



PROSTATE





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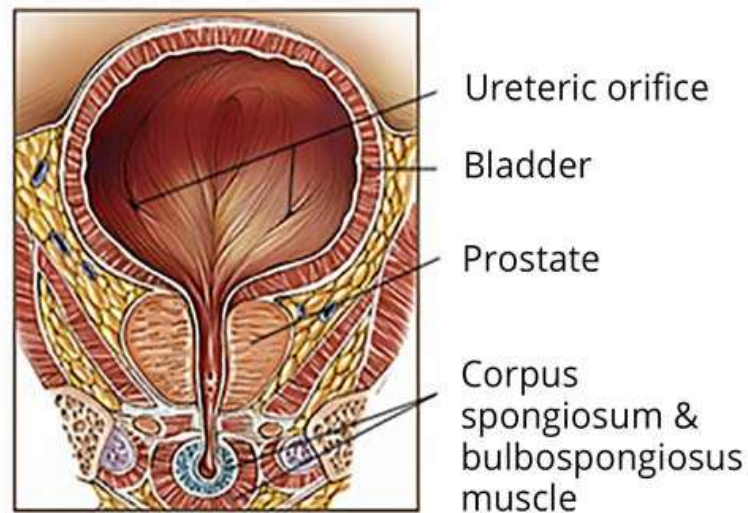
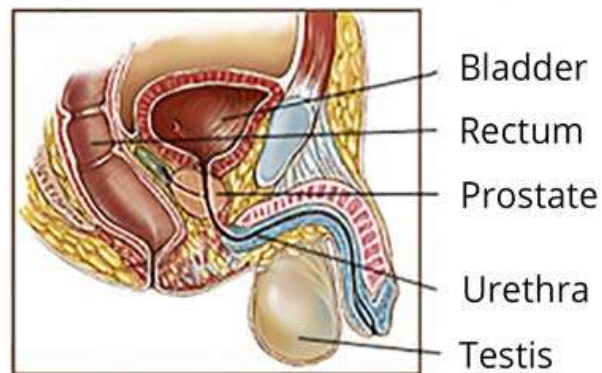
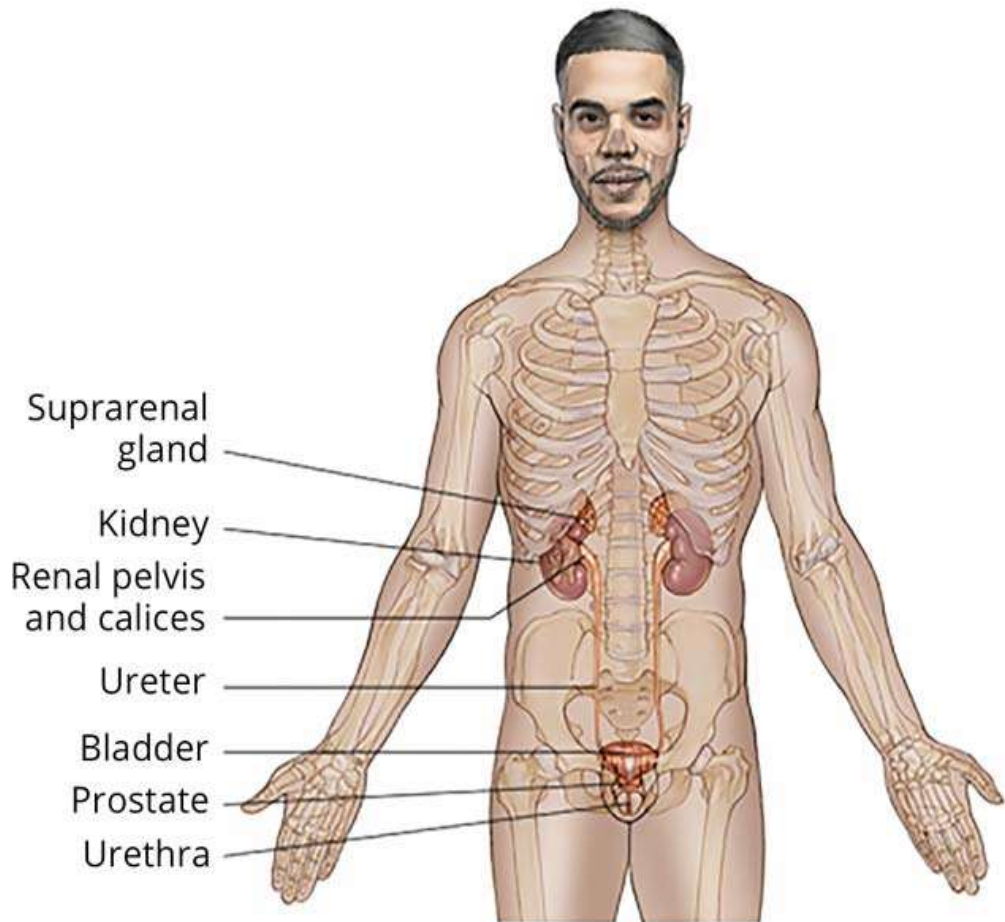
| Prostate

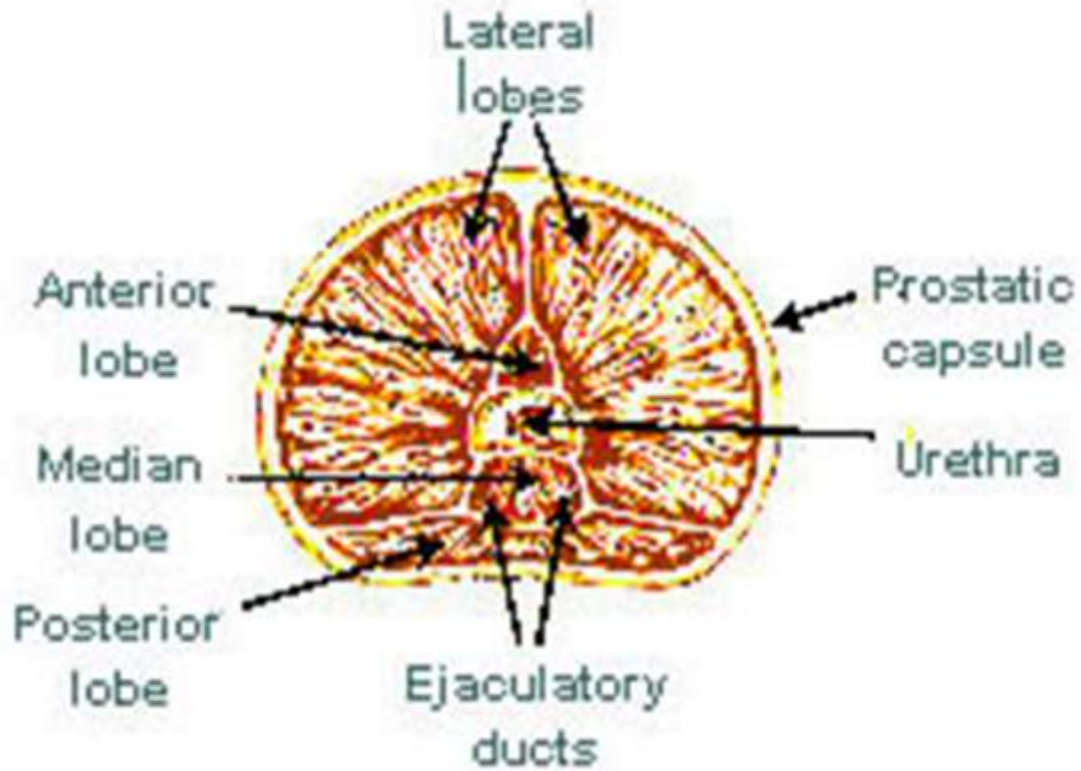
| Adenocarcinoma

Prostate Adenocarcinoma

- **Most common form of cancer in men**
- 2nd most deadly (lung)
- Occur in **peripheral zone PZ (posterior lobe)** of prostate (10-20%)
from TZ , (5-10%) may arise from CZ
- Classically posterior lobe
- Mets to prostate are very rare
- Methods of tumor spread:
 - Local invasion
 - Lymphatic
 - Hematogenous
- **Most common site for metastasis in Prostatic CA is bone (sclerotic lesion; purely osteoblastic)**







Risk factors

- **Age (>65)**
- **African Americans**
- **Family Hx**
 - 1st degree relative = 2X risk
 - 1st and 2nd degree relatives = 9X risk
- **High dietary fat**
- **Familial prostate CA gene**



Clinical features

- Early prostate cancer usually asymptomatic
- If symptomatic:
 - Obstructive symptoms: hesitancy, decreased force and caliber of the stream, sensation of incomplete bladder emptying ,straining to urinate, postvoid dribbling. ◆
 - Irritative symptoms: frequency, urgency , nocturia
- Back pain, incontinence
- Bone pain (metastasis)
- Leg pain and edema (nodal metastasis ; lymphatic and venous obstruction)

Urethra



Normal prostate
(posterior view)



Normal urine flow



Restricted urine flow

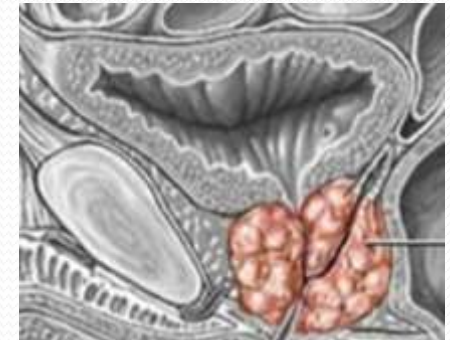
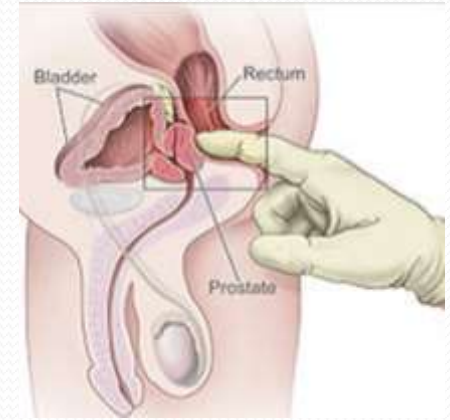
L.A. Rowley
MPC 2001

Prostate Adenocarcinoma

- **Investigations and Diagnosis:**

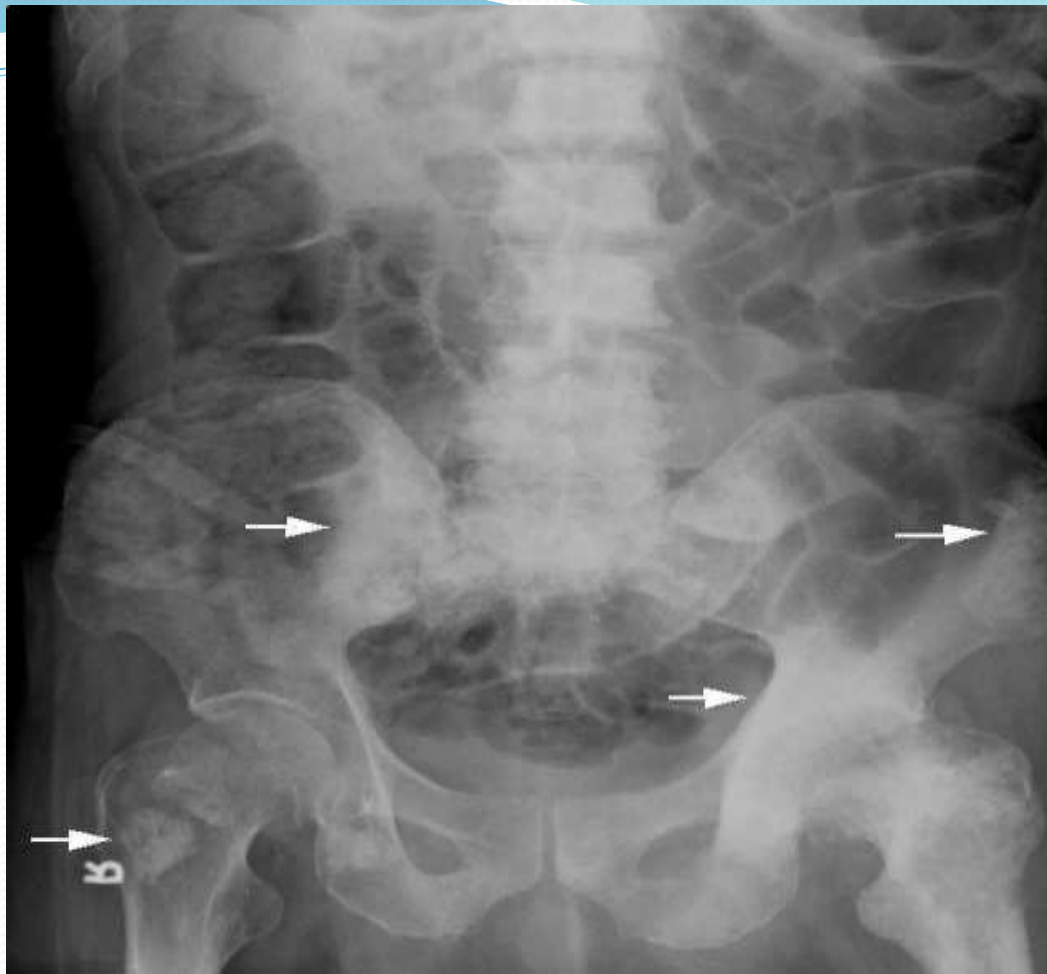
- Digital rectal exam (DRE) ; **findings:**
 - Nodularity with heterogenous texture
 - Stony Hard irregular surface
 - Absence of median sulcus
 - Asymmetry
 - Tethered rectal mucosa

50% of abnormal DREs are associated with prostate cancer, the remainder being benign hyperplasia, prostatic calculi, chronic prostatitis, or post-radiotherapy change



- Elevated PSA (not prostate cancer-specific)
 - Most PSA bound to protease inhibitors in blood:
 - Antichymotrypsin
 - Macroglobulin
 - Can measure % free versus bound PSA
 - Prostate cancer produces more bound PSA
 - ↑ total PSA with ↓ % free PSA
- Bone scan and CT scan to assess metastasis



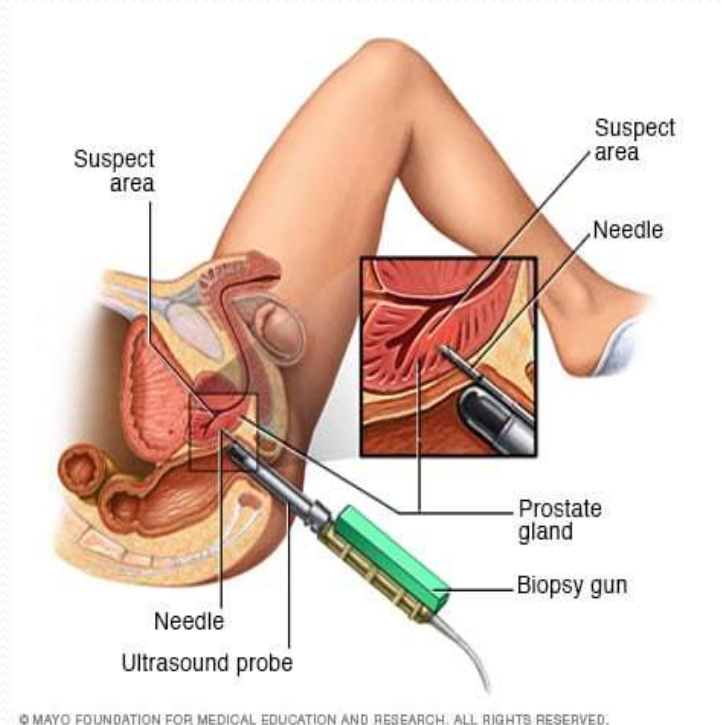


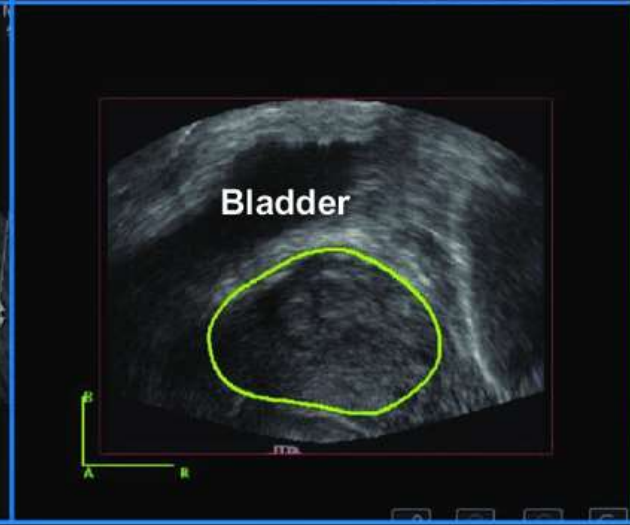
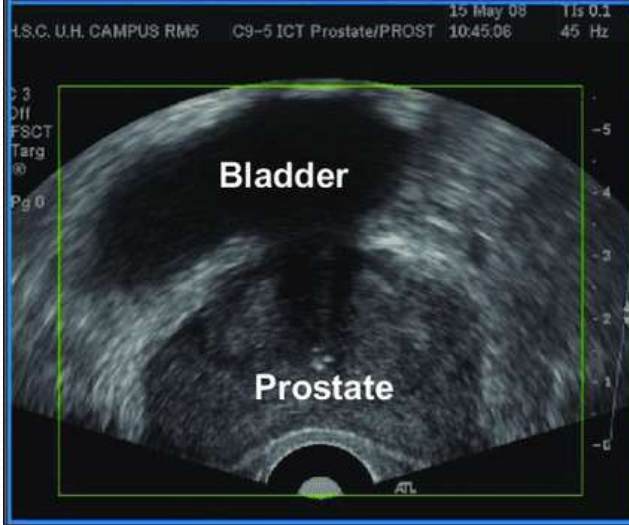
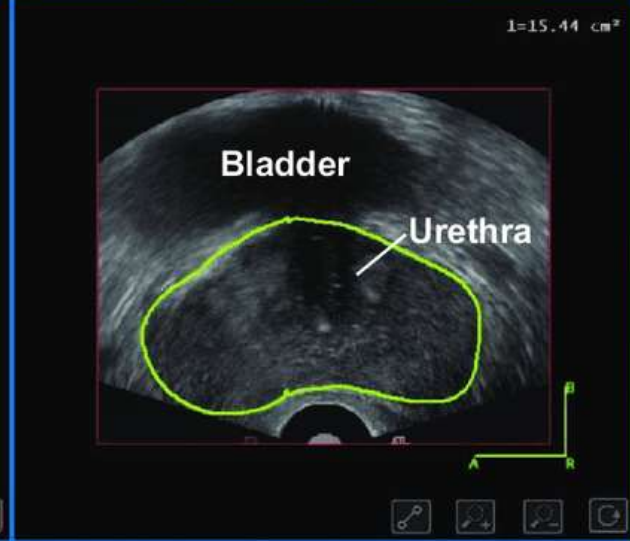
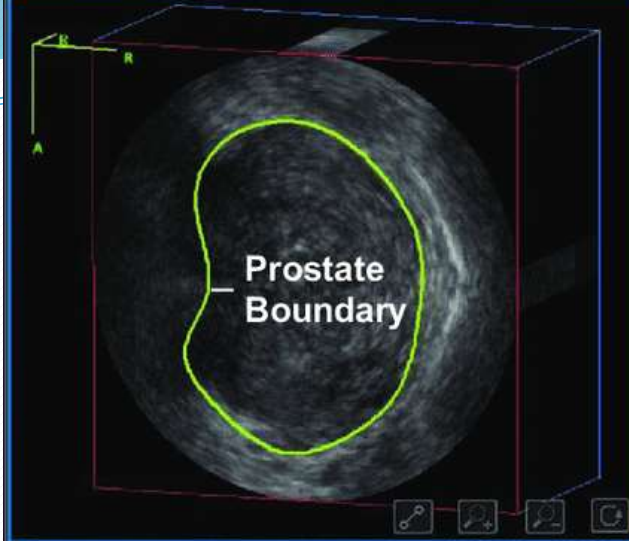
Diffuse osteoblastic bone metastasis

Prostate Adenocarcinoma

- **Investigations and Diagnosis:**

- **TRUS is useful in:**
 - prostatic biopsies under TRUS guidance
 - Staging information (detect extracapsular extension)
 - Measurement of prostate volume.
- **TRUS-guided needle biopsy**
 - Complications of prostatic biopsy
 - Vaso-vagal ,fainting immediately after the procedure.
 - Septicemia.
 - Rectal bleeding.
 - Mild hematospermia or hematuria, for up to three weeks





1=15.44 cm²

15 May 08 11:05 0.1
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3
DII
FSCT
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Staging

- The **TNM system** ; evaluates the size of the tumor, the extent of involved lymph nodes, and any metastasis.
- **Gleason's system (grading)**



Tumor	
T0	No evidence primary tumor
T1	Not detectable on DRE/imaging
T1 a/b	Incidental finding in specimen resected for another reason
T1c	Detected on biopsy for raised PSA
T2	Detectable on DRE/imaging, confined to prostate
T2a	In < one half of one lobe of prostate
T2b	In > one half of one lobe of prostate
T2c	In both lobes of prostate
T3	Spread outside prostate
T3a	Spread to prostate capsule
T3b	Spread to seminal vesicles
T4	Spread to local structures
Nodes	
N0	No spread to nodes
N1	Spread to pelvic nodes
Metastases	
M0	No evidence of spread outside the pelvis
M1a	Spread to distant lymph nodes e.g. para-aortic
M1b	Spread to bone
M1c	Visceral spread +/- bone e.g. liver, lungs

American Joint Cancer Committee prostate cancer staging guidelines

T1



Seminal vesicle

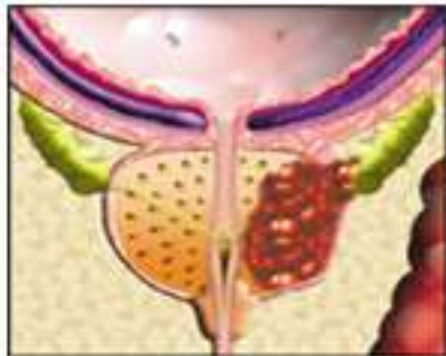
Rectum

External urinary sphincter muscle

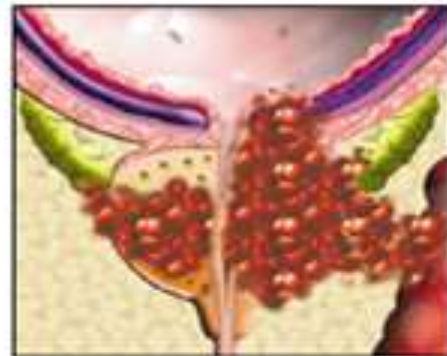
T2



T3



T4



Gleason's system

It is a system that relies upon the low-power appearance of glandular architecture under the microscope.

Primary grade - assigned to the dominant pattern of the tumor (has to be greater than 50% of the total pattern seen). ◆

Secondary grade - assigned to the next-most frequent pattern (has to be less than 50%, but at least 5% of the pattern of the total cancer observed).

Gleason sum : is the addition of the primary and secondary glandular patterns present on microscopic examination

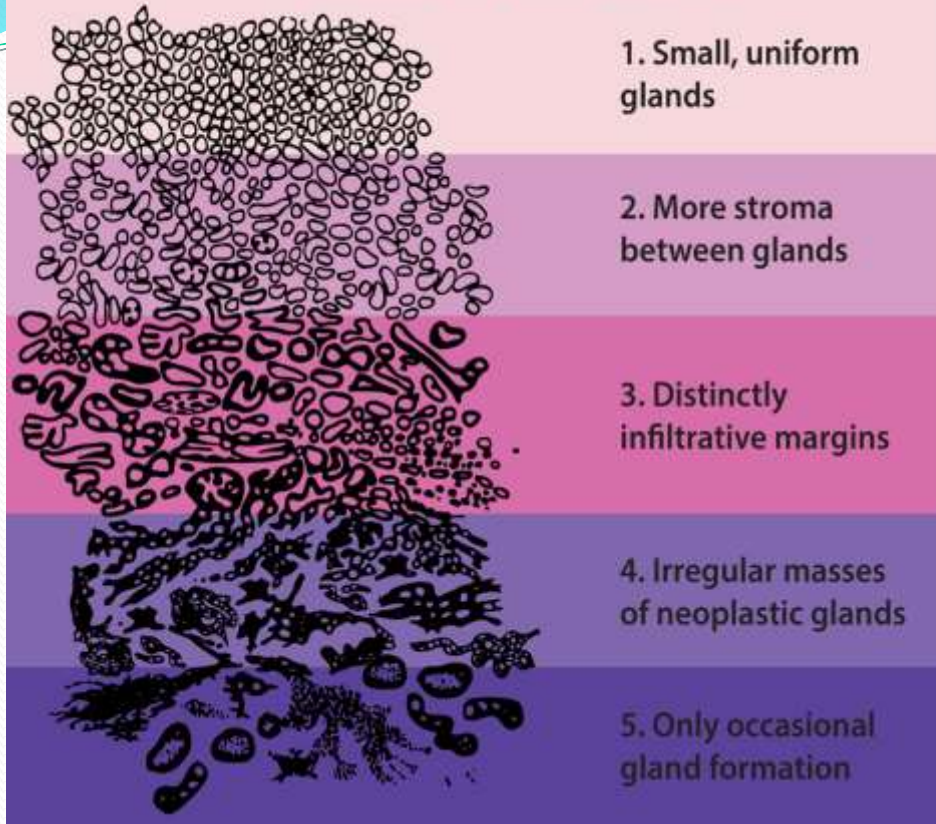
Higher Gleason score are more aggressive and have a worse prognosis.

e.g.

a Gleason $3+3 = 6$ adenocarcinoma carries a worse prognosis than a $3+2 = 5$ cancer of equivalent stage.

A Gleason $4+3=7$ adenocarcinoma carries a worse prognosis than a $3+4=7$ cancer of equivalent stage.

Gleason's Pattern



Well
differentiated

Moderately
differentiated

Poorly
differentiated/
Anaplastic

tumor grade (Gleason score out of 10)

- **2-4** represent **well differentiated**
- **5-7** represent **moderately differentiated**
- **8-10** represent **poorly differentiated**

Prostate cancer mortality risk

➤ **Prognostic factors :**

Tumor stage, grade , PSA value and PSA doubling time

	Low risk	Moderate risk	High risk
PSA	<10	10-20	>20
Gleason score	<7	7	8-10
stage	T1-2a	T2b-T2c	T3/4

Prognosis

- **T₁-T₂: comparable to normal life expectancy**
- **T₃-T₄: 40-70% 10-yr survival**
- **N₊ and/or M₊: 4 % 5 year survival**



General principles of management of localized prostate cancer

When considering treatment options for the man with localized prostate cancer, the following factors should be considered in the discussion:

- Patient's life expectancy and overall health status
- Tumor characteristics, including Gleason score, tumor stage, PSA levels, PSA velocity and PSA doubling times
- Risk stratification



Treatment protocol of prostate cancer

- If life expectancy <10 years, Watchful waiting
- If life expectancy > 10 years, asses the risk



Treatment

➤ **Low risk**

Active surveillance, PSA and biopsy every 6 months - 1 year

➤ **intermediate risk**

Without metastasis: Radical prostatectomy



With metastasis: Short course ADT (androgen deprivation therapy) then Radiotherapy

➤ **High risk:**

Localized: Radical prostatectomy + EBT (extra beam radiotherapy)

Locally advanced: Neoadjuvant hormonal + EBT

Metastasis: Hormonal therapy (LHRH agonist injection every 1-3 months or surgical castration (bilateral orchiectomy))

watchful waiting and active surveillance

Watchful waiting is based on the premise that some patients **will not benefit** from definitive treatment of the primary prostate cancer .

Active surveillance is based on the concept that some, but not all patients **may derive benefit** from treatment of their primary prostate cancer.

Advantages of active surveillance include avoidance of possible side effects and costs of definitive therapy that may be unnecessary, and maintaining quality of life.

Disadvantages include possibly missing an opportunity for cure, the risk of progression and/or metastasis, increased anxiety, increased physician visits and tests, and causing subsequent treatment to be more aggressive.

watchful waiting and active surveillance

Surveillance protocol (if life expectancy <10 years follow up may be less frequent) is as follows:

- Patients must have clinically localized disease and be candidates for definitive treatment and choose observation.
- DRE and PSA as often as every 6 months but at least every 12 months
- Repeat prostate needle biopsy within 6 months of diagnosis if initial biopsy was <10 cores
- Needle biopsy may be performed within 18 months if >10 cores obtained initially, then done periodically

radical prostatectomy

Radical (total) prostatectomy (RP) is excision of the entire prostate, including the prostatic urethra, with the seminal vesicles. It may be performed by open retropubic, perineal, laparoscopic, or robotically assisted laparoscopic approaches. ◆

RP is indicated for the treatment of men in **good health** with localized prostate cancer whose **life expectancy exceeds 10 years**, with curative intent.

Complication of the surgery :

1. intraoperative obturator nerve , ureteral or rectal injury **[early]** ◆
2. it results in high incidence of impotence but a low incidence of severe stress incontinence <2% **[late]**
3. bladder neck stenosis (bladder neck contracture) **[late]**
4. bleeding or infection may happen with any surgery

radical external beam radiotherapy (EBRT)

Indications

clinically localized prostate cancer
life expectancy >5 years.



Contraindications

- Severe lower urinary tract symptoms (risk of radiation cystitis)
- Inflammatory bowel disease (risk of radiation proctitis)
- Previous pelvic irradiation

brachytherapy (BT)

This is ultrasound-guided trans perineal implantation of **radioactive seeds**.

- **Indications for BT as monotherapy** ◆
BT is best for low-risk disease: localized T₁-2a, Gleason <6, PSA <10 ng/ml prostate cancer, with a life expectancy >5 years.
- **Indications for BT with EBRT**
 - In the non-protocol setting, patients with intermediate-risk prostate cancer are sometimes treated in combination: T₂b-T₂c, Gleason 7, PSA 10-20 ng/ml.

brachytherapy (BT)

- **Contraindications to BT**

- previous TURP (risk of incontinence)
- large-volume prostate (>60 mg), which causes difficulty with seed placement
- moderate to severe lower urinary tract symptoms (risk of retention).
- High-risk prostate cancer does not do well with BT monotherapy and should not be performed



Cryotherapy and HIFU

- These two **minimally invasive treatments** for localized prostate cancer
- they are viable alternatives to radical surgery or radiotherapy and that they are options for salvage treatment of organ-confined recurrent disease following radical radiotherapy



Cryotherapy

- Cryotherapy, or cryoablation, for prostate cancer is the controlled freezing of the prostate gland. The freezing destroys cancer cells. Cryotherapy is done under anesthesia. This treatment is **for men who are not good candidates for surgery or radiotherapy because of other health issues**. For this procedure, the prostate is imaged and measured. Special needles called "cryoprobes" are placed in the prostate under the skin. The needles are guided by ultrasound, to direct the freezing process. ◆
- **Complications** include ED, urinary retention, stress incontinence, and recto-urethral fistula (rare).

High-intensity focused ultrasound (HIFU)

- HIFU has the potential of **selective destruction** of tissues at depth without damaging intervening structures. Tissue is heated to the point of coagulative necrosis by high-energy ultrasound transmitted to the prostate using a transrectal device. ◆

Hormonal Therapy (androgen deprivation) :

Hormone therapy for prostate cancer is a treatment that stops the male hormone testosterone from being produced or reaching prostate cancer cells since most prostate cancer cells rely on testosterone to help them grow

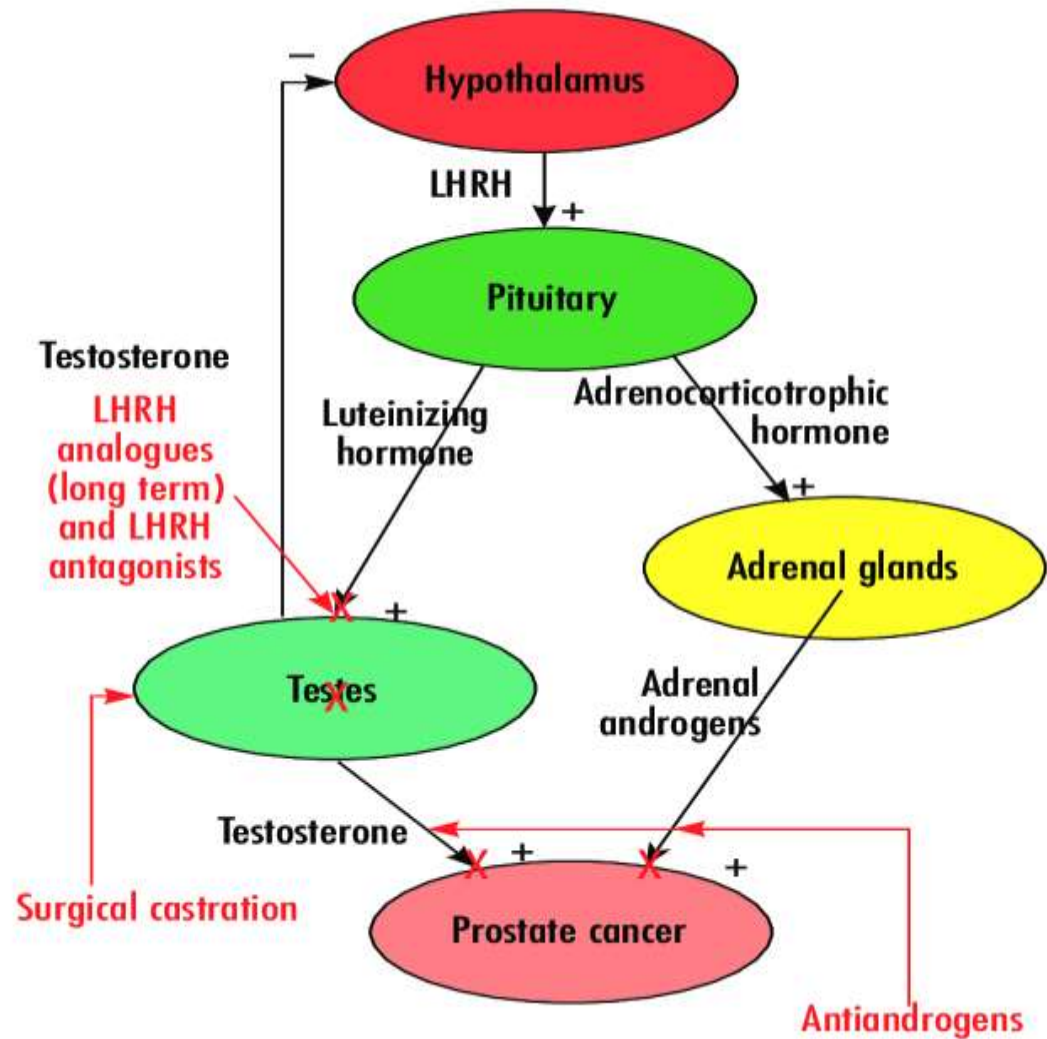
Hormone therapy causes prostate cancer cells to die or to grow more slowly

Androgen deprivation results in a reduction in PSA and clinical improvement in the majority of patients. However, most will still die within 5 years because of the development of **androgen-independent growth**

Hormonal Therapy (androgen deprivation) :

Mechanisms of androgen deprivation :

- **Surgical castration:** bilateral orchiectomy
- **Medical castration:** LHRH agonists, LHRH antagonists, estrogens
- **Antiandrogens** (steroidal or nonsteroidal): androgen receptor blockade at target cell
- **inhibitors of steroidogenesis**
- **Maximal androgen blockade (MAB):** medical or surgical castration plus anti-androgen



Hormonal Therapy (androgen deprivation) :

Side effects of bilateral orchiectomy and LHRH agonists/antagonists

- Loss of libido
- Hot flushes
- Weight gain and obesity
- Gynecomastia
- Anemia
- mood changes
- Metabolic syndrome (increased blood glucose and lipid profile)
- Osteoporosis and pathological fracture occur in patients on long-term treatment



Hormonal Therapy (androgen deprivation) :

Predictors of poor hormone therapy response include the following:

- More than 5 metastatic lesions
- Elevated alkaline phosphatase
- Anemia at presentation
- Poor performance status
- Low serum testosterone
- Failure of bone pain to improve within 3 months of treatment
- Failure of PSA to normalize within 6 months of treatment





THANKS