

CARCINOMA OF THE PROSTATE



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CARCINOMA OF THE PROSTATE



- CaP :is now one of the principal medical problems facing the male population.
- In Europe, an estimated 2.6 million new cases of cancer are diagnosed each year.
- In developed countries, about 15% of male cancers are prostate cancer
- In developing countries, about 4% of male malignancies are prostate cancer .

RISK FACTORS



- The risk of developing clinical CaP are not well known.
- Increasing age.
 - The probability of CaP developing in
 - ✦ a man under the age of 40 is 1 in 10,000;
 - ✦ for men 40–59 it is 1 in 103,
 - ✦ and for men 60–79 it is 1 in 8.
- Heredity:
 - If one first-line relative has the disease, the risk is at least doubled.
 - If two or more first-line relatives are affected, the risk increases 5- to 11-fold .
- The exogenous factors such as :
 - alcohol consumption,
 - exposure to ultraviolet radiation
 - and occupational exposure.
- A high content of animal fat in the diet may be important in increasing the risk of developing CaP .

- Possible protective agents for the development of prostate cancer include
 - vitamin E
 - selenium
 - and tomatoes (contain lycopenes, a strong antioxidant).

Pathology



- Over 95% of the cancers of the prostate are **Adenocarcinomas**.
- Of the other 5%,
 - 90% are transitional cell carcinomas,
 - and the remaining cancers are neuroendocrine (“small cell”) carcinomas or sarcomas.

Grading & Staging

- The Gleason grading system is the most commonly used grading system.
- pathologists assign a
 - primary grade to the pattern of cancer that is most commonly observed
 - secondary grade to the second most commonly observed pattern in the specimen.
- Grades range from 1 to 5 .
- If the entire specimen has only one pattern present, then both the primary and secondary grade are reported as the same grade.
- The Gleason score or Gleason sum is obtained by adding the primary and secondary grades together.
- As Gleason grades range from 1 to 5, Gleason scores or sums thus range from 2 to 10.
 - Well-differentiated tumors have a Gleason sum of 2–4,
 - moderately differentiated tumors have a Gleason sum of 5–6,
 - poorly differentiated tumors have a Gleason sum of 8–10.

The staging by TNM staging system.

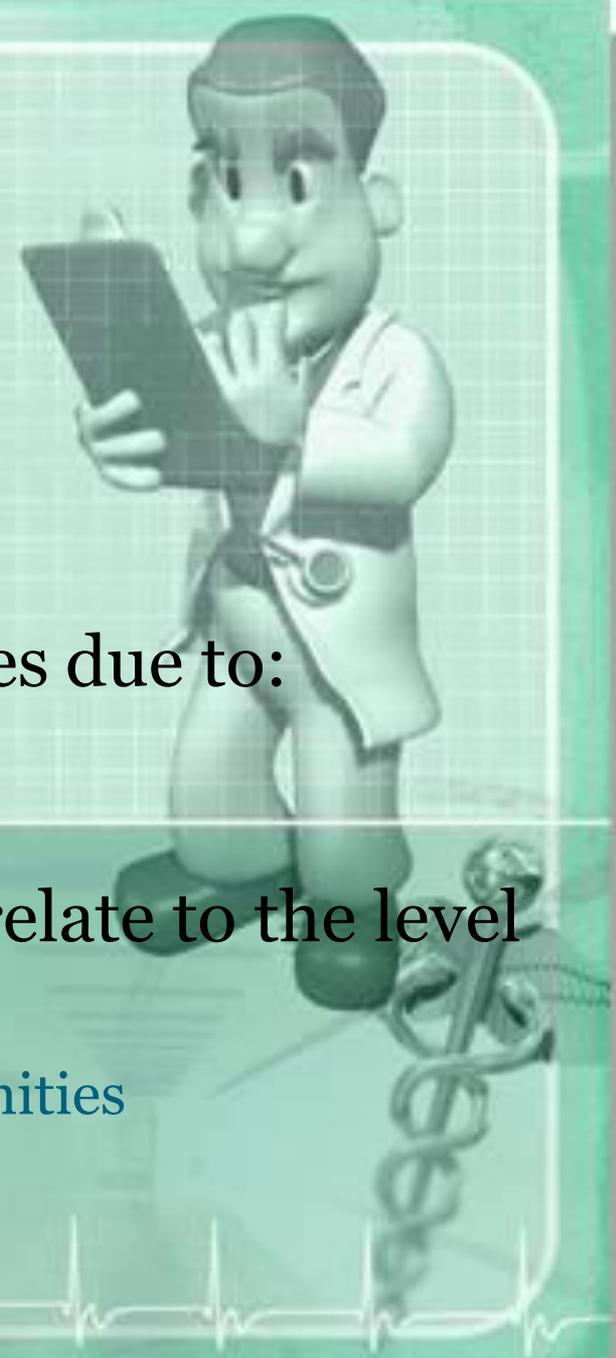
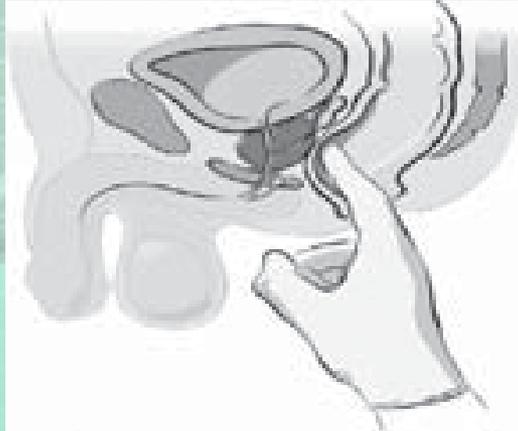
Diagnosis:



A. SYMPTOMS

- Most patients with early-stage CaP are asymptomatic.
- The presence of symptoms often suggests locally advanced or metastatic disease.
- Obstructive or irritative voiding complaints can result from:
 - ✦ local growth of the tumor into the urethra or bladder neck
 - ✦ direct extension into the trigone of the bladder.
- Metastatic disease to the bones may cause bone pain.
- Metastatic disease to the vertebral column may be associated with symptoms of cord compression including
 - paresthesias and weakness of the lower extremities
 - urinary or fecal incontinence.

Diagnosis:



B. SIGNS

- DRE. Induration
- lymphedema of the lower extremities due to:
 - locally advanced disease
 - bulky regional lymphadenopathy.
- Specific signs of cord compression relate to the level of the compression :
 - weakness or spasticity of the lower extremities
 - hyperreflexic bulbocavernosus reflex.

Diagnosis:



C. LABORATORY FINDINGS

1. Renal impairment can result from:
 - bilateral ureteral obstruction either from
 - ✦ direct extension into the trigone
 - ✦ retroperitoneal adenopathy.
2. Anemia may be present in metastatic disease.
3. Alkaline phosphatase = presence of bone Mt.
4. Acid phosphatase = disease outside the prostate.

D. TUMOR MARKERS—PROSTATE-SPECIFIC ANTIGEN (PSA)



- PSA is a serine protease produced by benign and malignant prostate tissues.
 - Normal PSA values are those ≤ 4 ng/mL.
 - PSA is tissue specific but not disease specific (PSA is not specific for CaP, as other factors such as BPH, urethral instrumentation, and infection can cause elevations of serum PSA).
- 1. PSA velocity**—PSA velocity refers to the rate of change of serum PSA. Patients whose serum PSA increases by 0.75 ng/mL/y appear to be at an increased risk of harboring cancer.
 - 2. PSA density**— The ratio of PSA to gland volume is termed the PSA density. The accepted ratio is (0.1-- 0.15).
 - 3. Age-adjusted reference ranges for PSA**—

Age (y)	PSA Normal Ranges (ng/mL)
40–49	0–2.5
50–59	0–3.5
60–69	0–4.5
70–79	0–6.5
 - 4. Racial variations in CaP detection**— American men presented with higher baseline serum PSA and PSA density.
 - 5. Molecular forms of PSA**— Approximately 90% of the serum PSA is bound to alpha-1-antichymotrypsin, and lesser amounts are free or are bound to alpha-2-macroglobulins. The cancers associated with >25% free PSA were more prevalent in older patients.

E. PROSTATE BIOPSY



- should be considered in men with:
 - an elevated serum PSA,
 - a suspicious DRE,
 - or a combination of the two.
- Prostate biopsy is best performed under TRUS .
- Biopsies are taken
 - ✦ throughout the peripheral zone of the prostate,
 - ✦ rather than just sampling an area abnormal on the basis of DRE or TRUS.

G. IMAGING



1. **TRUS**— is useful
 - in performing prostatic biopsies
 - in providing some useful local staging information if cancer is detected.
2. **Endorectal MRI** —
 - improves cancer detection and staging compared to the use of a standard body coil.
3. **Axial imaging (CT, MRI)**— of the pelvis in patients with CaP
 - to exclude lymph node metastases in high-risk patients who are thought to be candidates for definitive local therapy
4. **Bone scan**—
 - When prostate cancer metastasizes, it most commonly does so to the bone.
 - Soft tissue metastases (eg, lung and liver) are rare at the time of initial presentation.
5. **Antibody imaging**—
 - ProstaScint is a murine monoclonal antibody to an intracellular component of the prostate- specific membrane antigen (PSMA), which is conjugated to 111 indium.
 - After infusion of the antibody, single photon emission computed tomography (SPECT) images are usually obtained.

Differential Diagnosis:



- a) Other factors that elevate serum PSA include:
 1. BPH
 2. urethral instrumentation
 3. Prostatitis
 4. vigorous prostate massage.
- b) Induration of the prostate is associated:
 1. chronic granulomatous prostatitis
 2. previous TURP
 3. needle biopsy
 4. prostatic calculi.
- c) Sclerotic lesions on plain x-ray films and elevated levels of alkaline phosphatase can be seen in:
 - Paget's disease
 - ✦ PSA levels are usually normal
 - ✦ and x-ray findings demonstrate subperiosteal cortical thickening.

Treatment



A. LOCALIZED DISEASE (T1 and T2)

1. Watchful waiting and active surveillance—

- ✦ men with very well-characterized,
- ✦ early stage,
- ✦ low to intermediate grade cancer
- are followed very carefully
- treated at the first sign of subclinical progression
- based on serial and regular physical examinations, serum PSA measurements, and repeat prostatic biopsy

2. Radical prostatectomy—

- either perineal or retropubic approach.
- Perioperative complications include
 - DVT, pulmonary embolism, lymphocele , and wound infection.
- Late complications include
 - urinary incontinence
 - impotence.



Treatment



3. Radiation therapy—

• External beam therapy—

- Traditional external beam radiotherapy (XRT) techniques allow the safe delivery of 6500–7000 cGy to the prostate.

• Brachytherapy—

- Currently, with the use of computer software, one can preplan a precise dose of radiotherapy to be delivered by TRUS guidance. Implants can be permanent or temporary (iodine 125)

4. Cryosurgery and high-intensity focused ultrasound (HIFU)—

- Freezing of the prostate by using a multiprobe cryosurgical device.
- HIFU : using a rectal probe. This induces coagulative necrosis of benign and malignant prostate tissue.

Treatment

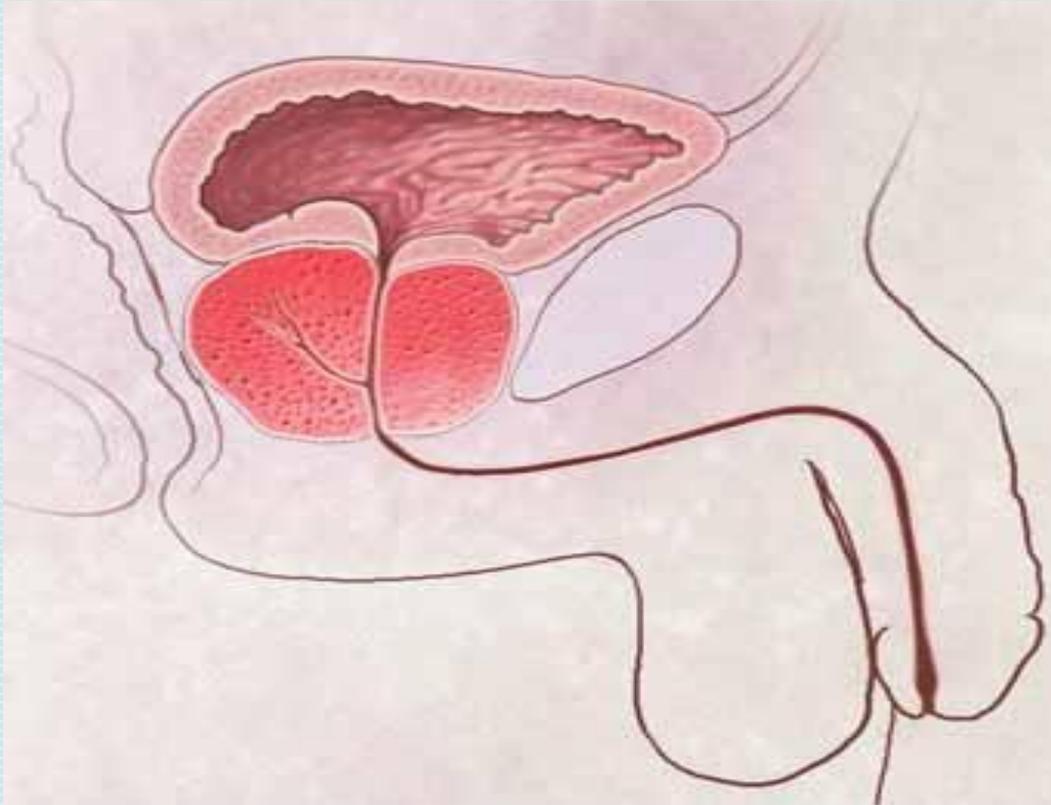


B. METASTATIC DISEASE

Endocrine therapy—

- Most prostatic carcinomas are hormone dependent
- Approximately 70–80% of men with metastatic CaP respond to various forms of androgen deprivation.
- Androgen deprivation may be induced at several levels along the pituitary-gonadal axis.
- Complete androgen blockade: Suppressing both testicular and adrenal androgens.
- Complete androgen blockade can be achieved by:
 - combining an antiandrogen with:
 - ✦ the use of an LHRH agonist
 - ✦ orchiectomy.
- Antiandrogens appear to act by competitively binding the receptor for DHT (e.g. Flutamide)

Prostatitis



Classification of Prostatitis : according to (NIDDK) (NIH).

Class		
1	Acute Bacterial Prostatitis (ABP)	
2	Chronic Bacterial Prostatitis (CBP)	
3	Chronic Pelvic Pain Syndrome (CPPS)	
A	Inflammatory CPPS (chronic non-bacterial prostatitis)	WBC in EPS,VB ₃ ,or semen and NO bacterial isolation
B	Non- Inflammatory CPPS (Prostatodynia)	NO WBC in EPS,VB ₃ ,or semen and NO bacterial isolation
4	Asymptomatic Inflammatory Prostatitis	Histological prostatitis

Acute Bacterial Prostatitis (ABP)



- Refers to inflammation of the prostate associated with a UTI.
- There is edema and hyperemia of the prostatic stroma.
- *E. coli* is the most common causative organism in patients with acute prostatitis.
- Other gram-negative bacteria (*Proteus*, *Klebsiella*, *Enterobacter*, *Pseudomonas*, and *Serratia* spp.)
- enterococci are less frequent pathogens.
- Anaerobic and other gram-positive bacteria are rarely a cause of acute prostatitis.

A. PRESENTATION AND FINDINGS



- ABP frequently affects adult men.
- Patients usually present with an abrupt onset of constitutional symptoms (fever, chills, malaise, arthralgia, myalgia, lower back/rectal/ perineal pain) and LUTS.
- They may also present with urinary retention due to swelling of the prostate.
- DRE reveals tender, enlarged glands that are irregular and warm.
- Urinalysis usually demonstrates WBCs and occasionally hematuria.
- Serum blood analysis typically demonstrates leukocytosis.
- PSA levels are often elevated.
- The diagnosis of prostatitis is made with microscopic examination and culture of the prostatic expressate and culture of urine obtained before and after prostate massage.
- Urethral catheterization should be avoided.
- Bladder ultrasonography may be useful in determining the amount of residual urine. TRUS is only indicated in patients who do not respond to conventional therapy.

Treatment:



- Treatment with antibiotics is essential in the management of acute prostatitis.
 - ✦ Empiric therapy directed against gram negative bacteria and enterococci should be instituted immediately,
 - Trimethoprim and fluoroquinolones have high drug penetration into prostatic tissue and are recommended for 4–6 weeks .
- The long duration of antibiotic treatment is to allow complete sterilization of the prostatic tissue to prevent complications such as chronic prostatitis and abscess formation .
- Hospitalization and treatment with parenteral antibiotics. Ampicillin and an aminoglycoside
 - Patients who have sepsis,
 - in acute urinary retention,
 - or have significant medical comorbidities
- Patients with retention should be managed with a suprapubic catheter.

Chronic Bacterial Prostatitis



- has a more insidious onset,
- characterized by relapsing, recurrent UTI
- caused by the persistence of pathogen in the prostatic fluid despite antibiotic therapy.

A. PRESENTATION AND FINDINGS



- Most patients with CBP typically present with:
 - LUTS and low back/perineal pain.
 - usually are afebrile
 - history of recurrent or relapsing UTI.
- Others are asymptomatic, but the diagnosis is made after investigation for bacteriuria.
- DRE of the prostate is often normal.
- Urinalysis demonstrates a variable degree of WBCs and bacteria in the urine
- PSA levels may be elevated.
- Diagnosis is made after identification of bacteria from prostate expressate or urine specimen after a prostatic massage, using the 4-tubes test .

Treatment:



- Antibiotic therapy is similar to that for acute bacterial prostatitis.
- In patients with CBP, the duration of antibiotic therapy may be 3–4 months. Using fluoroquinolones,
 - some patients may respond after 4–6 weeks of treatment.
- Despite maximal therapy, cure is not often achieved due to:
 - poor penetration of antibiotic into prostatic tissue
 - relative isolation of the bacterial foci within the prostate.
- TURP :has been used to treat patients with refractory disease.