



# Prostatic hyperplasia and cancer prostate

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## Lecture 4

**430 Pathology Team**

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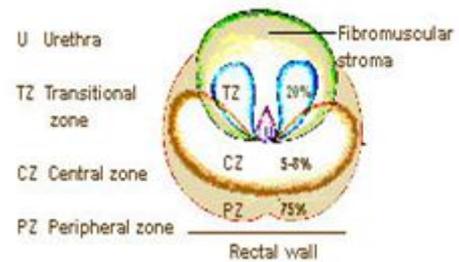
**Red: Doctors' and important notes.**  
**Green: Team notes.**

## Prostate gland:

- Prostate is a tubuloveolar organ **weighs 20 grams** in normal adult.
- Retroperitoneal organ, encircling the neck of bladder and urethra → **can give rise to urinary problems when enlarged.**
- Devoid of a distinct capsule
- Divided into four biologically and anatomically distinct zones or regions: the peripheral, central, and transitional zones, and the region of the anterior fibromuscular stroma
- Histologically normal prostate is composed of glands and stroma. The glands are lined by **two layers of cells**: a basal layer of low cuboidal epithelium covered by a layer of columnar secretory cells (**in malignancies the two layers are lost**)
- It is also normal to see papillary infoldings as well as corpora amylacea.

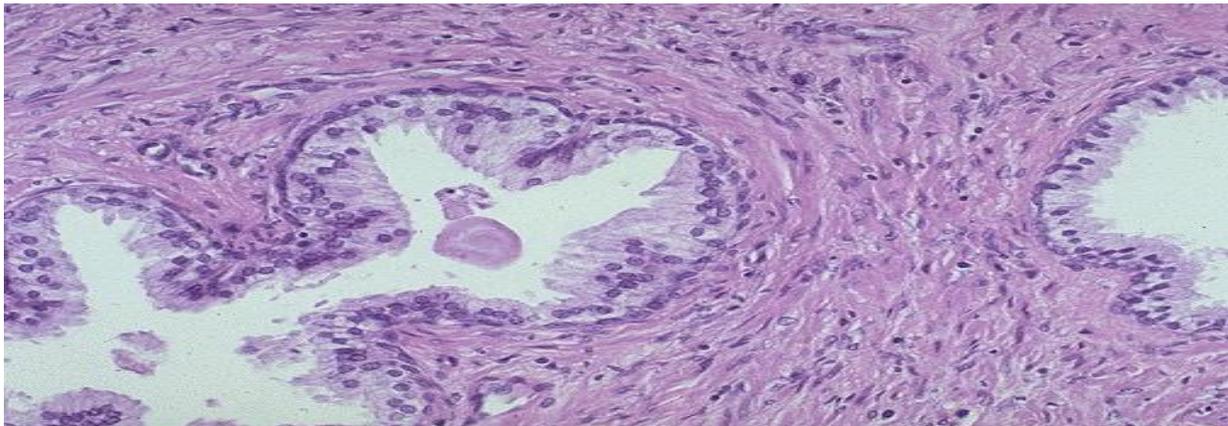
### **Zones of the Prostate:**

- Peripheral: **most carcinomas originate here (don't have urinary symptoms).**
- Central
- Transitional: **most hyperplasias arise here (develop urinary symptom).**



### **Histologically:**

The normal appearance of prostate glands and surrounding fibromuscular stroma



A small pink concretion (typical of the **corpora amylacea** seen in benign prostatic glands) appears in the gland just to the left of center. Note the **well-differentiated glands with tall columnar epithelial lining cells**. These cells **do not** have prominent nucleoli.

### **Two important pathological conditions of the prostate:**

1. Benign prostatic hyperplasia
2. Prostatic adenocarcinoma

## Benign Prostatic Hyperplasia (BPH):

- Extremely common lesion in men over age 50
- Incidence increase with age (20% in men over age 40, up to 70% by age 60, and **90% by age 70**)
- **Hyperplasia of both glands and stroma**

**Etiology:** related to the action of **androgen**. DHT, Dihydrotestosterone is the ultimate mediator for prostatic growth.

- Prepubertal castration (**removing the testicles**) prevents BPH (**because it prevents the androgen production**)

**Treatment: hormonal therapy (anti-androgen)**

**Morphology:**

- The prostate weighs between 60 and 100 grams( normal 20 gm)
- Almost exclusively in the transitional zone of the prostate gland
- Fairly large ,well defined **nodules** ,vary in color and consistency
- The **hallmark of BPH is nodularity** due to glandular proliferation or dilation and to fibrous or muscular proliferation
- Aggregation of small to large to cystically dilated glands
- Needle biopsy doesn't sample the transitional zone where BPH occur (**the transitional zone is in the central portion of the prostate which makes it hard to get there. However, needle biopsy is used in the investigation of prostatic adenocarcinoma because of its location on the peripheral zone**)

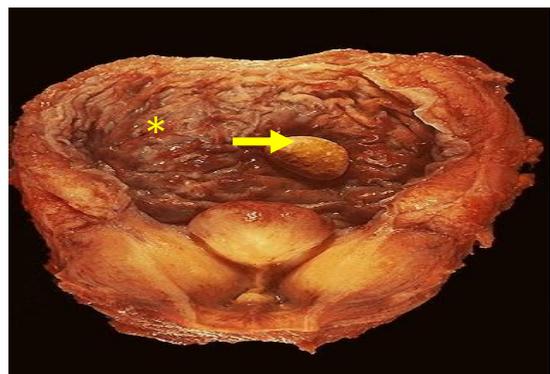


A normal prostate gland is about 3 to 4 cm in diameter. This prostate is enlarged due to prostatic hyperplasia, which appears nodular. Thus, this condition is termed either BPH (benign prostatic hyperplasia) or nodular prostatic hyperplasia



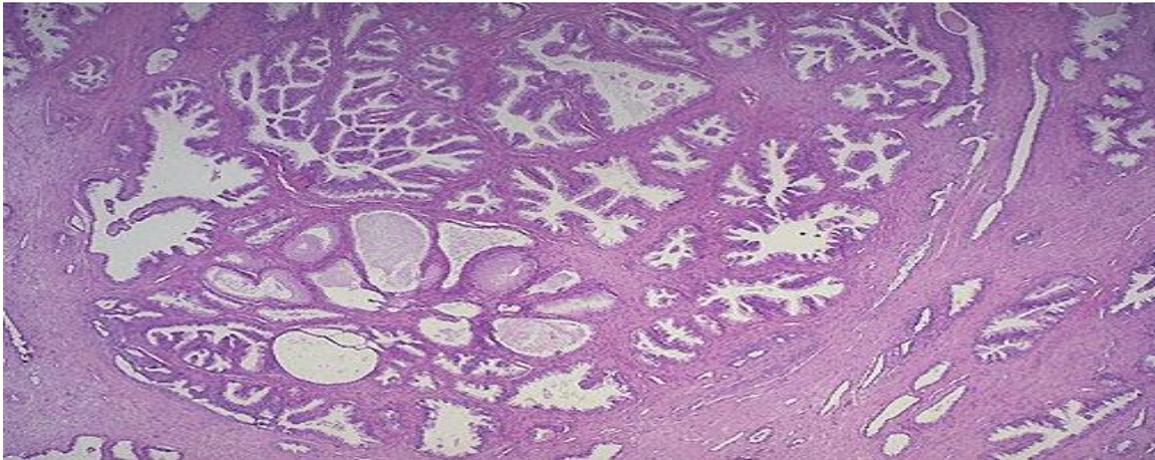
Nodules appear mainly in the lateral lobes. Such an enlarged prostate can obstruct urinary outflow from the bladder and lead to an obstructive uropathy

- The enlarged prostate gland seen here not only has enlarged lateral lobes, but also a greatly enlarged median lobe that obstructs the prostatic urethra.
- This led to obstruction with bladder hypertrophy, as evidenced by the prominent trabeculation of the bladder wall seen here from the mucosal surface (\*).
- Obstruction with stasis also led to the formation of the yellow-brown calculus (stone) (arrow).

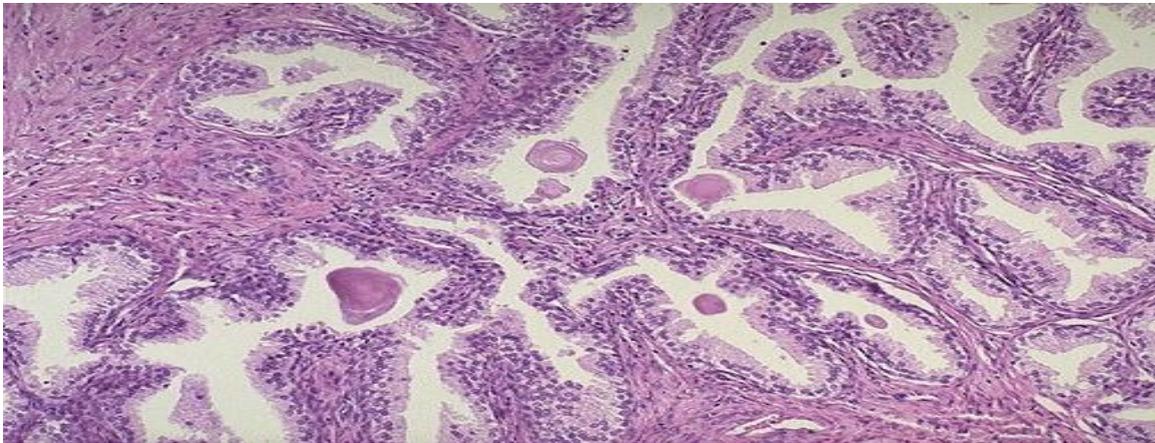


### Microscopically:

- Hyperplasia of both glands and stroma



BPH can involve both glands and stroma, though the former is usually more prominent. Here, a large **hyperplastic nodule** of glands is seen.



The glands are **well-differentiated** and still have **some** intervening stroma. The small laminated pink concretions within the glandular lumens are known as **corpora amylacea**.

**N.B:** presence of stroma is important in benign prostatic hyperplasia, because in prostatic adenocarcinoma the stroma is lost.

### Prostatic Adenocarcinoma:

- Adenocarcinoma of the prostate is the most common form of cancer in men
- **Second leading cause of cancer death (the 1<sup>st</sup> cause of death in men is lung cancer)**
- Disease of men over age 50 (rarely seen in younger age groups)
- More prevalent among **blacks** in the USA

### **Etiology**

- Several risk factors :
- Age, race, family history, hormone level, and environmental influences.
- **Androgen are believed to play a role in the pathogenesis**

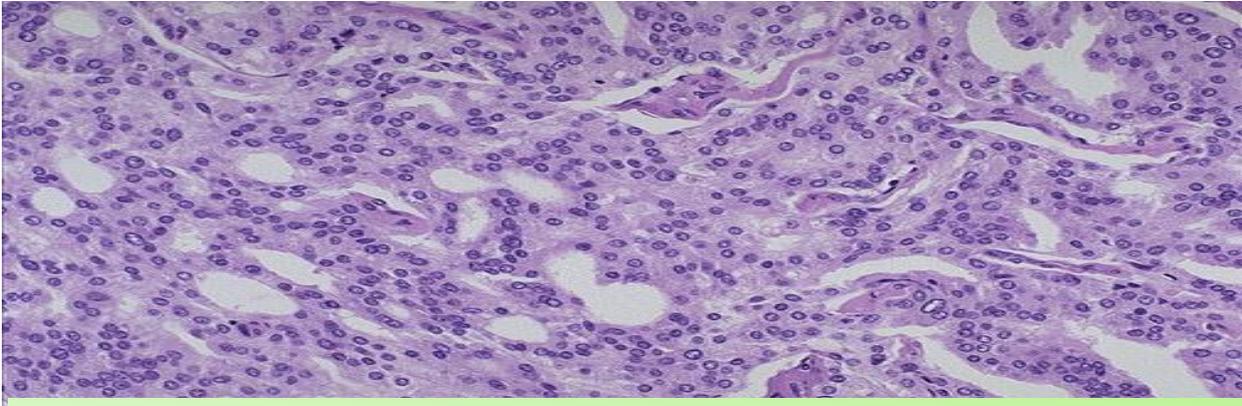
### **Morphology:**

- 70% arises in the peripheral zone of the gland
- Palpable in rectal exam
- cross-section of the prostate the neoplastic tissue is gritty (**resembling stones**) and firm

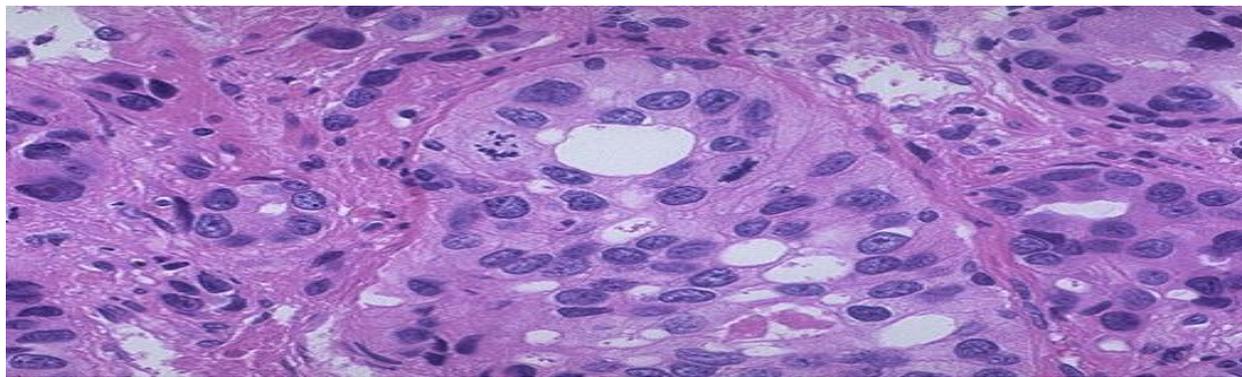


### On gross:

- Irregular yellowish nodules.
- Prostate glands containing adenocarcinoma are not necessarily enlarged.
- Adenocarcinoma may also coexist with hyperplasia.
- **However, prostatic hyperplasia is not a premalignant lesion (hyperplasia doesn't progress to malignancies)**



At high magnification, the neoplastic glands of prostatic adenocarcinoma are still recognizable as glands, but there is no intervening stroma and the nuclei are hyperchromatic.



Poorly differentiated prostatic adenocarcinoma demonstrates cells with nucleoli and mitotic figures.

### Microscopically:

- The glands are typically **smaller** than benign glands and are lined by a **single** uniform layer of cuboidal or low columnar epithelium.
- **Hyper-proliferation of the glands.**
- In contrast to benign glands, prostate cancer glands are more **crowded**, and characteristically lack branching and papillary infolding.
- The **outer basal cell** layer typical of benign glands is **absent**.
- **Nuclei are large** and often contain one or more large nucleoli
- Peri-neural invasion is common and typical. We can also see vascular and lymphatics invasion.

### Spread of prostatic Adenocarcinoma:

- By direct local invasion and through blood stream and lymph
- **Local extension** most commonly involves the seminal vesicles and the base of the urinary bladder
- **Hematogenous** extension occurs chiefly **to the bones**.
- The bony metastases are typically **osteoblastic** (**result in thickening of the bones. Tests to confirm the osteoblastic metastasize are : radiological investigations or high serum alkaline phosphatase**).
- **For your info: majority of cancers metastasize to bones are osteolytic**

### Grading and Staging:

- Gleason grading system is the best known for grading prostatic adenocarcinoma.
- Five grades on the basis of glandular pattern and degree of differentiation as seen under low magnification
- Grading is of particular important in prostate cancer ,because it is the best marker ,along with the stage ,for predicting prognosis
- Staging in prostate cancer depends on the TNM system. (T describes the size of the tumor and whether it has grown into nearby tissues. N describes any lymph nodes involved. M describes metastasis.)

### Clinical Course:

- Microscopic cancers are asymptomatic, discovered incidentally
- Patients with clinically localized disease do not have urinary symptoms
- Most arise peripherally ,away from urethra ,therefore ,urinary symptoms occur late
- Careful digital exam may detect some early cancers
- PSA (Prostate Specific Antigen) has been used in the diagnosis and management of prostate cancer (it is the best screening test performed now). The normal level of PSA should be less than 5 ng/ml. the levels are high in the majority of prostatic cancers. However, it can be increased in BPH as well as prostatitis.
- PSA is organ specific but not cancer specific 20% - 40% of prostate confined cancers have low PSA

### Treatment:

- Surgery ,radiotherapy ,and hormonal therapy
- 90% of treated patients expected to live for 15 years
- Currently the most acceptable treatment for clinically localized cancer is radical surgery
- Locally advanced cancers can be treated by radiotherapy
- Hormonal therapy (Anti-androgen therapy) could induce remission.

## Summary

- Normal weight of the prostate is 20 grams
- **BPH:** arise from transitional zone. Incidence increases with age (90% by age 70) usually present with urinary problems. Microscopically we see proliferation of both glands and stroma. On gross we see nodules. The cause is increase androgen secretion. In investigation we don't perform biopsy because it's unreliable. For treatment we give anti-androgens.
- **Prostatic adenocarcinoma:** arise from the peripheral zone. It is the most common form of cancer in men. 2<sup>nd</sup> leading cause of cancer death, more among blacks. Androgen plays a role in the pathogenesis. Microscopically, hyper-proliferation of the glands only which are lined by a single, the outer basal cell layer is absent. Hematogenous extension occurs chiefly to the bones and it is osteoblastics in nature.
- **Gleason grading system** is the best known for grading prostatic adenocarcinoma.
- **Staging** in prostate cancer depends on the TNM system
- **PSA** (Prostate Specific Antigen) has been used in the diagnosis and management of prostate cancer.

## Questions

1. A 66-year-old man visits his family physician with complaints of urinary frequency, hesitancy, and dysuria. Digital rectal examination reveals an enlarged prostate, and the consistency is rubbery and nodular. Serum prostate-specific antigen is modestly increased. Which of the following is most closely related to the pathogenesis of the likely disorder described here?

- (A) Dihydrotestosterone
- (B) Estrogen
- (C)  $\alpha$ -Fetoprotein
- (D) Human chorionic gonadotropin
- (E) Testosterone

**Answer:** (A) Dihydrotestosterone (DHT) is a major growth factor for prostatic tissue.

2. A 58-year-old African-American man presents to the emergency department with severe back pain. His history is negative for trauma and he has no other complaints. He denies urinary frequency, hesitancy, or dysuria. A digital rectal examination confirms the presence of a firm, hard, asymmetrical, and stony prostate. Imaging of the spine suggests osteoblastic involvement of the spine at lumbar vertebrae L3-L4. In addition to an increase in PSA, which serum marker might also be elevated?

- (A) Alkaline phosphatase
- (B) Androgens
- (C) Carcinoembryonic antigen-125
- (D)  $\alpha$ -Fetoprotein
- (E) Human chorionic gonadotropin

**Answer:** (A) serum alkaline phosphatase is an indicator of osteoblastic lesion in this advanced patient presentation.

**3. A 70-year-old healthy man goes to his physician for a routine check-up. On physical examination there is a firm nodule palpable in the prostate via digital rectal examination. Prostate biopsies are performed and on microscopic examination show small, crowded glands containing cells with prominent nucleoli within the nuclei. Which of the following is the most likely diagnosis?**

- (A) Adenocarcinoma of the prostate
- (B) Benign prostatic hyperplasia
- (C) Chronic prostatitis
- (D) Metastatic urothelial carcinoma

**Answer:** (A) Such a nodule at that age strongly suggests carcinoma. Microscopically, prostatic adenocarcinomas have irregular glands without intervening stroma. Large nucleoli are a characteristic microscopic feature.

**4. A 72-year-old man gets up several times during a football match to go to the restroom to urinate, even though he has had only one beer. This is a problem that has plagued him for several years. When he visits his physician for a checkup, on physical examination he has an enlarged, nodular prostate palpated on digital rectal examination. Laboratory studies show his serum prostate specific antigen is 5 ng/mL. Which of the following pathologic findings is most likely to be present on prostate biopsy in this man?**

- (A) Adenocarcinoma
- (B) Acute inflammation
- (C) Multiple infarctions
- (D) Nodular hyperplasia
- (E) Granulomatous inflammation

**Answer:** (D).BPH is a common finding in older males. And the increasing prostatic urethral obstruction leads to the classic symptoms of frequency and hesitancy with urination. The PSA can be mildly elevated with hyperplasia, but the level tends not to increase significantly over time.