

- Prostate: a gland that is located at the base of the bladder surrounding the prostatic urethra.
- It consists out of lobes and zones (3 zones >> the transitional periurethral zone, peripheral zone, and the central zone).
- Most of the prostate ca cases occur in the **peripheral zone** while 20% of it occurs in the transitional zone and very little percentage occurs in the central zone.
- Growth is hormonal dependent >> mainly **DHT**.
- It produces 25% of the seminal fluid / prostatic fluid mainly contains >> prostaglandins, acid phosphatase, PSA (prostate specific antigen)
- PSA: enzyme that splits the semenogelin and liquifies the semen / **PSA structure: Glycoprotein / member of the tissue kallikrein family (proteases)**
- Asymptomatic in 70% of the cases** (bcz it's mainly in the peripheral zone away from the urethra) >> incidental finding or screening.
- Screening (PSA) usually done after 51 yo unless there are risk factors, we start at 45 or even after 40 if there's strong family Hx
- Prostate Ca is adenocarcinoma in 95% of the cases.

Approach:

- Risk factors: **male > 50 yo**, **African Americans**, **family Hx**, smoking, long standing high androgen level, certain genetic mutations (BRCA2, P53 inactivation, C-myc activation) / **Note: BPH isn't a RF**
- Presentation: Asymptomatic (70% of cases), hematuria, LUTS, renal failure, symptoms of metastasis (bone pain, SOB, lymphadenopathy...)
- Examination: pallor, cachexia, lymphadenopathy, **DRE (Asymmetrical hard nodules, obliterated median sulcus, adherent rectal mucosa)**

Investigations:

- Labs** >> Basic (CBC, KFT, UA and culture) and **Tumor marker PSA** (elevated in prostate Ca bcz of **architectural distortion**)

PSA >> inc in BPH, prostate Ca, prostatitis, trauma, any manipulation (surgery, cath., biopsy)

- **Total level** (normal below 4 ng/ml, 4-10 elevated, >10 suspicious of malignancy) → If high you should order PSA metrics.

- **Ratio** (free / total) > prostate Ca elevates the bound more than the free > lower ratio > below 20% is suspicious.

- **Velocity** > Increase in PSA over one year >> if more than 0.75 it's suspicious.

- **Density** > total PSA / prostate volume >> if more than 0.15 it's suspicious.

- **Imaging** >> Multi-parametric MRI >> Localization and invasion → And for taking targeted biopsies (most imp.)

- **Biopsy** >> **TRUS guided biopsy** >> gold standard diagnostic tool

- ✓ Method > 12 biopsies are obtained, 6 from each lobe for "Gleason grading system (1-5)", we take the most prominent score for each lobe then we sum the score of both lobes.

- ✓ Complications > Infection (UTI, sepsis), Bleeding (Hematuria, Hematospermia, Rectal bleeding)

- For **staging** >> Bone scan + Abdomen, chest, pelvic CT with contrast.

- Direct spread >> Urinary bladder, seminal vesicle, Vas deferens // very late to the rectum (bcz of the presence of the rectovesical fascia)

- Lymphatic >> internal iliac

- Hematogenous >> 90% to the bone (osteoblastic lesions, elevated ALP), Lung, Brain, Liver.

In clinical practice there's nothing called "Normal PSA level" As it differs from one pt to another.

Random biopsies

Management:

- Mx of prostate ca is dependant on **Risk Assessment**
- Risk assessment is dependent on multiple things such as: Gleason grading system, PSA level ..etc
- Patients are divided into:

Low risk patients:

** Life expectancy less than 10 years >> **Watchful Waiting** (DRE every 6 months and PSA every year)

** Life expectancy more than 10 yrs >>> **Active Surveillance** (PSA / KFT/ DRE every 6 months, Biopsy every 2 yrs and MRI only if there's any progression)

** **Radical Prostatectomy** can also be done (pt preference, inability to follow up ...)

- **Complications of Radical Prostatectomy:** urinary incontinence, impotence, erectile dysfunction, obturator N injury, bladder neck stenosis)

High risk patients:

** No Mets (localized disease) >> **Radical Prostatectomy**

** Metastasis >>> **Androgen Deprivation Therapy = Castration (2 Types)**

- ✓ Surgical castration: Bilateral orchidectomy
- ✓ medical castration: GnRH antagonist / GnRH agonists (LHRH subcutaneous injections)

- **Complications of GnRH agonists** (LHRH injections) >> **Testosterone flare** >> Prevented by **Anti-androgen (Bicalutamide)** started 2 wks before LHRH injection then continued for 2 wks after
- During castration we monitor PSA and testosterone to make sure they are within castration range
- Castration range for Testosterone is below 50 >> If more than this then the tumor is Castration Resistant.
- Mx of Castration Resistant Prostate CA >> continue on androgen depletion therapy + chemotherapy (MC one used in prostate CA: **Docetaxel**), immunotherapy or radiotherapy.
- No need for Anti-androgen when giving other drugs of medical castration.

** If high risk + Mets and causing sever obstructive symptom >> do TURP (palliative)

Risk Group*	Grade Group	Gleason Score
Low/Very Low	Grade Group 1	Gleason Score ≤ 6
Intermediate (Favorable/Unfavorable)	Grade Group 2	Gleason Score 7 (3 + 4)
	Grade Group 3	Gleason Score 7 (4 + 3)
High/Very High	Grade Group 4	Gleason Score 8
	Grade Group 5	Gleason Score 9-10

TNM Staging Categories	
T	T1: No tumor felt on DRE or seen on ultrasound, but cancer cells found in prostate tissue
	T2: Tumor may be felt on DRE or seen on imaging, but it is only in the prostate
	T2a: Involves less than 1/2 of a prostate lobe
	T2b: Involves more than 1/2 of a prostate lobe (but not both lobes)
	T2c: Involves both prostate lobes
N	T3: Tumor has expanded outside the prostate and may have grown into the seminal vesicles
	T4: Tumor has expanded into other nearby tissues, such as the rectum, bladder, or wall of the pelvis
	NX: The lymph nodes have not been checked for cancer
M	N0: There is no cancer in nearby lymph nodes
	N1: Cancer has spread to nearby lymph nodes
	M0: Cancer has not spread past nearby lymph nodes
	M1: Cancer has spread past nearby lymph nodes to distant sites
	M1a: Cancer has spread to distant lymph nodes (outside of the pelvis)
	M1b: Cancer has spread to bones
	M1c: Cancer has spread to distant organs, including lung, liver, or brain