- 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.

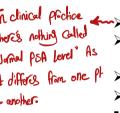
Approach:

- 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.
- if differs fam one pt > 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 thing burgeted 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.



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 ...)
 - <u>Complications of Radical Prostatectomy:</u> 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)
 - <u>Complications of GnRH agonists</u> (LHRH injections) >> <u>Testosterone flare</u> >> Prevented by <u>Antiandrogen (Bicalutamide)</u> 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: <u>Docetaxel</u>), 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	
Т	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 $\frac{1}{2}$ of a prostate lobe	
	T2b : Involves more than $\frac{1}{2}$ of a prostate lobe (but not both lobes)	
	T2c: Involves both prostate lobes	
	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	
N	NX: The lymph nodes have not been checked for cancer	
	NO: There is no cancer in nearby lymph nodes	
	N1: Cancer has spread to nearby lymph nodes	
M	MO: 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	