جامعة الملك سعود
King Saud University

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Summary file

Made by Sara Alaidarous ,
Sara Alobaid, Hessah Alalyan

Pathology

Prostate Pathology

439

Revised & Approved

Bassam Alasmari
Rania Almutiri

اللهم لا سهل الا ماجعلته سهلا و انت
تجعل الحزن إذا شئت سهلا

Objective

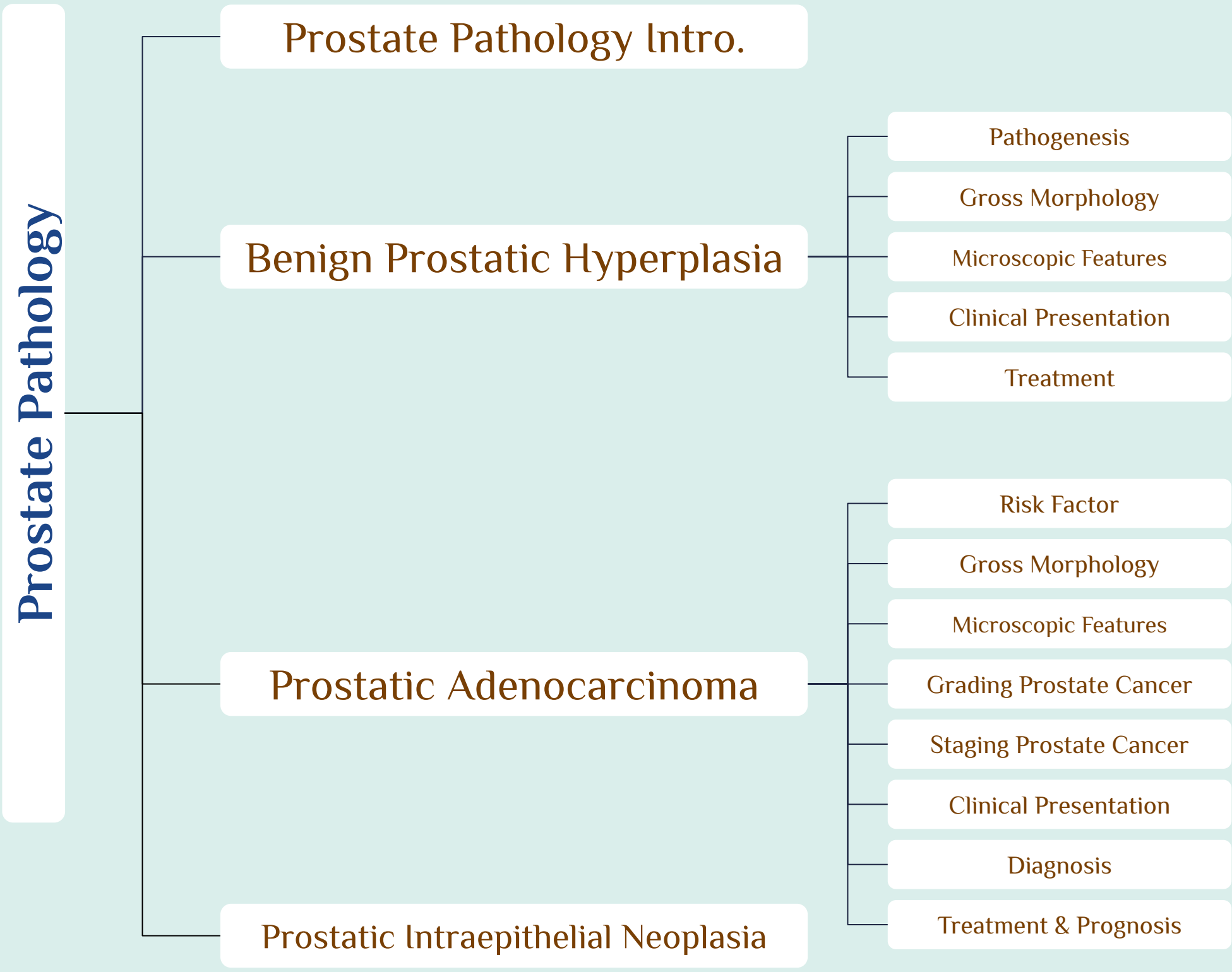
01

Know the epidemiology, pathogenesis and histopathologic features of:

Benign prostatic hyperplasia

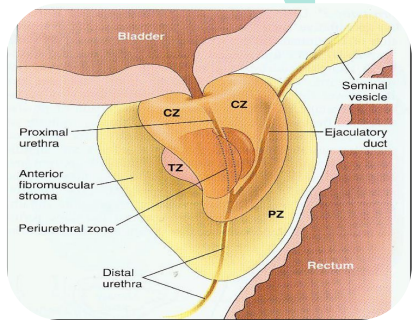
Carcinoma of the prostate

Overview

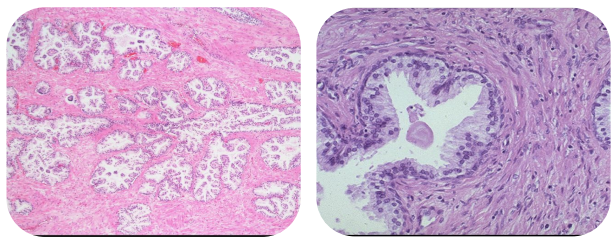


Prostate Pathology

Introduction



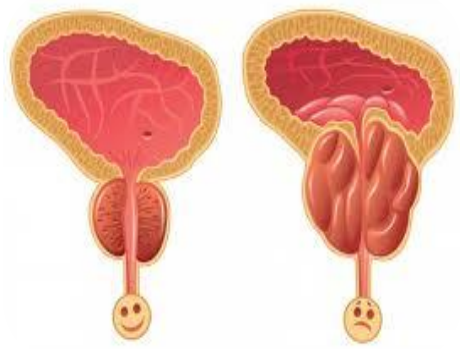
- The prostate weighs 20 grams in a normal adult male.
- It is a retroperitoneal organ, encircling the neck of bladder and urethra.
- It is devoid of a distinct capsule.
- The prostate is divided into **zones:**
  - **Central** zone.
  - **Peripheral** zone: most common zone of cancer.
  - **Transition** zones: surrounds the urethra and the. (most common zone of BPH.)
- Microscopically the prostate is a tubulo-alveolar organ. The prostate glands are lined by two layers of cells, basal cells and columnar secretory cells. IT IS VERY IMPORTANT to differentiate between Benign and Malignant. The Benign lesions always maintain these 2 layers (Basal & columnar), in Malignant they lose the basal layer.



Prostate Histology

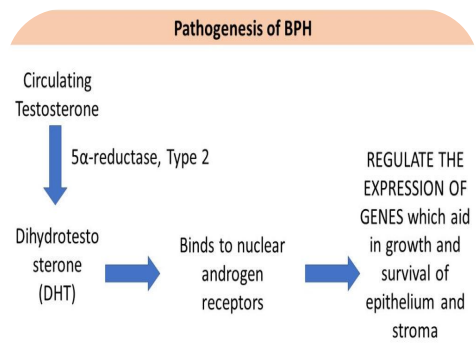
It has fibromuscular stroma and each gland has two layers basal layer and epithelial cell layers

Benign Prostatic Hyperplasia



- Benign prostatic hyperplasia (BPH) is also known as benign nodular hyperplasia.
- It is **extremely common** in men **> 50 years of age.** Incidence increase with age
  - 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 gland and stroma results in large nodular enlargement in the periurethral region (Transitional) of the prostate
- Once the nodules become large they compress the prostatic urethra causing either partial, or complete obstruction of the urethra
- BPH is **not a premalignant lesion.**

Pathogenesis of BPH

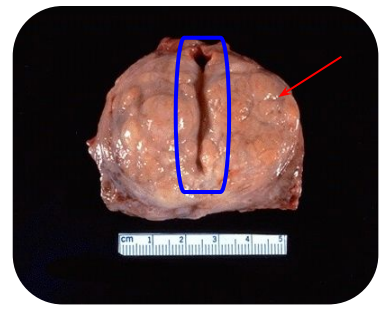


- The essential cause of BPH is unknown but the pathogenesis is related to the action of **androgens**.
- **Dihydrotestosterone (DHT)** is the **ultimate mediator for prostatic growth**:
  - It increases the proliferation of stromal cells.
  - Inhibits epithelial cell death.
- Therefore DHT is implicated in the pathogenesis of **both** benign prostatic hyperplasia and prostate cancer.
- Testosterone is converted to dihydrotestosterone by the **5-alpha reductase enzyme.**
  - Drugs that act as **inhibitors of 5-alpha reductase** have an important role in the **prevention and treatment of BPH** and prostate cancer.
- Prepubertal castration[1] prevents BPH.

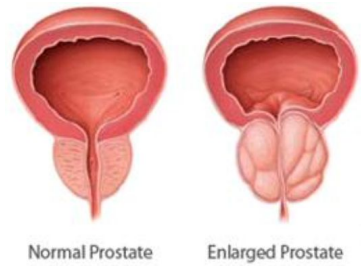
1. The process of removing the testicles

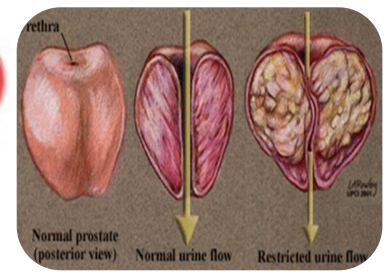
Benign Prostatic Hyperplasia

Gross Morphology



- The prostate weighs between **60 and 100 grams.**
- The hallmark of BPH is **nodularity** due to glandular and fibromuscular proliferation starting from **the transition zone** of the prostate.
- It compresses the wall of the urethra resulting in a slit-like orifice.
- **Cut-section**: nodules which vary in size, color and consistency.
  - depending on which element is proliferating more (glandular is softer vs. fibromuscular is firmer).

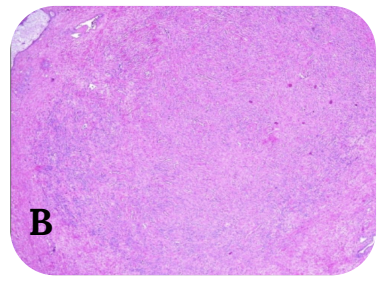


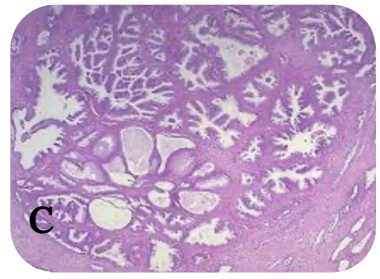


Microscopic Features

Since the main feature of BPH is nodularity, the nodules can be one of the following:

- **(B)** Purely **stromal nodules** composed mainly of fibromuscular elements.
- **(C) Fibroepithelial** with **both** glandular and fibromuscular component:
  - Aggregation of small to large to **cystically dilated glands.**
  - Lined by **two layers of epithelium**[1].
  - Surrounded by **fibromuscular stroma.**
- Needle biopsies do not sample the transitional zone where BPH occurs, therefore the diagnosis of BPH cannot be made on needle biopsy. We diagnose clinically by radiology. However, needle biopsy is good for diagnosing cancer, because it is in the peripheral zone





Clinical Presentation

- **Bladder hypertrophy:** the nodules compress the prostatic urethra causing urethral obstruction which leads to urinary retention and bladder hypertrophy.
- **Infection:** the inability to empty the bladder completely leads to an increased volume of residual urine, therefore infection.
- **Urinary frequency, Dysuria, Nocturia.**
- **Difficulty in starting and stopping the stream of urine.**
- **Some present with acute urinary retention. (Medical Emergency)**

Treatment

- **Mild** cases of BPH may be treated with **α-blockers and 5-α-reductase inhibitors.**
- **Moderate to severe** cases require **transurethral resection of the prostate (TURP).** They introduce a special device تقدر تكشط the prostate

- **Note:** Needle biopsies **do not sample** the transitional zone where BPH occurs, therefore the diagnosis of BPH **cannot be made on needle biopsy.**

1. Tall columnar epithelial cell layer and a peripheral layer of flattened basal cells

Prostatic Adenocarcinoma

Introduction

- 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.
- Tumor can **spread** by:
  - Direct local invasion, through blood vessels, and lymphatics.
- Local extension most commonly involves:
  - The **periprostatic tissue, seminal vesicles and the base of the urinary bladder** (leading to ureteral obstruction)[1].

Risk factors

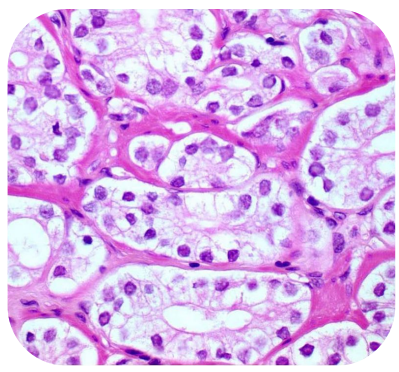
- **Age above 50.**
- **Race.**
- **Hormone level (increase level of androgens).**
- **Family history.**
- **Environmental influences.**

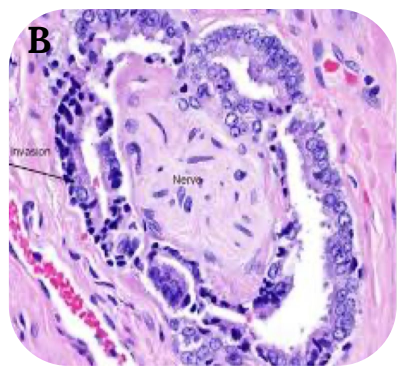
Gross morphology

- 70% of tumors arise in the **peripheral zone** in the posterior part of the gland.
- The tumor is **firm** and **gritty** and is **palpable**[2] on rectal exam.
- People use to screen for prostatic carcinoma by digital rectal examination

Microscopic features

- Most lesions produce **well-defined gland patterns.**
- The malignant glands are lined by a **single layer** of cuboidal or low columnar.
- **Large nuclei** and one or more **large nucleoli**.
- Nuclear pleomorphism is not marked.
- The outer **basal cell layer**, typical of benign glands, is **absent.**
- **Perineural invasion** is common. (B)





1. Because of the peripheral location, prostate cancer is less likely to cause urethral obstruction in initial stages, the manifestations occur late.
2. In opposite to BPH which is difficult to palpate because of deep origin (Transitional zone).

Prostatic Adenocarcinoma

Grading Prostate Cancer

- **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 pattern** within any given tumor.
- **Gleason Score:** is the final sum of two grades within the tumor:
  - **In biopsies**: the **most predominant** grade **+ most aggressive** grade are added and the final sum is **Gleason Score.**
  - **On resection**: the **predominant** grade + **second predominant** grade are added to give the **Gleason score**
- Gleason grading and scoring is very useful in predicting the **prognosis** of a patient.

What do you need to know for grading is that we use Gleason system and Gleason score, and both of them are important for prognosis

Staging Prostate Cancer

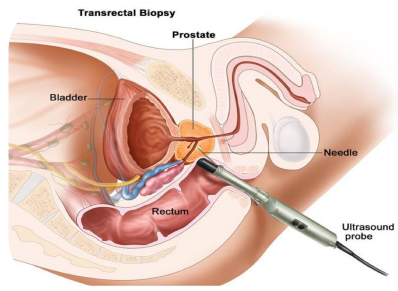
- Staging in prostate cancer depends on the **TNM (tumor size, lymph node, metastasis) system**.
- It is the **most important indicator of prognosis.** More important than grading

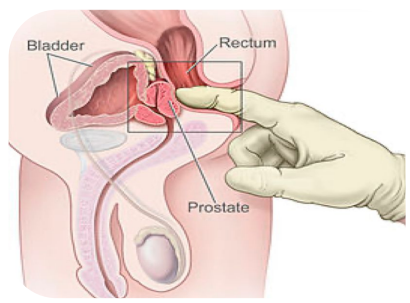
Clinical Presentation

- Microscopic (small size) cancers are **asymptomatic** and are discovered incidentally.
- Urinary symptoms occurs late.
- Occasionally patients present with **back pain caused by vertebral metastases.**

Diagnosis

- **Digital rectal examination**: may detect some early cancers.
- **PSA (Prostate Specific Antigen):** 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.





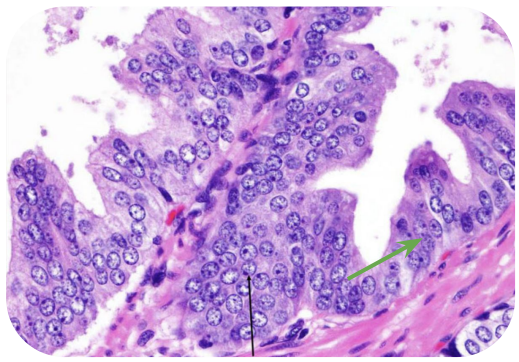
Prostatic Adenocarcinoma

Treatment

- **Surgery, radiotherapy and hormonal therapy** are used for treatment
- 90% of treated patients are 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** and **hormonal therapy**.
- Hormonal therapy (anti-androgen therapy) can induce remission.
- **Advanced, metastatic** carcinoma is treated by **androgen removal treatment**, either by **orchiectomy** or by hormonal **anti-androgen therapy**.

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.**



Basal layer

Prostatic Intraepithelial Neoplasia

- Prostatic intraepithelial neoplasia (**PIN**) is the **precursor** lesion for invasive carcinoma.
- It can be **low grade PIN** or **high grade PIN** (carcinoma in situ)[1].
- PIN like prostatic carcinoma occurs in the **peripheral zone.**

How to differentiate between benign & malignant (female doctor)		
	Benign	**Malignant**
Clinical symptoms	Symptomatic	Asymptomatic
Examination	Nothing (deep in transitional zone)	Firm (peripheral zone)
Microscopic	Two layers (basal and columnar epithelium)	One layer (only columnar epithelium)

1. You can find the **Basal layer** in this lesion because it's in situ

Summary

Prostatic tumors

Benign prostatic Hyperplasia

intro	❖ Benign nodular hyperplasia most commonly in the transition zone. ❖ The ultimate mediator Dihydrotesterone increase proliferation of stromal cells. ❖ Common above the age of 50, it is not premalignant.
Morphology	**Gross** (weight 60-100 grams) ❖ Nodular of varying size, color, and consistency. **Microscopic** ❖ Cystically dilated glands. ❖ **Two layer of epithelium.**
Clinical features	❖ Bladder hypertrophy. ❖ Infection. ❖ Urinary frequency, Dysuria, Nocturia. ❖ **Treatment**: Inhibitors of 5-alpha reductase.

Prostatic Adenocarcinoma

Intro	❖ Most common cancer above the age of 50, and among african americans. ❖ Androgens play a major role. ❖ **Risk factors**: age, race, hormonal level, family history, environmental factors.
Morphology	**Gross** ❖ Most commonly in the peripheral zone. ❖ Tumor is firm, gritty, and palpable on rectal exam. **Microscopy** ❖ Well-defined gland patterns, lined by a single layer of cuboidal cells. ❖ Large nuclei, large nucleoli, pleomorphism not marked.
Clinical presentation & diagnosis	❖ Asymptomatic, occasional back pain. ❖ **Digital rectal examination**: may detect early cancer. ❖ **Prostate specific antigens**: important in diagnosis and management, but a minority will have low PSA. ❖ **Transrectal needle biopsy**: required to confirm diagnosis.
Prognosis	❖ Depends on Gleason score & Stage of tumor. ❖ **Lymphatic metastasis**: first to obturator nodes, then to Para-aortic nodes. ❖ **Blood metastasis**: bone, osteoblastic in nature. ❖ 90% of treated patients are expected to live for 15 years. ❖ **Treatment**: Surgery, radiotherapy, Hormonal therapy.

QUIZ!

MCQs

01 | A 65-year-old man has had multiple, recurrent urinary tract infections for the past year. Escherichia coli and streptococcal organisms have been cultured from his urine during these episodes, with bacterial counts of more than 105/mL. He has difficulty with urination, including starting and stopping the urinary stream. Over the past week, he has again developed burning pain with urination. Urinalysis now shows a pH of 6.5, and specific gravity of 1.020. No blood or protein is present in the urine. Tests for leukocyte esterase and nitrite are positive. Microscopic examination of the urine shows numerous WBCs and a few WBC casts. Which of the following is the most likely condition predisposing him to recurrent infections?

A) Epispadias	B) Nodular prostatic hyperplasia	C) Phimosis	D) Posterior urethral valves	E) Prostatic adenocarcinoma	F)Vesicoureteral reflux

02 | A clinical trial of two pharmacologic agents compares one agent that inhibits 5α-reductase and diminishes dihydrotestosterone (DHT) synthesis in the prostate with another agent that acts as an α1-adrenergic receptor blocker The subjects are 40 to 80 years old. The study will determine whether symptoms of prostate disease are ameliorated in the individuals who take these drugs. Which of the following diseases of the prostate is most likely to benefit from one or both of these drugs?

A) Acute prostatitis	B) Adenocarcinoma	C) Chronic prostatitis	D) Leiomyoma	E) Nodular hyperplasia

03 | A 72-year-old man has had increasing difficulty with urination for the past 10 years. He now has to get up several times each night because of a feeling of urgency, but each time the urine volume is not great. He has difficulty starting and stopping urination. On physical examination, the prostate is enlarged to twice its normal size, but is not tender to palpation. One year ago, his serum prostate-specific antigen (PSA) level was 6 ng/mL, and it is still at that level when retested. Which of the following drugs is most likely to be effective in treatment of this man?

A) Estrogen (hormone)	B) Finasteride (5α-reductase inhibitor)	C) Mitoxantrone (chemotherapy agent)	D) Nitrofurantoin (antibiotic)	E) Prednisone (corticosteroid)

04 | A 71-year-old, previously healthy man comes to his physician for a routine health examination. On palpation, there is a nodule in his normal-sized prostate. Laboratory studies show a serum prostate-specific antigen (PSA) level of 17 ng/mL. A routine urinalysis shows no abnormalities. Which of the following histologic findings is most likely to be found in a subsequent biopsy specimen of his prostate?

A) Acute prostatitis	B) Adenocarcinoma	C) Chronic abacterial prostatitis	D) Nodular hyperplasia	E) Prostatic intraepithelial neoplasia

05 | What is the most common location of benign prostatic hyperplasia?

A) Central zone	B) Peripheral zone	C) Transitional zone	D)None of the above

06 | Initial metastasis of adenocarcinoma via lymphatics spreads to which one of the following?

A) Superficial inguinal node	B) paraaortic nodes	C) obturator nodes	D) Internal iliac nodes

MCQs Answer key	01	02	03	04	05	06
	B	5	B	C	C	C

Thank You!

We kept 438 pathology theme in the credits to remind you that this wonderful work was originally done by them

438 Khalid Alkhani

Team leader

439 Hamad Almousa

438 Lama Alzamil

Team Leader

439 Fatimah Alhilal

Team Subleader

Alhanouf Alhaluli

Done by the brilliant minds

Omar Alotaibi & Ahmad Alajlan

Note Taker

439 Mona Alabdely , Hamad Almousa

Edited by : 439 Pathology leaders