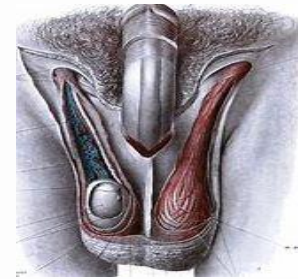
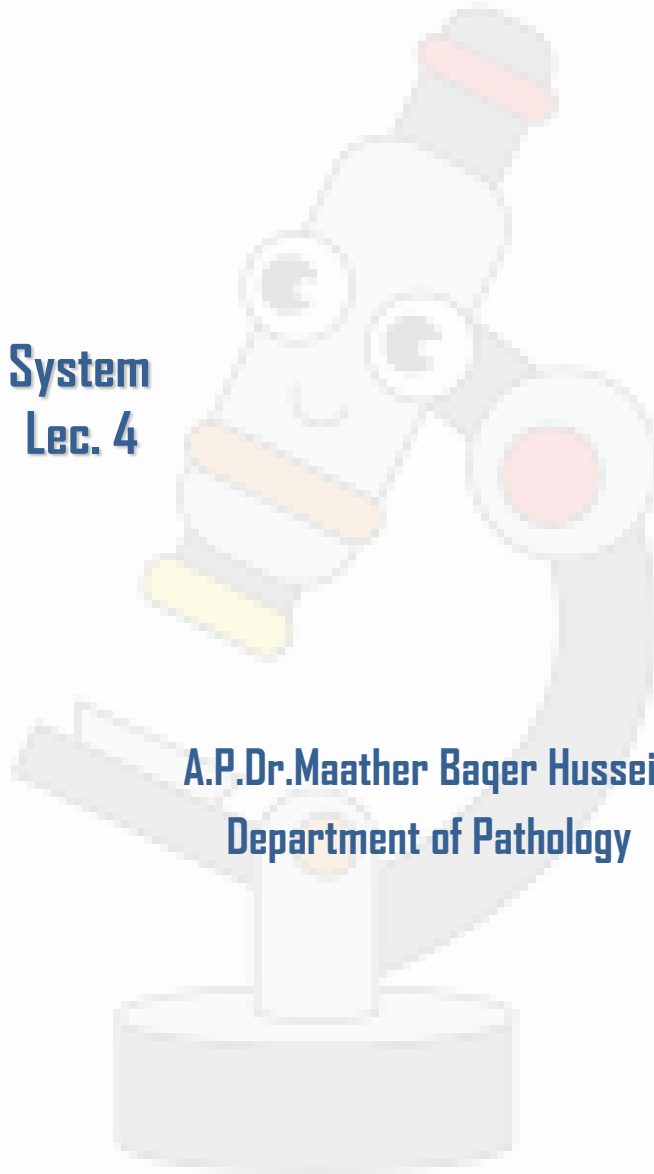


**Male Genital System  
Pathology Lec. 4**



**A.P.Dr.Maather Baqer Hussein  
Department of Pathology**



## Benign Prostatic Hyperplasia

- Very common
- Central zone proliferates
  - Is ccc by proliferation of both stromal and epithelial elements, result in enlargement of the gland and, in some cases, urinary obstruction.
- Histologic evidence of BPH is present in 20% of men by the age 40 years, 70% of men by age 60 years, and 90% by age 70 years; only half have clinically detectable prostate enlargement, and of those, only 50% develop clinical symptoms.

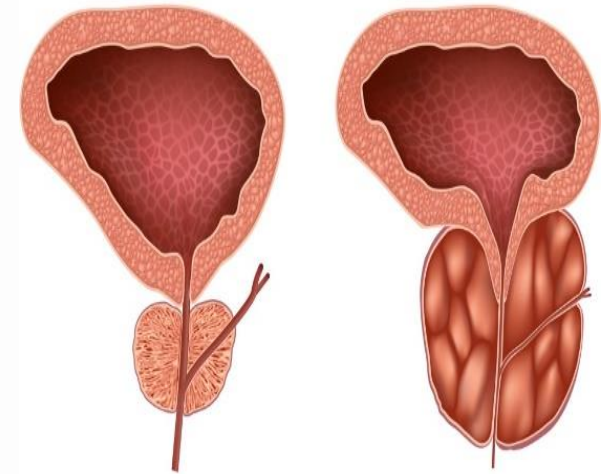
### Pathogenesis

Androgens have a central role in the pathogenesis of BPH.

DHT (dihydrotestosterone) , the active form of testosterone , is derived from testosterone by the action of  $5\alpha$ -reductase & stimulate stromal and glandular proliferation. DHT binds to nuclear androgen receptors and stimulates synthesis of DNA, RNA, growth factors, leading to hyperplasia.

This is the base for the current use of  $5\alpha$ -reductase inhibitors in the its treatment.

## Benign Prostatic Hyperplasia



Normal prostate

Enlarged prostate

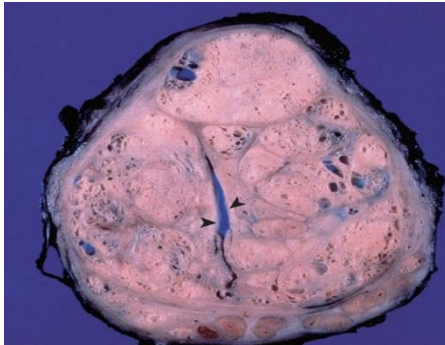
- **Diagnosis:-**

- The clinical diagnosis of BPH is based on a history of **lower urinary tract symptoms**, a **digital rectal exam**, and **exclusion of other causes of similar signs and symptoms**. The degree of **lower urinary tract symptoms** does not necessarily correspond to the size of the prostate.
- An enlarged prostate gland on rectal examination that is symmetric and smooth supports a diagnosis of BPH.
- However, if the prostate gland feels asymmetrical, firm, or nodular, this raises concern for prostate cancer.

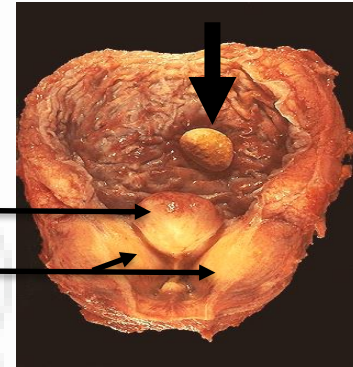


# Morphology

## Nodular prostatic hyperplasia



There are well-defined nodules that compress the urethra (**arrowheads**) into a slitlike lumen.

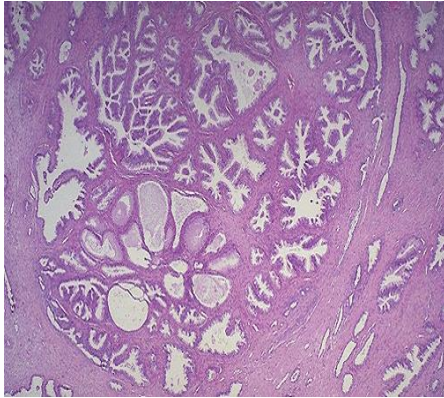


Enlarged lateral lobes and median lobe that obstructs the prostatic urethra. This led to obstruction with bladder hypertrophy, as evidenced by the prominent trabeculation of the mucosal surface. Obstruction with stasis also led to the formation of the yellow-brown stone (arrow).

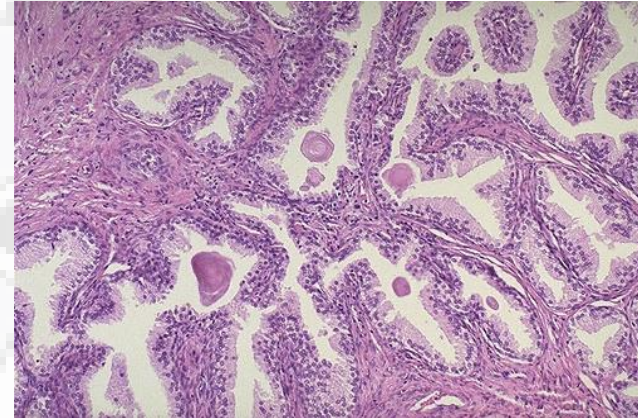


Nodules appear mainly in the lateral lobes. Such an enlarged prostate can obstruct urinary outflow from the bladder and lead to an obstructive uropathy.

## Prostatic nodular hyperplasia



**A- Low-power**  
Microscopically, benign prostatic hyperplasia can involve both glands and stroma, though the former is usually more prominent. Here, a large hyperplastic nodule of glands is seen

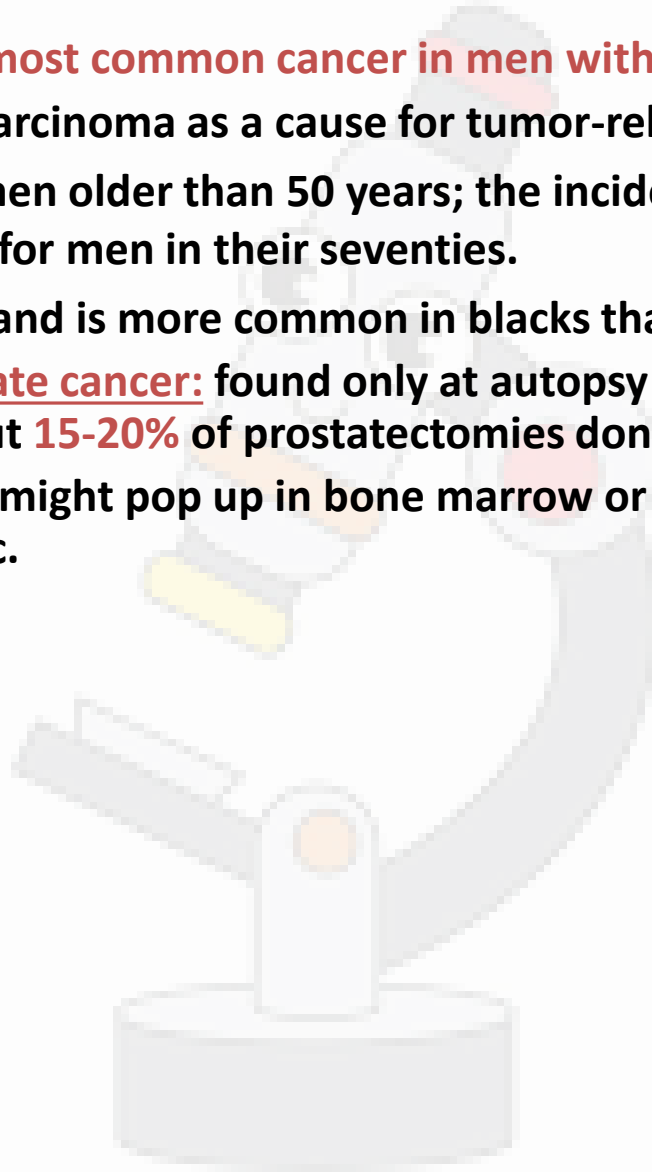


**B- Higher power hyperplastic glands, with the characteristic dual cell population:** The glands are well-differentiated and still have some intervening stroma. The small laminated pink concretions within the glandular lumens are known as corpora amylacea.

# Prostatic cancer

## Adenocarcinoma

- **Prostate cancer is the most common cancer in men with a 1 in 6 lifetime risk**  
Second cancer after lung carcinoma as a cause for tumor-related deaths among males.  
Occurs predominantly in men older than 50 years; the incidence increases from 20% for men in their fifties to 70% for men in their seventies.  
It is uncommon in Asians, and is more common in blacks than in whites.
- ❖ **Latent or hidden prostate cancer**: found only at autopsy (incidental prostate cancer) is more common, About **15-20%** of prostatectomies done.
- ❖ **Occult prostate cancer** might pop up in bone marrow or lymph node prior to becoming symptomatic.



- **Pathogenesis**

### **Etiology of prostate cancer:**

Hormones, genes, and environment are thought to be of pathogenetic importance

**A- The Androgens hormone play the significant role Prostate cancer cells depend on androgen interactions with AR to activate pro-growth and pro-survival genes.**

- **why :-**

- 1. Cancer of the prostate does not develop in males castrated before puberty.**(Castration is any action, surgical, chemical, or otherwise, by which an individual loses use of the testicles.)**
- 2. The growth of many prostatic carcinomas can be inhibited by orchiectomy or by the administration of estrogens such as diethylstilbestrol.**(Orchiectomy is a surgical procedure in which one or both testicles are removed.)**

### **B. Hereditary & Racial contributions**

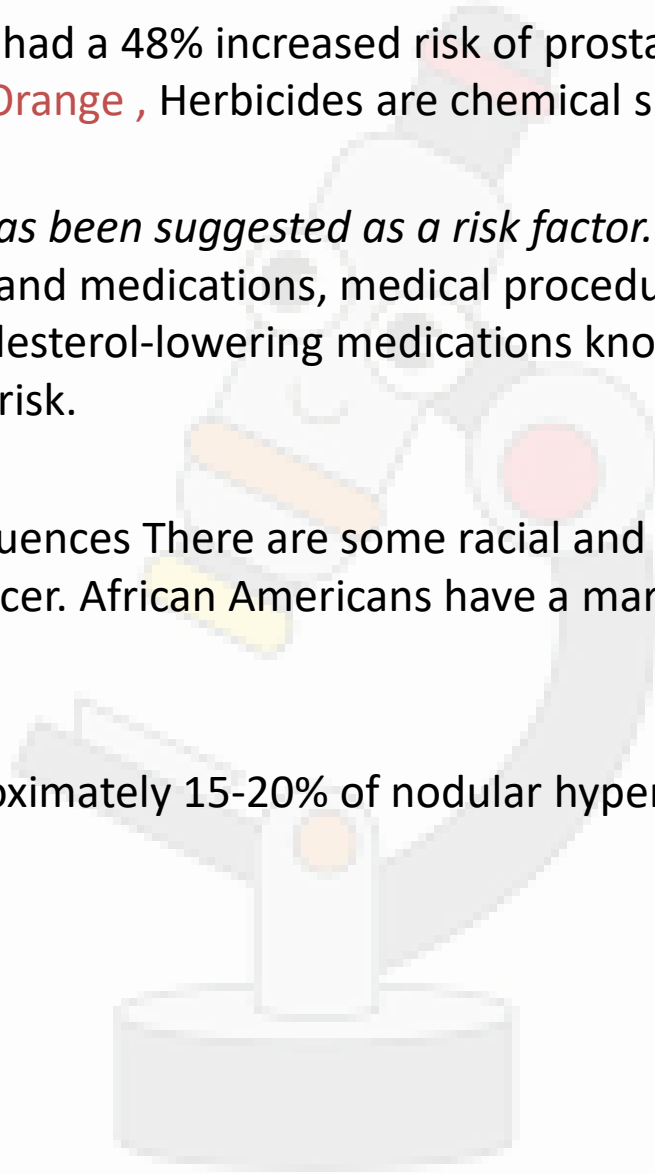
- Risk increases with the number of first-degree relatives with prostate cancer (one relative  $\frac{1}{4}$  two-fold increased risk; two relatives  $\frac{1}{4}$  five-fold increased risk) and the onset of disease occurs at an earlier age.
- BRCA2 mutations increase risk 20-fold, but most familial prostate cancers are associated with loci that only modestly affect risk.
- Several risk loci are associated with innate immunity, suggesting that inflammation can underlie prostate cancer development

### **C. Environmental influences**

- exposed to **Agent Orange** had a 48% increased risk of prostate cancer recurrence following surgery. [**Agent Orange** , Herbicides are chemical substances used to control unwanted plants.
- **Diet High in animal fat** has been suggested as a risk factor. There are also some links between prostate cancer and medications, medical procedures, and medical conditions. Use of the cholesterol-lowering medications known as statins may also decrease prostate cancer risk.

**D. Racial and geographic** influences There are some racial and geographic differences in the incidence of prostatic cancer. African Americans have a markedly higher incidence as compared to whites.

**E. Nodular hyperplasia** Approximately 15-20% of nodular hyperplastic prostates harbour carcinoma.

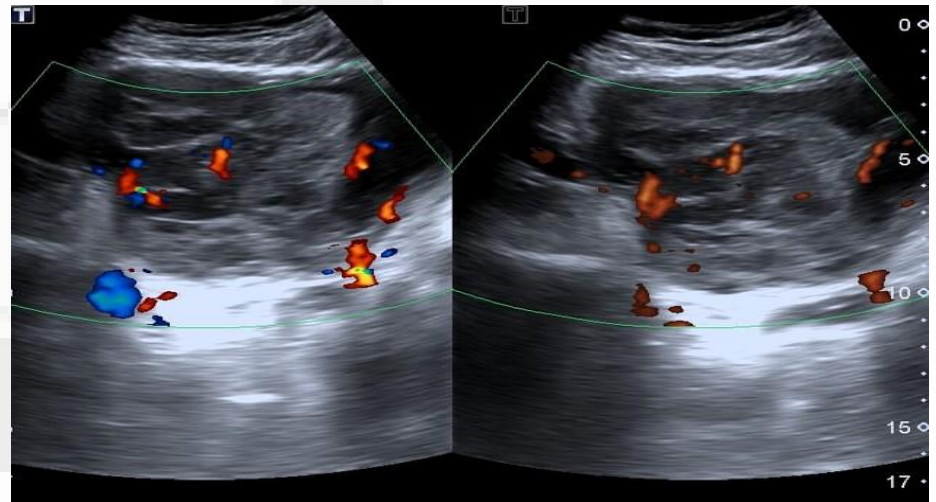




## Diagnosis:-

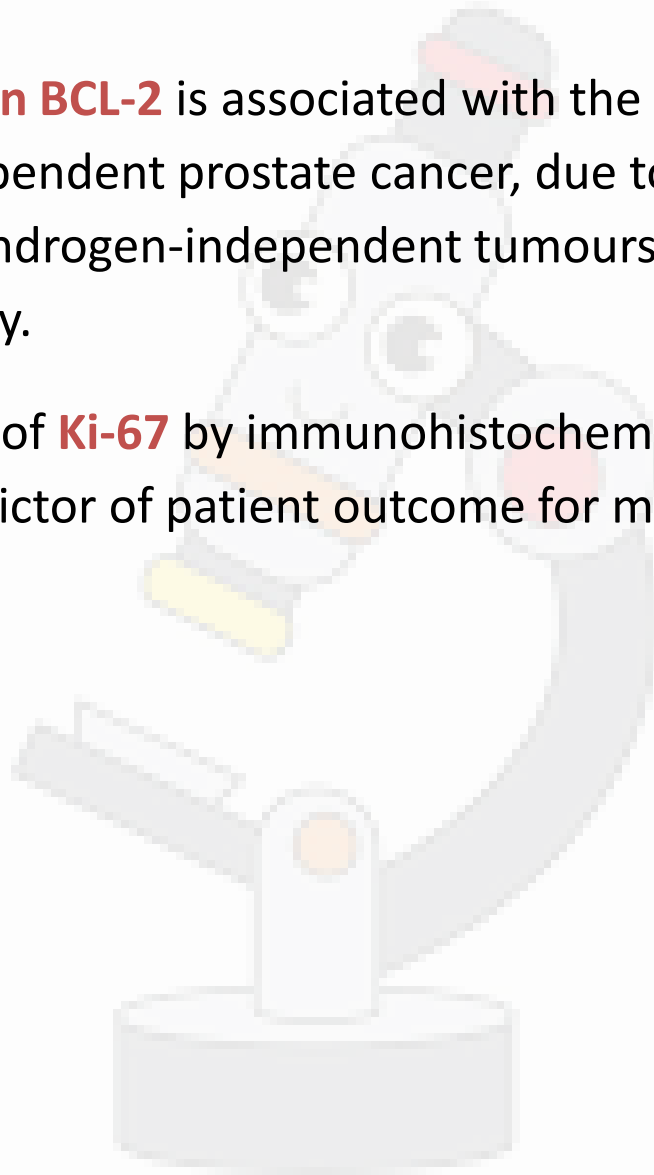
### History & examination :-

- Early prostate cancer usually has no clear symptoms. Sometimes prostate cancer does cause symptoms, often similar to those with benign prostatic hyperplasia, include frequent urination, nocturia (increased urination at night), difficulty starting and maintaining a steady stream of urine, hematuria (blood in the urine), and dysuria (painful urination).
- Metastatic prostate cancer that has spread to other parts of the body can cause additional symptoms. The most common symptom is bone pain, often in the vertebrae (bones of the spine), pelvis, or ribs.



## Tumor markers:-

- The **oncoprotein BCL-2** is associated with the development of androgen-independent prostate cancer, due to its high levels of expression in androgen-independent tumours in advanced stages of the pathology.
- The expression of **Ki-67** by immunohistochemistry may be a significant predictor of patient outcome for men with prostate cancer.

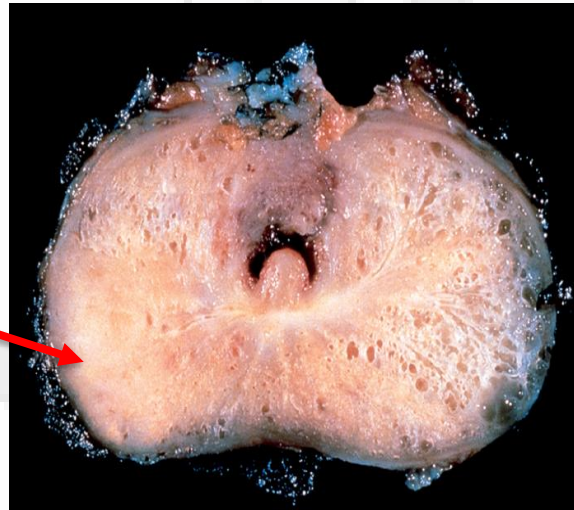


## •Gross features

## Adenocarcinoma of the prostate



Extensive tumor appearing as an irregularly shaped, yellowish mass in a gland that is also involved by nodular hyperplasia.

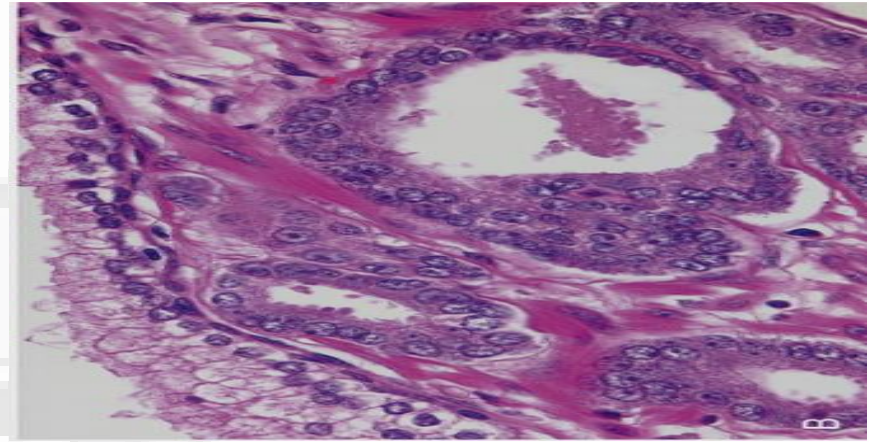
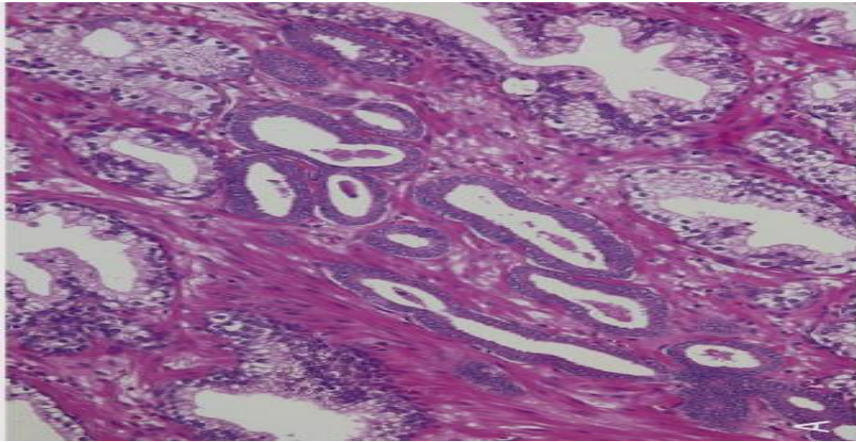


Carcinomatous tissue is seen on the posterior aspect (lower left). Note the solid whiter tissue of cancer in contrast to the spongy appearance of the benign peripheral zone on the contralateral side.

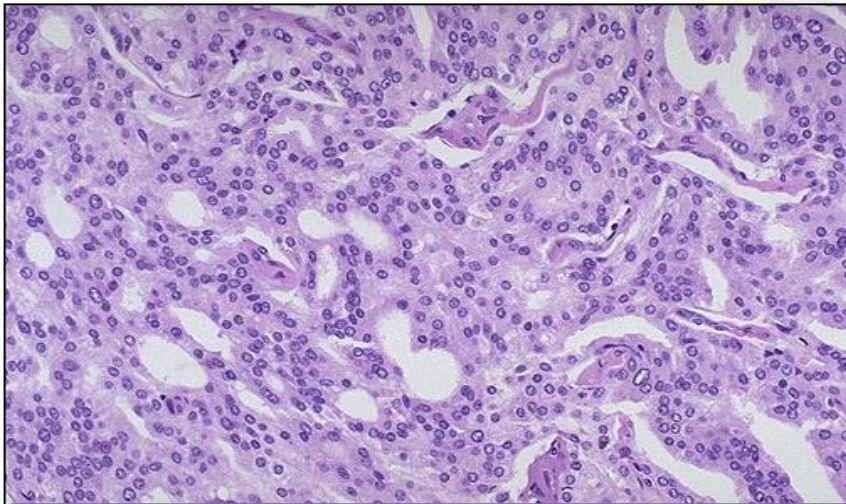


These sections through a prostate removed via radical prostatectomy reveal irregular yellowish nodules, mostly in the posterior portion (seen here superiorly).

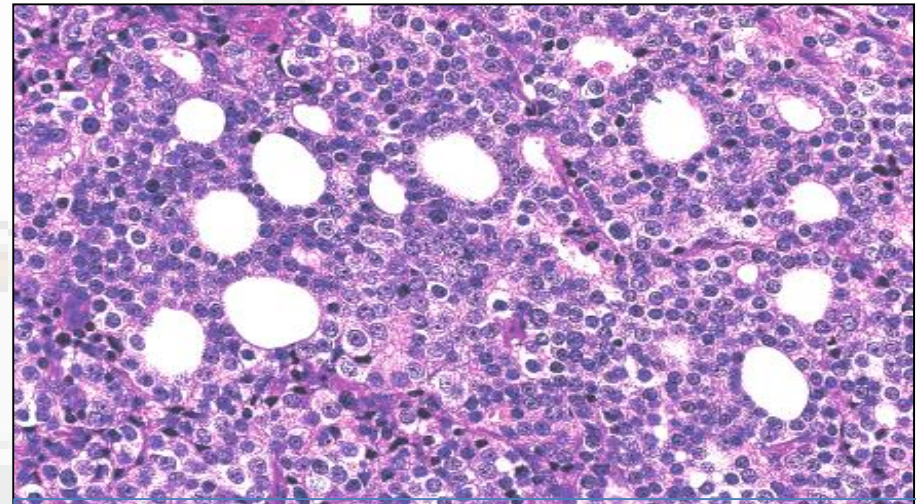
## Prostatic adenocarcinoma



**A, a small focus of adenocarcinoma of the prostate shows small glands crowded in between larger benign glands. B, Higher magnification shows several small malignant glands with enlarged nuclei, prominent nucleoli, and dark cytoplasm.**



**Prostatic adenocarcinoma back to back glands**



**Prostatic adenocarcinoma lymph node metastasis**

## Metastases:

Regional lymph nodes

Axial skeleton (causing miserable bone pain often with osteoblastic lesions)

Leptomeninges (not the brain tissue).

## Staging of Prostate Cancer

### PROSTATE CANCER STAGES

- |                  |   |
|------------------|---|
| <b>Stage I</b>   | - the cancer is small and only in the prostate  |
| <b>Stage II</b>  | - the cancer is larger and may be in both lobes of the prostate but is still confined to the prostate   |
| <b>Stage III</b> | - the cancer has spread beyond the prostate to close by lymph glands or seminal vesicles  |
| <b>Stage IV</b>  | - the cancer has spread to other organs such as the bone and is referred to as metastatic cancer. If prostate cancer spreads, or metastasizes, to the bone, you have prostate cancer cells in the bone, not bone cancer |

# Histologic Grading of Prostatic adenocarcinoma:

## Gleason grading system:-

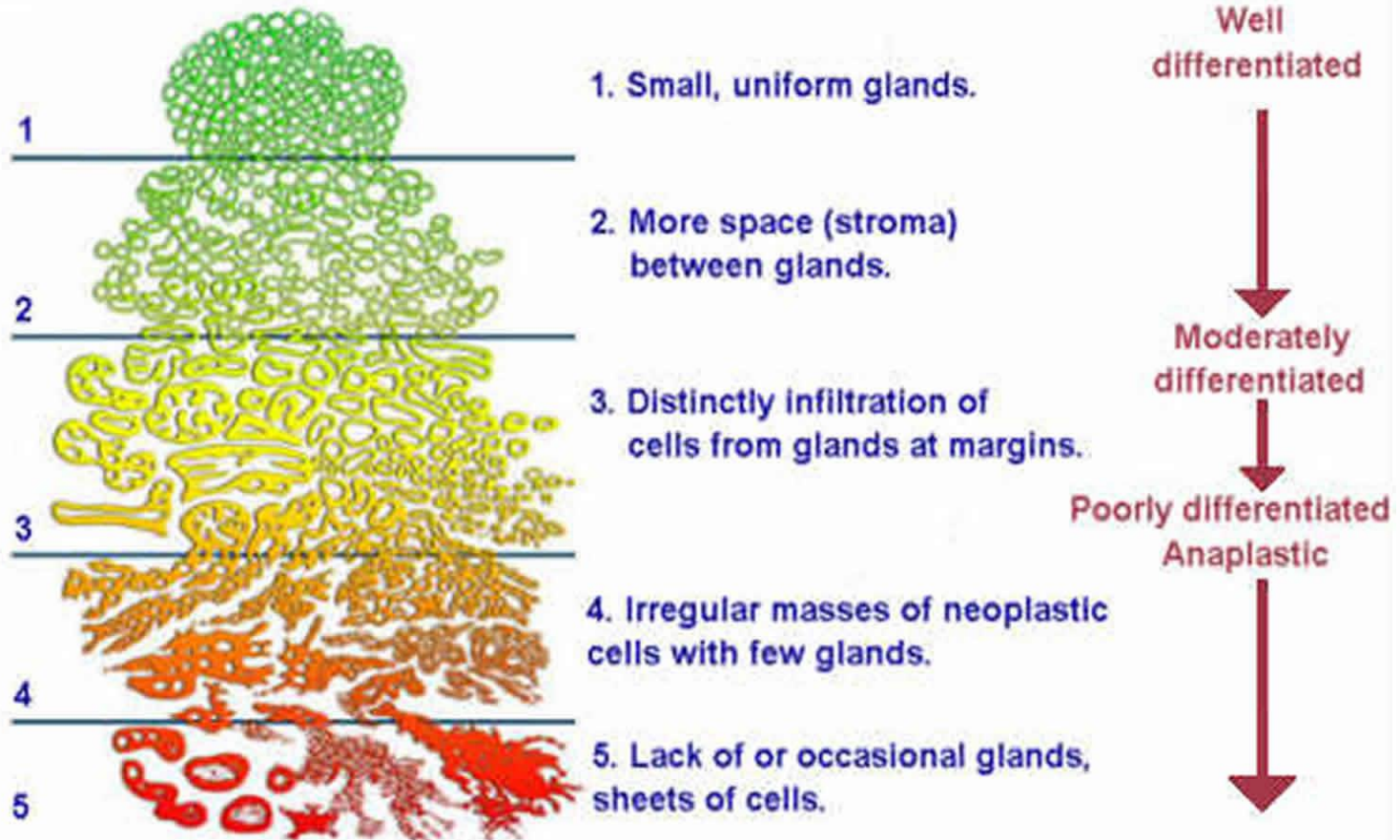
is given to prostate cancer based upon its microscopic appearance.

is used in routine practice to help evaluate the prognosis of men with prostate cancer using samples from a prostate biopsy.

- A total score is calculated based on how cells look under a microscope, with the first half of the score based on the dominant, or most common cell morphology (scored 1—5), and the second half based on the non-dominant cell pattern with the highest grade (scored 1—5). These two numbers are then combined to produce a total score for the cancer.

For example, if the Gleason score is written as “3+5 = 8”, it means most of the cancer is primarily pattern 3 and to a lesser amount pattern 5. The two numbers are then added together to create a Gleason score of 8.

# Gleason's Pattern Scale



*Gleason scoring system* is predominant as :-

**Low grade** or well differentiated corresponding to score **2-4**.

**Medium grade** or moderate differentiated corresponding to score **5-7**.

**High grade** or poor differentiated corresponding to score **8-10**.



**THANK YOU  
FOR YOUR  
ATTENTION**