Prostate Pathology

Objectives

- Understand the basic anatomical relations and zones of the prostatic gland.
- Know the epidemiology, pathogenesis and histopathological features of benign prostatic hyperplasia and carcinoma of the prostate.

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Editing File

Color index :
Main text (black)
Female Slides (Pink)
Male Slides (Blue)
Important (Red)
Dr's note (Green)
Extra Info (Grey)

Introducion

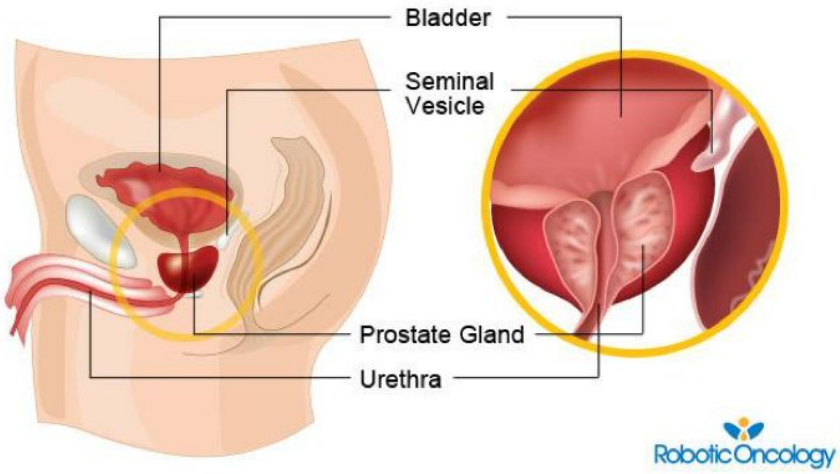
The prostate weighs 20 grams in a normal adult male.
It is a retroperitoneal organ, encircling the neck of bladder and urethra.

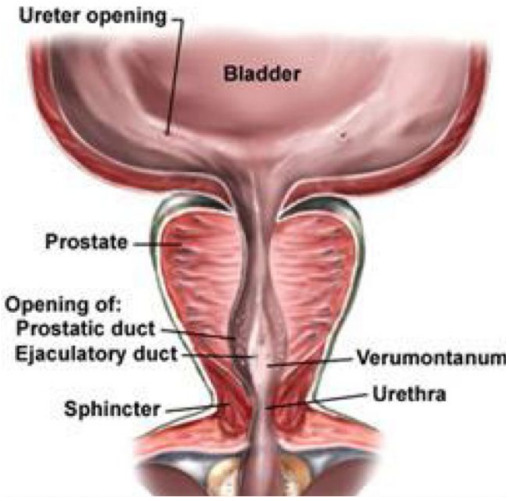
It is devoid of a distinct capsule.
The prostate is **divided** into different zones. They are:

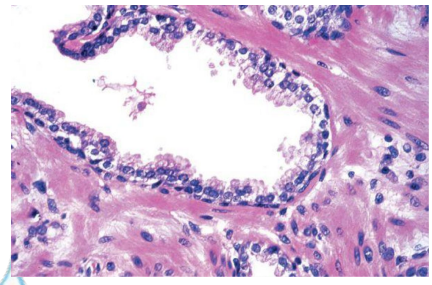
- **Central, Peripheral and Transitional zones.**

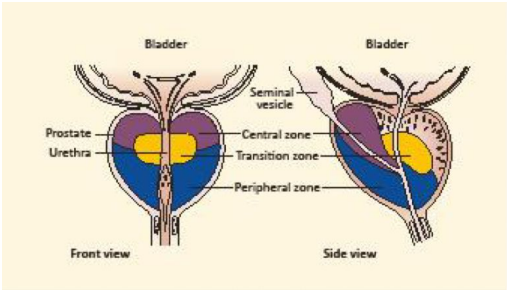
The **transition** zone is the middle area of the prostate, between the peripheral and central zones. It surrounds the urethra as it passes through the prostate.
The majority of prostate cancers are **found in the peripheral zone and Benign prostatic hyperplasia** in the transitional zone.

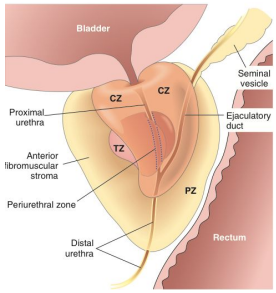
Microscopically the prostate is a tubulo-alveolar organ. The prostate glands are lined by two layers of cells, basal cells and columnar secretory cells











Benign Prostatic Hyperplasia (BPH)

Overview

- Also known as **benign nodular hyperplasia.**
- Extremely common lesion in men over age 50.
  - About 20% men have BPH by age 40.
  - About 70% men have BPH by age 60.
  - About 90% men have BPH by age 80.
- Hyperplasia of glands and stroma results in large nodular enlargement in the periurethral region of the prostate.
- Once the nodules become large they compress the prostatic urethra causing either partial, or complete obstruction of the urethra.

Pathogenesis

IMPORTANT

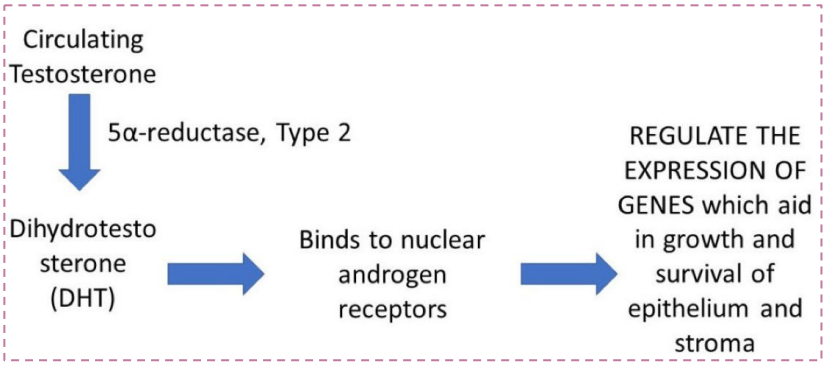
The essential cause of BPH is unknown BUT The pathogenesis is related to the action of androgens.

Dihydrotestosterone (DHT) is the ultimate mediator for prostatic growth: It increases the proliferation of stromal cells & Also Inhibits epithelial cell death.

Therefore DHT is implicated in the pathogenesis of both benign prostatic hyperplasia (BPH) and prostate cancer.

Testosterone is converted to dihydrotestosterone (DHT) by **5-alpha reductase enzymes.**

Drugs that act as inhibitors of 5-alpha reductase, therefore have an important role in the prevention and treatment of BPH and prostate cancer. Prepubertal castration prevents BPH.

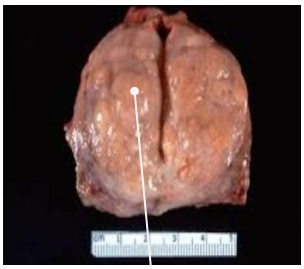


Benign Prostatic Hyperplasia (BPH)

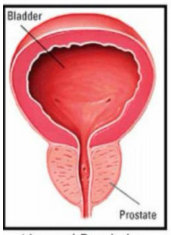
Morphology

IMPORTANT

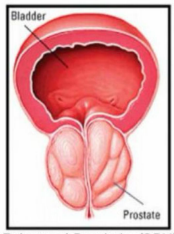
Gross	Microscopic
• The prostate weighs between 60 and 100 grams (normal = 20). • The **hallmark** of BPH is **nodularity** due to glandular and fibromuscular proliferation. • Nodular hyperplasia begins in the inner aspect of the transition zone. • Cut-section shows **nodules** which vary in size, **color** and **consistency** depending on which element is proliferating more (glandular or fibromuscular). • It **compress** the wall of the **urethra** resulting in a **slit-like orifice.**	• the main feature of BPH is nodularity. • The nodules can be: A. purely stromal nodules composed mainly of fibromuscular element. B. fibroepithelial with both glandular and fibromuscular component. C. There is **aggregation** of small to large to cystically dilated glands, lined by two layers of epithelium **surrounded** by fibromuscular stroma. • Needle biopsy doesn't sample the transitional zone where BPH begins and occurs, therefore the diagnosis of BPH cannot be made on needle biopsy.



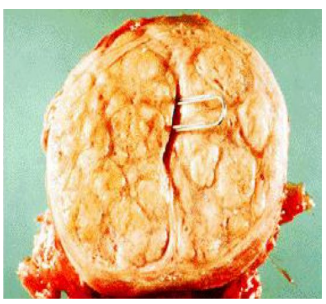
Nodular lesion

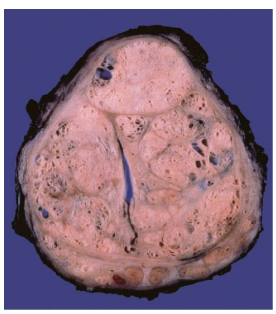


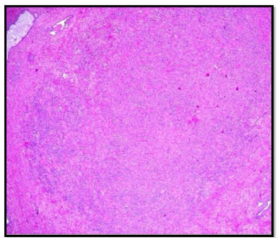
Normal Prostate

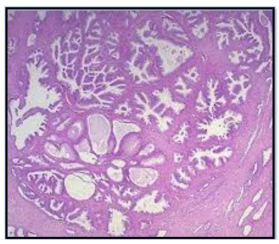


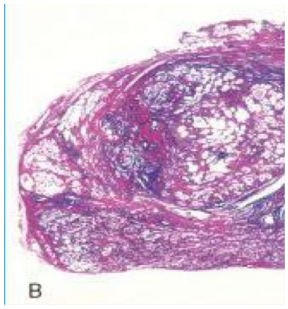
Enlarged Prostate (BPH)

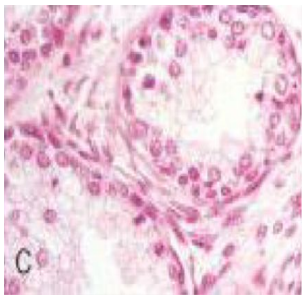


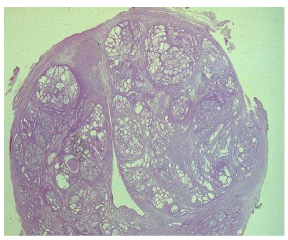


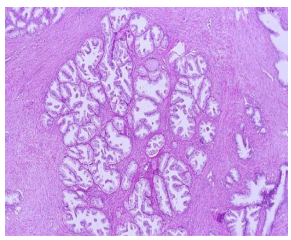












Benign Prostatic Hyperplasia (BPH)

Clinical Features

The inability to empty the bladder completely leads to increase volume of residual urine → therefore infection.

Some patients present with **acute urinary retention (medical emergency).**

01 The nodule compress the prostatic urethra → urethral obstruction → leads to retention of urine in the bladder →bladder hypertrophy.

02

03 **Difficulty** in starting and stopping the stream of urine.

04

05 Increased urinary **frequency, Nocturia, Dysuria.**

Treatment

Mild cases of BPH may be treated with **α-blockers and 5-αreductase inhibitors.**

Moderate to severe cases require **transurethral resection of the prostate (TURP).**

Clinical Note

Diagnostic procedures/imaging :

Urodynamic testing: Attempts to reproduce patient's symptoms in a simulated environment by filling the bladder with fluid & Assesses for detrusor overactivity, urinary incontinence, bladder compliance, urine flow curve

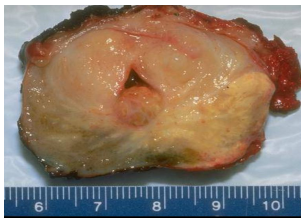
Transrectal ultrasound: Not necessary for diagnosis of BPH, but helps with accurately estimating prostate volume & Important for prostate biopsy under ultrasound guidance when assessing for possible prostate cancer

Cystoscopy: Office procedure to view the prostate, bladder, urethra with a camera & Assists in operative planning for BPH and to rule out other anatomic causes

Prostatic Adenocarcinoma

Overview

- It is the most common form of cancer in men over the age of 50 years.
- It is more prevalent among African Americans.
- Androgens are believed to play a major role in the pathogenesis.
- These tumors show a wide range of clinical behaviors



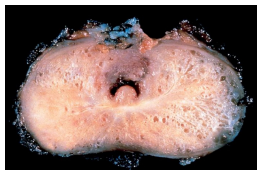
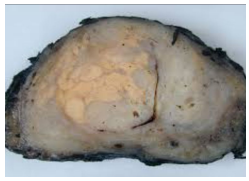
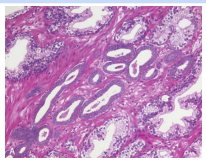
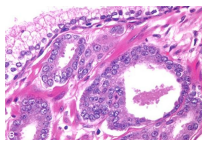
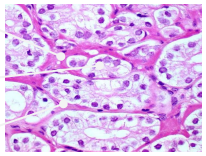
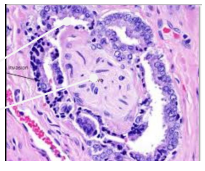
Risk Factors

Age above 50, race, family History, hormone level (Androgens) and environmental influences.

TMPRSS2-ETS gene mutation is present in 40% to 60% of prostate cancer

Morphology

IMPORTANT

Gross	A.70% of tumors arise in the **peripheral** zone in the posterior part of the gland. B.The tumor is firm and gritty and is palpable on rectal exam. C.Tumor can spread by: direct local invasion and through blood vessels and lymphatics. D.Local extension most commonly involves: the periprostatic tissue, seminal vesicles and the base of the urinary bladder (leading to ureteral obstruction).	 
Microscopic	1.Histologically,most lesions are adenocarcinomas that produce well-defined gland patterns. 2.The malignant glands are lined by a **single** layer of cuboidal or low columnar epithelium with large nuclei and one or more large nucleoli. 3.Nuclear pleomorphism is not marked. 4.The outer basal cell layer, typical of benign glands, is absent. 5.Perineural invasion is common.	   

Prostatic Adenocarcinoma

Grading

Not important just know that we use **Gleason system** for Grading

- **Gleason system** is a histological grading and scoring system for prostatic adenocarcinoma done on the microscopic level.
- There are five grades (1 to 5) depending on the degree and pattern of differentiation as seen microscopically:
  - Grade 1 = well-differentiated
  - Grade 5 = very poorly differentiated.
- Prostate carcinomas usually have more than one type of grade in the tumor mass/pattern within any given tumor.
- The two most common types of grades/most predominant pattern (grade) and the most aggressive seen in the biopsy for each cancer patient are added and the final sum is called the Gleason score (the predominant & second predominant on resection).
- Gleason grading and scoring is very useful in predicting the prognosis of a patient.

Staging

- Staging in prostate cancer depends on the TNM (tumor size, lymph node, metastasis) system.
- It is the **most important indicator of prognosis.**
- Nodular hyperplasia (BPH) is NOT a premalignant lesion.

Diagnosing

- Careful digital rectal examination: may detect some early cancers.
- PSA (Prostate Specific Antigen): (tumor marker) are important in the diagnosis and management of prostate cancer. However, a minority of prostate cancers may have low PSA.
- PSA is organ-specific but **NOT** cancer specific thus it can increase in BPH and prostatitis.
- Transrectal needle biopsy: is required to confirm the diagnosis.

Normally its 4 , if its more than that it might be:

- Hyperplasia
- Prostatitis
- Ischemia
- Adenocarcinoma

Prognosis

- The prognosis depends on the Gleason score and stage of tumor.
- Metastases: first spread via lymphatics initially to the obturator nodes and eventually to the para-aortic nodes.
- Hematogenous extension occurs chiefly to the bones.
- The bony metastasis are typically osteoblastic in nature.

Prostatic Adenocarcinoma

Clinical Features

01 Microscopic (small size) cancers are asymptomatic and are discovered incidentally.

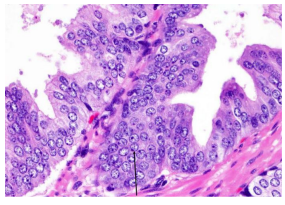
02 Most arise in the peripheral zone, away from the urethra and therefore urinary symptoms occurs late

03 Occasionally patients present with back pain caused by vertebral metastases.

Treatment

1. Surgery, radiotherapy and hormonal therapy are used for treatment , 90% of treated patients are expected to live for 15 years.
2. Currently the most acceptable treatment for clinically localized cancer is radical surgery.
3. Locally advanced cancers can be treated by radiotherapy and hormonal therapy.
4. Hormonal therapy (anti-androgen therapy) can induce remission.
5. Advanced, metastatic carcinoma is treated by androgen removal treatment, either by orchiectomy or by hormonal anti-androgen therapy.

Prostatic Intraepithelial neoplasia(PIN)



Prostatic intraepithelial neoplasia **(PIN)** is the **precursor lesion for invasive carcinoma.**

It can be low grade PIN or high grade PIN (high grade PIN is like carcinoma in situ).

PIN like prostatic carcinoma occurs in the **peripheral zone.**

Keywords

BENIGN PROSTATIC HYPERPLASIA (BPH)	• prostate cancers are found in the peripheral zone and Benign prostatic hyperplasia in the transitional zone. • Nodular hyperplasia is NOT a premalignant lesion • Dihydrotestosterone (DHT) is the ultimate mediator for prostatic growth : increases the proliferation of stromal cells & Inhibits epithelial cell death. • nodularity due to glandular and fibromuscular proliferation. • nodules can be: composed mainly of fibromuscular element OR fibroepithelial with both glandular and fibromuscular component • 2 layers of cells • Increased urinary frequency, Nocturia, Dysuria. • acute urinary retention
Prostatic Adenocarcinoma	• Androgens are believed to play a major role in the pathogenesis. • TMPRSS2-ETS gene mutation • arise in the peripheral zone • tumor is irm and gritty and is palpable • The malignant glands are lined by a single layer of cuboidal or low columnar epithelium. • Commonly there is perineural invasion. • outer basal cell layer Is • Gleason system For grading • patients present with back pain caused by vertebral metastases. • PSA (Prostate Specific Antigen) Is increased • bony metastasis are typically osteoblastic in nature.
Prostatic Intraepithelial neoplasia(PIN)	• precursor lesion for invasive carcinoma. • occurs in the peripheral zone.

IF YOU WANT A SUMMARY CLICK HERE

YOU VS MCQs

Question 1

Which of the following statements is TRUE about benign prostatic hyperplasia (BPH)?

- patients present with urinary frequency and nocturia.
- mainly affects the peripheral part of the prostate.
- main treatment for BPH is surgery.
- An elevated PSA is not seen with BPH.

Question 2

Which of the following is not a symptom of benign prostatic hypertrophy (BPH)?

- Fecal incontinence
- Dribbling
- Nocturia
- Difficulty urinating

Question 3

What is a transurethral resection of the prostate (TURP)?

- Resection of the prostate through the urethra
- Removal of the prostate
- A nonsurgical procedure
- Laser surgery to resect the prostate

Question 4

Which of the following is the most appropriate screening test for prostate cancer?

- Rectal ultrasound
- Digital rectal examination
- Prostate-specific antigen
- Prostate needle aspiration

1- A / 2-A / 3- A / 4-C

YOU VS MCQs

Question 5

In benign prostatic hyperplasia, the prostate is ____ on digital rectal examination.

- Solid
- Tender
- Non Tender
- Could be both

Question 6

What is the most commonly performed procedure to treat symptomatic benign prostatic hyperplasia patients?

- Prostate Full Resection
- Catheter
- Transurethral resection of the prostate
- Biopsy

Question 7

_____antigen is measured in patients with benign prostatic hyperplasia to rule out prostate cancer.

- TMPRSS2-ETS gene mutation
- Prostate-specific antigen
- Alpha fetoprotein
- HCG

Question 8

What is the most common mutation In Prostatic Adenocarcinoma

- TMPRSS2-ETS gene mutation
- BRCA1
- P53
- NTRK1

5- C / 6- C / 7- B / 8-A

Cases

1.A 78-year-old man was admitted to the hospital due to acute urinary tract obstruction. For the past few years, he has had recurrent bouts of cystitis. Two days before being admitted to the hospital, he could not urinate at all. What is the probable cause of bladder outlet obstruction in this patient?

A.Nephrogenic metaplasia	B.Nodular prostatic hyperplasia	C.Urothelial cell carcinoma of the bladder	D.Urethral stricture

2.A 68-year-old man is found to have an elevated serum PSA level (9.5 ng/mL, normal = 0 to 4 ng/mL). Biopsy of the prostate gland reveals a poorly differentiated adenocarcinoma.Which of the following best describes the putative precursor of this malignant neoplasm?

A.Basal cell hyperplasia	B.Chronic prostatitis	C.Nodular hyperplasia of the prostate	D.Prostatic intraepithelial neoplasia

3.A 55-year-old man presents with urinary symptoms of urgency and frequency. Rectal examination reveals an enlarged prostate. Laboratory studies show an elevated serum PSA level of 4.9 ng/mL. The patient subsequently undergoes a prostate needle biopsy series, which demonstrates two cancer-positive needle cores: Gleason grades 2+2(4) and 3+2(5). Which of the following is the appropriate diagnosis?

A.Adenocarcinoma	B.Nodular prostatic hyperplasia	C.Prostate intraepithelial neoplasia	D.Squamous cell carcinoma

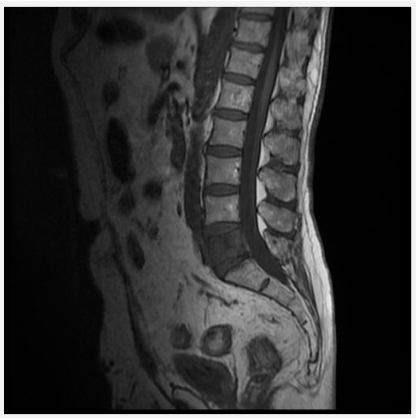
1-B / 2-D / 3-A

NEED EXPLANATION ? CLICK HERE

Cases

EXTRA CASES MAY REQUIRE EXTRA INFO

1.A 70-year-old man comes to the office because of progressive lower back pain. He first noticed the pain a few months ago at the grocery store. It is most severe at night and is not relieved by rest, exercise, medication or change in position. He has not had any recent trauma. He also reports difficulty initiating urination and dysuria for the past 6 months. He is a retired veteran and lives alone. Past medical history is noncontributory. Family history is significant for colorectal cancer in his father. Vitals are within normal limits. Neurological examination and straight leg raise test are normal. MRI of the lumbar spine is performed and shown: Further evaluation of this patient will most likely show which of the following?



A.Paraspinal tenderness	B.Irregular prostate on digital rectal examination	C. Reduced chest expansion	D.Inguinal lymphadenopathy

2.A 48-year-old man presents to the office because of perineal pain for the past 4 months. He states that the pain is dull, constant and has been interfering with daily activities. He also reports mild pain during urination but denies urinary frequency, urgency or straining. Past medical history is significant for migraine headaches. Family history is unremarkable. Vitals are within normal limits. Physical examination including digital rectal examination is normal. There is no suprapubic pain on palpation. Urinalysis shows no abnormality. Expressed prostatic secretion shows 2 leukocytes/hpf, but culture does not grow a pathogenic organism. What is the most likely diagnosis in this patient?

A.Chronic bacterial prostatitis	B.Benign prostatic hyperplasia	C.Chronic abacterial prostatitis	D.Cystitis

3.A 71-year-old man comes to the emergency department because of severe lower abdominal pain for the last 4 hours. He has not urinated for the past 24 hours and adds that he has had poor urine flow and difficulty initiating urination for the past 6 months; he also needs to get up multiple times throughout the night to urinate. He denies weight loss, dysuria, or urinary urgency. He has had seasonal allergies for the past week, for which he started taking diphenhydramine as needed. He does not use tobacco or illicit drugs. Vitals are within normal limits. Physical examination shows a palpable mass in the suprapubic area. A symmetric, enlarged, non-tender prostate is palpated on digital rectal examination. Urinary catheter is placed with immediate collection of 700 mL of urine and relief of the patient's symptoms. Which of the following is the most likely cause of this patient's symptoms?

A.Prostate adenocarcinoma	B.Bladder outlet obstruction	C.Transitional cell carcinoma of bladder	D.Chronic abacterial prostatitis

1-B / 2-C / 3-B

Pathology Team

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- رند ابا الخيل
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