

# PROSTATE PATHOLOGY

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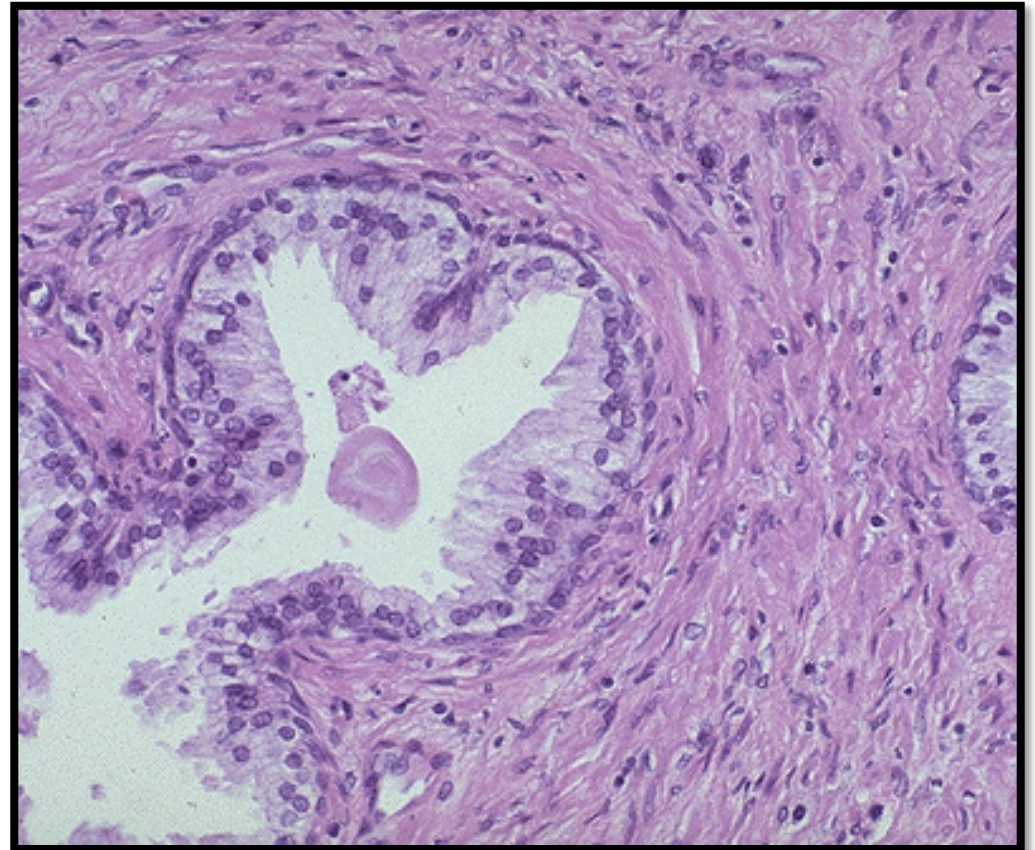
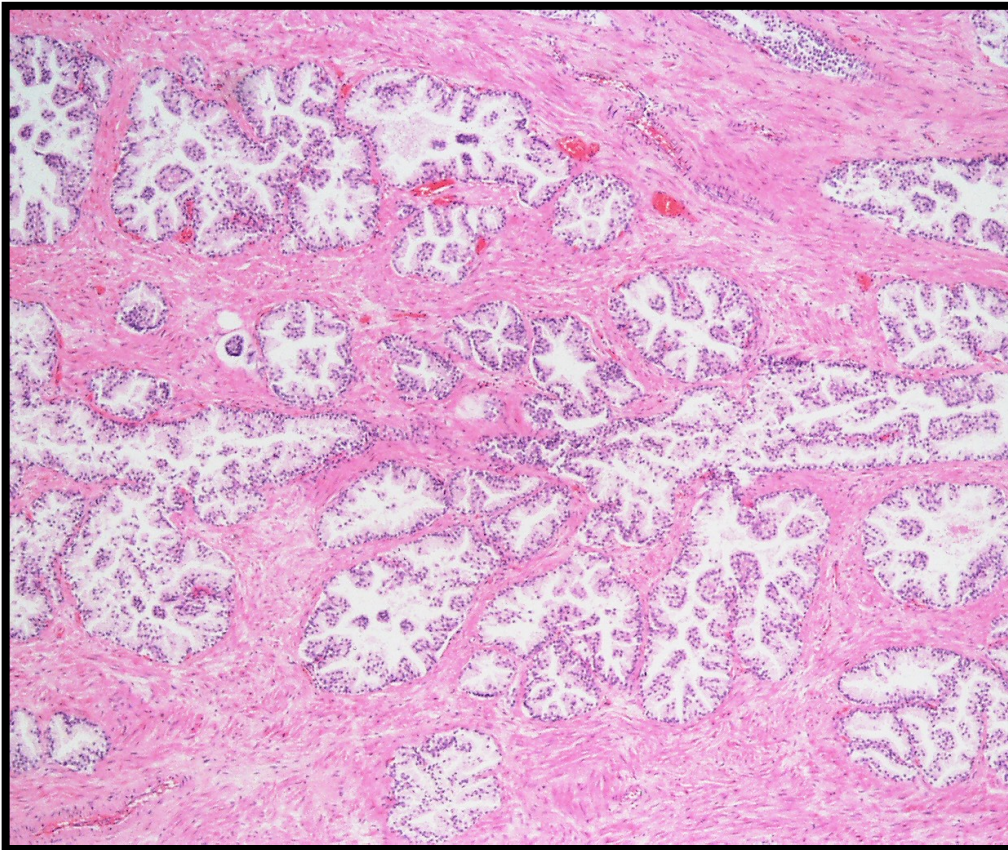
# OBJECTIVES

- 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.

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

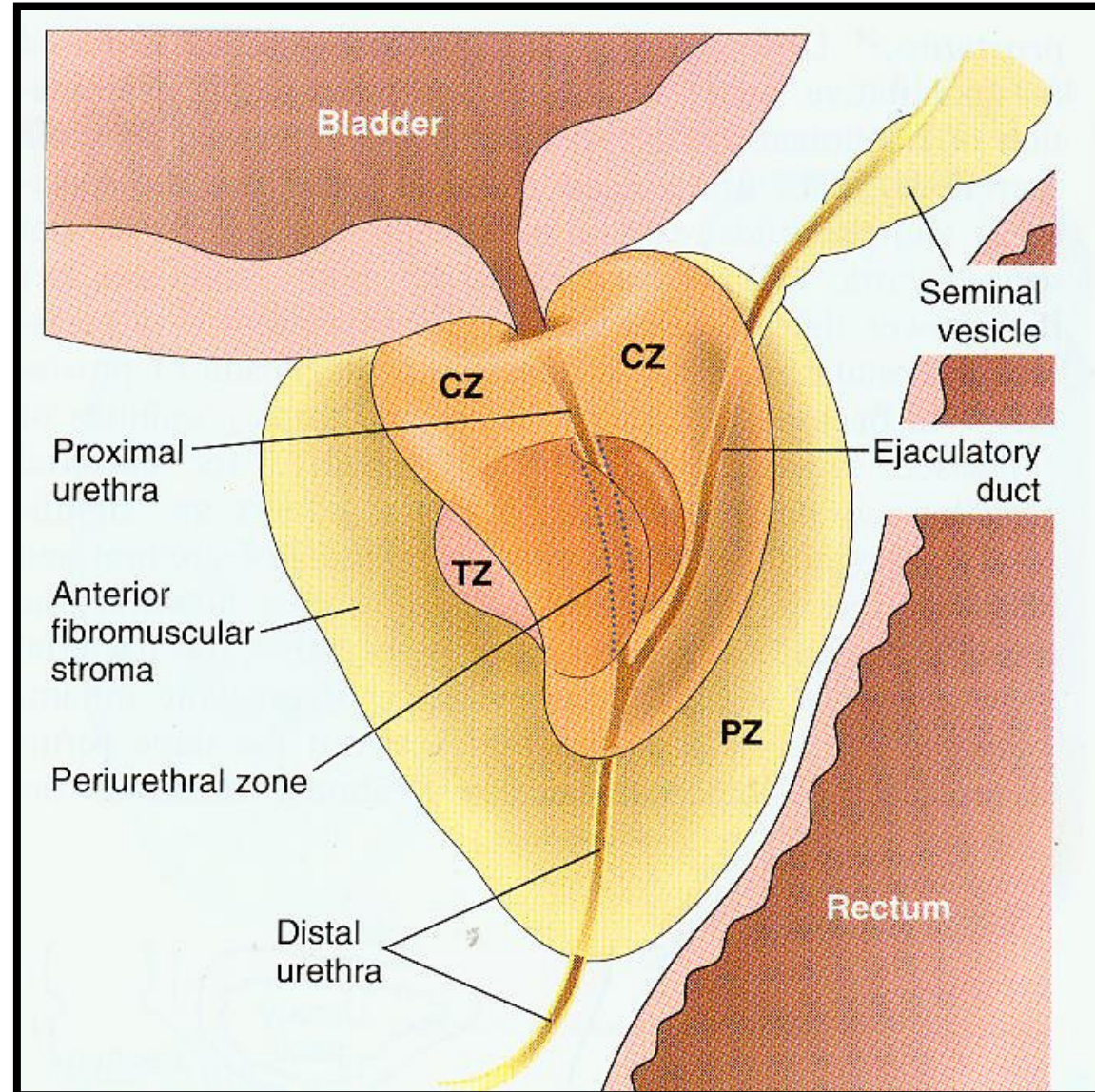
# PROSTATE HISTOLOGY



# INTRODUCTION

- The prostate is divided into different zones: 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 nodular hyperplasia in the *transitional zone*.

# PROSTATE ZONES



# BENIGN PROSTATIC HYPERPLASIA

- Benign prostatic hyperplasia (BPH) is also known as benign nodular hyperplasia.
- It is extremely common in men over the age of 50 years.
  - About 20% men have BPH by age 40
  - About 70% men have BPH by age 60
  - About 90% men have BPH by age 80
- BPH is not a premalignant lesion.

# BENIGN PROSTATIC HYPERPLASIA

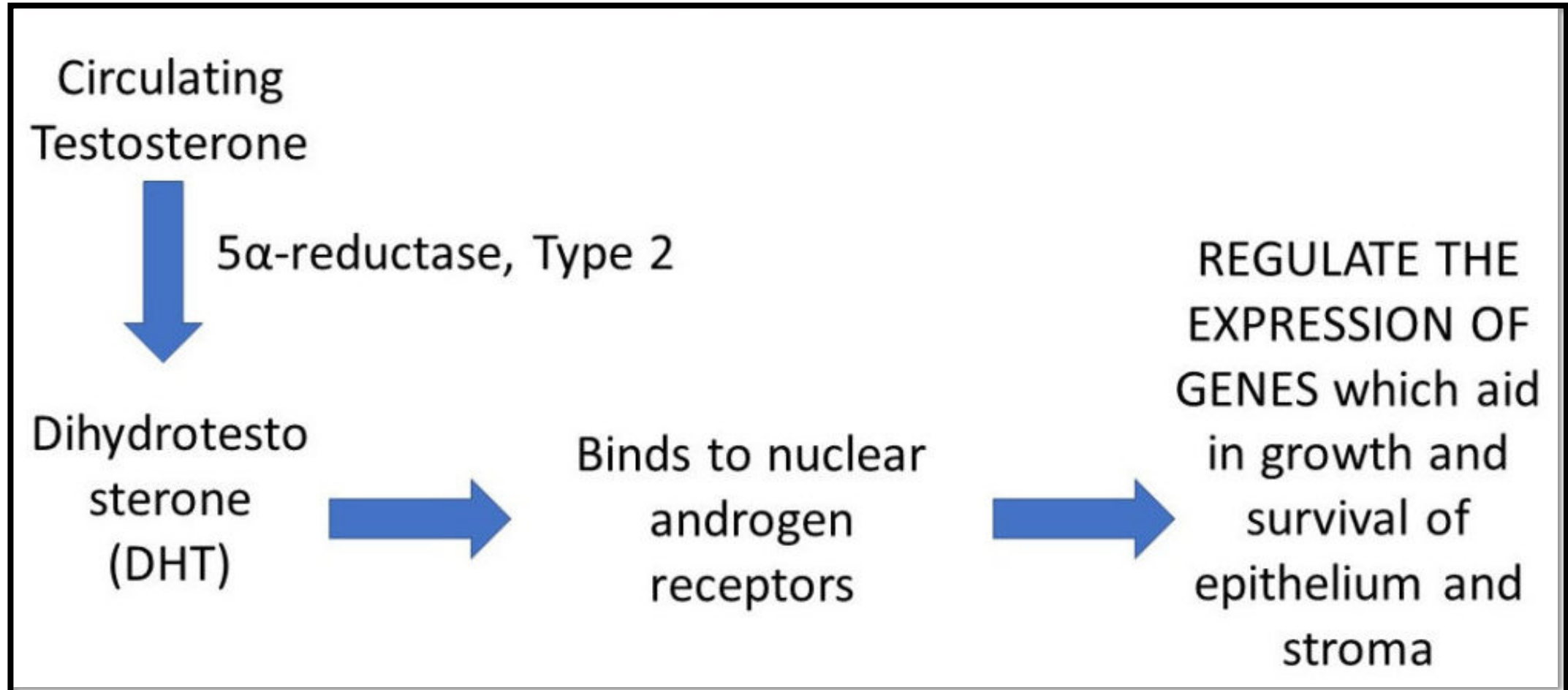
- Hyperplasia of glands and stroma results in large nodular enlargement in the periurethral region of the prostate.
- Once the nodules become large they compress the prostatic urethra causing either partial, or complete obstruction of the urethra.
- The essential cause of BPH is unknown but the pathogenesis is related to the action of androgens.
- Prepubertal castration prevents BPH.



# PATHOGENESIS OF BPH

- Dihydrotestosterone (DHT) is the ultimate mediator for prostatic growth. It increases the proliferation of stromal cells and 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, therefore have an important role in the prevention and treatment of BPH and prostate cancer.

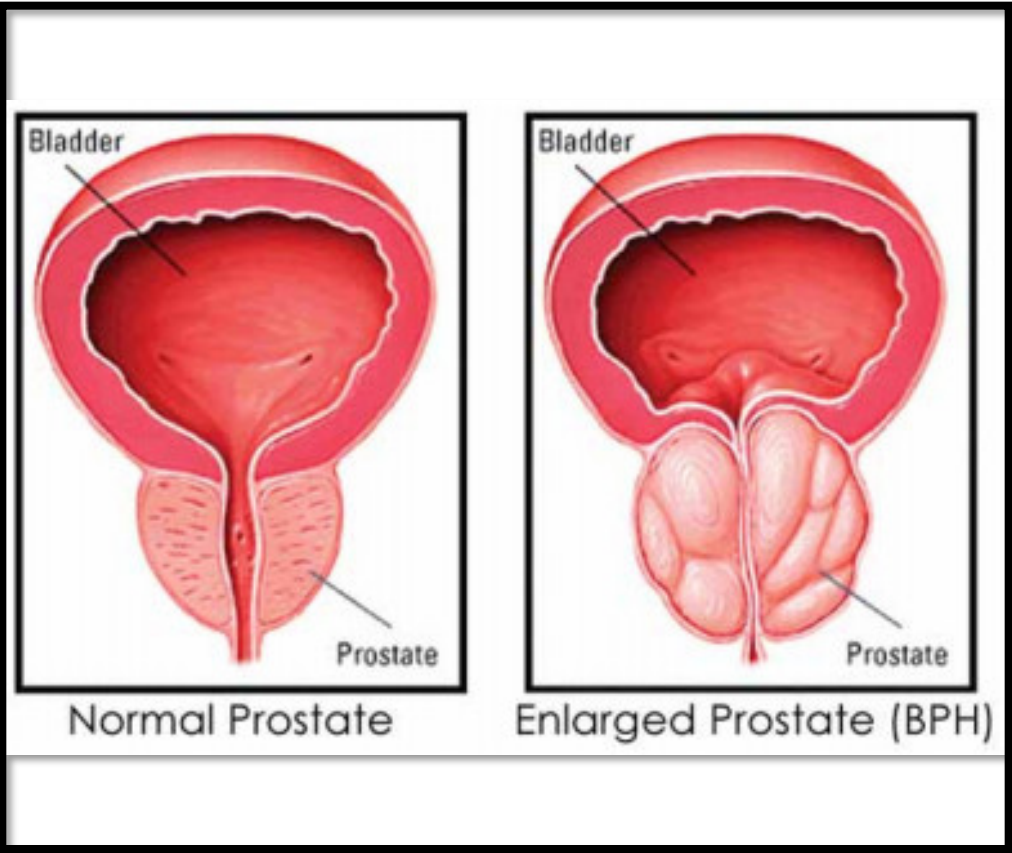
# PATHOGENESIS OF BPH



# GROSS MORPHOLOGY

- The prostate weighs between 60 and 100 grams.
- The hallmark of BPH is nodularity due to glandular and fibro-muscular proliferation starting from the inner aspect of the prostate gland “the transition zone”.
- Cut-section shows nodules which vary in size, color and consistency depending on which element is proliferating more (glandular vs. fibro-muscular).
- It compresses the wall of the urethra resulting in a slit-like orifice.

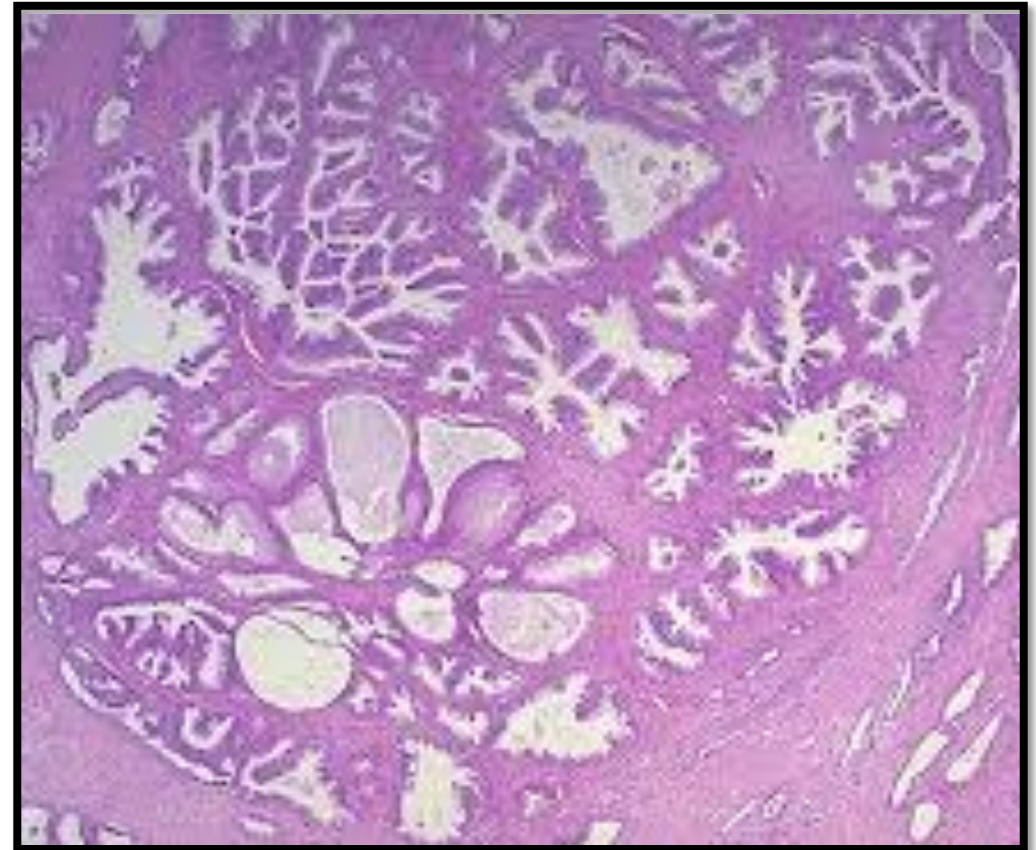
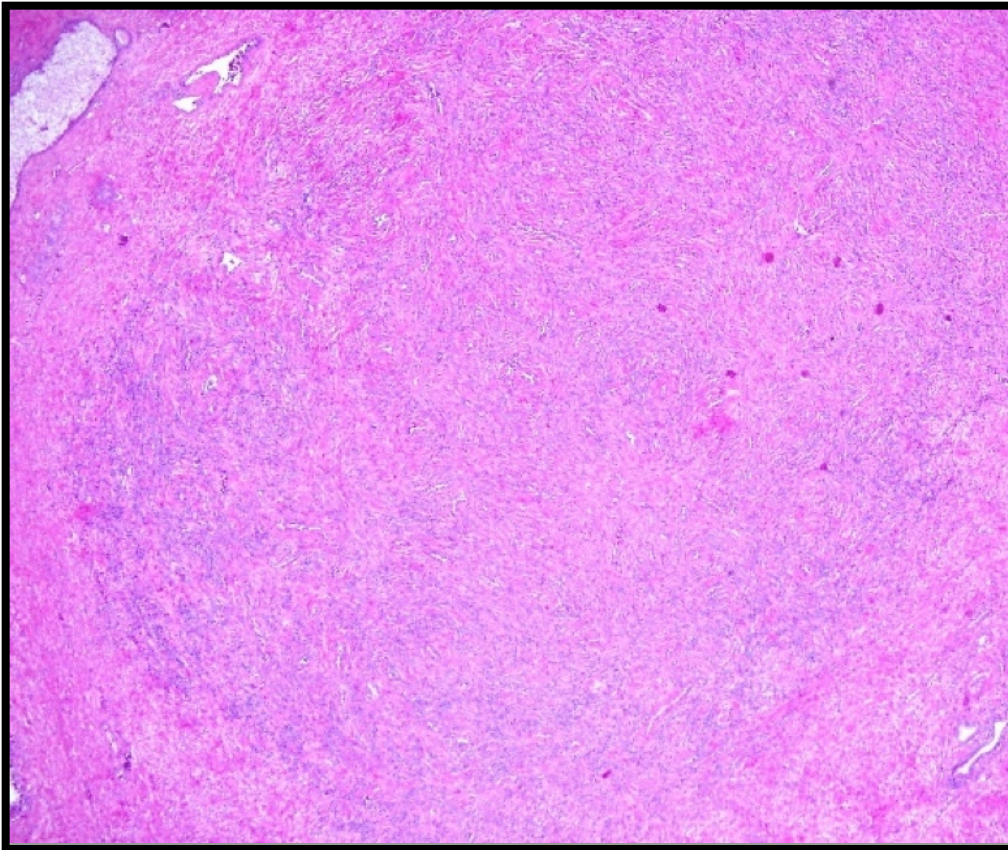
# GROSS MORPHOLOGY



# MICROSCOPIC FEATURES

- The main feature of BPH is nodularity, the nodules can be one of the following:
  - purely stromal nodules composed mainly of fibromuscular elements
  - fibroepithelial with both glandular and fibromuscular component; an aggregation of small to large to cystically dilated glands, lined by two layers of epithelium 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.

# MICROSCOPIC FEATURES



# CLINICAL PRESENTATION

- The nodules compress the prostatic urethra → urethral obstruction → retention of urine in the bladder → bladder hypertrophy
- The inability to empty the bladder completely leads to an increased volume of residual urine → therefore infection
- Increased urinary frequency
- Nocturia
- Difficulty in starting and stopping the stream of urine
- Dysuria
- Some patients present with acute urinary retention.

# TREATMENT

- Mild cases of BPH may be treated with  $\alpha$ -blockers and 5- $\alpha$ -reductase inhibitors.
- Moderate to severe cases require transurethral resection of the prostate (TURP).



# PROSTATE ADENOCARCINOMA

- It is the most common form of cancer in men over the age of 50 years.
- It is more prevalent among African Americans.
- Risk factors include: age, race, family history, hormone level (androgens) and environmental influences.
- Androgens are believed to play a major role in the pathogenesis.
- Tumor can spread by direct local invasion and 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).

# 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 on rectal exam.

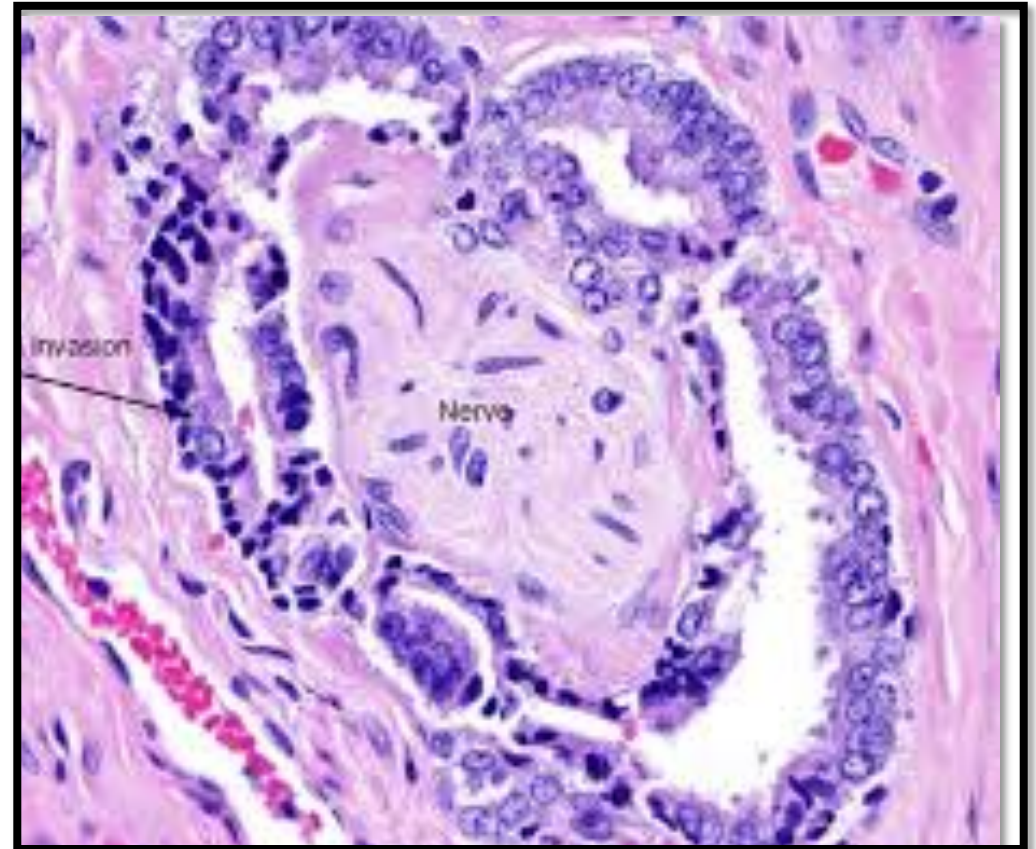
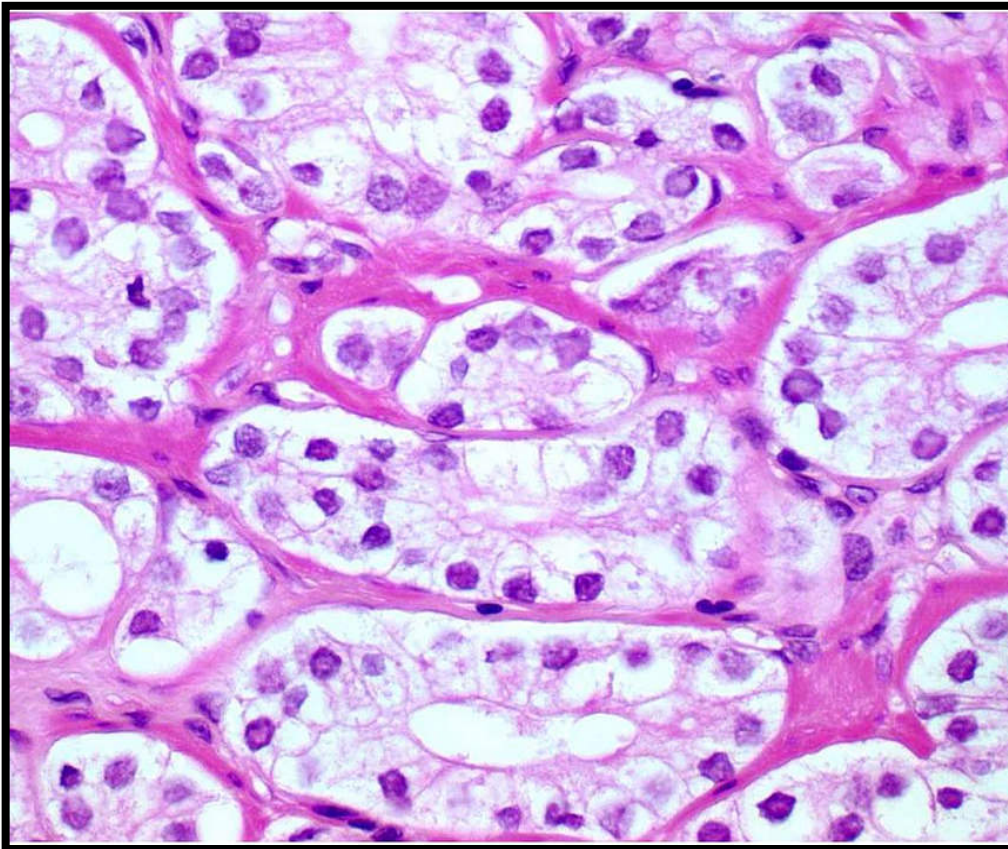
# GROSS MORPHOLOGY



# MICROSCOPIC FEATURES

- Most lesions are adenocarcinomas that produce well-defined gland patterns.
- The malignant glands are lined by a single layer of cuboidal or low columnar epithelium with 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.

# MICROSCOPIC FEATURES



# 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 (in which they range from, grade 1 = well-differentiated to grade 5 = very poorly differentiated).
- Prostate carcinomas usually have more than one pattern within any given tumor. In biopsies, the most predominant pattern (grade) and the most aggressive are added and the final sum is called the Gleason Score (the predominant & second predominant on resection).
- Gleason grading and scoring in prostate cancer is very useful in predicting the prognosis of a patient.

# STAGING PROSTATE CANCER

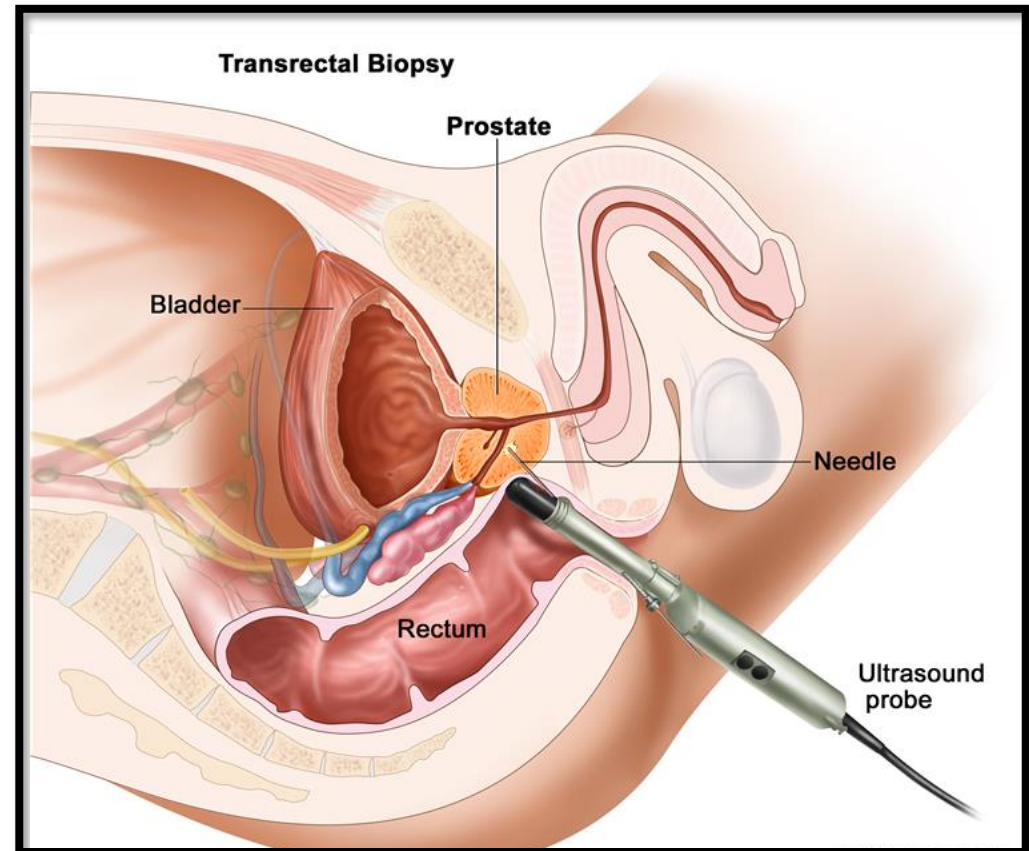
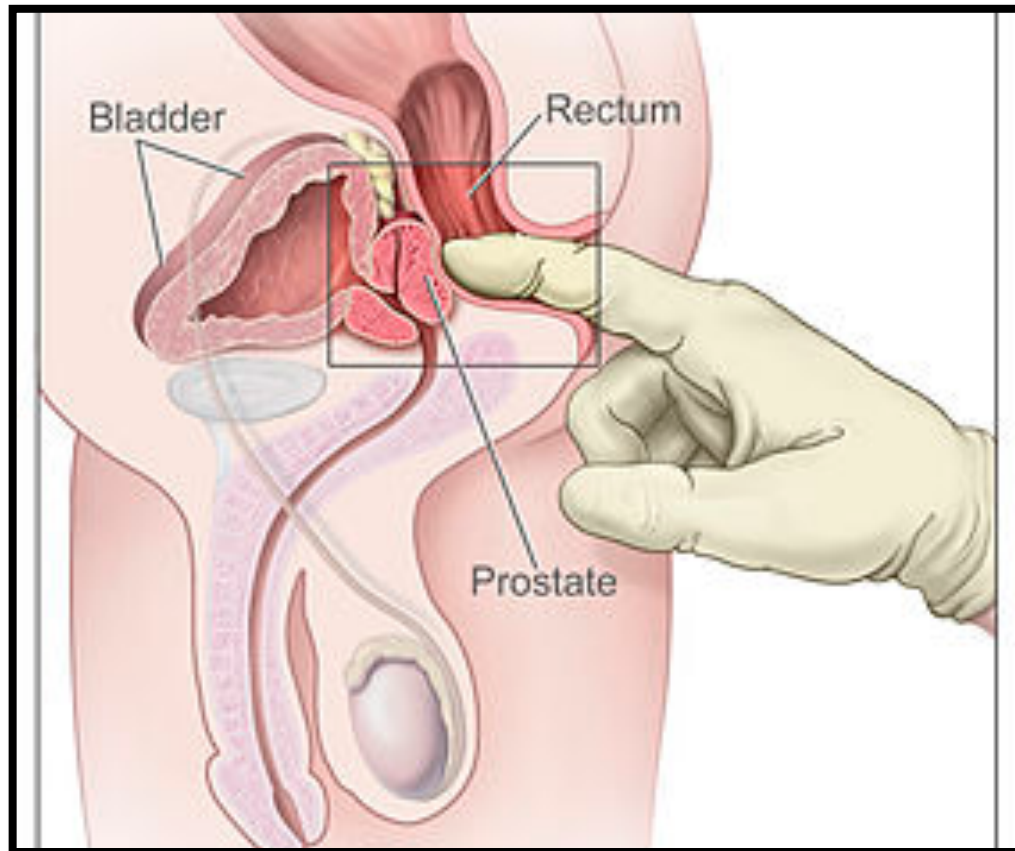
- Staging in prostate cancer depends on the TNM system.
- It is the most important indicator of prognosis.

# CLINICAL PRESENTATION

- Microscopic (or very small size) cancers are asymptomatic and are discovered incidentally.
- Most tumors arise in the peripheral zone, away from urethra and therefore urinary symptoms occur late.
- Occasionally patients present with back pain caused by vertebral metastases.
- Careful digital rectal examination may detect some early cancers.
- PSA (Prostate Specific Antigen) levels 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.
- A transrectal needle biopsy is required to confirm the diagnosis.



# CLINICAL PRESENTATION



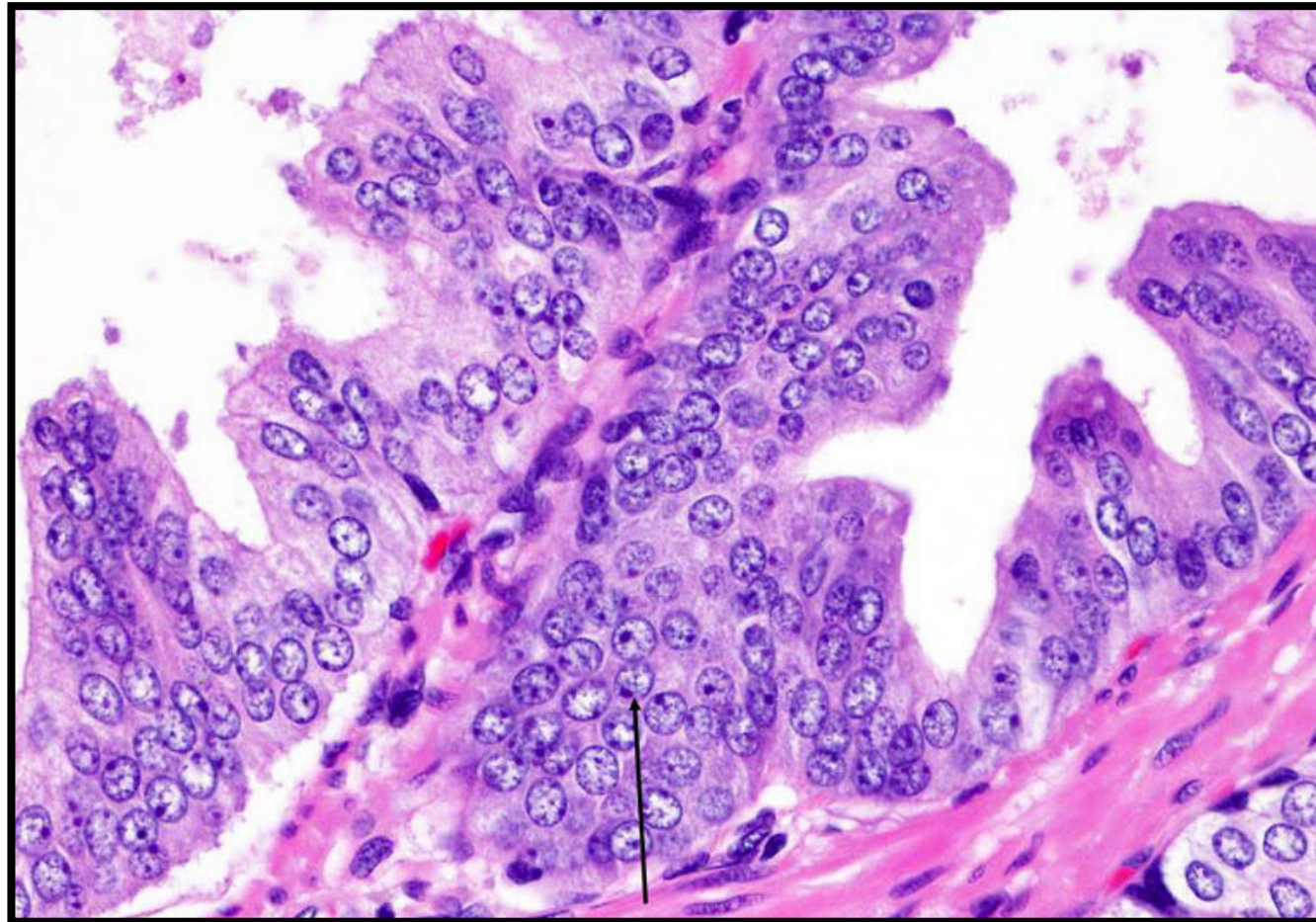
# TREATMENT

- Surgery, radiotherapy and hormonal therapy are used for treatment and 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.
- 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 INTRA-EPITHELIAL 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).
- PIN like prostatic carcinoma occurs in the peripheral zone.

# PROSTATIC INTRA-EPITHELIAL NEOPLASIA



# REFERENCES

- Kumar V, Abbas AK, Aster JC. Robbins Basic Pathology. 10<sup>th</sup> ed. Elsevier; 2018. Philadelphia, PA.



# THANK YOU

End of Lecture