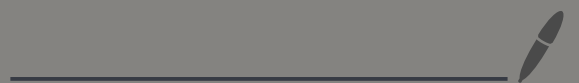
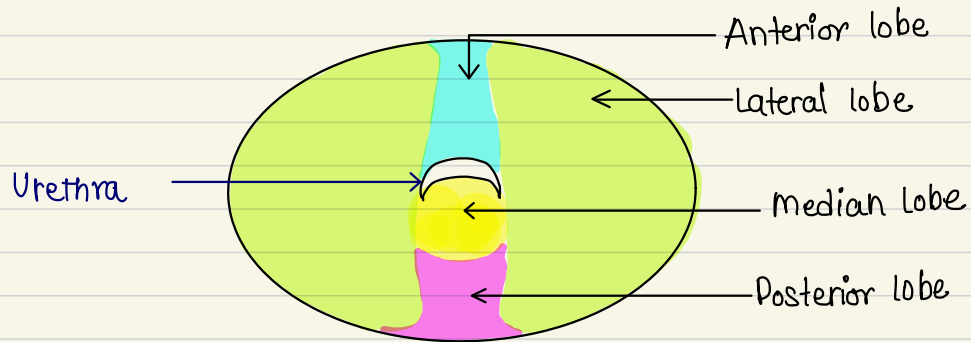


Prostate



Anatomy

• Lobes



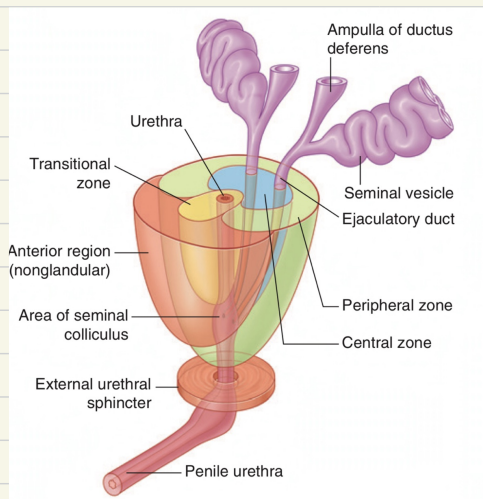
- Anterior Lobe
 - Without glandular part
 - Also called isthmus.

- Median Lobe
 - Anteriorly - Prostatic urethra
 - Posteriorly - Ejaculatory duct
 - Base of median lobe extends into the bladder
 - ↳ Uvula vesicae
 - ↳ Enlarged in BPH - Stagnation of urine

McNeal

• Zones

- Transitional - Surrounds proximal urethra [m/c affected by BPH]
 - ↳ Short unbranched glands
- Central - Surrounds ejaculatory duct [Ca < 2% but highly invasive type]
- Peripheral zone - Surrounds distal urethra [80% of Carcinomas]
 - ↳ Long branched glands
- Anterior fibromuscular zone - Non glandular.



• Blood Supply -

- Middle Rectal art.
- Internal Pudendal art.
- Inferior vesical art.

Prostatic Calculi

- | | |
|---------------------------|--|
| • <u>Endogenous</u> | • m/c composition- Ca PO_4 (m/c prostatic calculi) |
| • <u>Exogenous</u> | • Stone from kidney / Bladder which gets stuck in prostatic urethra (Rare)
Usually incidently detected while doing TURP.
No active treatment required for endogenous stones. |
| • <u>Corpora Amylacea</u> | • Tiny Calcified lamellated bodies found in glandular alveoli of prostate.
• Precursor lesions for prostatic stones |



Prostatitis

• <u>Acute Bacterial</u>	• <u>Organisms</u> - E. coli • Staphylococcus • Streptococcus faecalis • Neisseria Gonorrhoe • Chlamydia
• <u>C/E</u>	• Fever • Perineal Pain • Digital Rectal exam - Tender boggy prostate ↳ Massaging may lead to Septicemia.
• <u>Mx</u>	Antibiotics for at least 2-3 weeks.
• <u>Chronic Bacterial</u>	• <u>Aetiology</u> ↳ Sequela of inadequately treated acute prostatitis. ↳ Chlamydia • <u>Dx</u> - 3 glass urine test ↳ 1st glass with initial voided sample shows urine containing prostatic threads. • <u>Mx</u> - Antibiotic X 4-6 weeks.
• <u>Abscess</u>	• May cause urinary retention → Suprapubic Catheterisation. • <u>Mx</u> - Abscess should be drained without delay by: a) Perurethral Resection (Unroofing of whole cavity) b) Using a needle via transrectal/perineal route.

Symptoms

• LUTS

Lower Urinary Tract Symptoms

Storage (Irritative Symptoms)

- Frequency [Earliest, M/c]
- Urgency
- Incontinence
- Nocturia
- Pain

Voiding (Obstructive Symptoms)

- Weak Stream
- Hesitancy
- Urinary Retention
- Incomplete emptying
- Post void dribbling

Post Mictural LUTS

- Voiding & Post mictural symptoms are common in Bladder Outlet Obstruction.
- Storage symptoms common in Neurogenic Bladder

Investigations

• <u>Digital Rectal Exam</u>	<u>BPH</u> • Firm • Rubbery • Mucosa mobile	<u>Cancer</u> • Hard • Mucosa fixed
• <u>Urine Examination</u>	Routine & microscopy Look for sugar & blood in urine. Culture & sensitivity.	
• <u>USG - KUB</u>	Gives an idea of Prostate volume size Residual urine in Bladder Status of upper urinary tract (Hydronephrosis)	
• <u>Serum PSA</u>	Prostate specific Antigen - Glycoprotein For patients of 50-69 yrs : • 0-3 ng/ml - Normal / BPH → Pt has prostatic symptoms ↓ No Biopsy needed ↓ Start on BPH Rx. • >3-4 ng/ml - BPH / cancer / Prostatitis ↓ Antibiotics ↓ Repeat PSA after 6 weeks. • >10-15 ng/ml - Locally advanced cancer • >25-30 ng/ml - Metastatic Ca	
	* PSA value is not affected by Digital Rectal Exam * PSA velocity - Change in PSA levels with time. ↳ If >0.75 ng/ml/yr → Indicative of Cancer	

* Free PSA is more sensitive - ↓ in % of free PSA

* BPSA (Nickel); i PSA (intact) ⇒ ↑ in benign conditions

* Pro PSA - ↑ in Cancer

- Biopsy
 - 1) Trans Rectal Ultrasound (TRUS) guided Trucut biopsy - ↳ Traditional / Most common.
 - Minimum 16 biopsies taken
 - Can be done under local anaesthesia
 - Anterior lobe biopsy is difficult
 - ↑ chances of Sepsis.
 - 2) Transperineal biopsy
 - Done under GA.
 - Anterior lobe biopsy easily done
 - ↓ chances of sepsis
 - Indications - 1) Anterior lobe biopsy
2) Raised PSA but negative TRUS guided biopsy.
 - 3) Trans perineal Template - latest

- Uroflowmetry
 - Measure of Urine flow rate (UFR)
 - Accurate measurement - If patient void > 200 cc of urine
 - UFR > 15-20 ml/sec - Normal
 - 10-15 ml/sec - Equivocal
 - < 10 ml/sec - Bladder Outlet obstruction.

- Cystometry
 - Bladder pressure measurement
 - > 80 cm of H₂O - High
 - 60-80 cm of H₂O - Equivocal
 - < 60 cm of H₂O - Normal.
 - ✧ BOO/BPH → High pressure & low flow rate
 - ✧ Neurogenic bladder → Very low pressure & low flow rate.

✧ Marion's Disease (Prostatism Sans Prostate)

- Patient has features of LUTS but prostate is normal.
- Common in young patients.
- Due to hypertrophy of Internal Sphincter.

Prostate specific antigen (PSA)

- ① Prostate specific antigen is a protease produced from the prostatic epithelium secreted in the semen to cleave and liquefy the seminal coagulum formed after ejaculation.
- ② PSA is organ specific. (N) value = 4 ng/ml of plasma.
More than 10 ng/ml is significant.
- ③ PSA elevation occurs not only in carcinoma but also in prostatic hyperplasia & prostatitis. But the increase is much more in carcinoma than in benign conditions.
- ④ 2 Forms $\longrightarrow$ Major, bound form - $\uparrow$ ses in carcinoma
Minor, free form. - $\uparrow$ ses in benign conditions.
- ⑤ PSA density i.e. PSA level/g of prostate tissue is more relevant.
- ⑥ Pro PSA, initial inactive part, whose assessment is more useful in prostatic cancer along with PSA. When PSA = 4 ng/ml form of Pro PSA (-2) assay is useful to decide whether prostate biopsy is essential/not.
- ⑦ PSA is sensitive for carcinoma prostate but not specific
PSA velocity = $> 2 \text{ ng/mL/year}$ [rate of change in PSA in one year]
PSA doubling time = < 12 months [time period when man's PSA doubles]
Free to total PSA ratio = % free PSA < 25
PSA density = $> 0.5 \text{ ng/mL/g}$ Δ assessment of PSA isomers
- ⑧ Serial estimation of PSA is very useful to suspect spread & recurrence after treatment - PSA velocity estimation.
- ⑨ 25% men with PSA = $4-10 \text{ ng/mL}$ show prostate carcinoma.
20% men with (N) PSA = $1-4 \text{ ng/mL}$ will show prostate Ca.
PSA $> 10 \text{ ng/mL}$ suggestive of prostate Ca.

} different forms of PSA

10

PSA > 35 ng/mL - almost diagnostic of advanced Ca of prostate.

11

↓ in PSA after therapy suggests adequate ablation

12

Men aged > 50 yrs & PSA ≥ 3 ng/mL should undergo prostatic biopsy.

Benign Prostatic Hyperplasia (BPH)

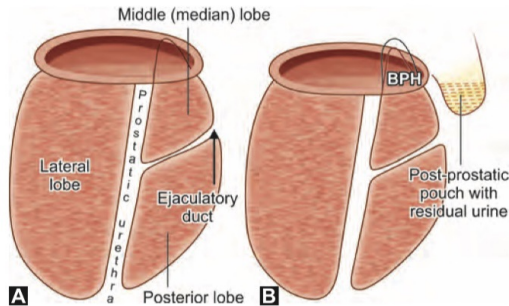
• Starts in 5th decade of life. • Incidence ↑ with age					
• <u>Components</u>	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 50%; text-align: center;"><u>Static</u></th><th style="width: 50%; text-align: center;"><u>Dynamic</u></th></tr> </thead> <tbody> <tr> <td style="vertical-align: top;"> • Due to Stromal Hypertrophy Mediated by DihydroTestosterone • T 5α reductase → DHT </td><td style="vertical-align: top;"> • Due to ↑ smooth muscle tone. Mediated α_{1A} receptors. </td></tr> </tbody> </table>	<u>Static</u>	<u>Dynamic</u>	• Due to Stromal Hypertrophy Mediated by DihydroTestosterone • T 5α reductase → DHT	• Due to ↑ smooth muscle tone. Mediated α_{1A} receptors.
<u>Static</u>	<u>Dynamic</u>				
• Due to Stromal Hypertrophy Mediated by DihydroTestosterone • T 5α reductase → DHT	• Due to ↑ smooth muscle tone. Mediated α_{1A} receptors.				
• <u>Effects</u>	a) Urethra - Prostatic urethra lengthened [2x original length] Distortion of urethra if only one lateral lobe enlarges b) Bladder - Due to BOO, musculature of Bladder Hypertrophies to overcome obstruction & appears trabeculated.				
• <u>IPSS</u>	<u>International Prostate Symptom Score -</u> • 0-7 Mild BPH → Observation & Reassessment • 8-19 Moderate BPH • 20-35 Severe } mx				
<u>Management</u> <u>Medical</u>	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; vertical-align: top;"> a) <u>α_{1A} blockers</u> • Tamsulosine • Alfuzosine • Quick onset (few days) </td><td style="width: 50%; vertical-align: top;"> b) <u>5α reductase inhibitors</u> • Finasteride • Dutasteride • Slow onset (Months) • Sustained effect ↓ In 6 months <table style="width: 100%;"> <tr> <td style="width: 50%; text-align: center;"> 25-30% Reduction in Prostatic volume </td><td style="width: 50%; text-align: center;"> 50% reduction in PSA </td></tr> </table> </td></tr> </table> * Combination of both provides best medical management.	a) <u>α_{1A} blockers</u> • Tamsulosine • Alfuzosine • Quick onset (few days)	b) <u>5α reductase inhibitors</u> • Finasteride • Dutasteride • Slow onset (Months) • Sustained effect ↓ In 6 months <table style="width: 100%;"> <tr> <td style="width: 50%; text-align: center;"> 25-30% Reduction in Prostatic volume </td><td style="width: 50%; text-align: center;"> 50% reduction in PSA </td></tr> </table>	25-30% Reduction in Prostatic volume	50% reduction in PSA
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* If a patient is on 5α reductase for 6 months

↳ PSA value is calculated by multiplication with 2.

Pathology

- ◆ BPH usually involves median and lateral lobes or one of them.
- ◆ It involves adenomatous zone of prostate, i.e. submucosal glands.
- ◆ Median lobe enlarges into the bladder.
- ◆ Lateral lobes narrow the urethra causing obstruction.
- ◆ *Urethra above the verumontanum* gets elongated and narrowed.
- ◆ *Bladder* initially takes the pressure burden causing *trabeculations*, *sacculations* and later *diverticula* formation.
- ◆ Enlarged prostate compresses the prostatic venous plexus causing congestion, called as *vesical piles* leading to *haematuria*.



Figs 26.109A and B: (A) Prostate anatomy; (B) Retention of urine in bladder due to BPH.

- ◆ Incrimination of BPH as the source of haematuria before excluding other causes is termed as “*Decoy prostate*”.
- ◆ *Kidney and ureter:* Backpressure causes *hydroureter* and *hydronephrosis*.
- ◆ Secondary ascending infection can cause *acute* or *chronic pyelonephritis*.
- ◆ Often severe obstruction can lead to obstructive uropathy with *renal failure*.
- ◆ BPH causes *impotence*.

Clinical features

Lower urinary tract symptoms (LUTS)

Symptoms of voiding

- Hesitancy
- Poor flow not improving by straining
- Dribbling even after micturition
- Intermittent stream—stops and starts
- Poor bladder emptying
- Episodes of near retention

Symptoms of storage

- Frequency
- Nocturia
- Urgency
- Urge incontinence
- Nocturnal incontinence

• Surgical

- 75% of improvement in IPSS
- Urine flow rate $\uparrow$ by 9-18% after TURP.

Indications

- 1) Hydronephrosis - **Most important**
- 2) Acute / Chronic Retention of urine
- 3) Recurrent UTI
- 4) Gross haematuria
- 5) Bladder diverticulae secondary to BPH
- 6) flow rate $< 10 \text{ ml/sec}$ & pressure $> 80 \text{ cm of H}_2\text{O}$

• TURP

Trans Urethral Resection of Prostate

- Strips of tissue are cut from bladder neck till verumontanum.
- The chips of prostate are removed by **Ellik evacuator**.
- Following TURP, Haemostasis performed; and a 3 way foley's is used to irrigate till outflow is pale pink.
- This is done to prevent further bleeding from forming clots.
- Catheter is left for 2-3 days.

• Irrigating fluid - To get a clear field of vision

(i) 5% dextrose & distilled water $\rightarrow$ Hypotonic solⁿ
 $\hookrightarrow \uparrow$ Risk of TURP syndrome

(ii) **Isotonic glycine** - **Best irrigating fluid**

(iii) Normal Saline - **Only used in Bipolar TURP (B-TURP)**.

• LASER procedures

- Holmium Laser Enucleation of Prostate (HoLEP)
- Transurethral Laser Incision of Prostate (TULIP)

• Other Surgeries

Rarely done -

- Retropubic prostatectomy (Millin) [superceded by HoLEP]
- Transvesical prostatectomy
- Perineal (Young's)

LASERS used - • **Best** - KTPA green light LASER [532nm]

- Causes vapourisation of tissue
- Haemostatic
- Can be used in patients on anticoagulants

• **M/C** - Ho:YAG laser

Complications of TURP

• <u>Haemorrhage</u>	• m/c during surgery. • Due to [• <u>Badenoch</u> arteries [5'o clock & 7'o clock] m/c • <u>Smaller Flock</u> arteries [10'o clock] • Both arteries are branches of Inferior Vesical artery.
• <u>Clot Retention</u>	3 way foleys to prevent this
• <u>TURP Syndrome</u>	Water Intoxication / Dilutional Hyponatremia • Occurs due to absorption of fluid used for irrigation at the time of TURP. (Hypotonic solⁿ) • Can give rise to CCF, Hyponatremia & Haemolysis. • C/E - within 4-6 hrs of surgery • Confusion / Disoriented • Nausea / Vomiting • Mx - a) If serum Na < 120 mEq/L → Severe → 3% Hypertonic Saline [Gradual correction required → Not more than 8-10 mEq/L/day] • Rapid correction → Central Pontine Demyelination / Myelinolysis. • b) If serum Na > 120 mEq/L → Fluid restriction. • Prevention - Use of isotonic glycine as irrigating fluid. faster surgeries (use of LASERS)
• <u>Retrograde Ejaculation</u>	m/c complication overall (60-70%) → Due to Bladder Neck injury
• <u>Incontinence</u>	Injury to external sphincters if surgery extended beyond verumontanum
• <u>Stricture</u>	• m/c site - Bladder Neck • If a large resectoscope is used → m/c site → Meatal Stenosis.
• <u>Reoperation</u>	After 8 years of TURP, 15-18% require reoperation. Reason include technically imperfect primary procedure
• <u>Erectile impotence</u>	- 5% ; usually in patients whose potency is waning

PI-RADS

• <u>PI-RADS 1</u>	Very low (Clinically significant Ca highly unlikely)
• <u>PI-RADS 2</u>	Low (Clinically significant Ca unlikely)
• <u>PI-RADS 3</u>	Intermediate (Equivocal)
• <u>PI-RADS 4</u>	High (Clinically significant Ca likely)
• <u>PI-RADS 5</u>	Very High (Clinically significant Ca very likely)

Prostatic Cancer

Risk Factors

- Increasing age
- ↑ Testosterone exposure
- African american males
- Obesity
- BRCA 2 > BRCA1
- GSTP-1 gene on Chr 11 → M/C gene
- Alcohol
- Smoking

Screening

Starts after 50 years of age · (Annual screening)

- Digital Rectal Exam (DRE)
- PSA
- DRE + PSA (Best modality)

Gleason Score

- Grading for prostatic cancer.
- Find the most common occurring gland type & 2nd most common occurring gland type.
- Grade both types from 1 (well differentiated) to 5 (poorly diff)
- Add both scores → Gleason score
- Min. gleason score - 2 • Max. gleason score - 10

Risk group	ISUP grade group	Gleason score
Low	Grade group 1	≤ 6
Intermediate Favourable	Grade group 2	7 (3+4)
Intermediate Unfavourable	Grade group 3	7 (4+3)
High	Grade group 4	8
High	Grade group 5	9/10

• <u>Staging</u>	• T_x - Primary tumor can't be assessed • T₀ - No evidence of primary tumor • T_i - Tumor not palpable clinically nor visible with imaging. • T_{1a} - Incidental Histological findings in < 5% of tissue resected • T_{1b} - Incidental Histological findings in > 5% of tissue resected • T₂ - Tumour confined within prostate • T_{2a} - involves 1/2 of one lobe or less • T_{2b} - more than 1/2 of one lobe but not other lobes • T_{2c} - involves both lobes • T₃ - Tumor extends through prostatic capsule • T_{3a} - Extracapsular extension (V/L or B/L) • T_{3b} - Invade seminal vesicles • T₄ - Invasion of adjacent structures • N - 1st draining lymph node - Obturator LN • M - M₀ - No Distant metastasis M₁ - M/C to Bone → vertebral column → due to Batson Plexus ↓ M/C - Lumbar vertebrae. osteoblastic > osteolytic
• <u>Partin Table</u>	Tells about risk of recurrence after radical prostatectomy. Takes in account: (a) Serum PSA (b) Clinical stage (c) Gleason score
• <u>d'Amico classification</u>	Tells about risk of recurrence & based on same 3 criterions.
• <u>Jewett & Whitmore Staging</u>	Old staging system.

• Management

a) Early

T_1, T_{2a} with No Mo

<70 years age
>10 yrs expected life span
G₃/G₄/G₅ disease

↓
Radical Prostatectomy

>70 years age
<10 yrs expected life span
G₁/G₂ disease

↓
Active Surveillance

↓
• 3-6 monthly by DRE & PSA

• Radical Prostatectomy

Removal of • Prostate
• Seminal vesicles
• Obturator Lymph nodes
• Iliac LN

• Complications

• Impotence
• Erectile Dysfunction
• Sepsis
• Incontinence

b) Locally advanced

$T_{2b}; T_3; T_4$ with No/N₁ & Mo

<70 years age
>10 yrs expected life span
G₃/G₄/G₅ disease

↓
Brachytherapy

↓
• Iodine ¹²⁵
• Palladium
• 68-70 Gy of RT

↓
Good Response

↓
Observation

↓
Residual disease

↓
Radical Prostatectomy

>70 years age
<10 yrs expected life span
G₁/G₂ disease

↓
Brachytherapy
±
ADT

c) Metastatic Any stage with M₁.

1st line - ADT

• ADT Androgen Deprivation Therapy

a) Surgical Castration - Bilateral Subcapsular orchiectomy

b) Medical Castration -

- LHRH analogues [Goserelin (Zoladex)
Buserelin +
- LHRH antagonist - Degarelix
- Anti Androgens
[Flutamide
Enzalutamide (Xtandi)
Abiraterone (Zytiga)

* Analogues cause initial surge in LH

↓
↑ Testosterone
↓

PSA Flare in 10 days → Antiandrogens prevent this

* Tumor becomes Hormone Resistant in few years

• Hormone Resistant a) Chemotherapy [Paclitaxel
Cabazitaxel

b) Radiotherapy

c) Radio Pharmaceutical therapy

- Used for Hormone Resistant Bony metastasis
- Earlier - Strontium 89
- Now - Radium 223 (acts via α-rays)

d) Sipuleucel T (Provenge)

- T-cell vaccine
- CD54 extract
- Individually created for each patient.

* M/I prognostic factor - Stage of the disease

