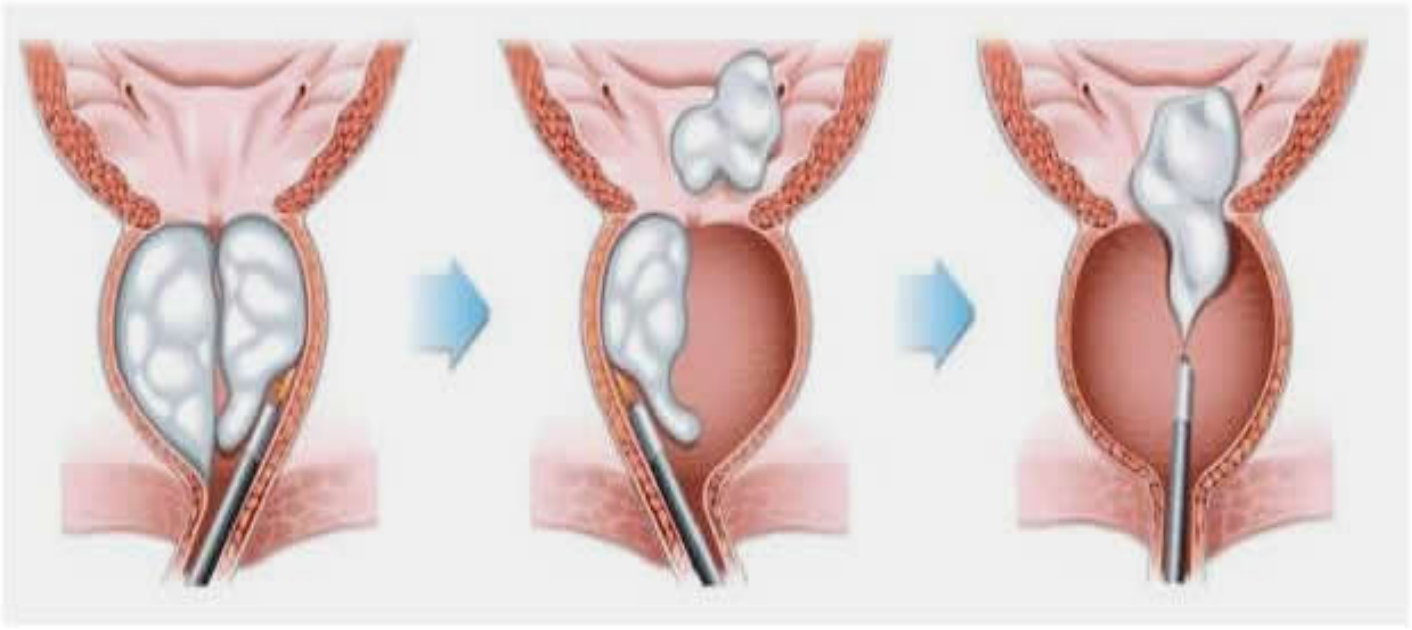


TUIP



TURP LOOP

Laser Prostatectomy



Treatment Options

Invasive Surgery

Open Prostatectomy

Involves surgical removal of the inner portion of the prostate via a suprapubic or retropubic incision in the lower abdominal area.

Characteristics[12]

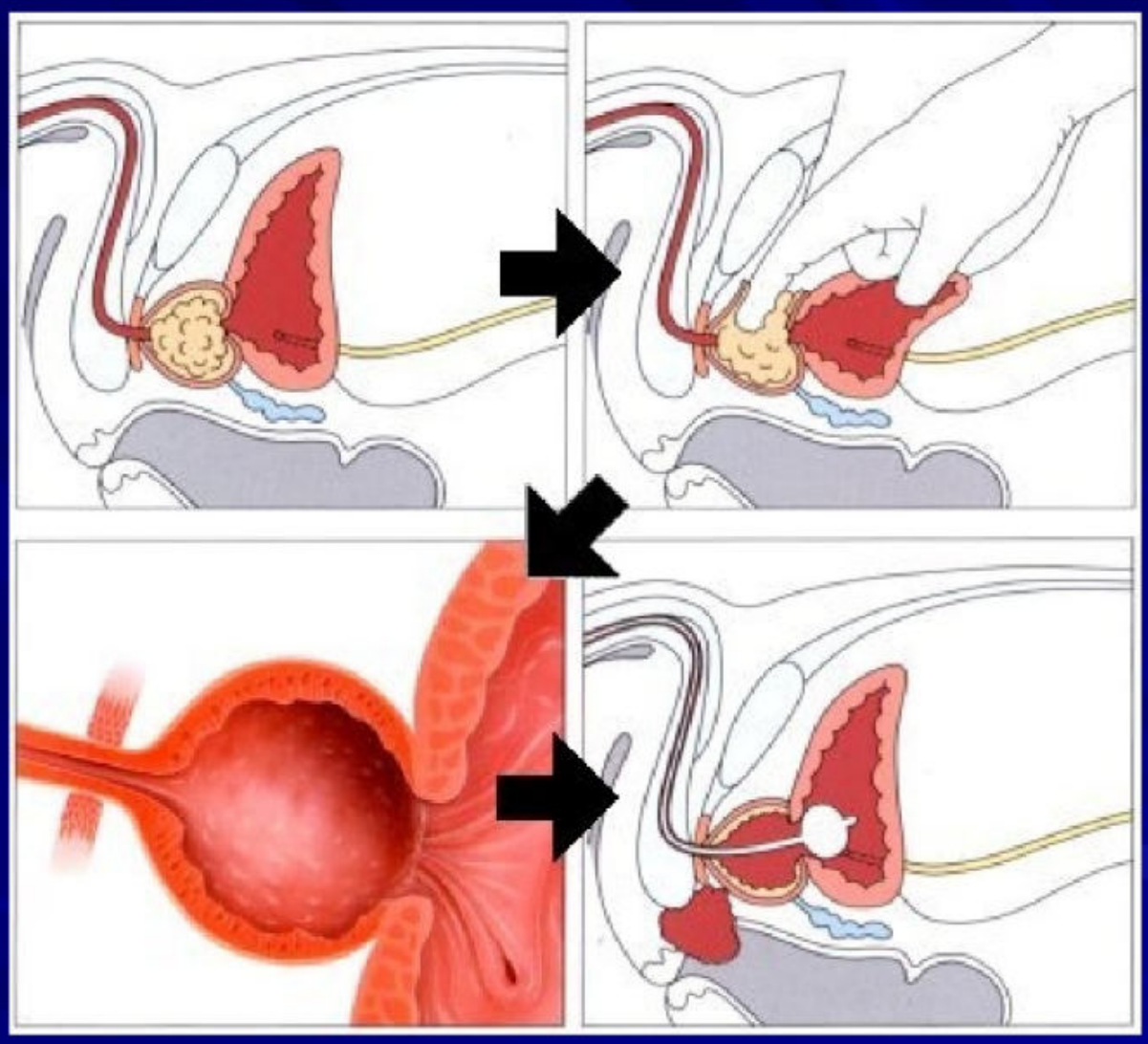
- Typically is performed on patients with larger prostate volumes (>80 - 100 mL)
- Effective for men with:
  - Very enlarged prostate glands
  - Bladder diverticula (pockets)
  - Stones

Side Effects[12]

- Associated with a longer hospital stay
- Risk of blood loss, transfusion significantly greater than with transurethral procedures

Open prostatectomy

- Open prostatectomy can be done either Tranvesical, perineal or Retropupic prostatectomy.
- In recent years the suprapubic & retropubic approaches for BPH have been limited to approximately 10% of patients.
- Indications for suprapubic prostatectomy are a gland size greater than 100g, cystolithotomy or diverticulum excision.
- Most post op complications are similar to TURP, however, wound infection & thromboembolism are additional complications.



Prostate cancer

Prostate Cancer

Statistics

- Most common non-cutaneous malignancy in men in North America
- 2nd most common cause of cancer-related deaths in men
- 1 in 7 men will be diagnosed
- Lifetime risk of being diagnosed with prostate cancer is 18% but risk of dying of prostate cancer is only 3%

Prostate Cancer Risk Factors

- Established
  - Advancing age
  - Presence of androgens
  - Family history (1st degree relative)
  - African ancestry
- Potential
  - High dietary fat
  - Obesity
  - Inherited mutations (*BRCA1* or *BRCA2* genes)
  - Vitamin D or E deficiency
  - Selenium deficiency?

Prostate Cancer: Presentation

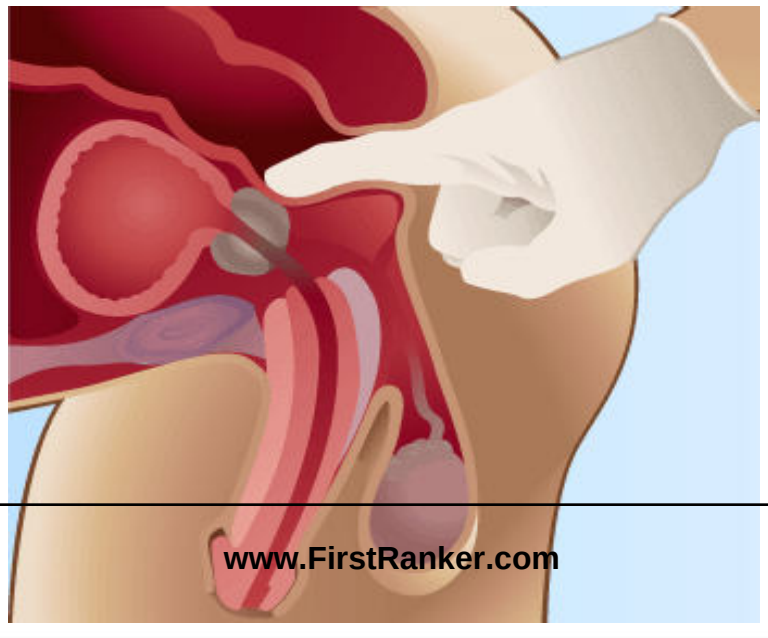
- Early stages usually asymptomatic
  - Most cases detected by serum PSA **screening**
  - Palpable nodule or firmness on DRE
- Advanced stages
  - Urinary retention/renal failure
  - Bone pain
  - Anemia
  - Weight loss, fatigue
  - Spinal cord compression

Disease Screening

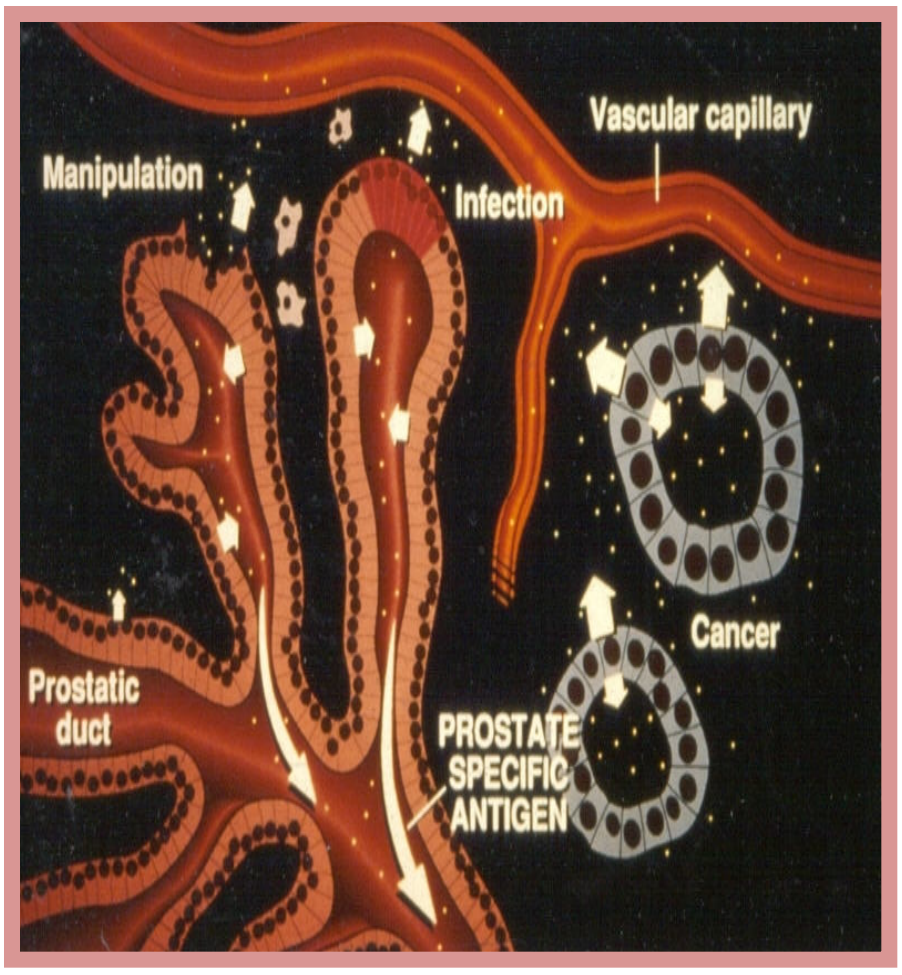
- Goal
  - To identify the presence of disease at a stage when treatment can be given that will cure it
- Use a combination of DRE and PSA

Digital Rectal Examination

- DRE (digital rectal exam) has a 50% positive predictive value
- DRE alone is not a good screening tool
- BUT it is an important part of screening



What is PSA (Prostate Specific Antigen)?



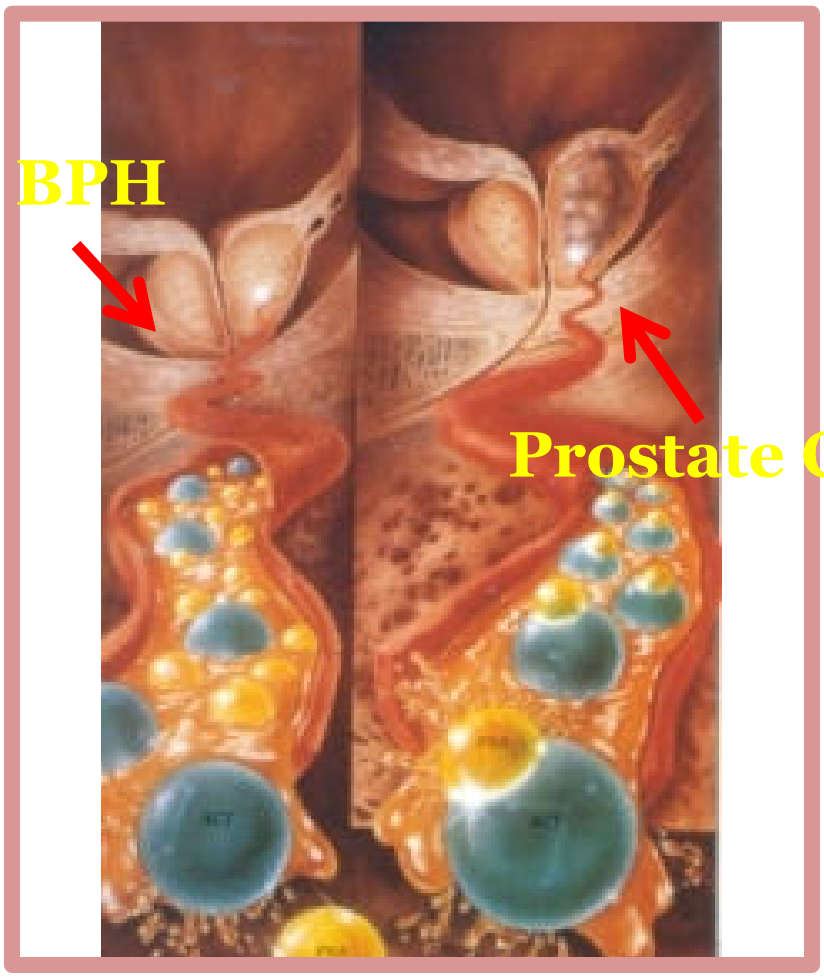
- A Serine protease (enzyme) found in the prostate
- Secreted by prostate epithelial cells
- Found in ejaculate
- As diagnostic tool for:
  - Screening
  - Staging
  - Prognostic indicator
  - Surveillance

Prostate Cancer: Screening with PSA

- No clear cut-point between normal and abnormal PSA levels. Even PSA cut-off of 1.1 ng/ml misses up to 15% of prostate cancer **(The Cancer Prevention Trial – 2003)**
- Positive predictive value for PSA > 4ng/ml = 30% (i.e. About 1 in 3 men with elevated PSA have prostate cancer detected at time of biopsy
- PPV increases to 45-60% for PSA > 10ng/ml
- Nearly 75% of cancers detected in the grey zone (PSA 4-10) are organ confined; potentially curable.
- ~~<50% of prostate cancers organ confined if PSA >10~~

Free/Total PSA Ratio:
A Way to Improve Specificity

- Prostate cancer maybe associated with more protein-bound PSA (less free PSA) than in BPH
  - F/T ratio is lower in patients with prostate cancer
  - Can improve test specificity
  - Useful when total PSA in 4-10 ng/ml range



Prostate Cancer:
Diagnosis

- Indications for transrectal ultrasound (TRUS) guided biopsy
  - Palpable nodule on DRE
  - Elevated serum PSA
- Biopsy involves 10-18 needle cores taken mostly from the peripheral zone of the prostate

Imaging

CT:

used only when extensive L.N. disease is suspected and it is based only on the size of the nodes thus false +ve and -ve are common.

MRI:

not useful because of the cost and the overlap in the appearance of benign & malignant processes, but its more accurate than TRUS for staging extracapsular extension and seminal vesicle involvement.

Bone scanning:

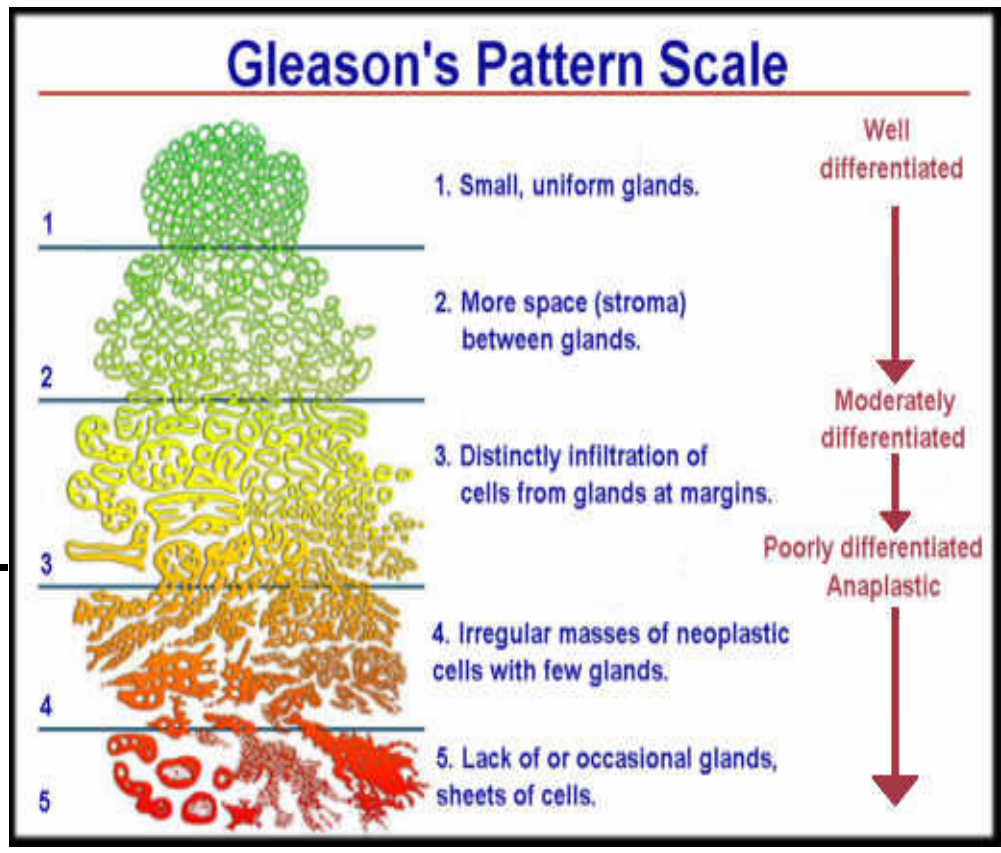
most common way to assess systemic metastasis.

False +ve rate is less than 2%.

Diagnosis is confirmed by plain radiographs, thin section CT or MRI and bone biopsy

Prostate Cancer: Pathology

- Adenocarcinoma
- Gleason "grade" is from 1-5 based on glandular architecture
- Gleason score is the total primary grade (1-5) + secondary grade (1-5) = 2-10
  - 4-6/10=well-differentiated
  - 7/10=moderately differentiated
  - >8/10=poorly differentiated



Prostate Cancer:

Staging

- Can spread to adjacent organs (seminal vesicles, bladder), lymph nodes, bone
- Most bone mets are **osteoblastic**
- Prior to initiating treatment consider
  - Bone scan (PSA>10, Gleason Score >7)
  - CT scan pelvis/abdomen (PSA >10, Gleason Score >7))
  - These tests are typically not required in asymptomatic men with low risk prostate cancer

1. The size and extent of the primary Tumor (T category)

- T1 - The tumor is not detectable with a digital rectal exam (DRE) or imaging but is found in prostate tissue from a biopsy or surgical treatment.
  - T1a - Cancer is found in 5% or less of the removal tissue.
  - T1b - Cancer is found in more than 5% of the removed tissue.
  - T1c - Tumors are found by needle biopsy done for a high PSA.
- T2 - The tumor is detectable with a DRE or imaging but is confined to the prostate.
  - T2a - Cancer is in no more than one half of one side of the prostate.
  - T2b - Cancer is in more than half of one side of the prostate.
  - T2c - Cancer is in both sides of the prostate.
- T3 - Cancer has grown outside the prostate and may have grown into the seminal vesicles.
  - T3a - Cancer has spread outside the prostate but not to the seminal vesicles.
  - T3b - Cancer has spread to the seminal vesicles.
- T4 - Cancer has grown into other nearby tissues, such as the urethral sphincter, rectum, bladder or wall of the pelvis

Whether the cancer has spread to nearby lymph Nodes (N Category)

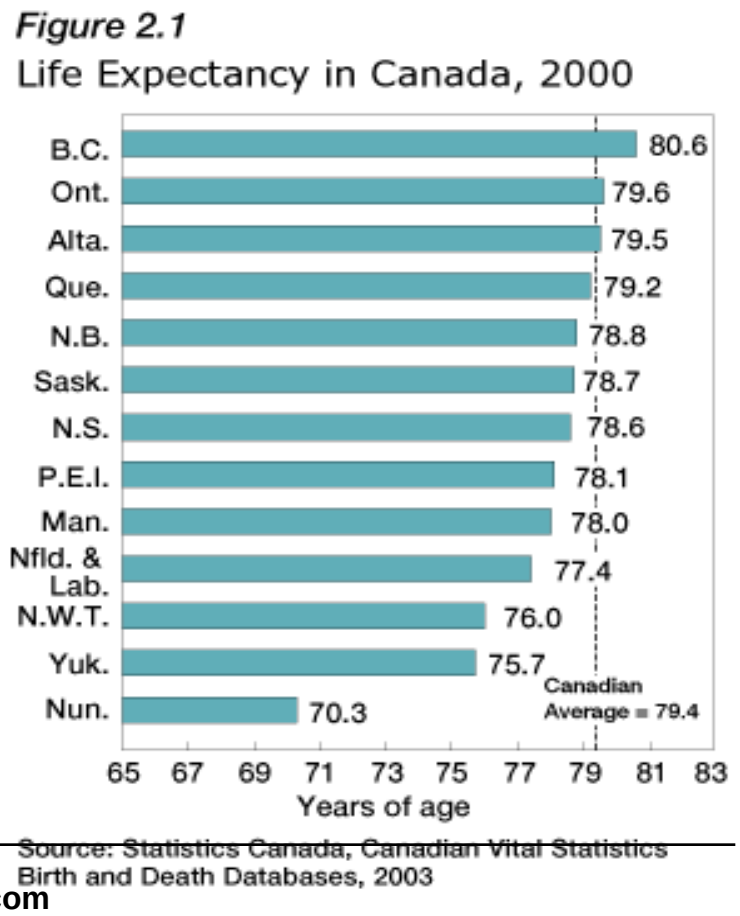
- NX - The lymph nodes have not been assessed for cancer.
- N0 - There is no cancer in nearby lymph nodes.
- N1 - Cancer has spread to nearby lymph nodes.

The absence or presence of cancer outside the prostate, or Metastasis (M Category)

- MX - It is unknown if cancer has spread to distant sites.
- M0 - The cancer has not spread to distant sites.
- M1 - Cancer has spread to distant sites.
  - M1a - Cancer has spread to distant lymph nodes.
  - M1b - Cancer has spread to bones.
  - M1c - Cancer has spread to distant organs

Prostate Cancer Treatment

- Considerations
  - Patient's age
  - Co-morbid health conditions
  - Tumor stage
  - Tumor grade (Gleason score)
  - Often a patient choice
  - Surgery and



Treatment

- Early stage Cancer
  1. Radical Prostatectomy
  2. External Beam Radiotherapy
  3. Radioactive Seeds (Brachytherapy)
  4. Active Surveillance
  5. Observation – Watchful Waiting

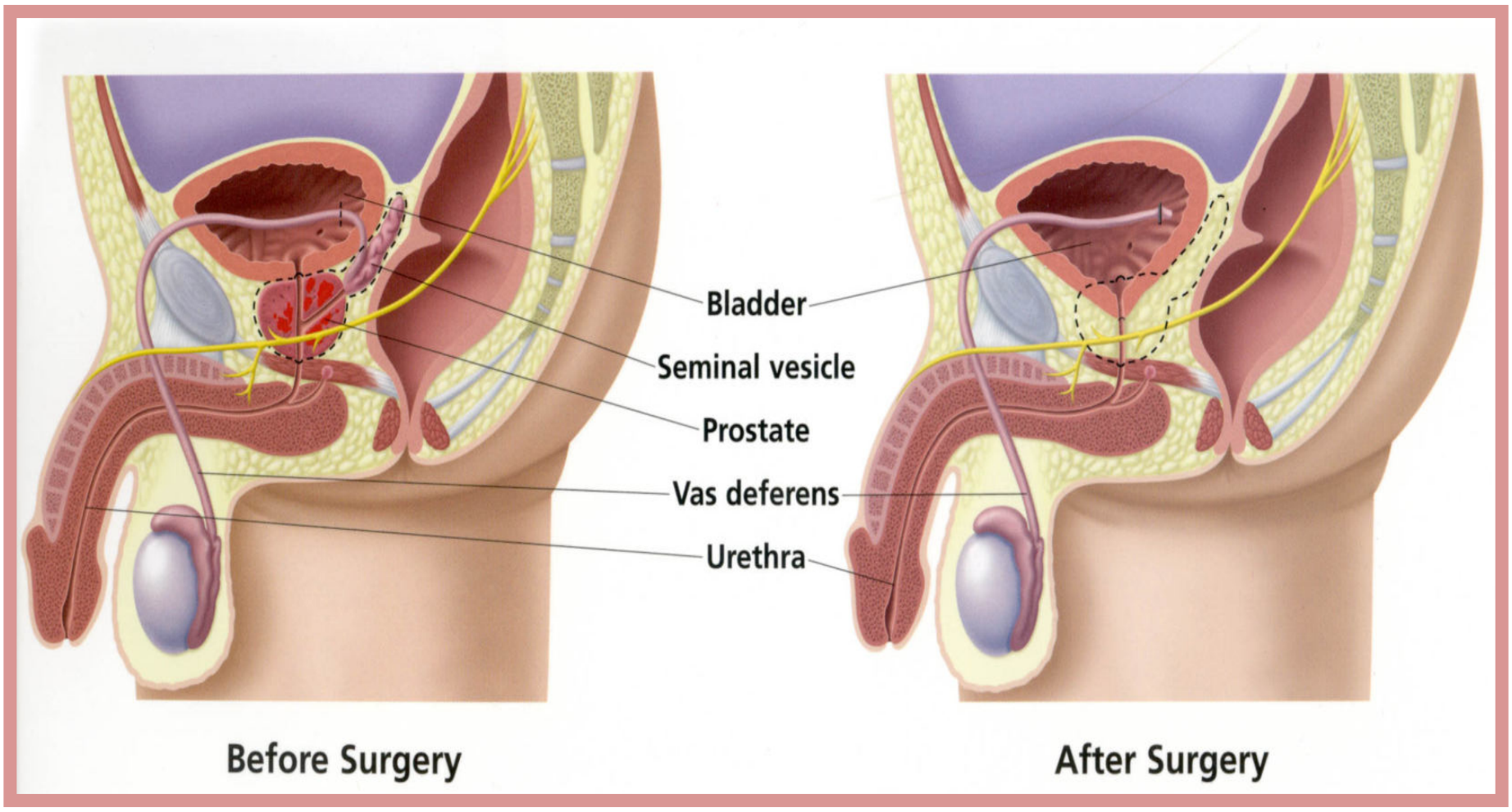
Prostate Cancer Treatment:

1. Radical Prostatectomy

- Radical Prostatectomy
  - Complete surgical removal of entire prostate, seminal vesicles
  - Considered a good treatment for men <70 years of age with clinically organ confined cancer who are healthy
  - Open or laparoscopic/robotic approaches

Prostate Cancer Treatment:

1. Radical Prostatectomy



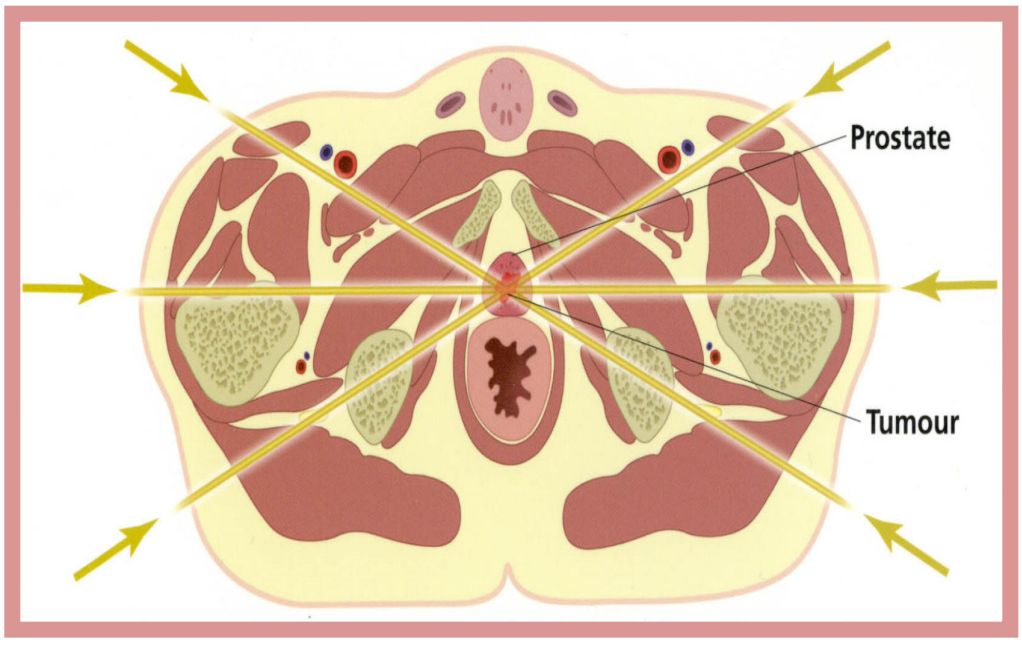
Prostate Cancer Treatment:

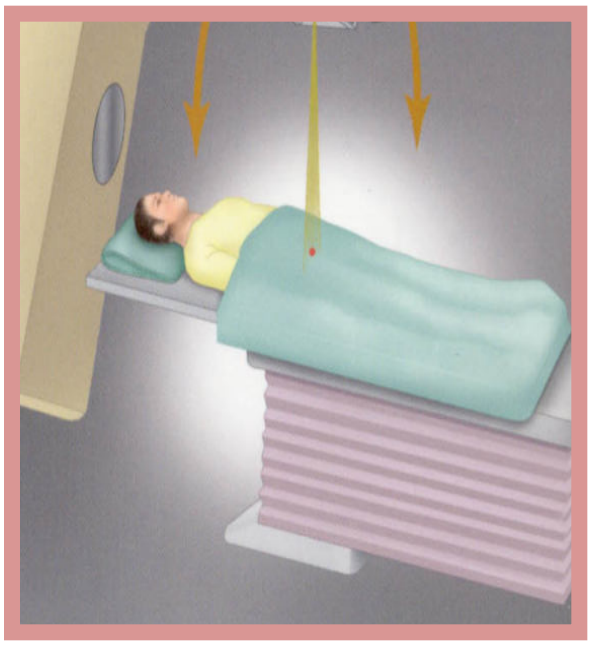
Radiotherapy

- Radiotherapy Options
  - External Beam
  - Brachytherapy (seed implant)
  - Concept of maximizing dose to the tumor and minimizing collateral damage
- Curative options for patients at high risk for morbidity from radical prostatectomy
  - Age, medical co-morbidities
  - Patient preference

Prostate Cancer Treatment:

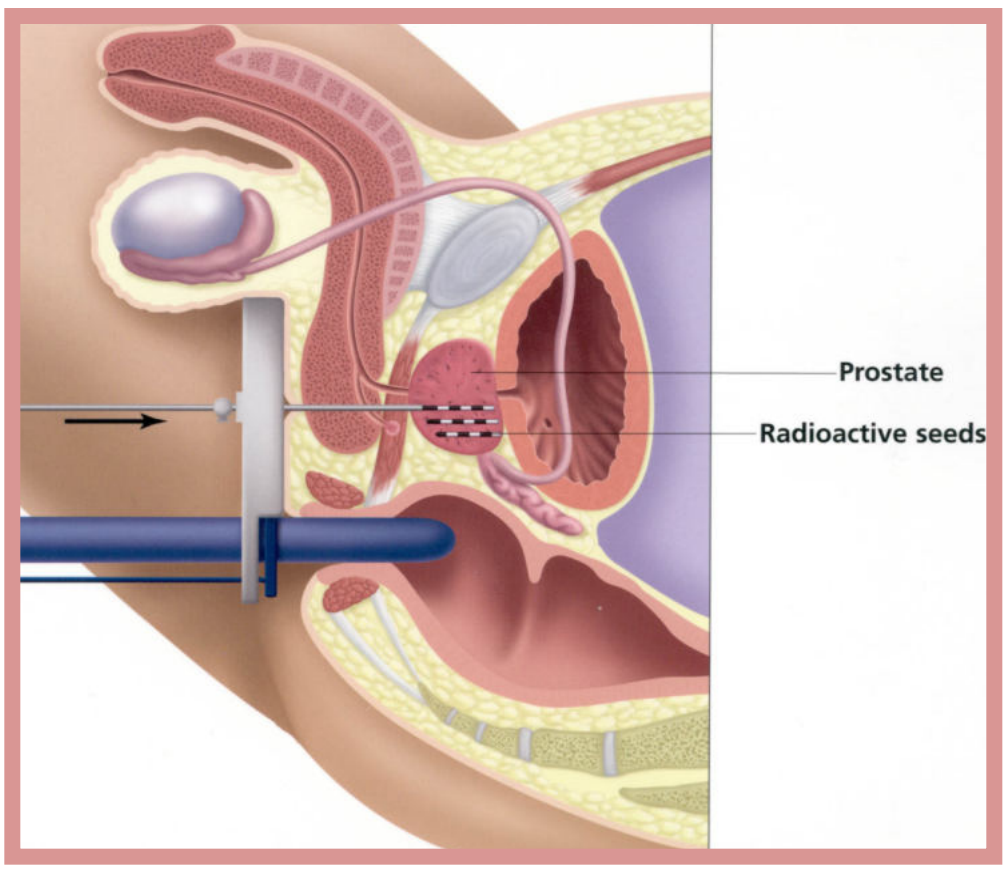
2. External Beam Radiotherapy





Prostate Cancer Treatment:

3. Brachytherapy



Prostate Cancer Treatment:

4. Active Surveillance

- Observing low grade tumors in men <70 yrs and >10 yr life expectancy
- Delay definitive treatment until it is necessary and cancer is still curable
- Goal is to delay potential treatment-related morbidity
- Monitor DRE, PSA, and periodic repeat biopsy
- Ideal candidate:
  - PSA < 10
  - Normal DRE
  - Gleason <7 (low grade)
  - Only 1-3 / 12 biopsy cores positive

Prostate Cancer. Treatment:

5. Watchful Waiting

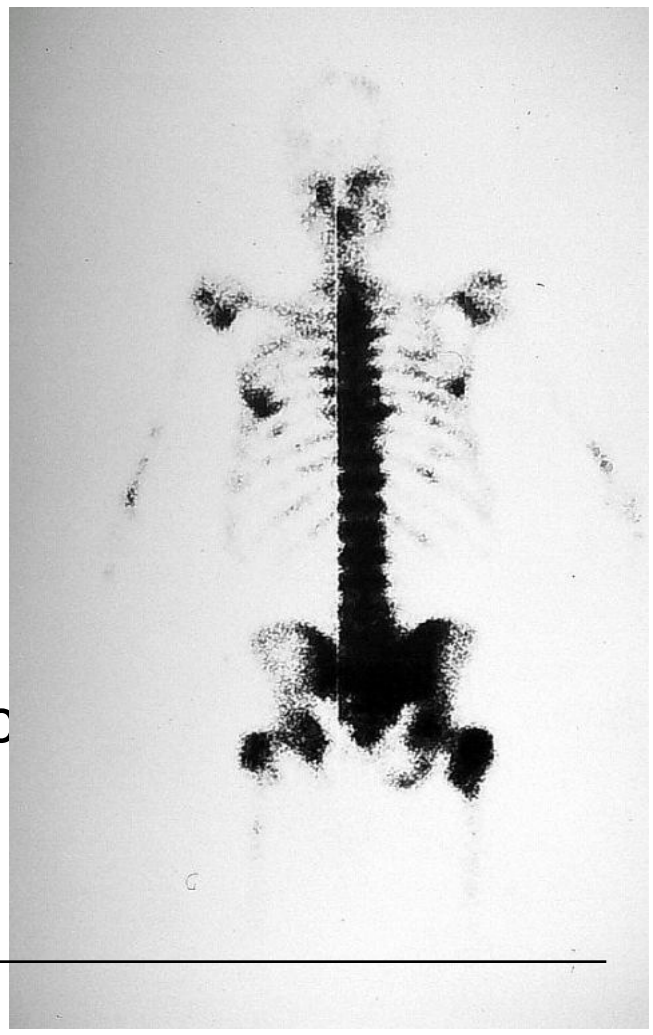
- Observing low grade tumors in men >70 yrs or <10 yrs life expectancy
- Institute hormonal therapy when patient becomes symptomatic
- No curative intent

Advanced or Metastatic Prostate Cancer

- Not curable disease
- Goals shift to disease control
- Development of cancer cells unresponsive to androgen deprivation
- Typically occurs slowly over time, although it can occur rapidly

Advanced Prostate Cancer: Treatment

- Androgen Deprivation (Hormonal Rx)
  - Orchidectomy
  - LHRH analogues
  - Antiandrogens
- Supportive therapies
  - Analgesics
  - Steroids
  - Bisphosphonates/Vitamin D/Calc for bone health
- Chemotherapy
  - Taxotere, Docetaxel
  - Last line of treatment



Prostate Cancer Prognosis

- Depends upon grade, stage and treatment
- Early stage/well-differentiated Ca treated by radical prostatectomy:
  - 85% + 10 year survival
- Metastatic disease
  - <10% 5 year survival

PROSTATITIS

Definition

- Infection &/ or inflammation of the prostate

Epidemiology

- Overall prevalance in men is 5
- higher risk age 20 – 50 & >70

Pathogenesis

- Tissue around prostatic acini become infiltrated by inflamatory cells.
- Organisms:
  - G-ve (E.coli, pseudomonas, klebsiella , serratia, Enterobacter aerogenes.)
  - G+ve 5-10 %

  (staph aureus, saprophyticus, streptococcus faecalis)
- Aetiology ???

Risk factors

- UTI
- Acute epididymitis.
- Urethral catheters.
- Transurethral surgery
- Intraprostatic duct reflux
- Phimosis
- Prostatic stones

Segmented urine cultures

- Localize bacteria to specific part of the urinary tract.
- first voided 10ml ---------- urethritis & prostatitis VB1
- Midstream urine ----------cystitis VB2
- Prostatic massage
- 10 ml post massage---------- prostatitis VB3
- EPS ---------- prostatitis

Classification

- Class 1: acute bacterial prostatitis
- Class 2: chronic bacterial prostatitis.
- Class 3: chronic pelvic pain syndrome
  - **3a** inflammatory non-bacterial : wbc in EPS, VB3 or semen.
  - **3b** non-inflammatory : no wbc in Eps , vb3 or semen.
- Class 4: Asymptomatic inflammatory prostatitis

Evaluation

- Class 1: acute bacterial prostatitis
  - E.coli common
  - Associated with LUT infection.

Class 1

- Acute onset fever.
- Chills
- Nausea &vomiting
- Perineal & sp pain
- Irritative urinary symptoms (frequency, urgency, dysuria)
- Obstructive (hesitancy, strangury, UR, intermittency)
- Signs:
- Systemic toxicity
- Suprapubic tenderness.
- Palpable bladder with UR
- Tender DRE

- Systemically well
  - Oral quinolone ciprofloxacin 500 BID
  - 2-4 weeks
- Systemically unwell
  - I.V antibiotic
  - Aminoglycoside+3rd generation cephalosporins
  - Pain relief

- Prostatic abscess
  - Persistant symptoms:
  - Fever while on antibiotic.
  - TRUS ???? PAIN
  - Transurethral management

Class2

- Previous history of recurrent UTI
- Chronic episodes of pain & voiding dysfunction
- DRE: tender, enlarged & boggy prostate

Class 3

- Chronic pelvic pain syndrome
- Both types present with:
  - >3 months localized pain.

  (perineal, suprapubic, penile , groin or ext. genitalia)

  Pain with ejaculation.

  LUTS
- ED
- Symptoms can recur over time
- Affect patient's quality of life

Class 4

- Incidental histological Dx in prostate specimens.

Evaluation

- Hx
- NIH- CPI questionnaire:
- Pain (location, severity, frequency)
- Voiding (obstructive , irritative symptoms)
- Impact on quality of life.

Evaluation

- Segmented urine culture & EPS
  - Cultures –ve
  - high Leucocyte count >10/ HPF
  - Favor Dx inflammatory chronic pelvic pain syndrome

Treatment

- Alpha- blockers: improve urinary flow,& reduce intraprostatic ductal reflux
- Anti inflammatory drugs NSAID
- 5 alph reductase inhibitors :improve intraprostatic ductal reflux.
- Microwave heat therapy

Non- inflammatory chronic pelvic pain syndrome

- Treatment:
  - Drugs: analgesia (tricyclic antidepressent, anti inflammatory, muscle relaxants, 5- alpha reductase inhibitors
  - Biofeedback.
  - psychological

Thank You