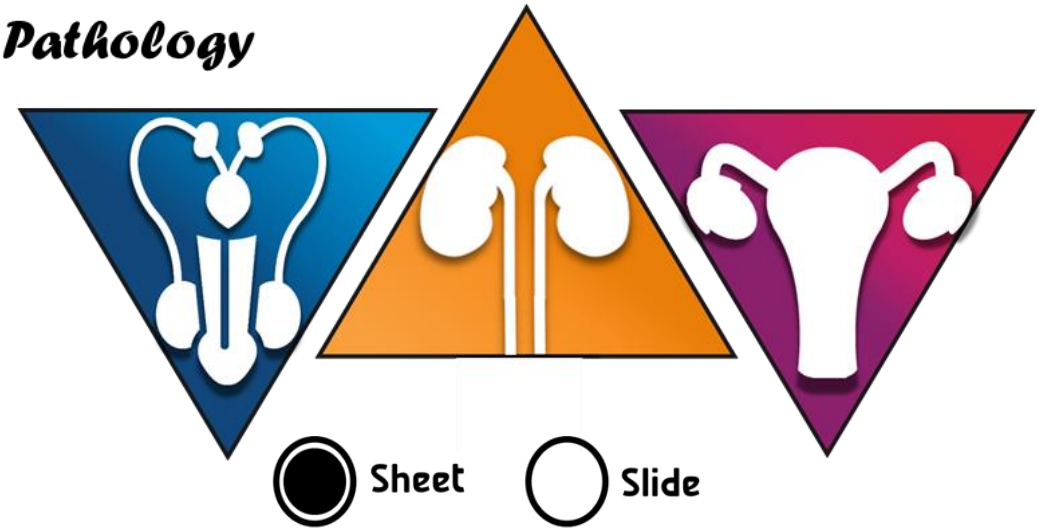
Urogenital system

Pathology



Number: - 1

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Everything in the slide –including pictures- is added so you don't need to refer back to the slides .Good Luck

Testicular Neoplasms:

Peak incidence at 15-34 years old.

The most common tumours in men among this age group and causes 10% of cancer deaths.

Classified into :

I. **Germ cell tumours** : (95%); all are malignant in postpubertal males .(this is the topic of this sheet)
II. **Sex cord-stromal tumours**: (<5%) generally benign.(we will not talk about them)

Risk factors of testicular neoplasms:

1. **whites** > blacks

2. **Cryptorchidism** : failure of descending of one or both testis. 3-5 folds risk of cancer in the undescended testis, and an increased risk of cancer in the contralateral descended testis.

3. **Intersex syndromes**: -

-Androgen insensitivity syndrome : in which the patient is genetically a male(XY in karyortyping) but phenotypically he looks like a female due to insensitivity (resistance) of androgens in the peripheral tissues .

-**Gonadal dysgenesis** : a congenital developmental abnormality affecting both males and females characterized by failure to develop normal functioning gonads so they end up with streak(functionless)gonads .

4. **Family history**: Relative Risk (RR) is 4X higher than normal in fathers and sons of affected patient and 8-10X in their brothers.

5. **The development of cancer in one testis** markedly increased risk of neoplasia in the contralateral testis.

6. **An isochromosome *of the short arm of chromosome 12**, i(12p), is found in virtually all germ cell tumors, regardless of their histologic type.

* isochromosome is an abnormal metacentric chromosome formed by the duplication of one arm of a normal chromosome with deletion of the other arm. Both arms of the metacentric chromosome are thus genetically identical. It may arise from transverse instead of longitudinal division of the centromere during cell division

7**. Most** testicular tumours in **post pubertal males** arise from the in situ lesion (precursor lesion) **intratubular germ cell neoplasia** with the *exception* of spermatocytic seminomas in adults and yolk sac tumours and teratomas in kids, since the three mentioned tumors don't originate from intratubular germ cell neoplasia.

Testicular germ cell tumours are sub-classified *(due to differences in clinical behaviour, treatment modality and outcome)* into:

I. **seminomatous germ cell tumours** : including:
-seminoma
- spermatocytic seminomas

II. **Non-seminomatous germ cell tumours (NSGCT):** include embryonal carcinomas, yolk sac tumours, choriocarcinomas and teratomas .

The histologic appearances of a specific tumour may be:

1. **Pure** (composed of a single histologic type) 40% of cases, less common.

2. **Mixed** (composed of multiple histologic types like you see embryonal carcinoma and seminoma or yolk sac tumor with teratoma and embryonal carcinoma) 60% of cases, more common.

Let's start talking about testicular neoplasms in more details.

1)Seminomas:

Prototype of seminomatous germ cell tumours, Make up to 50% of all testicular tumours –**most common.**

- Classic seminoma:

Peak is 40-50 years old

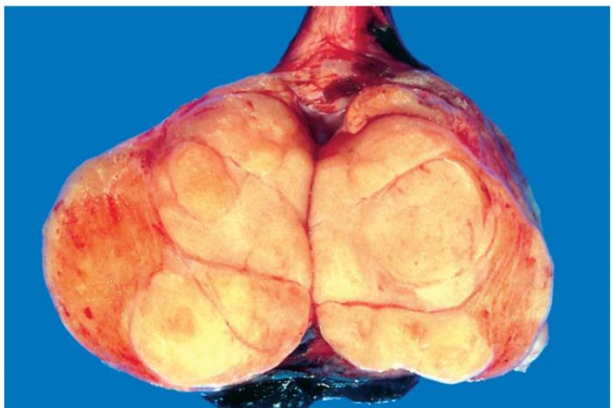
Rare in prepubertal children , never happen in infants

Confined to the testis : Progressive painless enlargement of the testis

Morphology :

Grossly: soft, well-demarcated tumours, usually **without haemorrhage or necrosis.**

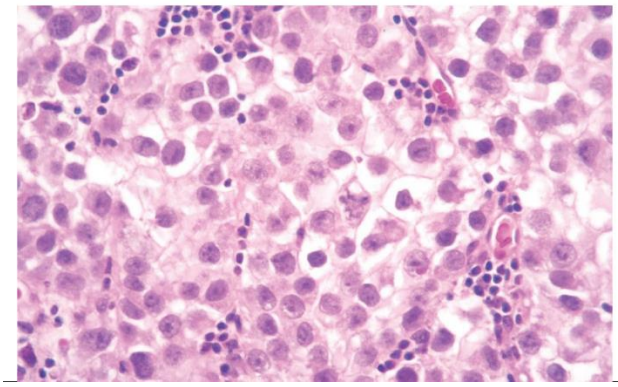
Seminoma of the testis appearing as a well circumscribed, pale, fleshy, homogeneous mass



Histologically: large, uniform cells with distinct cell borders, clear, glycogen-rich cytoplasm, round large nuclei, and 1-2 conspicuous nucleoli The cells arrayed in small lobules with intervening delicate fibrous septa.

A lymphocytic infiltrate usually is present in the septa (a unique characteristic that is characteristic of seminomas)

Microscopic examination reveals large cells with distinct cell borders, pale nuclei, prominent nucleoli, and lymphocytic infiltrate.



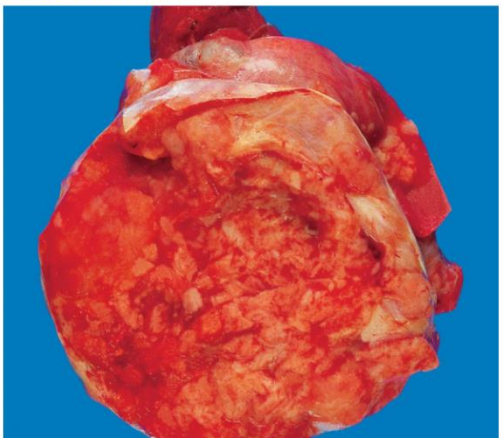
2) Embryonal carcinomas

Peak is 20-30 years old

More aggressive than seminoma

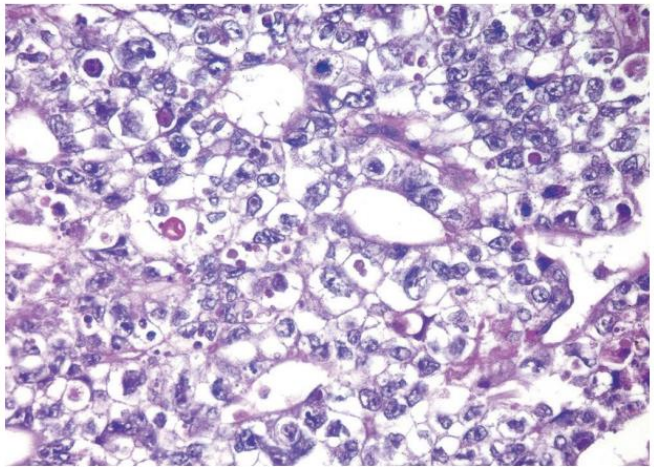
Grossly: Are **ill-defined** masses **containing foci of haemorrhage and necrosis**

The tumor is hemorrhagic



Microscopically: The tumor cells are large and **primitive**-looking. With basophilic cytoplasm, indistinct cell borders, large nuclei, prominent nucleoli, **pleomorphic (cells don't look like each other,** variable in cellular and nuclear size and shape**)** and increased mitotic activity,

Sheets of undifferentiated cells & primitive gland -like structures. The nuclei are large and hyperchromatic



3)yolk sac tumours :

The most common primary testicular neoplasm in children<3 years with very good prognosis

In adults pure form of yolk sac tumours is rare so mixed forms(such as they have yolk sac tumours with embryonal carcinoma and teratoma) are commoner with worse prognosis compared to children .

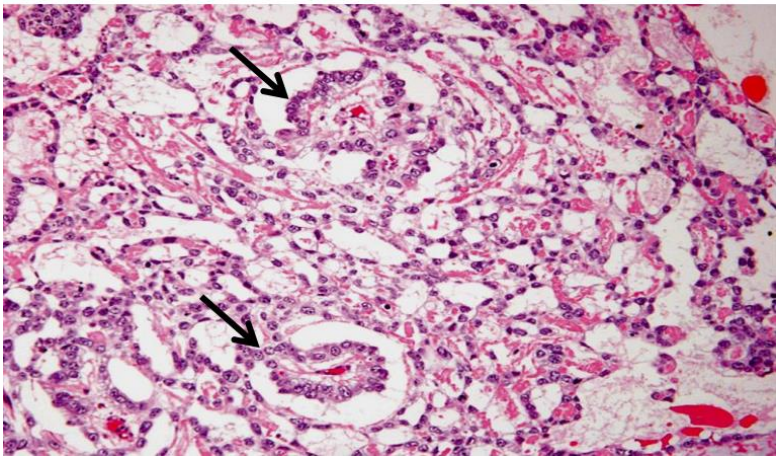
Grossly: large and may be **well demarcated**.

Histologically: - The tumor is composed **of low cuboidal to columnar** epithelial cells forming Microcysts, Lacelike (reticular) patterns.

A distinctive feature is the presence of structures resembling primitive glomeruli, called Schiller-Duvall bodies.

-tumor cells secrete **Alpha Feto Protein (AFP)** can also be detected in the serum.- **so whenever you see schiller-duvall bodies you should order AFP test .**

Schiller-Duvall bodies.



NOTE: the **yolk sac** is related to the ***FETUS*** so you can remember that it has elevated levels of Alpha ***FETO*** protein(AFP).

4)***CHORIO***carcinomas :

Peak is 20-30 years old

highly malignant form of testicular tumor.

♣ its "pure" form is rare, constituting less than 1% of all germ cell tumours

- This neoplasm can **also arise in the female genital tract**

-tumor cells secrete Human ***CHORIO***nic Gondotropin (HCG)

so there is **Elevated serum level of HCG**.

Remember :

CHORIOcarcinoma has elevated levels of human ***CHORIO***noic gondadotropin (HCG)

Grossly: The primary tumours often are small (<5 cm) so patients present to the medical attention late. **palpable nodule with NO testicular enlargement**

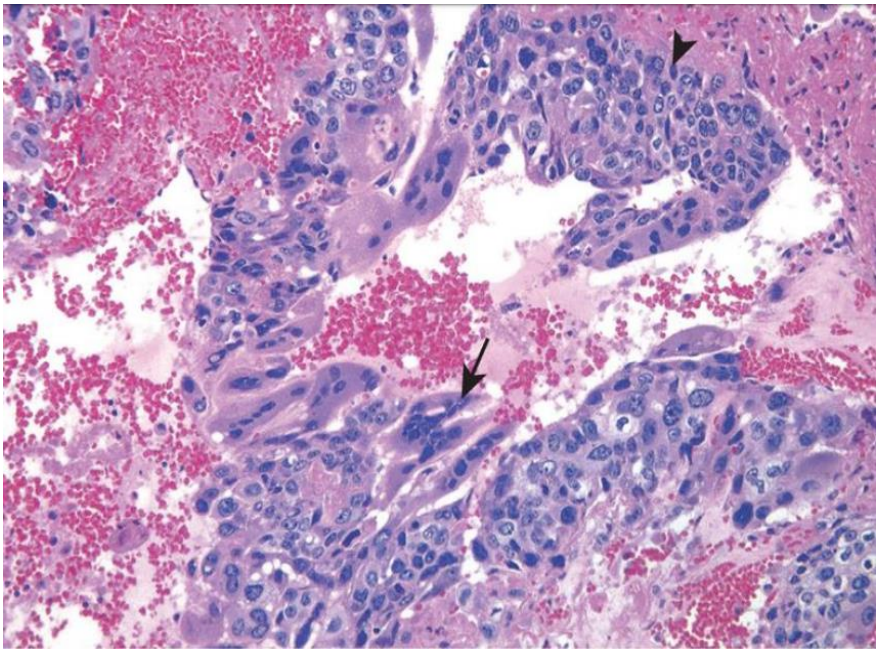
Poor prognosis

Haemorrhage and necrosis are extremely common so you see sheets of cells in a necrotic or hemorrhagic background.

Microscopic examination:

Syncytiotrophoblasts: large multinucleated cells with abundant eosinophilic vacuolated cytoplasm containing HCG. So syncytiotrophoblasts are the cells that **secrete HCG** .

Cytotrophoblasts: more regular polygonal cells, with distinct borders and clear cytoplasm; grow in cords or masses and have a single, fairly uniform nucleus.



Arrowhead,upper right-> cytotrophoblas

Arrow.middle->syncytiotrophoblas

5)teratomas

-The neoplastic germ cells **differentiate along somatic cell lines showing various cellular or organoid components**. reminiscent of the normal derivatives of more than one germ layer.

Remember we have 3 germ cell layers ectoderm(which gives rise to our epidermis, neural tissue, hair, nails, sebaceous glands ,oral and nasal lining) ,mesoderm(which gives rise to our mesenchymal tissue like bone, cartilage, blood vessels ,connective tissue ,cardiac and smooth muscles)and endoderm(which gives rise to our stomach ,liver ,pancreas, urinary bladder ,large and small intestines) . in teratomas you have cells derived from more than one germ layer for example you may see a full tooth with adjacent pancreatic tissue! or bone with respiratory epithelium and so on (two components from different germ layers are enough to call it teratoma).

-**Can affect All ages**

-**Pure forms of teratoma are common in infants and children , being second in frequency only to yolk sac tumours**

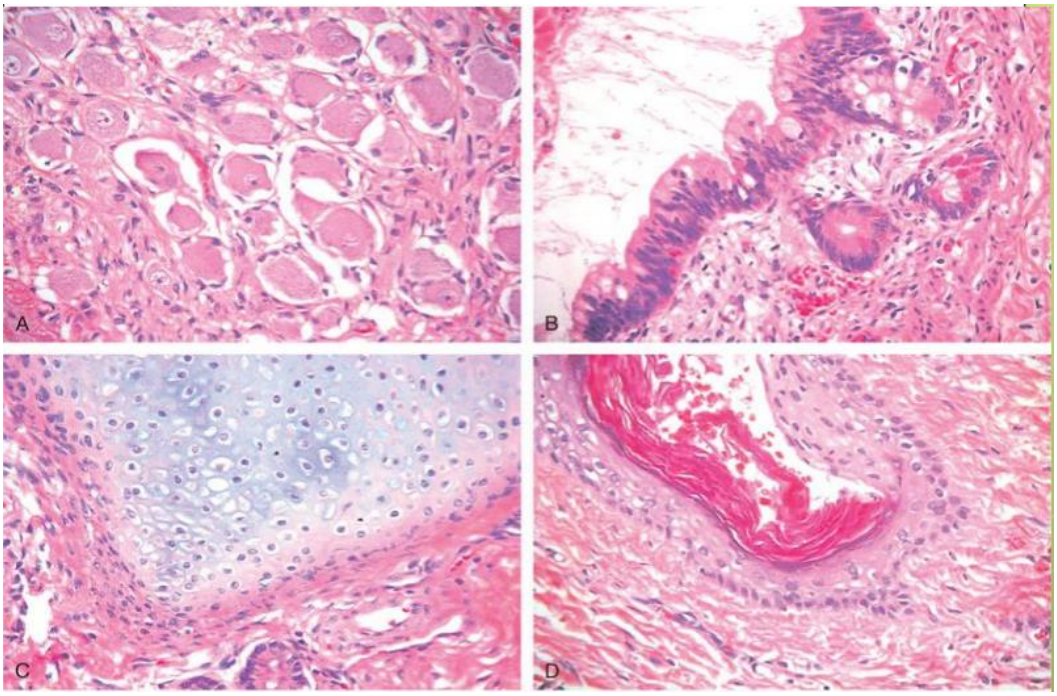
-In adults, pure teratomas are rare, constituting 2% to 3% of germ cell tumours. However, the frequency of teratomas mixed with other germ cell tumours is approximately 45%.

-Grossly: firm masses containing cysts and recognizable areas of cartilage→ it depends basically on the components of the tumor

-Histologically:

1**. Mature** teratomas: a heterogeneous, collection **of differentiated cells** or organoid structures, such as neural tissue, muscle bundles, islands of cartilage, clusters of squamous epithelium, etc

2. **Immature** teratomas: - Share histologic features with **fetal or embryonal tissues(undifferentiated cells)**



A-D->four different fields from the same testicular teratoma. This figure shows:
A->neural(ectodermal)

b->glandular (endodermal)

c->cartilage (mesodermal)

d->squamous epithelial elements (ectodermal)

Clinical Features of testicular germ cell neoplasms:

-present most frequently with a **painless testicular mass that is non-translucent**

-Some tumours, especially **NSGCT, may have metastasized widely by the time of diagnosis in the absence of a palpable testicular lesion.**

Biopsy of a testicular neoplasm is **absolutely contraindicated**, because it's associated with **a risk of tumor spillage** , it means if you do a biopsy you will **UPSTAGE** the patient's tumor (if he had stage 1 (pT1)meaning that the Tumor is limited to testis then if you do biopsy you will shift him to higher stage

The standard management of a solid testicular mass is **radical orchiectomy** (surgical removal of the testis), based on the presumption of malignancy. After you do it you send it to the histopathology lab to confirm diagnosis.

NOTE : Treatment modality differ between metastazied tumor and non metastasized tumor(metastases determine treatment modality)

Seminomas and nonseminomatous tumours

differ in their behaviour and clinical course :

I. **Seminomas:**

often remain **confined** to the testis for long periods and may reach considerable size before diagnosis. **Metastases most commonly in the iliac and para-aortic lymph nodes**, particularly in the upper lumbar region**. Haematogenous** metastases occur **late** in the course of the disease.

II. **Nonseminomatous germ cell neoplasms:**

tend to **metastasize earlier**(may be the 1st manifestation is metastasis), **by lymphatic & haematogenous (liver and lung mainly) routes.**

Metastatic lesions may be **identical** to the primary testicular tumor or **different containing elements of other germ cell tumours.**

*Assay of tumor markers secreted by germ cell tumours:

- HCG is *always* elevated in patients with choriocarcinoma

- HCG may be **minimally elevated** in individuals with other germ cells tumours (GCTs) containing **syncytiotrophoblastic cells(since they secrete HCG)**

-AFP is increased in lesions with yolk sac tumor component.

- lactate dehydrogenase (LDH) level correlate with the <u>tumor burden</u> (tumor size or load).

- tumor or serum markers which are mentioned above are helpful in:

-**diagnosis** (they are elevated when there is tumour, but after treatment they drop down to normal if the tumour is completely excised)

- **follow up** (you follow up the patient by making sure that the levels are within normal limits. if they are elevated this may indicate metastases of the original tumor or an affected contralateral testis)

TREATMENT:

- Seminoma:

Extremely radiosensitive. Tends to remain localized for long periods

Best prognosis (>95% of patients with early-stage disease can be cured).

-Nonseminomatous germ cell tumours:

histologic subtype DOES NOT influence the therapy.

90% of patients achieve **complete remission with aggressive chemotherapy, and most are cured**. *The exception is choriocarcinoma, which is associated with a poorer prognosis (since this tumor doesn't cause testicular enlargement so it's associated with late diagnosis)*

Prostate gland pathology

Normally the prostate is a **small gland** weighing 20-30 grams and measuring 3-4 cm in diameter.

The zone of the prostate surrounding the urethra –periurethral zone is known as **transitional zone and it is the most common site of benign enlargement of prostate** that's why they present with urethral obstructive symptoms –as we will discuss in the following slides - while **the peripheral zone is the most common site of prostate carcinoma**

Benign prostatic hyperplasia-BPH (nodular hyperplasia)

extremely common cause of prostatic enlargement in men >40; frequency **rises with age**.

androgen-dependent proliferation of both stromal and epithelial elements so it does not occur in males with genetic diseases that block androgen activity.

Pathogenesis:

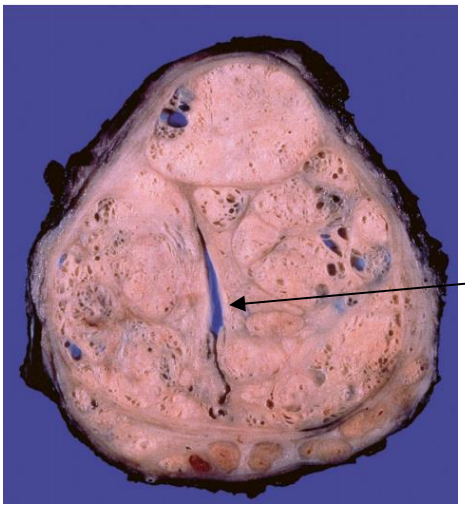
Dihydrotestosterone (DHT) is synthesized in the prostate from circulating testosterone by the action of the enzyme **5α-reductase, type 2.**

DHT supports the growth and survival of prostatic epithelium and stoma cells by binding to androgen receptors *Although testosterone can also bind to androgen receptors and stimulate growth*, **DHT is 10 times more potent.**

Morphology:

BPH **occurs in the transition zone of the prostate.**

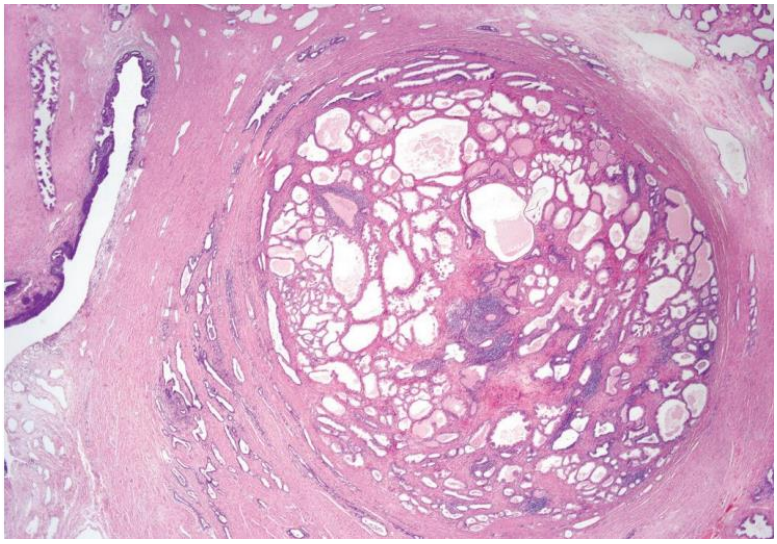
Grossly: Prostatic enlargement (60 and 100 g), many well circumscribed nodules bulging from the cut surface .**Compressed urethra**.



Microscopically

hyperplastic nodules composed of proliferating glandular elements and fibromuscular stroma.

The hyperplastic glands are lined by tall, columnar epithelial cells and a peripheral layer of flattened basal cells.



Well demarcated nodules at the right with compressed urethra to the left

Clinical features:

(The presence of symptoms depends on the level of hyperplasia so it may be asymptomatic as well.)

Because BPH preferentially involves the inner portions of the prostate, the most common manifestations are lower urinary tract obstruction as:

- Difficulty in starting the stream of urine **(hesitancy)**

- Intermittent interruption of the urinary stream **(intermittency)**

-**urinary urgency, frequency, and nocturia,** all indicating bladder irritation.

- **Increased risk of urinary tract infections (due to stasis)**

TREATMENT:

Agents that **inhibit the formation of DHT from testosterone (5-alpha reductase inhibitors)** or **that relax prostatic smooth muscle by blocking α1-adrenergic receptors** with or without Surgery depending on the severity of the symptoms.

prostatic carcinoma

Affecting **men >50 years of age**. The **most common form of cancer in men in this age group**

Nowadays there is **significant drop in prostate cancer mortality, due to increased detection of the disease** through screening HOW?

By measuring prostate specific antigen-**PSA** (free: total) ratio. Then determining if the PSA ratio is favourable or grey zone or unfavourable (at risk) for prostate cancer. Also by the **digital rectal examination** .

PATHOGENESIS

1. **Androgens**. Provide the "soil," within which prostate cancer develops that's why Cancer of prostate does not develop in males castrated (surgically or chemically) before puberty. Cancers regress in response to surgical or chemical castration

2. **Heredity**: increased risk among first-degree relatives of patients with prostate cancer.

3. **Environment:**

Raise of Geographical variations incidence in Japanese immigrants to US -> due to differences in life styles .

Diet: westernized dietary habits

4. **Acquired somatic mutations: The most common** gene rearrangements in the prostate cancer is **fusion genes** consisting of androgen regulated promoter of the **TMPRSS2 gene** and the coding sequence of **ETS** family transcription factors. **(TMPRSS2-ETS fusion genes)**

Clinical Features

- 70% - 80% arise in the **peripheral zone of prostate glands**

No urethral obstructive symptoms at least in early stages since it starts in the periphery

Palpable as irregular hard nodules on digital rectal examination.

- **elevated serum prostate-specific antigen (PSA)** level screening tests.

Bone metastases (axial skeleton) ->**osteoblastic (bone-producing) lesions** on bone scans**-X-ray**, the opposite to breast cancer which produces osteolytic lesions upon metastases.

We may encounter many defeats

but We MUST NOT be defeated .