Prostate gland

Consists of 5 lobes

Anterior, posterior, middle and two lateral.

Histologically: it is composed of glands and fibromuscular stroma.

The glands have two layers of cells: Basal: (flattened or cuboidal); luminal: (tall or columnar).

Stromal tissue (muscles & fibrous tissue):

❖ ***The most important categories of prostate diseases are.***

1. Prostatitis.
2. Nodular hyperplasia.
3. Prostatic carcinoma.

1. Prostatitis

- It is divided into three categories:

a) ***Acute bacterial prostatitis*** (2–5% of cases), caused by the same organisms associated with other acute urinary tract infections (Mainly due to **E.coli).** Presents with sudden onset of fever, chills, dysuria, perineal pain, and bladder outlet obstruction; it may be complicated by sepsis. digital rectal examination is contraindicated, as pressure on the boggy, exquisitely tender prostate can cause bacteremia. ***Microscopically***, there are **neutrophils** (mainly) & macrophages infiltration in the glands.

b) ***Chronic bacterial prostatitis*** (2–5% of cases), also caused by common uropathogens. It usually is associated with recurrent urinary tract infections bracketed by asymptomatic periods. Presenting manifestations include low back pain, dysuria, and perineal and suprapubic discomfort. ***Microscopically***, there are lymphoid infiltrate & glandular injury.

c) Chronic pelvic pain syndrome (90%–95% of cases). It can be subdivided into **inflammatory cases**, which are associated with leukocytes in prostatic secretions, and **noninflammatory cases**, in which leukocytes are absent. It is characterized by chronic pain localized to the perineum, suprapubic area, and penis. Pain during or after ejaculation is a prominent finding. The etiology is uncertain.

2. Nodular hyperplasia of the prostate (benign prostatic hyperplasia [BPH]).

Normally, the prostatic parenchyma can be divided into 4 biologically distinct regions, include the peripheral, central, transitional, & periurethral zones.

Note: most hyperplastic lesions arise in the inner transition zone, while most carcinomas (70%–80%) arise in the peripheral zones.

As a result, carcinomas are often detected by rectal examination, whereas hyperplasias are more likely to cause urinary obstruction.

- **Age:** BPH frequency rises with age, it is present in a significant number of men by 40 years of age, and rises progressively thereafter, reaching 90% by the eighth decade of life. (>40yrs=20%, >60yrs=70% >70yrs=90%).
- Periurethral portion is involved.
- Present with urinary obstruction.
- Hyperplasia of stroma and epithelial cells.

Pathogenesis of nodular prostatic hyperplasia

Although the cause of BPH is incompletely understood, excessive androgen-dependent growth of stromal and glandular elements has a central role.

- BPH does not occur in males who are castrated before the onset of puberty or in males with genetic diseases that block androgen activity.
- Dihydrotestosterone (DHT), the ultimate mediator of prostatic growth, is synthesized in the prostate from circulating testosterone by the action of the enzyme **5α-reductase, type 2.** DHT binds to nuclear androgen receptors, which regulate the expression of genes that support the growth and survival of prostatic epithelium and stromal cells. Although testosterone can also bind to androgen receptors and stimulate growth, DHT is 10 times more potent.

The importance of DHT in causing nodular hyperplasia is supported by clinical observations in which **an inhibitor of 5α-reductase** such as finasteride (proscar) is given to men with this condition. Such treatment markedly reduces the DHT content of the prostate and, in turn, reduces prostate volume and BPH symptoms

Clinical features.

Only 10% of men are showing clinical features of prostatic hyperplasia.

- features are divided into

I. **obstructive symptoms** include: hesitancy or difficulty initiating the stream, straining, a reduced flow, an intermittent stream or a sensation of incomplete emptying.

II. **Irritative symptoms** include: frequency, urgency, nocturia and urge incontinence.

Morphology of Nodular Prostatic Hypeplasia.

Gross.

The prostate is **enlarged** (300 grams or more).

The cut surface contains **multiple, well circumscribed nodules,**

- **Mic.**

Both glandular & fibromuscular stroma tissues are proliferated within hyperplastic nodules.

The hyperplastic glands are lined by tall, columnar epithelial cells & a peripheral layer of flattened basal layer, & the glandular lumina contain inspissated, proteineous secretory material called **Corpora amylacea**.

Note: Nodular hyperplasia is **NOT** considered to be a **premalignant lesion**

But **it may coexist with it**

3. Carcinoma of prostate

- **The most common form of cancer in males.**
- **Second most common cause of cancer related deaths in men older than 50 years of age, after carcinoma of the lung.**

- **Etiology**.

1. **Hormonal factors.** Androgen are of central importance, suggested by the following facts:

I. Cancer of prostate **does not develop in males castrated before the puberty**, **indicating that androgen likely play a part in its development.**

II. The growth of many carcinomas of prostate **can be inhibited by orchiectomy or by the administration of estrogens.**

2. **Hereditary factors**
   - Increased risk of disease among first-degree relatives of patients.
   - The incidence is highest among African-Americans than in Scandinavian countries & Asians.
   - Aggressive, clinically significant disease is more common in African-Americans than in Caucasians.

3. Environmental factors
   - Increased with **certain industries** (Cadmium).
   - Among Japanese immigrants to the United States the incidence of the disease rises. Also, as the diet in Asia becomes more westernized, the incidence in this region of the world is increasing. However, the relationship between specific dietary components and prostate cancer risk is unclear.

4. <u>Acquired genetic aberrations</u>

- The most common gene rearrangements in prostate cancer create fusion genes consisting of the androgen-regulated promoter of the TMPRSS2 gene and the coding sequence of ETS family transcription factors.
- TMPRSS2-ETS fusion genes are found in approximately 40% to 60% of prostate cancers in Caucasian populations, and they occur relatively early in tumorigenesis.

- **<u>Clinical features</u>**.

According to stage of cancer:

1. During early stages/ mainly silent/ diagnosed incidentally on routine digital rectal examination, because most of cancers are aroused at peripheral area of gland.
2. More extensive disease/produce urinary obstructive symptoms.
3. More aggressive carcinomas/ discovered due to metastases (bone metastases, which are commonly to axial bones).

Important Note:

<u>Bone metastases of prostatic carcinoma are either</u>

I. **<u>Osteolytic (destructive) lesion.</u>**
II. **<u>Osteoblastic (bone producing) lesion</u>**, **COMMONEST** one & indicate advanced cancer.

4. Other sites of metastases are **<u>lung/pleura</u>**, liver, adrenal, **<u>lymph nodes & Perinural invasion</u>** is very common (in 85% of cases), is suggested of extraprostatic extension.

- **<u>Screening tests</u>**
  - Screening tests for diagnosis of prostatic carcinomas are:
    1. Prostatic specific antigen (**PSA)** serum levels.
    2. Digital rectal examination.
    3. Transrectal sonography & needle biopsy.

<u>All these tests should be used in combination in diagnosis of prostatic carcinomas.</u>

- **<u>Morphology of prostatic carcinomas</u>**
  - About 70% to 80% of prostatic carcinomas arise in the outer (peripheral) glands & hence may be palpable as irregular hard nodules by rectal digital examination.
  - Carcinomas detected clinically are usually not visible grossly. More advanced lesions appear as firm, gray-white lesions with ill-defined margins that infiltrate the adjacent gland.

Mic

- Most cases are Adenocarcinoma with variable degrees of differentiation, ranging form well differentiated (small glands with irregular infiltration of stroma) to anaplastic carcinoma (irregular shaped glands).
- Gland formations:
  1. Lined by single cell layer, **no basal layer**
  2. The glands are small, **crowded** together and characteristically lack branching and papillary infolding.
  3. Nuclei are large, contain **1-2 nucleoli**
  4. Mitotic figures are uncommon
- **Perineural invasion is common**
- In approximately 80% of cases, prostatic tissue removed for carcinoma also harbors presumptive precursor lesions, referred to as high-grade prostatic intraepithelial neoplasia (HGPIN).

Grading of prostatic carcinoma.

Gleason system, which depends on certain features, include

1. Degree of glandular differentiation
2. The architecture of the neoplastic glands
3. Nuclear grading & mitotic activity.

Gleason system is consisting of five grades.

Testis

Normal testicular tissue:

- 250 lobule.
- 4 tubule in each lobule.
- Each tubule is composed of:
  Basement membrane, sertoli cells, germ cells .
- The interstitial cells are (Leydig cells).

Cryptorchdism (undescended testis) & Testicular Atrophy.

Cryptorchidism: is a failure of testicular descent into the scrotum.

- Normally, the testes descend from the abdominal cavity into the pelvis by the third month of gestation & then through the inguinal canals into the scrotum during the last 2 months of intrauterine life.

- In majority of cases the cause is unknown.
- It affects 1% of male
- It is difficult to diagnose before the age of 1 year, particularly in premature infants, because testicular descent into the scrotum is not always complete at birth.
- The condition is bilateral in approximately 10% of affected patients.

- **Predisposing factors**

1. Hormonal abnormalities. Mainly androgen abnormalities (androgen is important for descending of testes from the pelvis to scrotum).
2. Intrinsic testicular abnormalities.
3. Mechanical problems (obstruction of the inguinal canal).

- **Complications of cryptorchidism**

1. Trauma.
2. Torsion.
3. Inguinal hernia, in 10%- 20% of cases.
4. Sterility (bilateral cryptorchidism, because undescended testes become atrophic. For unclear reasons, even unilateral cryptorchidism may be associated with atrophy of the contralateral descended gonad).
5. Testicular cancer, failure of testicular descent is associated with 3-5 fold increase risk of malignancy, & also there is increase cancer risk in **contralateral** normal descending testis.

- Surgical placement of the undescended testis into the scrotum (orchiopexy) is recommended by 18 months of age to decrease the likelihood of testicular atrophy, infertility, and testicular cancer.

Gross

Small, firm, brown testis.

Mic

1. There is marked hyalinization & thickening of basement membrane of seminiferous tubules.
2. There are prominent leydig cells, hyperplastic sertoli cells, & atrophy of germ cells.

Causes of testicular Atrophy.

1. Atherosclerosis.
2. Orchitis (inflammation of testes) mainly mumps.
3. Cryptorchidism.
4. Hypopituitarism.

5. Radiation.
6. Liver cirrhosis.
7. Females hormones therapy.

Testicular Neoplasms.

- Less than 1% of all male malignancies.
- Peak age of incidence 15-34 years.
- More in whites than in blacks.
- 95% of these tumors arise from germ cells, and almost are malignant (aggressive but curable tumors). By contrast, sex cord-stromal tumors derived from Sertoli or Leydig cells are uncommon and usually benign.

Causes of testicular neoplasia:

The cause of testicular neoplasms is poorly understood. It may be due to

1) Cryptorchidism.
2) Intersex syndromes, including androgen insensitivity syndrome and gonadal dysgenesis.
3) Extra copies of the short arm of chromosome 12, usually due to the presence of an isochromosome 12 [i(12p)], are found in virtually all germ cell tumors.
4) Oncogenic mutations in *KIT* which are found in up to 25% of tumors.

Classification of testicular neoplasia (WHO Classification)

1. **Intratubular germ cell neoplasia.** It is mean that the malignant changes are limited to the lining of seminiferous tubules, & it is now widely believed that most testicular tumors arise from intratubular germ cells tumors.
2. **Seminoma** (classic, tubular)
3. **Spermatocytic seminoma (spermatocytic tumor).**
4. **Non seminomatous germ cell tumors.**

   Embryonal carcinoma

   Yolk sac tumor

   Choriocarcinoma

   Teratomas (mature, immature, with malignant transformation)

   Mixed

Clinical features:

- Patients present most frequently with a painless testicular mass that is nontranslucent.
- Some tumors, especially nonseminomatous germ cell neoplasms, may have metastasized widely by the time of diagnosis in the absence of a palpable testicular lesion

- Seminomas and nonseminomatous tumors differ in their **behavior** and **clinical course** as:

Seminomas often remain confined to the testis for long periods and may reach considerable size before diagnosis. Metastases most commonly are encountered in the iliac and paraaortic lymph nodes, particularly in the upper lumbar region. Hematogenous metastases occur late in the course of the disease.

Nonseminomatous germ cell neoplasms tend to metastasize **earlier**, by lymphatic as well as hematogenous routes. Hematogenous metastases are most common in the liver and lungs.

Seminoma.

- Mostly between the 3rd- 5th decades of life.
- Account for about 50% of testicular germ cell neoplasms.
- They are histologically identical to ovarian dysgeminoma & germinoma occurring in CNS.

Gross.

- **large, soft, well demarcated**, usually homogenous, may contain foci of **coagulative necrosis**, but usually **without hemorrhage**.

Mic.

Seminoma are composed of:

- Large cells with distinct cell borders.
- Clear, glycogen- rich cytoplasm.
- Round nuclei with conspicuous nucleoli,

Tumors cells are arranged in lobules with intervening fibrous septa, A lymphocytic infiltrate is usually present.

* Seminoma **never** occurs in children.
* In about 15% of cases, syncytiotrophoblasts are present; these cells are the source of the minimally **elevated serum human choriogonadotropin (hCG).**
* Seminoma is **+ve for placental alkaline phosphatase.**
* Seminoma is **-ve for alpha feto-protein**.
* Seminomas often remain confined to the testis for prolonged time & may reach considerable size before diagnosis

Spermatocytic Seminoma.

- (formerly called spermatocytic seminoma)
- Occurs in older men than other testicular tumors (beyond 50 years of age).

- Contain a mixture of small, medium sized cells and multinucleate tumor cells.
- Do not metastasize in contrast to classic seminoma.

Embryonal carcinoma

- Ill-defined invasive masses containing foci of hemorrhage & necrosis.
- Cells are large, indistinct cell borders, basophilic cytoplasm, & large nuclei with prominent nucleoli.

Yolk sac tumors.

- Most common primary testicular neoplasm in children younger than 3 years of age.
- In adults, often seen admixed with embryonal carcinoma.
- Histological examination showing:

1. Low cuboidal to columnar epithelial cells forming sheets, glands, papillae, & microcysts.
2. Presence of Schiller-Duvall bodies (structures resembling primitive glomeruli).

These tumors often have eosinophilic hyaline globules containing α_1-anti-trypsin and alpha fetoprotein (AFP), which can be demonstrated by immunohistochemical techniques

Choriocarcinoma.

- These tumors are usually mixed with other germ cell tumors.
- Arise in placenta, ovary, mediastinum or abdomen.
- Choriocarcinoma usually small, but almost presented with metastases (mainly to the lungs, liver, CNS).
- Microscopically: sheets of small cuboidal cells (cytotrphoblastic cell) mixed with large, multinucleated syncytial cells(syncytiotrophoblstic cells),
  HCG can be identified in the syncytiotrophoblastic cells by IHC staining

Teratomas.

- Most second germ cell tumor in children under 3 years, following the yolk sac tumors.
- They are usually pure, & almost never show metastases, & are associated with many Down's syndrome, klinefelter's syndrome, spina bifida.
- in postpubertal males are malignant, being capable of metastasis regardless of whether they are composed of mature or immature elements.
- Microscopically, three major variants of pure teratoma are recognized:

I. Mature Teratomas.

Contain fully differentiated tissues from one or more germ cell layers (e.g neural tissue, cartilage, adipose tissue, bone, and epithelium).

II. **Immature Teratomas.** Usually are seen in adults, & they are contain immature tissue resemble to fetal tissue (primitive neural tissue, immture cartilage tissue…..etc).

III. **Teratomas with malignant transformation.** Characterized by:

The development of frank malignancy in preexisting teratomatous elements, usually in the form of a squamous cell carcinoma or adenocarcinoma.