Prostate Cancer

- RFs —> **Age** , African American , Family hx, High fat /red meat intake , Obesity .. protective factors —> Vit E
- Origin : glandular >> ***Adenocarcinoma*** … or Stromal >> **epithelial** & **Non epithelial**
- Cytological features : Hyperchromatic enlarged nuclei+ prominent nucleoli + ***basal cell layer is absent***
  ➔ Use high molecular- weight keratin immunohistochemical staining

  - Precursors : 1) Prostatic intraepithelial neoplasia (PIN) / similar to ca in a high grade
    2) Atypical small acinar proliferation (ASAP) / high risk

Symptoms& signs :

- More common in **peripheral zones** —> obstruction appears late —> **asymptomatic** in early stage
- Penetration of the prostatic capsule/ common & perineural space & bladder trigone —> **Obstructive/irritative voiding**
- Bone &lumbar spine —> **bone pain** & symptom of cord compression.
- Direct ***Rectal exam*** —> Induration or nodularity , consistency, size, symmetry, median sulcus ?—> do further investigations
- LAP , signs of cord compression.

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Laps

- Anemia, elevated APT & Serum acid phosphatase
- Azotemia / bilateral ureteral obstruction, extension into the trigone

- **Prostate specific Antigen PSA**

  ➔ Glycoproteins… Produced by normal & malignant tissue —> Liquefies the semen & dissolves the cervical mucus.
  ➔ It's a diagnostic , screening tool & for risk-stratifying —> the higher the value , the higher the risk
  ➔ You can say roughly … Normal is **< 4 ng/ml** —> actually there is no normal value .. it depends !
  ➔ Can be false positive for : BPH, Trauma, Iatrogenic, Prostatitis.
  ➔ Can be false negative for : 5α-reductase inhibitors (finasteride) , high BMI, Hemodilution.
  ➔ Attempts a t refining PSA have included:

PSA velocity/ kinetics

- the rate of change by time
- PSA increases by 0.75ng. /ml . year —> cancer !
- Very rapid PSA increases—> prostatitis

PSA density

- *Ratio of PSA to gland volume*
- *PSA > 0.1 or 0.15*
- *require TRUS*

PSA isoforms

-low Free/ total PSA —> can suggest pCA
- ratio < 20% , Total > 10

- **Prostate cancer antigen 3 (PCA3)**
  ➔ noncoding, prostate-specific mRNA … 75% accuracy

➢ Low-risk	PSA =< 10ng/ml	Gleason =< 6	T1 & T2a
➢ Moderate-risk	PSA 10-20 ng/ml	Gleason =7	T2b
➢ High-risk	PSA >20 ng/ml	Gleason 8-10	T2c

Diagnosis & Evaluation :

Do PE & laps ? —> ***Prostate biopsy*** —> Most definitive dx :

- By TRUS , take 6 biopsies under GA, local analgesia …… or 12 biopsies—> supersaturated biopsy
- Complications: Hematospermia, hematochezia, and hematuria

Grading and staging

1) ***Gleason system***
   - ➔ According the *glandular architecture* under the microscope —> **Grade** 5 out of 5
   - ➔ Take two grades from 5 (primary & secondary grades) according to the most commonly observed
   - ➔ Take the sum —> get the **score** from 10
   - ➔ 2–4 mild differentiated, 5–7 moderate differentiated, 8–10 poorly differentiated.

2) ***TNM***
   - ➔ Depends on TRUS and DRE Only
   - ➔ clinical T stage —> is a relatively weak prognostic factor.

Stage	Definition
Primary tumor	
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Clinically, the tumor is neither palpable nor visible with imaging
T1a	Tumor is an incidental histologic finding in 5% or less of tissue resected
T1b	Tumor is an incidental histologic finding in more than 5% of tissue resected
T1c	Tumor identified with needle biopsy (eg, because of an elevated PSA level)
T2	Tumor confined within the prostate
T2a	Tumor involves one-half of one lobe or less
T2b	Tumor involves more than one-half of one lobe but not both lobes
T2c	Tumor involves both lobes
T3	Tumor extends through the prostate capsule
T3a	Extracapsular extension (unilateral or bilateral)
T3b	Tumor invades seminal vesicle(s)
T4	Tumor is fixed or invades adjacent structures other than seminal vesicles: bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall
Regional lymph nodes	
NX	Regional lymph nodes were not assessed
N0	No regional lymph node metastasis
N1	Metastasis in regional lymph node(s)
Distant metastasis	
MX	Distant metastasis cannot be assessed (not evaluated with any modality)
M0	No distant metastasis
M1	Distant metastasis
M1a	Nonregional lymph node(s)
M1b	Bone(s)
M1c	Other site(s) with or without bone disease

Imaging

1) TRUS —> as Hypoecheoic region in periphery
2) ***Multi parametric MRI*** —> highest accuracy
3) Axial imaging (CT, MRI) —> for staging
4) Bone scan
5) Antibody imaging —> PSMA & SPECT

- ➔ Most guidelines recommend screening >50 years
- ➔ Every 2-3 years for men with PSA <1ng/dl

Treatment

- based on the ***grade and stage*** of the tumor, the ***life expectancy*** of the patient, its associated morbidity.

1) ***Watchful waiting & surveillance***
   - ➔ 89yrs old, high PSA , Gleason 10 , low life expectancy < 10 yrs, no Metz —> **Waiting & Observe**
   - ➔ By serial DRE & PSA assessments every 6 months, follow-up TRUS-guided biopsies /1 year —> **Surveillance**
   - ➔ Cancers are usually treated at the first sign of subclinical progression

2) ***Radical Prostatectomy***
   - ➔ Lymph node dissection, seminal vesicles , the entire prostate is excised, by laparoscopes —> T1-T2 , N0M0
   - ➔ PSA should fall to undetectable levels within ***6*** weeks of surgery in most cases.
   - ➔ For ? Life expectancy>10, Tumor confined to prostate (T1-T2), Moderate differentiation, PSA < 20

3) ***Cryosurgery***
   - ➔ for localized CaP, less invasive.
   - ➔ Freezing of the prostate is carried out by using a multiprobe cryosurgical device/ Radiotherapy

4) ***Focal therapy***
   - ➔ For multifocal lesions (cancerous glands interspersed with normal ones)

5) ***Hormone (androgen deprivation) with Radiotherapy***
   - ➔ Mostly are androgen dependent/ receptors(testosterone)
   - ➔ For pt with ***metastatic*** disease, Or low grade& pt 89yrs , with low life expectancy+Metz —> ADT+ &Radio/chemo
   - ➔ So … use a LHRH agonists : ***goserelin acetate***, ***triptorelin pamoate***, ***histrelin acetate***, ***leuprolide acetate***.
   - ➔ Or … use a LHRH antagonist : Degarilex , Estrogen
   - ➔ in cases of METASTASIS: bilateral orchiectomy/ same effect of ADT
   - ➔ Taxane-based chemotherapy : docetaxel, cabazitaxel
6) ***Open prostatectomy*** : is contraindicated ! ❌