

Lecture 2: Prostatic Hyperplasia & Prostate Cancer

wiseGEEK

▣ Important

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▣ Explanation

Benign Prostatic Hyperplasia

Features

Pathogenesis

Morphology

Microscopy

Clinical Features

Treatment

Prostatic Adenocarcinoma

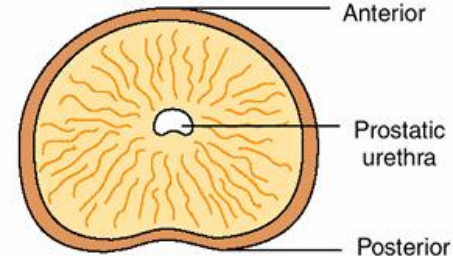
Features

Morphology

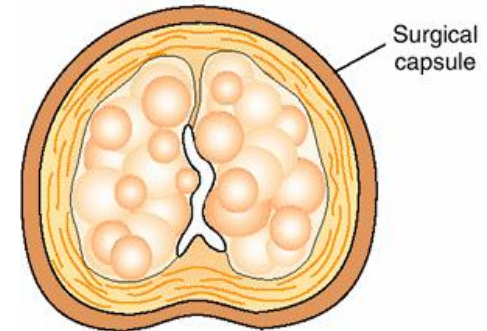
Microscopy

Clinical Features

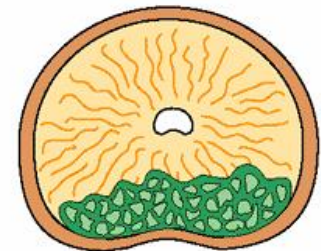
Treatment



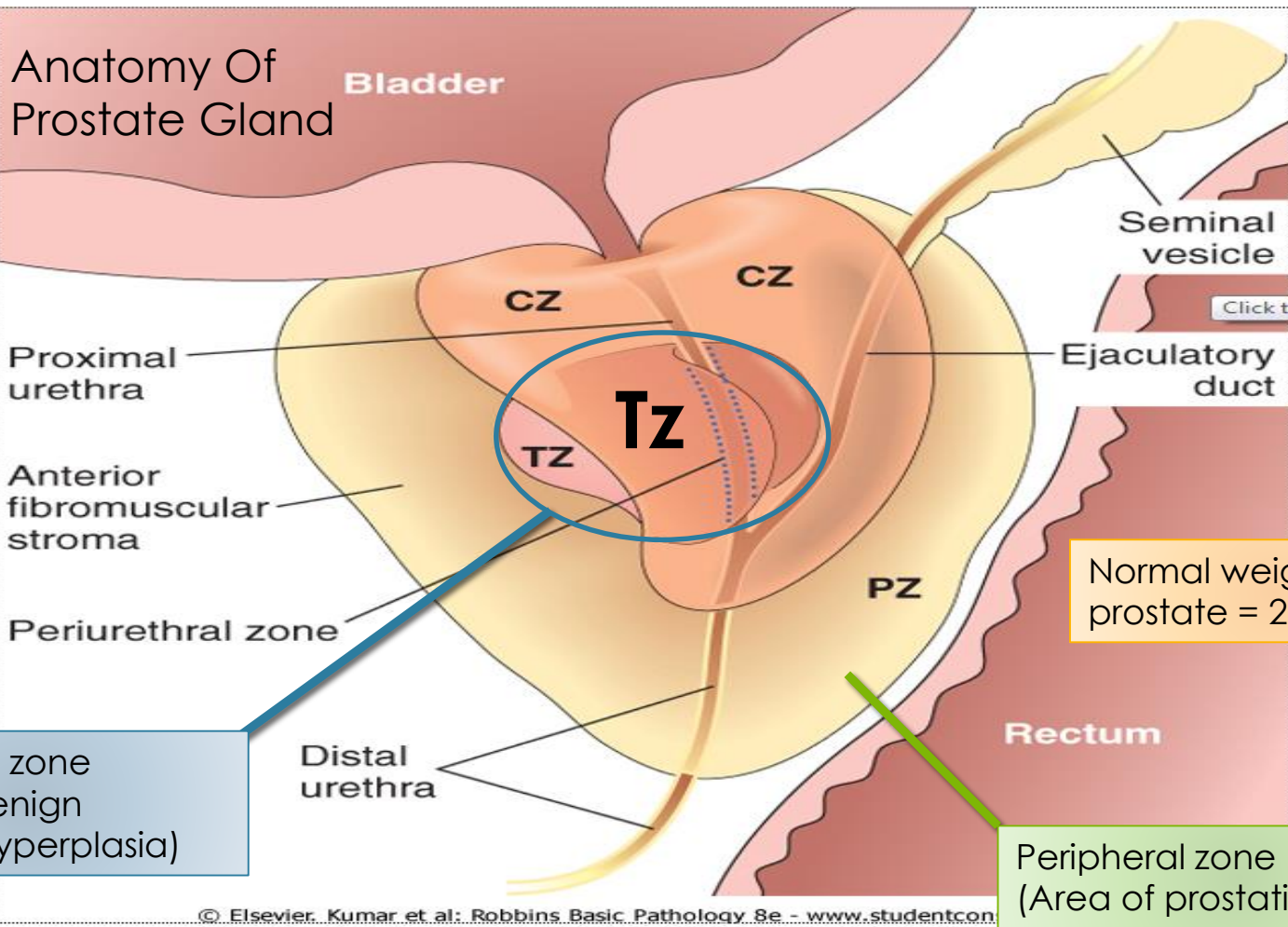
NORMAL PROSTATE



NODULAR PROSTATIC HYPERPLASIA



CARCINOMA OF PROSTATE



Transitional zone
(area of benign prostatic hyperplasia)

Normal weight of prostate = 20gm

Peripheral zone
(Area of prostatic cancer)

Benign Prostatic Hyperplasia (BPH) also called “Benign Nodular Hyperplasia”

Features :

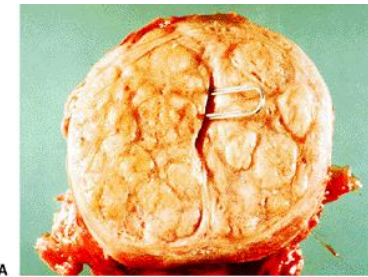
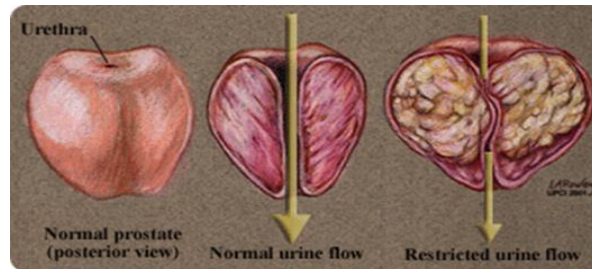
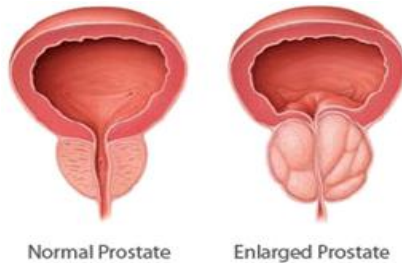
- Extremely **common** lesion in men over the **age of 50**.
- 20% in men over the age of 40, up to 70% by age 60, and 90% by age 80.
- Hyperplasia of glands and stroma results in large **nodular enlargement** in the **periurethral region of transitional zone** of the prostate.
- Once the nodules become large, they compress the prostatic urethra causing either partial, or complete obstruction of the urethra.
- Nodular hyperplasia is **NOT a premalignant** lesion. (**No fear of becoming malignant**)

Pathogenesis :

- The essential cause of BPH is unknown.
- 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 and inhibits epithelial cell death.
- **DHT** is implicated in the pathogenesis of **both benign prostatic hyperplasia (BPH) & prostate cancer**.
- Testosterone is converted to dihydrotestosterone (DHT) by **5-alpha reductase enzyme (type 2)** inside the cell.
- 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 (**removal of testes**) prevents BPH, **because these have low amount of androgens**.

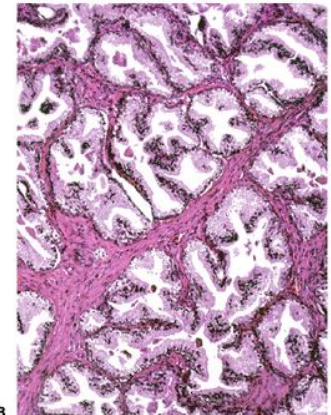
Morphology :

- The prostate weighs between 60 and 100 grams
- The hallmark of BPH is **nodularity** due to glandular & fibromuscular proliferation.
- Nodular hyperplasia begins in the inner aspect of the prostate gland, **the transitional zone**.
- Cut-section shows nodules which vary in size, color and consistency depending on which element is proliferating more (**glandular or fibromuscular**).
- It compresses the wall of the urethra resulting in a **slit-like orifice**.



Microscopy :

- Microscopically, the main feature of BPH is **nodularity**.
- The glandular lumina contain material proteinaceous called **corpora amylacea**.
- The nodules can be: **Stromal** or **Fibroepithelial**
 - Purely **stromal** nodules composed mainly of **fibromuscular element**.
OR
 - **Fibroepithelial** with both **glandular** and **fibromuscular** component. There is aggregation of small to large to cystically dilated glands, lined by two layers of epithelium surrounded by fibromuscular stroma.
- Hyperplastic glands are lined by two cell layers: **inner columnar** & **outer flattened basal cells**.

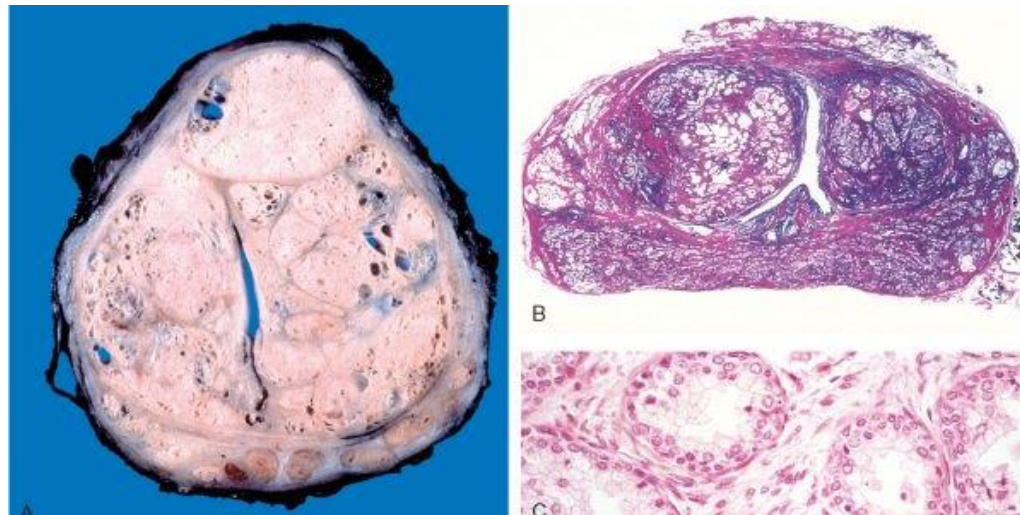


Clinical Features : (in 10% of patients)

- The nodule compresses the prostatic urethra and causes **urethral obstruction**. This leads to **retention of urine** in the bladder (may be acute in some patients) with associated **urinary bladder hypertrophy**.
- Increased urinary frequency.
- Nocturia. (The need to wake and pass urine at night)
- Dysuria. (Painful or difficult urination)
- Difficulty in starting and stopping the stream of urine (Hesitancy).
- Urinary tract infection due to urine retention "stasis"
(Inability to empty the bladder completely → ↑volume of residual urine → infection)
- Absence of the appropriate treatment for urine retention would lead to **hydronephrosis**.

Treatment :

- Mild cases of BPH may be treated with α -blockers (which cause relaxation of prostatic smooth muscle) and 5- α -reductase inhibitors.
- Moderate to severe cases require transurethral resection of the prostate (TURP)



Prostatic Adenocarcinoma

Features :

- One of the **most common** cancers in men.
- Second leading cause of cancer deaths **after lung cancers**.
- Disease of men over age **50**.
- More prevalent among African Americans.
- These tumors show a wide range of clinical behaviors.
- **Etiology**: Several risk factors: Age, race, family history, hormone level (androgens) and environmental influences.
- **Androgens** are believed to play a major role in the **pathogenesis**.

Morphology :

- 70% arises in the **peripheral zone** of the posterior part of the gland.
- Tumor is firm and gritty and is **palpable** on rectal exam.
- Spread by **direct local invasion** and through **blood stream** and **lymph**.
- **Metastases** first spread via **lymphatics**: initially to the obturator nodes and eventually to the para-aortic nodes.
- Hematogenous extension occurs chiefly to **the bones** (vertebral column). The bony metastasis are typically **osteoblastic**.
(In general, Metastases are either osteoblastic or osteolytic and this one enhances osteoblastic activity)
- Local extension most commonly involves the **periprostatic tissue**, **seminal vesicles** and the **base of the urinary bladder** (leading to **urethral obstruction**).

Needle biopsy doesn't sample the transitional zone where BPH begins and occurs, therefore **the diagnosis of BPH can't be made on needle biopsy**.

However, **it could be used to diagnose prostate cancer** because it is mostly found in the peripheral zone.

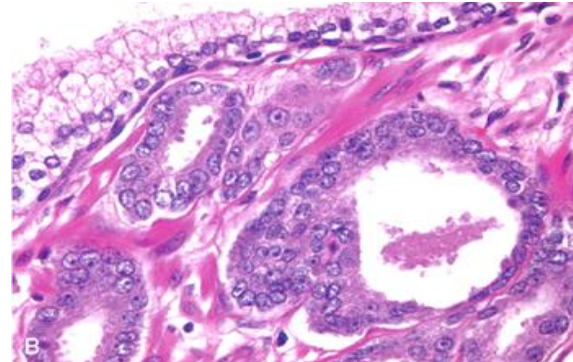
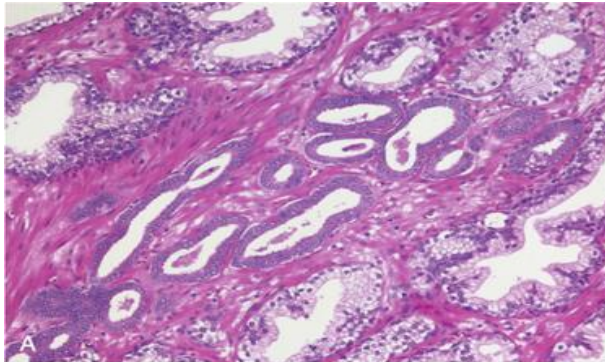


Microscopy :

- Most lesions are adenocarcinomas that produce well-defined gland patterns.
- The malignant glands are lined by a **single layer** (Not Like BPH) of cuboidal or low columnar epithelium.
- The **outer basal cell layer** (typical of benign glands) is **absent**.
- **Large nuclei** and one or more large nucleoli.
- Pleomorphism is not marked.
- Commonly there is perineural invasion (**the tumor invades neurons**)

Prostatic Intraepithelial Neoplasia (PIN)

- 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 carcinoma occurs in the peripheral zone.



Gleason Grading and Scoring

- Gleason system is a histological grading and scoring system for prostatic adenocarcinoma done **on the microscopic level**.
- Gleason Grading and Scoring in prostate cancer is very useful in predicting prognosis of a patient.
- 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 and grade 5= very poorly differentiated).
- The two most common types of grades seen in the biopsy for each cancer case are added to produce a combined Gleason score.
- Score 2-4 being well-differentiated neoplasm. score 5-6 intermediate-grade neoplasm .score 7 moderately - poorly differentiated neoplasm. score 8-10 high-grade neoplasm.

Staging

- Staging in prostate cancer depends on the TNM system. It is **the most important** indicator of prognosis.
- The TNM staging system is based on the size and/or extent (reach) of the primary tumor (T), whether cancer cells have spread to nearby (regional) lymph nodes (N), and whether metastasis (M), or the spread of the cancer to other parts of the body, has occurred.



[Prostate Cancer: Gleason Score](#)
(click here)

Clinical features :

- Microscopic (very small size) cancers are **asymptomatic** and are discovered incidentally.
- Most arise in **the peripheral zone**, away from urethra and **therefore the urinary symptoms occur late**.
- Occasionally, patients present with **back pain** caused by vertebral metastases.
- Careful digital rectal examination (see picture below) may detect some early cancers.
- **PSA (Prostate Specific Antigen)** levels are important in the diagnosis and management of prostate cancer. However, 20% - 40% of prostate confined cancers have low PSA.
- **PSA** is **organ specific** but not cancer specific because it could be increased in BPH and prostatitis.
- A **transrectal needle biopsy** is required to confirm the diagnosis.



Treatment :

- Surgery (if **localized**), 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** 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**.

Summary

(from Robbin's basic pathology)

SUMMARY

Benign Prostatic Hyperplasia

- BPH is characterized by proliferation of benign stromal and glandular elements. DHT, an androgen derived from testosterone, is the major hormonal stimulus for proliferation.
- BPH most commonly affects the inner periurethral zone of the prostate, producing nodules that compress the prostatic urethra. On microscopic examination, the nodules exhibit variable proportions of stroma and glands. Hyperplastic glands are lined by two cell layers: an inner columnar layer and an outer layer composed of flattened basal cells.
- Clinical symptoms and signs are reported by 10% of affected patients and include hesitancy, urgency, nocturia, and poor urinary stream. Chronic obstruction predisposes to recurrent urinary tract infections. Acute urinary obstruction may occur.

SUMMARY

Carcinoma of the Prostate

- Carcinoma of the prostate is a common cancer of older men between 65 and 75 years of age. Aggressive, clinically significant disease is more common in American blacks than in whites, while clinically insignificant occult lesions appear to occur at equal frequencies in these two races.
- Prostate carcinomas range from indolent lesions that will never cause patient harm to aggressive fatal tumors.
- The most common acquired mutations in prostatic carcinomas are *TPRSS2-ETS* fusion genes and mutations that activate the PI3K/AKT signaling pathway.
- Carcinomas of the prostate arise most commonly in the outer, peripheral gland and may be palpable by rectal examination, although currently many are nonpalpable.
- Microscopically, they are adenocarcinomas with variable differentiation. Neoplastic glands are lined by a single layer of cells.
- Grading of prostate cancer by the Gleason system correlates with pathologic stage and prognosis.
- Most localized cancers are clinically silent and are detected by routine monitoring of PSA concentrations in older men. Bone metastases, often osteoblastic, typify advanced prostate cancer.
- Serum PSA measurement is a useful but imperfect cancer screening test, with significant rates of false-negative and false-positive results. Evaluation of PSA concentrations after treatment has great value in monitoring progressive or recurrent disease.

Thank You!

We hope you found this helpful and informative.

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