



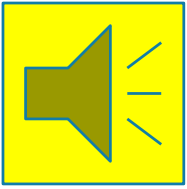
Pathology

Subject :

Lec no : lec-22-

Done By : Hala AL Beshtawe □□□□□ □□□□□ □□□□ □□□□

وَقُلْ رَبِّ زِدْنِي عِلْمًا



- Cancer is the second leading cause of death in the United States.
- Some cancers are highly curable, whereas others are virtually always fatal.

NOMENCLATURE:

(Tumor) ^{ورم / كتلة} **Neoplasm** = ^{كتلة با يورت من طفرات} New growth of transformed cells producing a mass.

What are **TRANSFORMED** cells?

- Cells that have undergone several mutations leading to features of :

1. Uncontrolled growth
2. Uselessness
3. Persistence ^{مقاومة بيت الطية واللايا}

NEOPLASIA

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NEOPLASM

- Abnormal mass of tissue, the growth of which **EXCEEDS** and is **UNCOORDINATED** with that of the normal tissues and **PERSISTS** in the same way even **AFTER REMOVAL** of the stimulus which produced the change.
- There is a **loss of responsiveness to normal growth controls**, resulting in **continuous proliferation of cells**.
- In common medical usage, a **neoplasm** often is referred to as a **tumor**.
- ❖ **Oncology**: Is the **study of tumors** (from oncos, “tumor,” and logos, “study of”).

According to a tumor's clinical behavior, two main types of neoplasms:

- **Benign neoplasm** = Limited new growth **without** local invasion or spread.

1. Innocent.
2. Remain localized.
3. Amenable to local surgical removal.
4. Patients generally survive.

- **Malignant neoplasm** = Invasive growth locally, which also spreads to distant sites.

- May be fatal.

❖ **Cancer** Is a general term for all malignant growths of whatever type.

عن الطراب كان → Benign
→ malignant

Components of neoplasms:

-All tumors whether benign or malignant have 2 basic components: Parenchymal cells and stromal cells.

→ the main part of Cancer

(1) **The parenchyma:** made up of transformed or neoplastic cells.

- Determines its biologic behavior, and it is this component from which the tumor derives its name.

تكونه tumor و also

(2) **The stroma:** supporting, host-derived, non-neoplastic, made up of connective tissue, blood vessels, and host-derived inflammatory cells.

- Crucial to the growth of the neoplasm.

- Amount & type of stromal cells may contribute to the consistency and appearance of tumors.

- If there is stromal proliferation \rightarrow hardness of the tumor \rightarrow Scirrhus tumor \rightarrow Desmoplasia.

- If there is lack of stromal cells, the tumor may be soft or cystic.

less stromal cells
cyst / soft



Serous cystadenocarcinoma of ovary



\rightarrow more stromal cells

Scirrhus Carcinoma of breast
 \rightarrow or hard

Tumors of Epithelial Cell Origin

*دائماً ادا اپتري ال (tumor) مي سايبرس جى (epithelial) يکون Benign ۽ تڪون الخليا المکونه epithelial ۽ لکن بيه استنادات سے کمر لاجتا

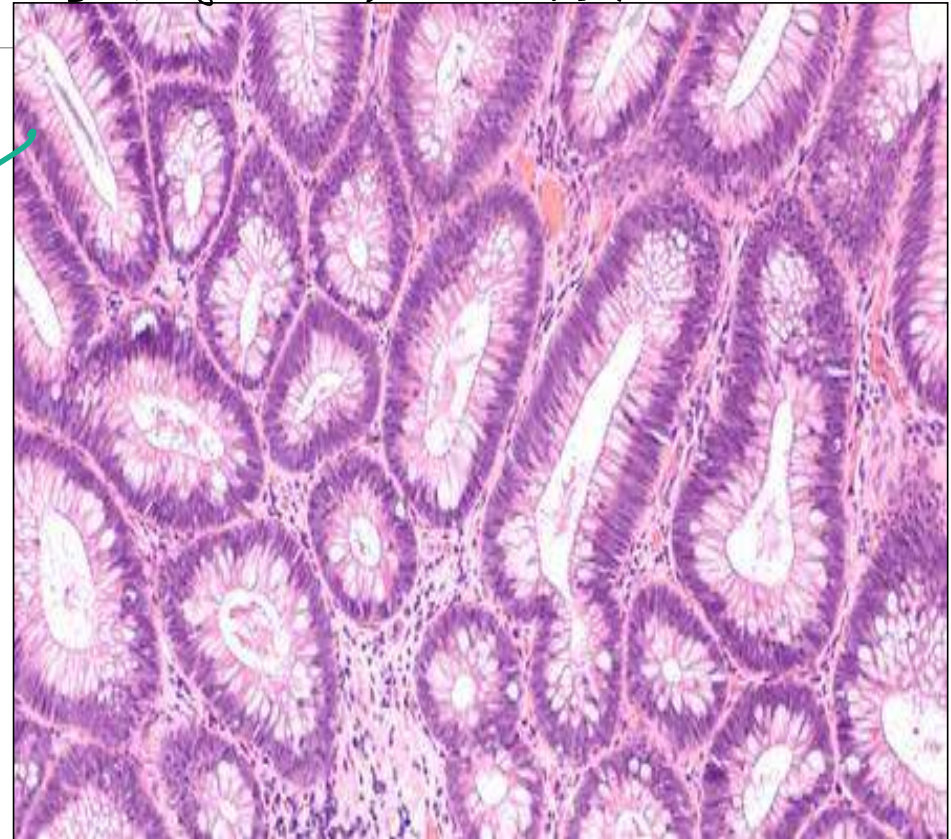
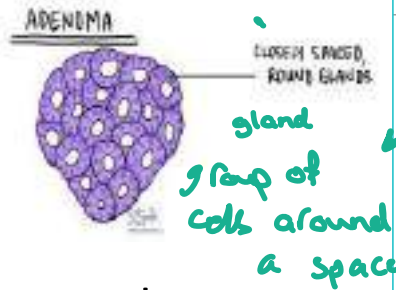
Benign Epithelial tumors:

خليا (tumor) تصيف حول space ۽ تڪون gland
او تڪون derived from gland

1. Adenoma:

Benign epithelial neoplasm that produces **glandlike structures**, or benign epithelial neoplasms that are **derived from glands** but lack a glandular growth pattern.

Cystadenoma: Hollow ^{اکتو} **cystic masses** that typically arise in the **ovary**.



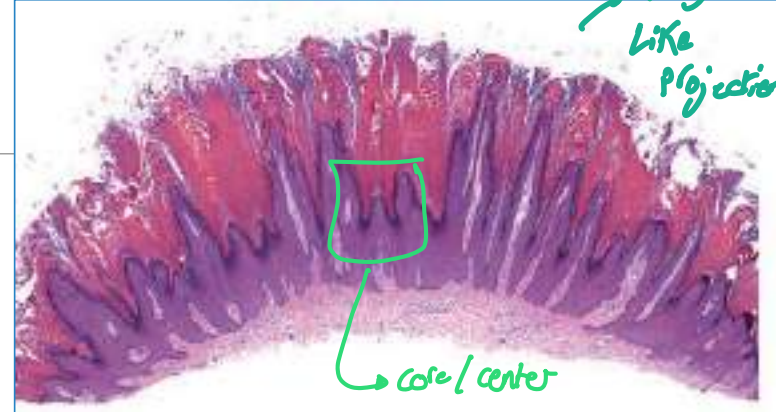
warts

Squamous cell Papilloma (skin warts)

2. Papilloma:

Epithelial tumor forming finger-like fronds/projections from any epithelial surface, with a connective tissue core/center.

↳ could be blood vessels



finger-like projection

core/center

Colonic adenomatous polyp

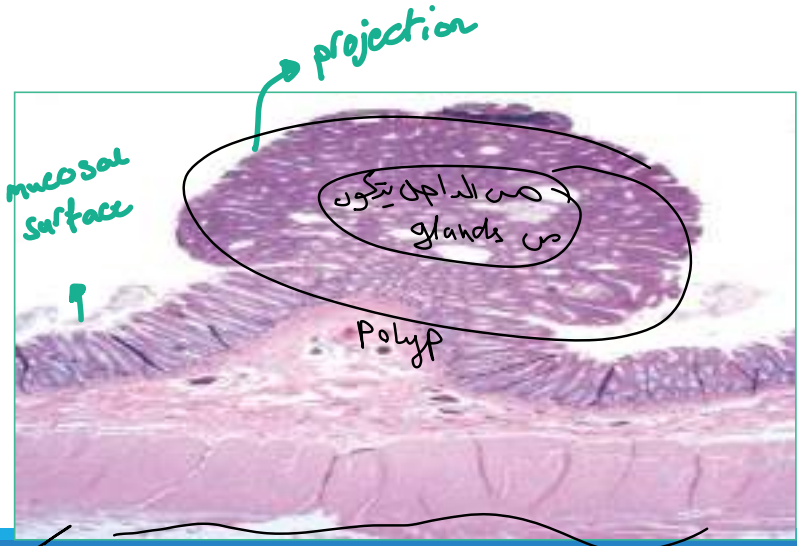
3. Polyp:

benign
Malignant

General term: Ineoplastic/non-neoplastic! A mass projecting from the mucosal surface of a hollow organ.

↳ Can contain Adenomas inside it

Colon
Stomach



projection

mucosal surface

Polyp

glands

very long

Malignant epithelial tumors (Carcinomas):

1. Squamous cell carcinoma: from squamous cells or produce squamous cells
e.g. skin, mouth, cervix, bronchus...etc

2. Adenocarcinoma: from glandular origin or grow in glandular pattern, e.g.
G.I.T., endometrium, breast, kidney, thyroid...etc

Tumors of **Connective tissue** cell origin

1. Benign: Named by tissue of origin with the attached suffix – **oma** / *there are some exceptions*

e.g. **fibroma**, **lipoma**, **chondroma**...etc

fibrow ✓ *↳ Adipose tissue* *↳ Cartilage*

2. Malignant connective tissue tumors: **SARCOMA:** Prefix (origin)+ suffix (sarcoma)

e.g. Osteosarcoma, liposarcoma, angiosarcoma, leiomyosarcoma, rhabdomyosarcoma...

bone ✓ *↳ inner lining blood vessel* *↳ smooth muscles* *↳ stratified muscle*



Very Imp

Exceptions (these are malignant, but end with oma)

- ① Leukemia, Lymphoma
- ② Glioma → glial cells in Brain
- ③ Melanoma → Melanocytes
- ④ Mesothelioma → mesothelial cells
- ⑤ Retinoblastoma → Retina
- ⑥ Seminoma... → germ cell tumor

Mixed Tumors:

→ epithelial
→ Connective

1. Single germ cell tumors: Derived from **one** germ cell layer that differentiates into more than one cell type (divergent differentiation).

e.g., *Mixed tumor of the Salivary Gland (pleomorphic adenoma)

Fibroadenoma of the breast.

↳ parotid gland

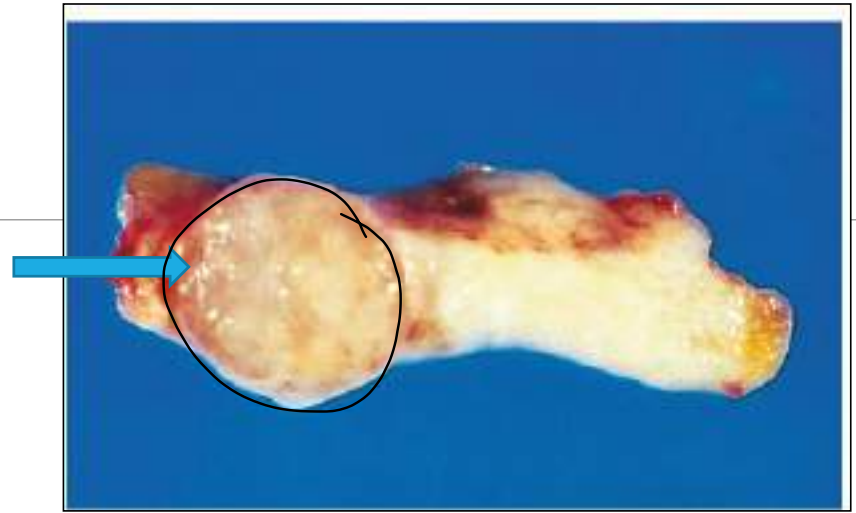
germ cell layers
embryo → الجنين

- endoderm
- mesoderm
- ectoderm

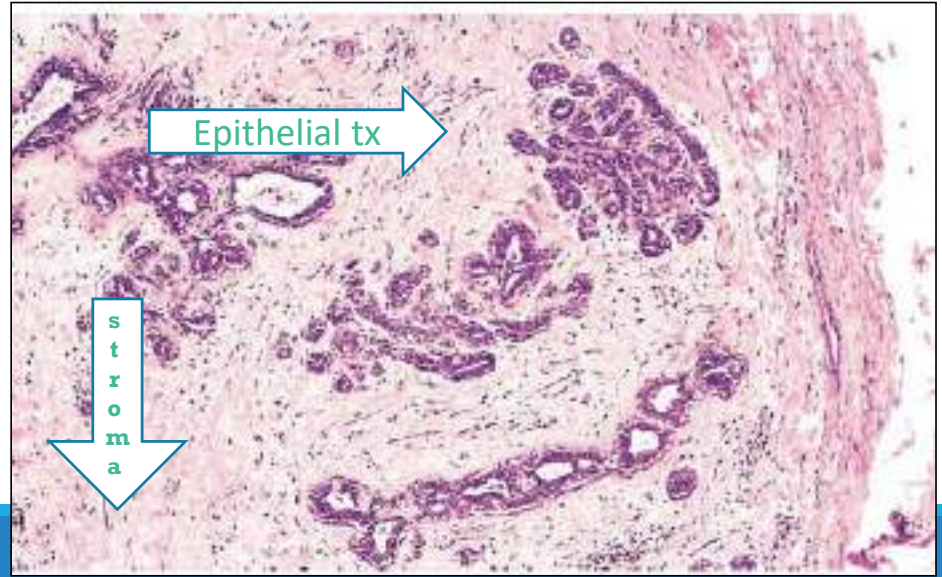
1. Fibroadenoma of breast

Fibrous gland benign

Gross: The ^{capsule}tan-colored, encapsulated small tumor is sharply demarcated from the whiter breast tissue.

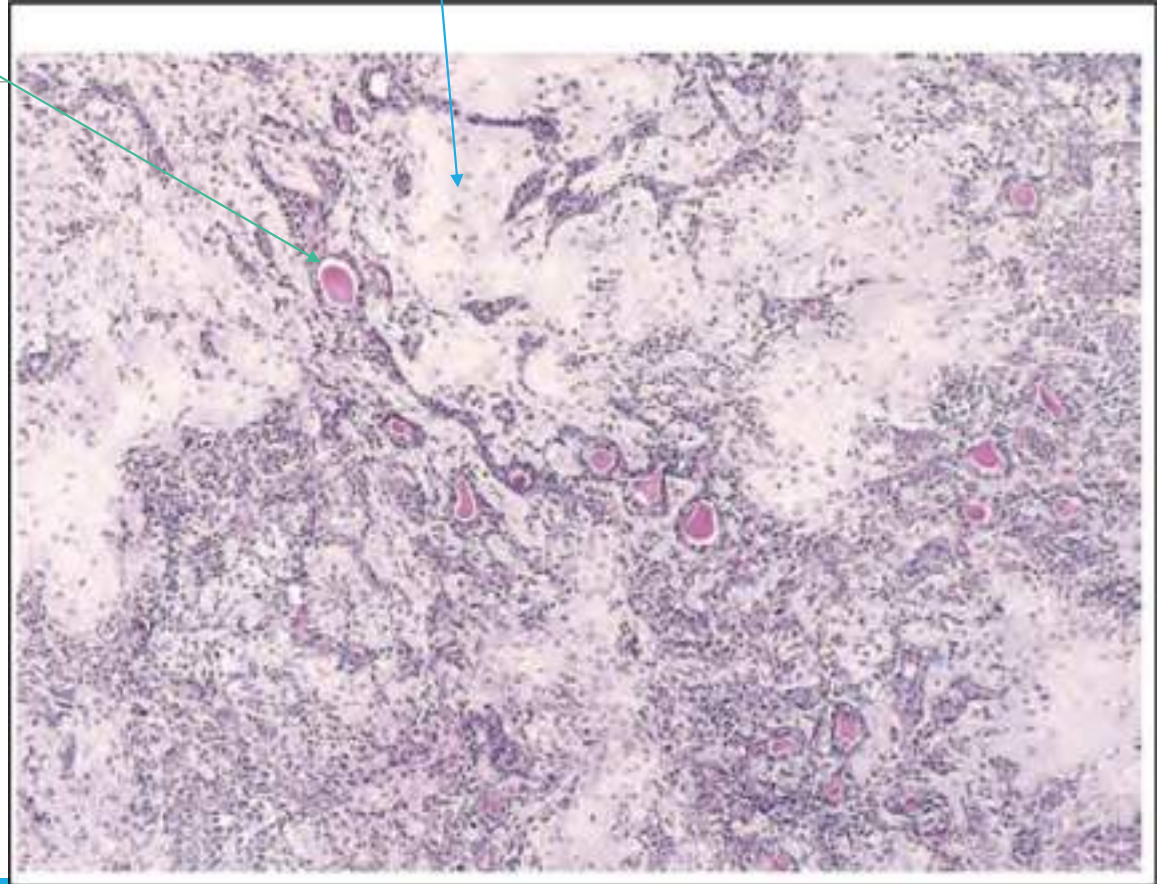


The fibrous capsule (right) sharply delimits the tumor from the surrounding tissue

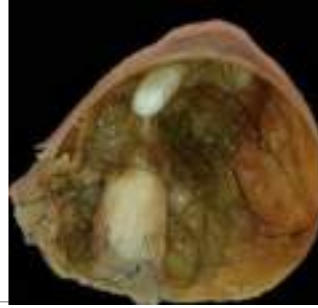


2. Pleomorphic adenoma: {Mixed tumor} → parotid gland

Composed of epithelial cells and myxoid stroma resembling cartilage



ovaries ← female }
testis ← male } نسا وذكور



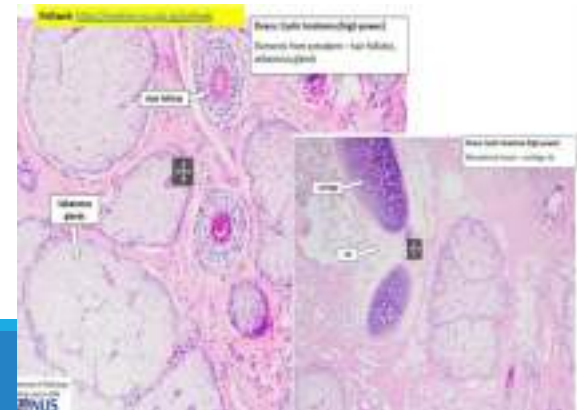
2. Teratomas: Made of a variety of parenchymal cell types that are derived from **more than one germ cell layer** formed by totipotential germ cells that are able to form **ectoderm, endoderm & mesoderm** (**normally present in the testis, ovary & sometimes abnormally present in sequestered midline embryonic rests**).

-May be **benign or malignant** depending on the structure, site, age, and sex.

-May contain **skin, sebaceous & mucus glands, hair, cartilage, bone, teeth, respiratory epithelium, glial tissue...etc.**

anything

-Usual location is the **ovary or testis**



Tumors of primitive fetal origin:

Blastoma: from immature tissue.

-May arise in the kidney, liver, retina...etc.

e.g. * Nephroblastoma

* Retinoblastoma.

* hepatoblastoma

-The majority of these tumors are **malignant** & occur in infants & children.

↳ ends with oma {exception}

Some 'tumors' are NOT true neoplasms

↪ Not tumor → but some could be

□ **Hamartoma:** Tumor-like developmental malformation in which there is abnormal mixing of normal components of the organ, either in the form of a change in quantity or arrangement of tissue elements.

↳ tissues from the same organ

□ **Choristoma:**

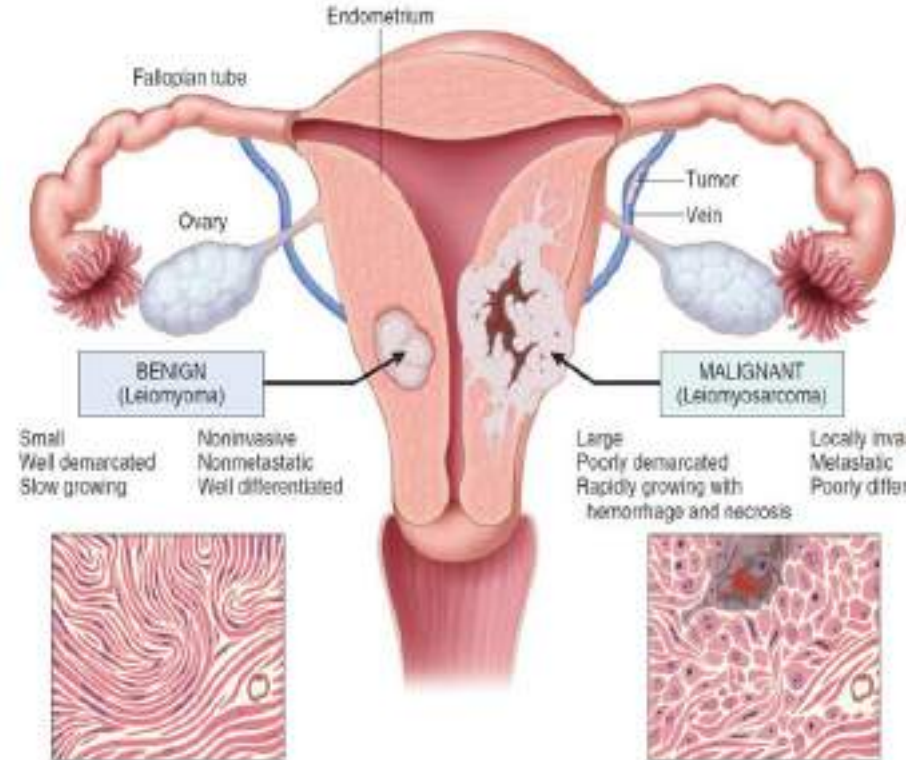
- ^{يولد مع الجسم} Congenital anomaly where different types of tissue ^{موجود بجان على tissue} grow ectopic to the region. e.g. - Meckle's Diverticulum in the small intestine containing gastric tissue.

↳ tissue from an organ grows in An Abnormal place
of different organ 3 ↓

Characteristics of benign and malignant neoplasms

Tumors can be distinguished on the bases of:

- Differentiation & anaplasia
- Rate of growth
- Presence of capsule
- Local invasion (علاوة على ذلك، (تسبب) الدم يبتلع فيه)
- Distant metastasis



1- Differentiation:

* هذه التسمية هذه الخلايا الموصولة بال (mass) في الخلايا الطبيعية الموصولة د tissue
← أصلاً
← أصلاً

- This indicates the degree of resemblance of the tumor cell to its parenchymal cell of origin, both functionally & morphologically.

- Benign tumors are composed of well-differentiated cells that closely resemble their normal original tissue.
يشبه ال Normal tissue

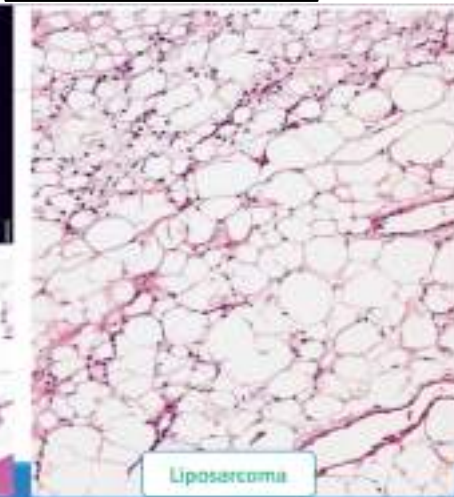
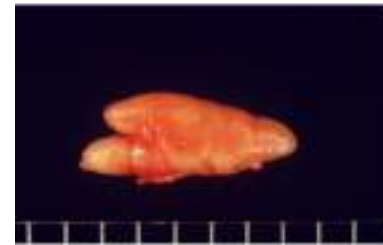
- While malignant neoplasms exhibit a wide range of parenchymal cell differentiation (well-moderately-poorly differentiated).

-Example -

- Cells of a lipoma may look exactly like normal fat cells

↳ benign
↳ well differentiated

a well differentiated
very close to normal





When a tumor **cell loses differentiation**, it gradually **gains features** of **DYSPLASIA**

- **Dysplasia** is a disorderly proliferation of cells with **loss of architectural orientation**
- It may precede malignancy. → Dysplasia → Doesn't mean

ANAPLASIA= Severe Dysplasia: Total loss of differentiation

Malignant

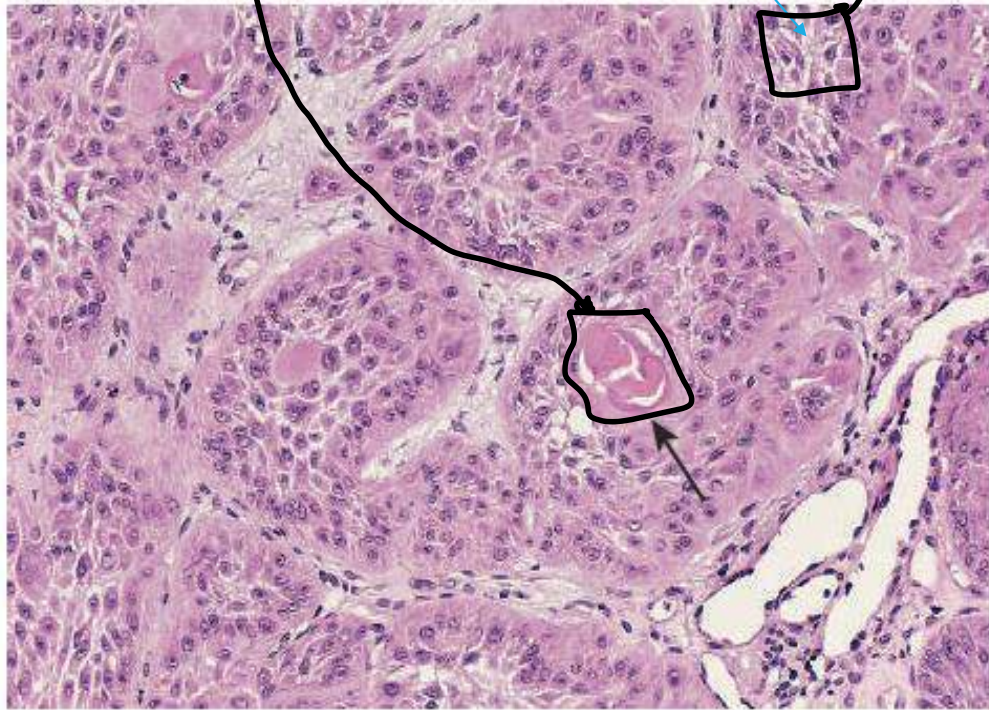
ممكن بتكون مفرطه مرحله تست ل malignancy

Cytological Features of Dysplasia

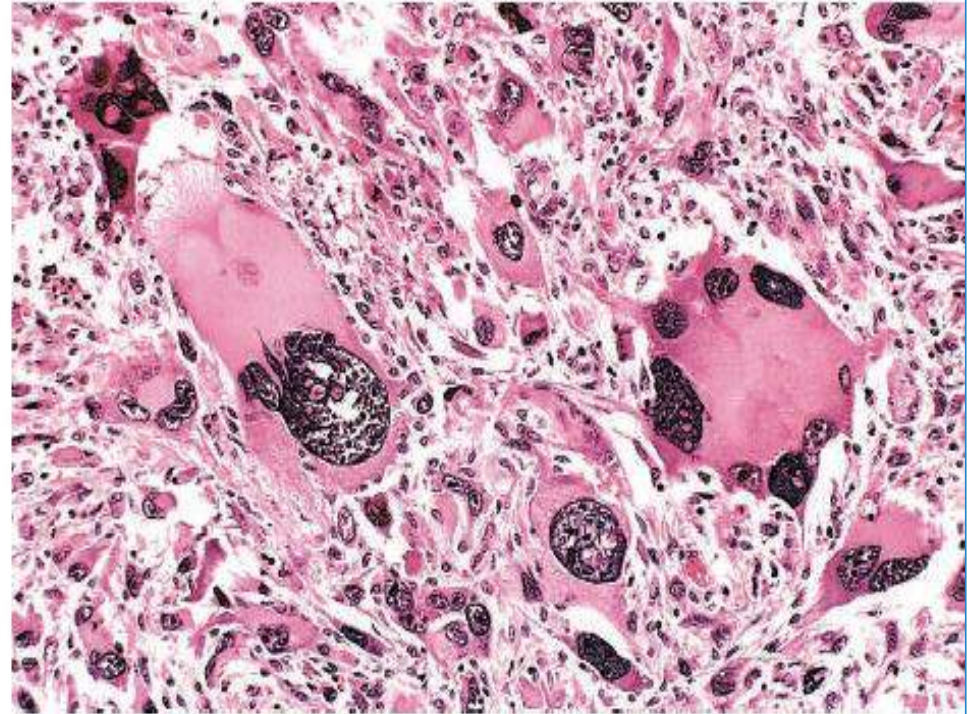
1. Increased nuclear size ↑ N/C ratio
2. PLEOMORPHISM: Variation in nuclear & cell size & shape
3. Loss of differentiating features
4. HYPERCHROMASIA: Increased nuclear DNA content. → very condensed → Dark
5. Nucleoli: Prominent, may be multiple
6. Mitotic figures: Increased → *Replication*
↳ *Abnormal mitotic figures* → *eg: mitotic spindle*
7. Abnormal mitoses: may be present
8. Loss of Polarity: Failure of orientation and polar arrangement of an epithelial surface

Well-differentiated squamous cell carcinoma of the skin. The tumor cells are strikingly similar to normal squamous epithelial cells, with **intercellular bridges** and **necks of keratin** (arrow)

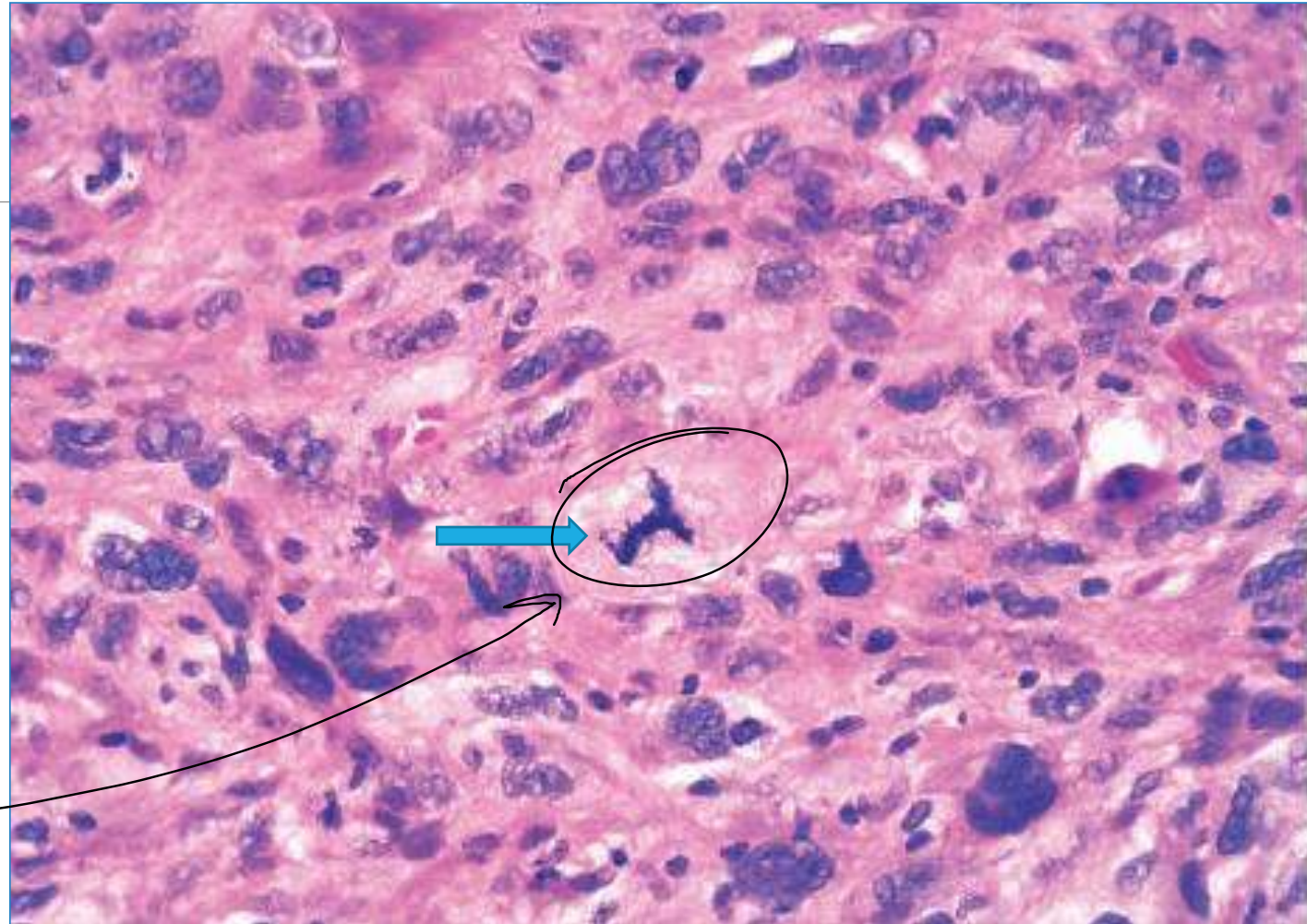
↳ junctions



Pleomorphic malignant tumor *Anaplasia* (rhabdomyosarcoma). Note the marked variation in cell and nuclear sizes, the hyperchromatic nuclei, and the presence of tumor giant cells



High-power detailed view of **anaplastic tumor** cells shows cellular and nuclear variation in size and shape. The prominent cell in the center field has an **abnormal tripolar spindle mitotic figure**



Dysplasia can be:

- Mild, Moderate or Severe.

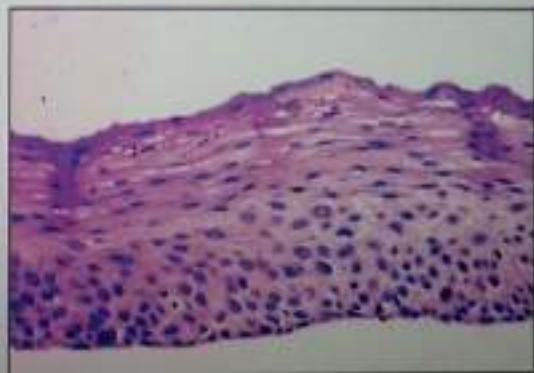
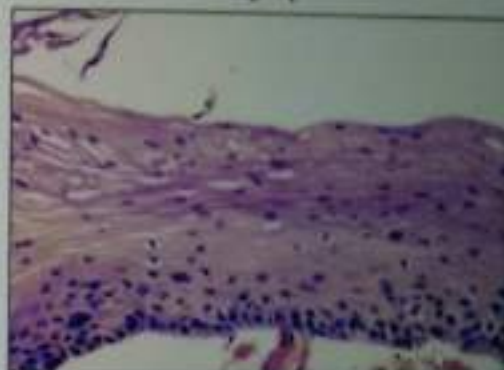
* When dysplastic changes are marked and involving the **entire thickness** of the epithelium & associated with **an intact basement membrane**, the lesion is referred to as **severe dysplasia or carcinoma in situ (CIS)**.

❖ Mild to moderate dysplasias sometimes regress completely if inciting causes are removed.

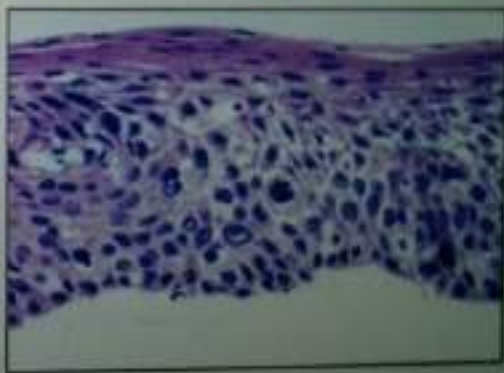
Normal



Mild dysplasia

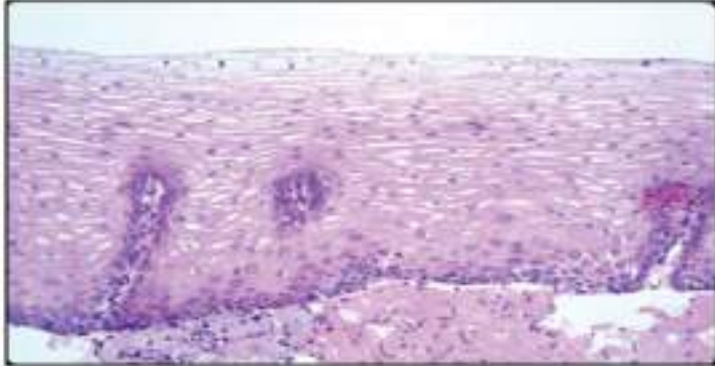


Moderate dysplasia

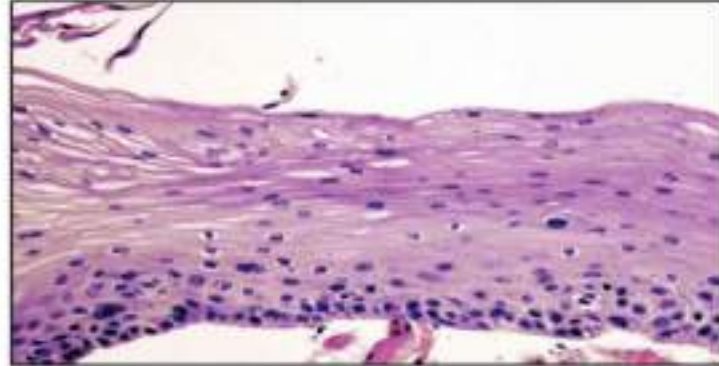


Severe dysplasia

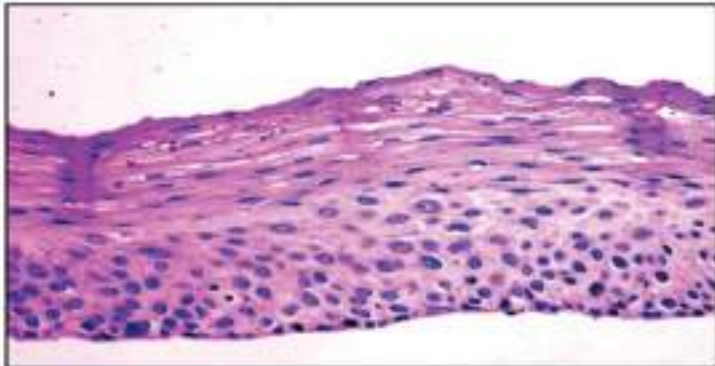
Normal



Mild dysplasia

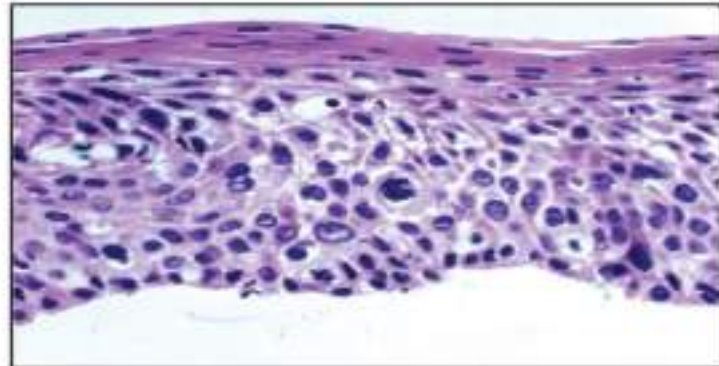


→ lower 1/3



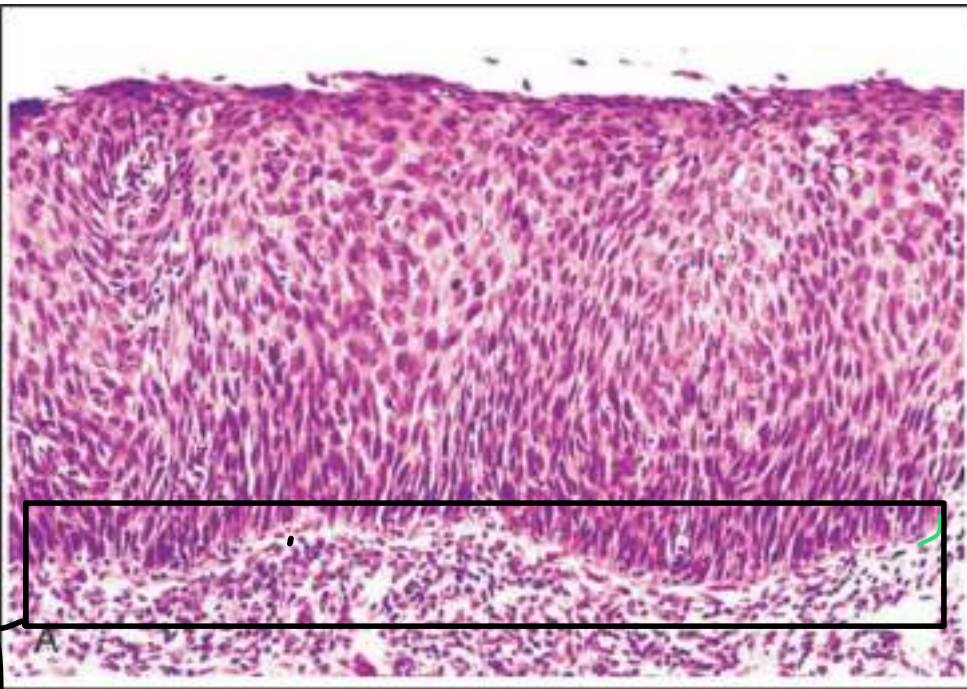
← lower 2/3

← Moderate dysplasia



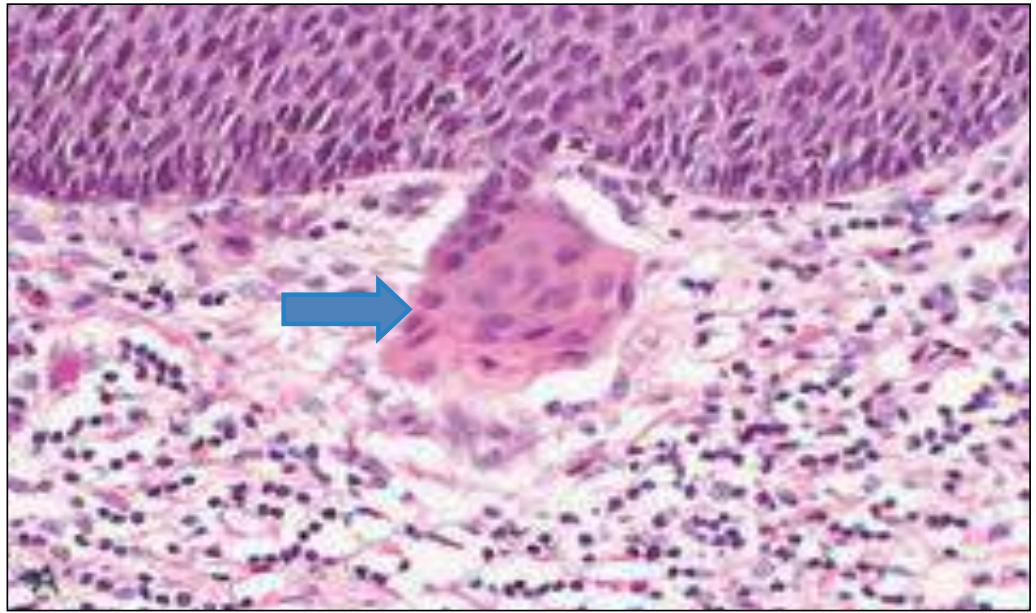
Severe dysplasia

↳ Full tissue



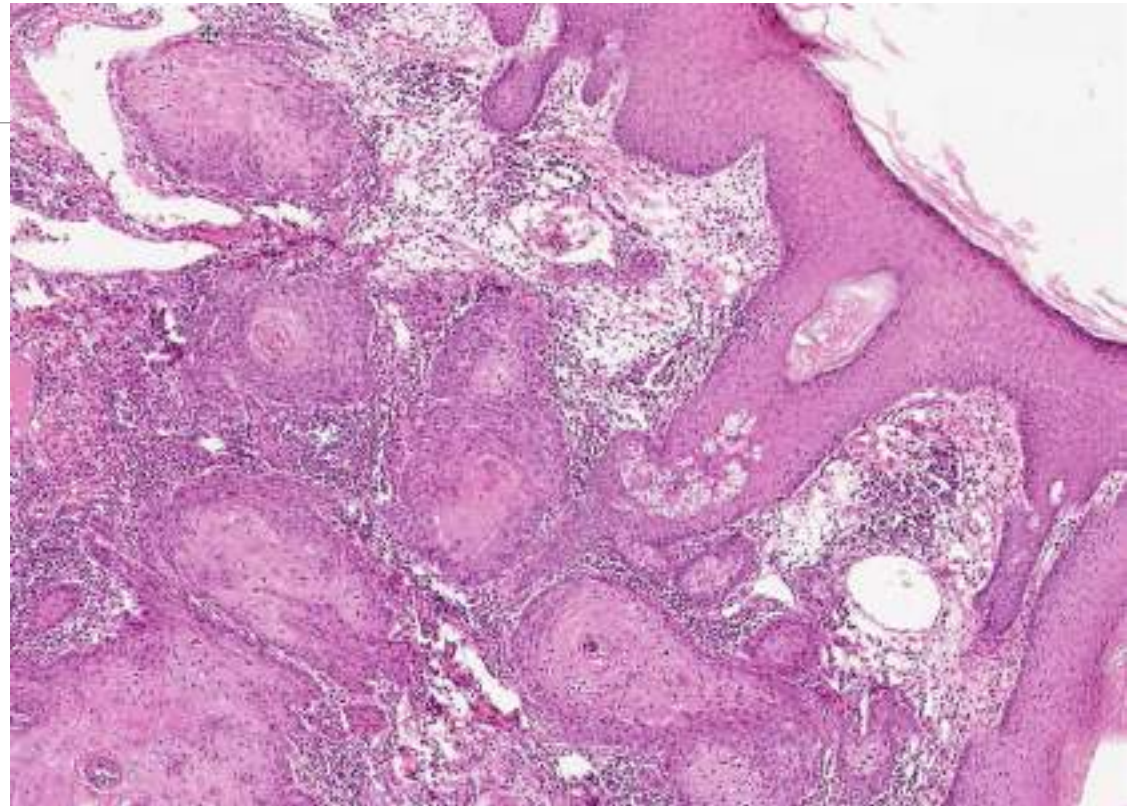
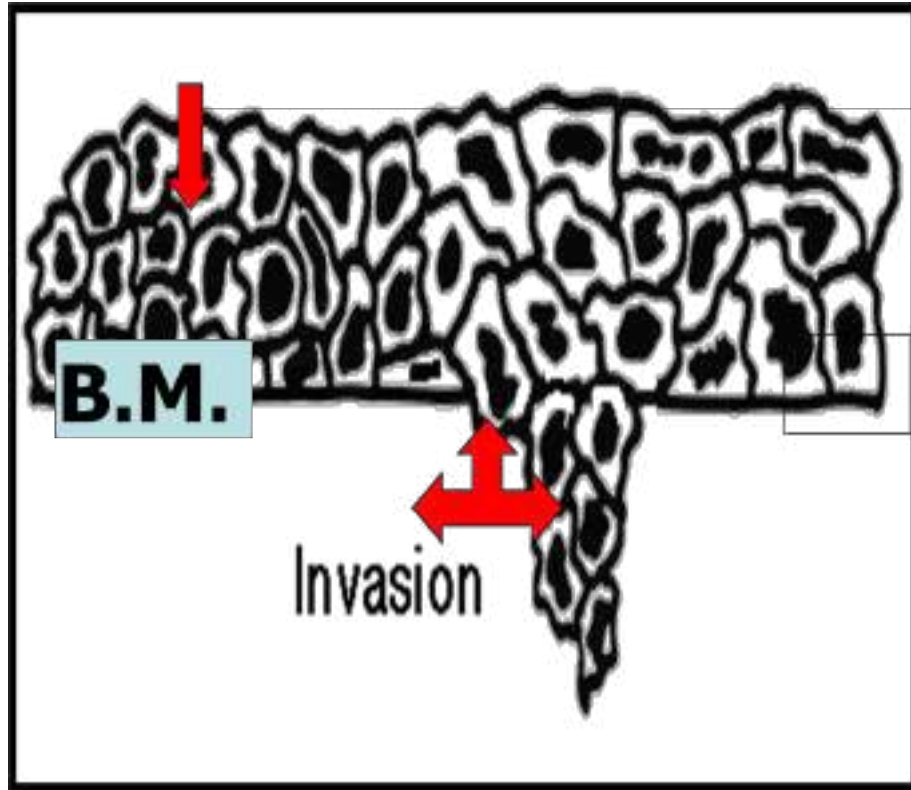
↳ white area → basement membrane
↳ if the dysplasia is only above it
we call it {Carcinoma in situ}

Small invasion under the basement membrane we call it



Microscopic view of squamous carcinoma in situ of the cervix with micro invasion of the basement membrane (arrow)

↳ large amount under the Basement



Invasive squamous cell carcinoma

2- Rate of growth

- Usually slow in benign & rapid in malignant tumors.
- Rate of growth usually correlates with level of differentiation.
- Exceptions:
 - Hormonal influences: e.g. ^{Benign} Leiomyoma of uterus in pregnancy (grow very fast)
 - Some malignant tumors may outgrow their blood supply --> C. ischemic necrosis, so grow slowly

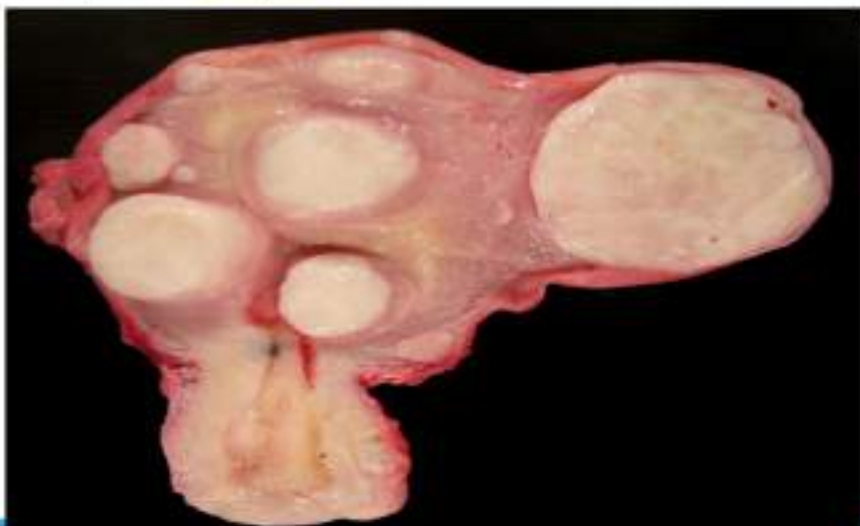
3- Local invasion & Encapsulation

صندوقه و حزينه →

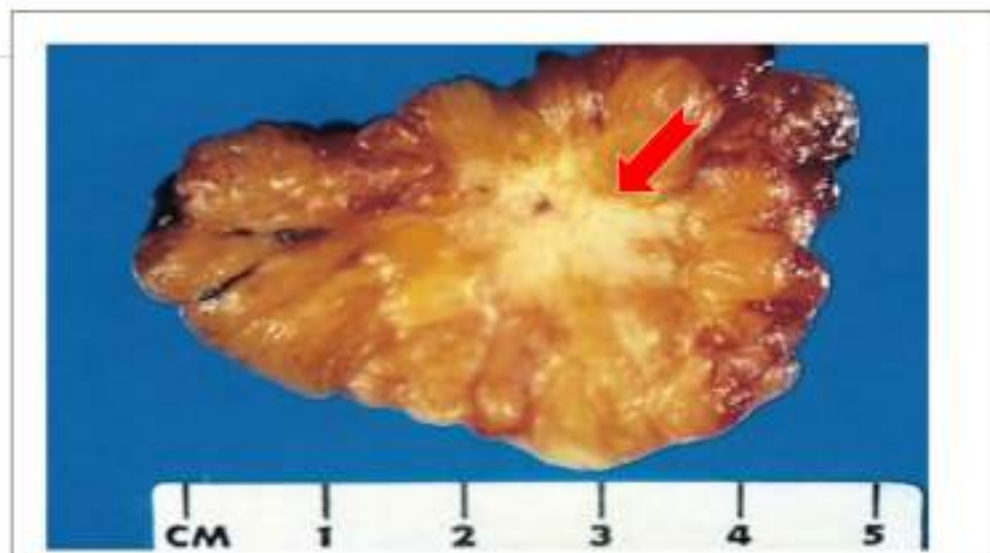
- Benign tumors: frequently have a fibrous capsule or are well-demarcated and do not have the capacity to invade the normal tissue. → these are exceptions
- Most benign tumors grow as cohesive expansile masses that remain localized to their sites of origin.
- Malignant tumors lack well-defined capsules and progressively invade & destroy surrounding tissue

Next to the development of metastases, invasiveness is the feature that most reliably distinguishes cancers from benign tumors

Leiomyomata: uterus showing multiple shiny, white, well-demarcated but unencapsulated leiomyomas in the wall of the uterus.



Invasive ductal carcinoma of the breast. This malignant tumor is non-encapsulated, infiltrating the surrounding breast substance, & is stony-hard (scirrhous) on palpation.



4- Metastasis:



- Spread of malignant tumors to distant sites that are physically discontinuous with the primary tumor and unequivocally marks a tumor as malignant.
- Proportionate to the size and differentiation of the primary tumor
- **Most important factor in the diagnosis of malignancy** ✦
- All tumors can potentially metastasize except **BASAL CELL CARCINOMA** & **most 1ry brain tumors**

metastasis 1st 2nd

Routes of metastases:

1. Lymphatics

2. Blood vessels (hematogenous spread)

3. Seeding within body cavities/ Transcoelomic Spread

1- Lymphatic Spread:

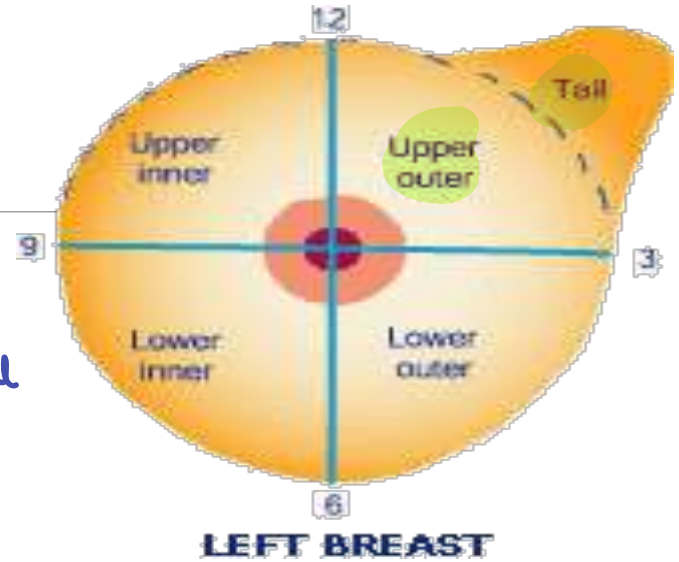
→ Malignant

→ mostly epithelial

- All cancers, but more characteristic in Carcinoma.

- Spread follows the anatomical route of drainage e.g.

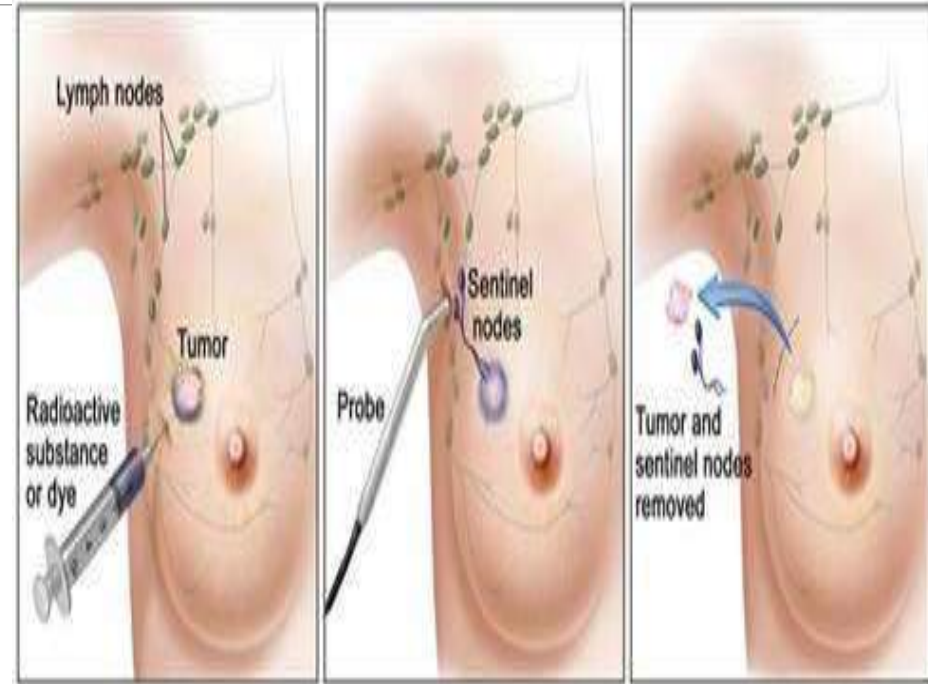
- Breast cancer in upper outer quadrant → axillary L.N. → closest one



IMPORTANT IN SURGICAL RESECTION:

■ Sentinel Lymph Node:

- The first regional lymph node that receives lymph flow from a primary tumor.
- Usually outlined with a blue dye.
- Biopsy from sentinel lymph node allows determination of the extent of spread of the tumor.
- Not all enlarged L.N.s indicate Mets
e.g. Reactive hyperplasia



⇒ a clinical method doctors use during surgery :-

* they use a dye to mark the first lymph node

* they remove it and test it, if

- no tumor they stop
- There is a tumor → they remove the next one

* there is No Benign lymph node tumor

* a lymph node either is inflamed → Reactive hyperplasia

or lymphoma

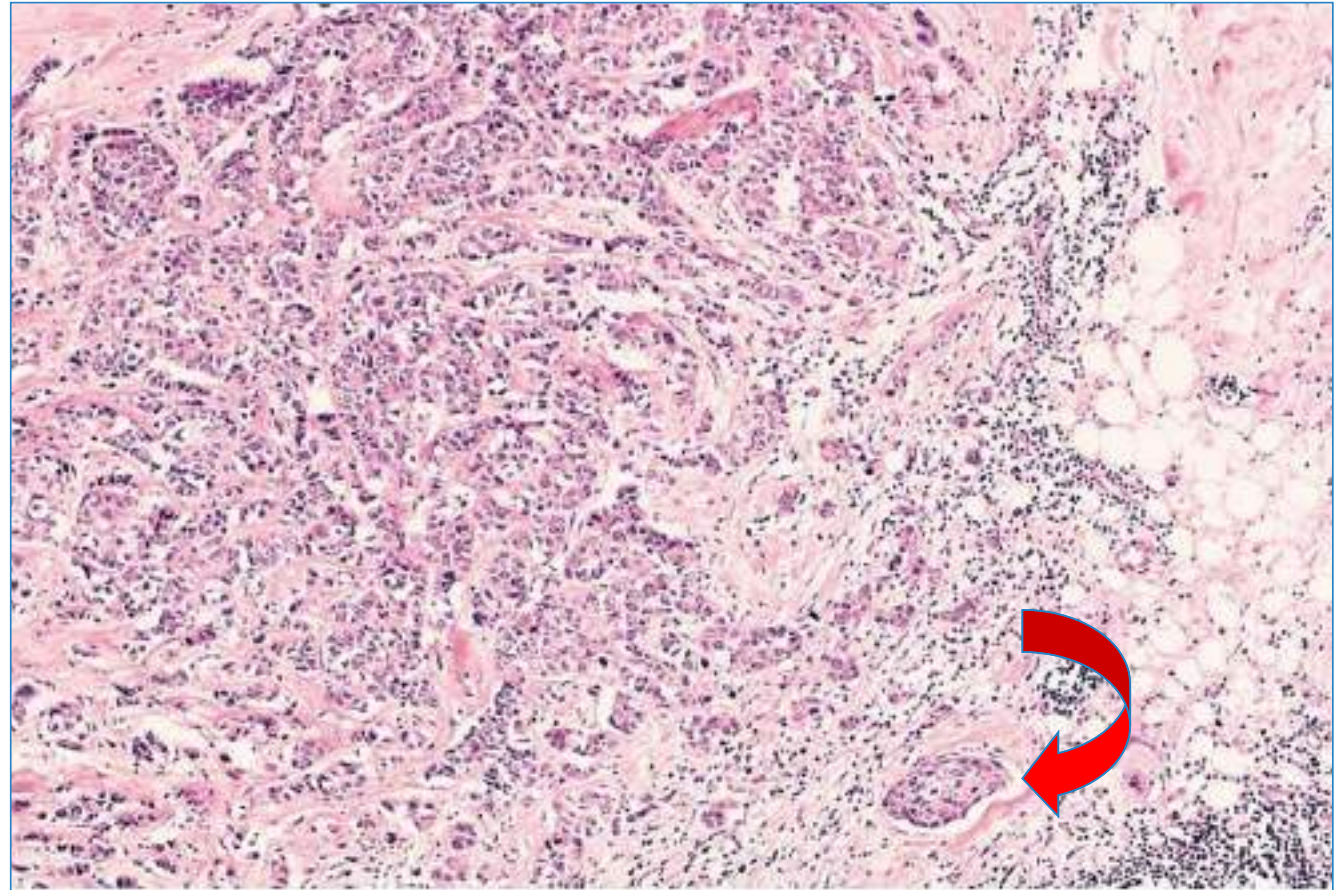
* melanocytes either has a malignant tumor → melanoma

or it's benign → Nevus (mole) → 

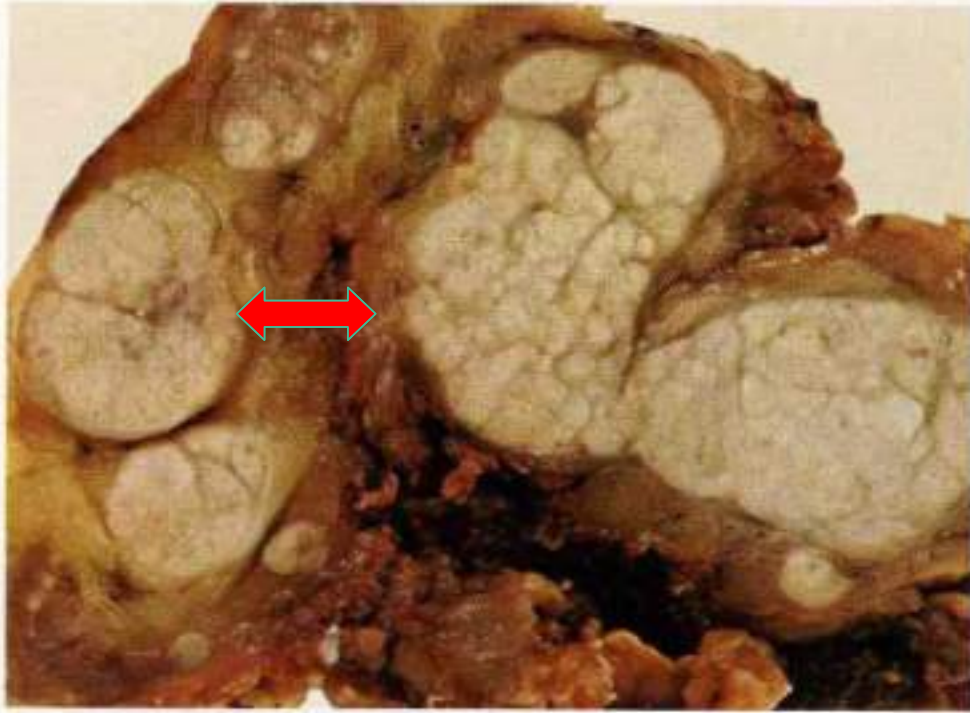


Breast carcinoma: There is **no capsule**. Nests & cords of tumor cells **invading breast stroma, fat & lymphatic vessel (arrow)**

lymphatic invasion



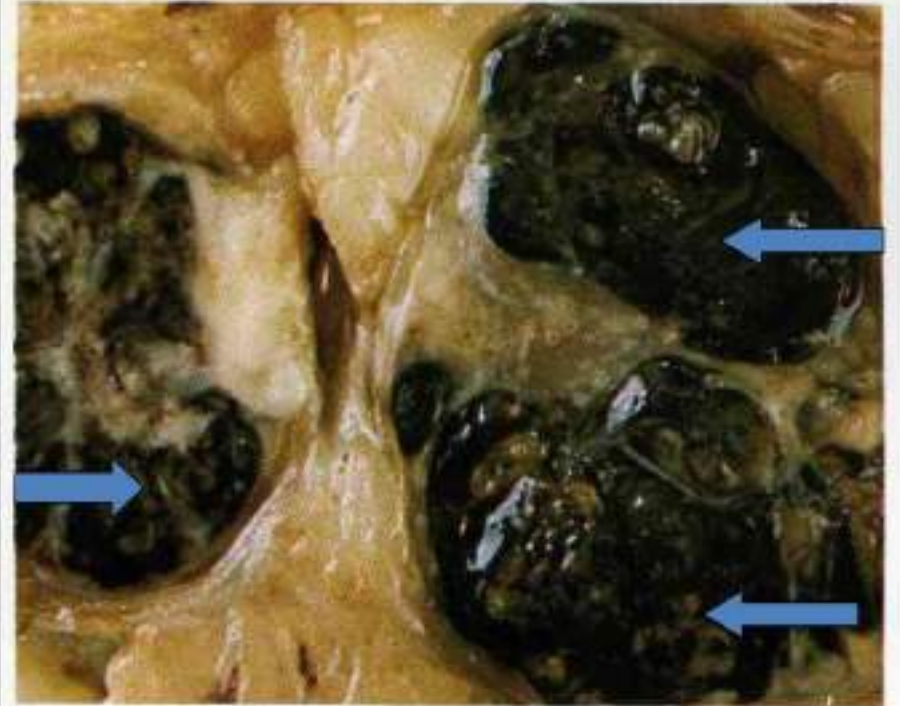
Secondary carcinoma: lymph nodes. Several enlarged mesenteric lymph nodes. The enlargement is caused by the presence of greyish-white deposits of secondary carcinoma from a (primary rectal adenocarcinoma.)



2.31 Secondary carcinoma: lymph nodes

Secondary melanoma: lymph nodes are enlarged & largely replaced by melanin-laden secondary deposits of malignant melanoma.

black pigment abs



2.32 Secondary melanoma: lymph nodes

2- Hematogenous spread:

↪ connective tissue

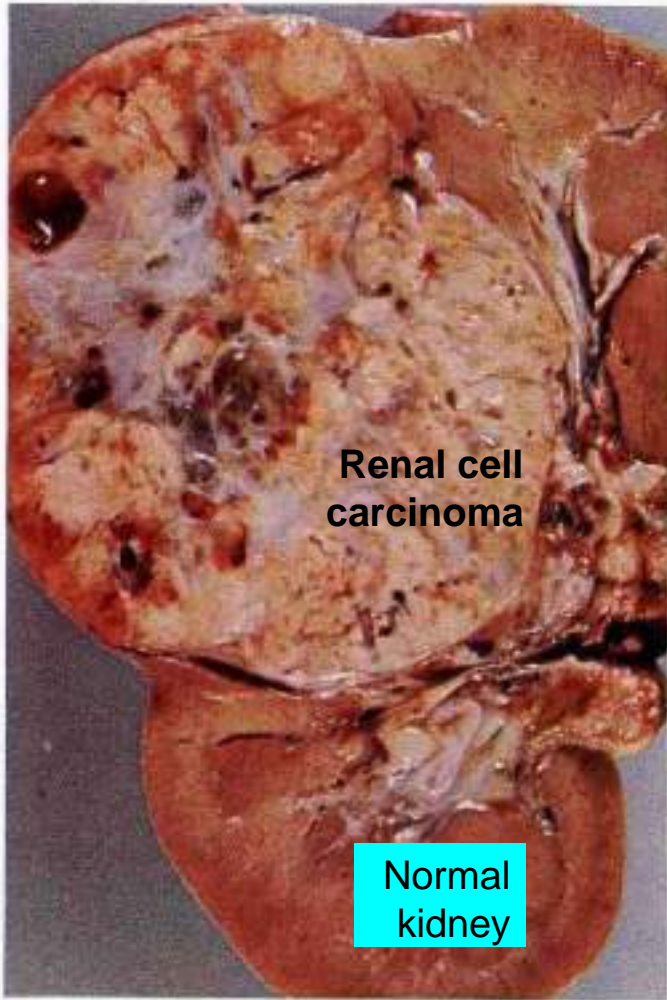
- More characteristic of **Sarcoma** but may occur in carcinoma.

- Veins, with thinner walls, are more readily penetrated than arteries.
- With the venous invasion, the blood-borne cells follow the venous flow draining the site of the tumor:
 - All portal venous blood flow drainage to the liver as in cancers of GIT.
 - All systemic venous blood flow to the lungs & bones.
 - The *liver, lungs, and bones* are the *commonest three sites involved in hematogenous metastatic secondaries*.

Bones → is not known why

kidney (Renal cell carcinoma)

The tumor forms a large smooth rounded mass in the upper pole of the kidney which has extended into the hilum & infiltrate renal vein. This **cancer usually spread by the blood.**



Renal cell carcinoma

Normal kidney

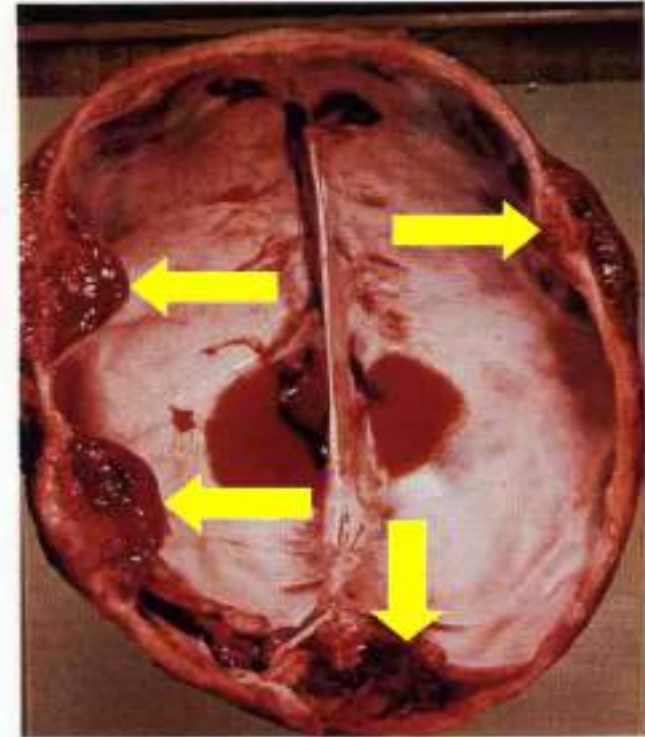
Liver, studded with multiple whitish metastatic cancer secondaries.



© Elsevier, Kumar et al: Robbins Basic Pathology 8e - www.studentconsult.com

Secondary neuroblastoma: skull. Four large hemorrhagic, malignant neuroblastomatous secondary deposits in the skull.

↳ From adrenal gland



13.80 Secondary neuroblastoma: skull

A multiple lesions in one organ → mostly metastatic

3- Transcoelomic spread:

- Within a natural body cavity like peritoneal or pleural cavity, e.g.:
 - CA of the ovary tends to spread widely through the peritoneal surface
 - CA of the upper lobe of lung to the lower lobe through the pleural surface
 - CA of colon across peritoneum to S.I. & distant parts of the colon
 - CNS tumors may penetrate the cerebral ventricles & be carried by the CSF to be reimplanted on the meningeal surfaces, either in the brain or the spinal cord.

Peritoneal seeding by malignant cells of colonic adenocarcinoma .



Summary : Differences between benign & malignant neoplasms

■ BENIGN

- Well-differentiated
- Low mitotic index
- Slow Growth
- With capsule
- No invasion
- No metastases

vs

MALIGNANT

- Various or Anaplastic
- High mitotic index
- Rapid growth
- No capsule
- Invasion
- Metastases