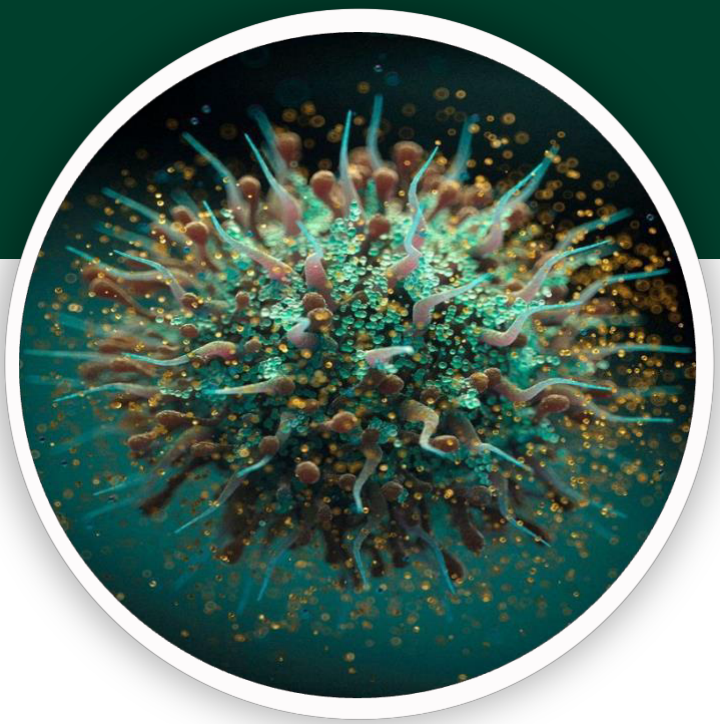


Pathology | Final 6

Neoplasia Pt.2

Written by: NST Members

Reviewed by: NST Members

RECALL

In the last lecture, we agreed that neoplasms are new growths with specific genetic mutations that allow them to grow autonomously. We also said that neoplasms can be benign or malignant

Characteristics of malignant neoplasms

1. Differentiation and anaplasia
2. Increased rate of growth
3. Local invasion
4. Metastasis

Differentiation (التشابه)

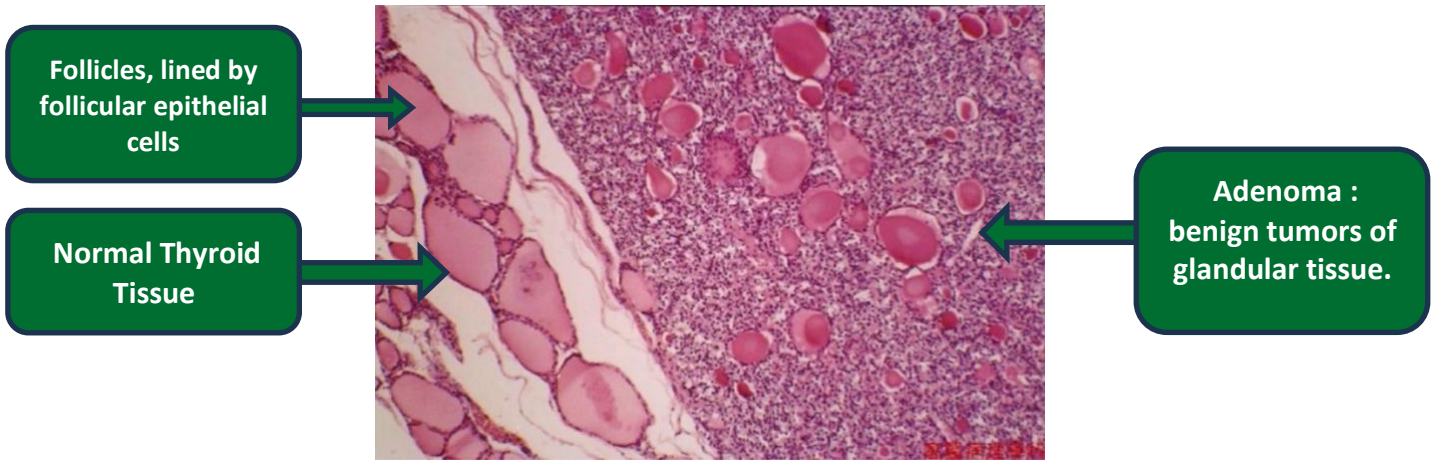
The extent to which neoplastic cells (tumor cells) resemble the cells they originated from, both morphologically and functionally.

The more the difference, the more the differentiation is. Which means the worse the behavior of the tumor.

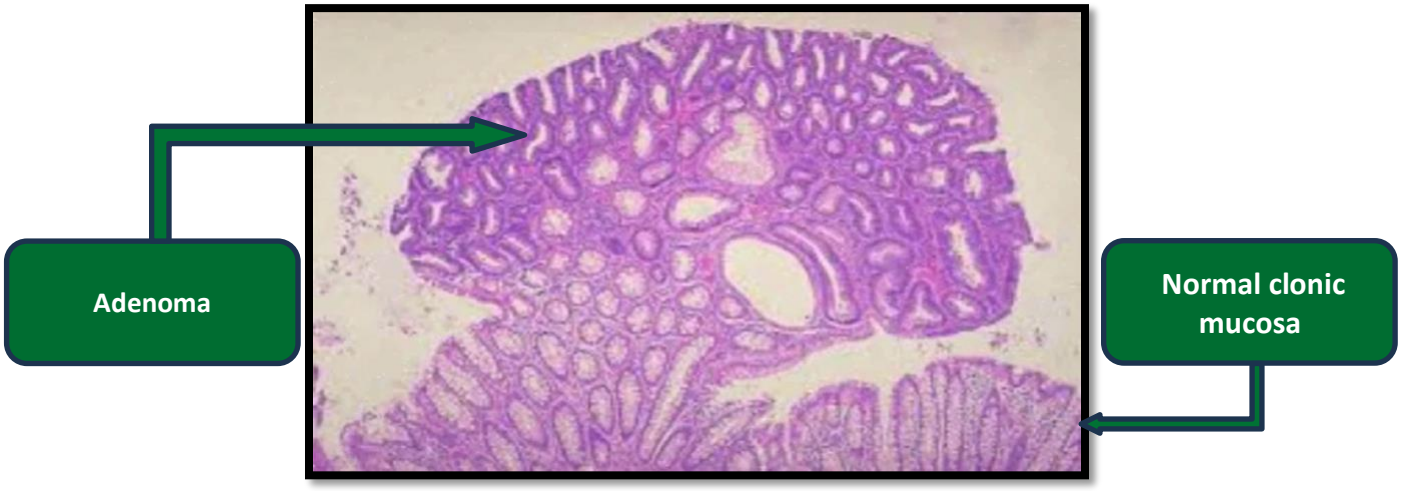
Benign tumors: well, differentiated

Benign tumors **always resemble** their **parent cells morphologically and functionally**, that's why we call them **well differentiated.**

Example: Pituitary adenoma can **look exactly** like normal pituitary gland and **(morphologically similar)** and can **secrete** hormones secreted from that gland **(functionally similar).**



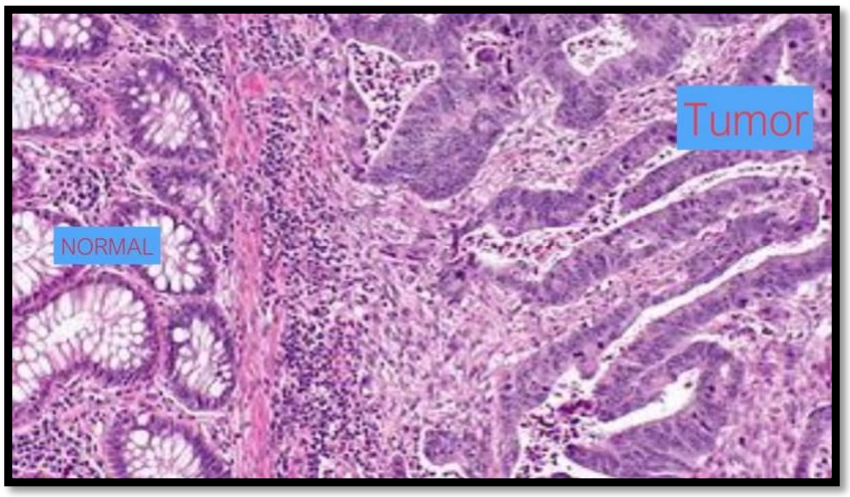
Example: colon adenoma looks almost **exactly the same (morphologically similar)** as the normal glandular tissue (almost, because there is **no benign tumour that is a carbon copy of the original tissue)**, and it performs the **same function (functionally similar).**



Malignant neoplasms: less differentiated or de-differentiated

Malignant tumors are functionality and morphologically less similar to the original tissue, which is why the called less differentiated or de-differentiated.

Example: malignant tumors arising from colonic glandular tissue are called adenocarcinoma, and they are **less similar to the normal tissue morphologically (they become elongated)** and **functionally**.



❖ Malignant neoplasms have a **wide range of differentiation:**

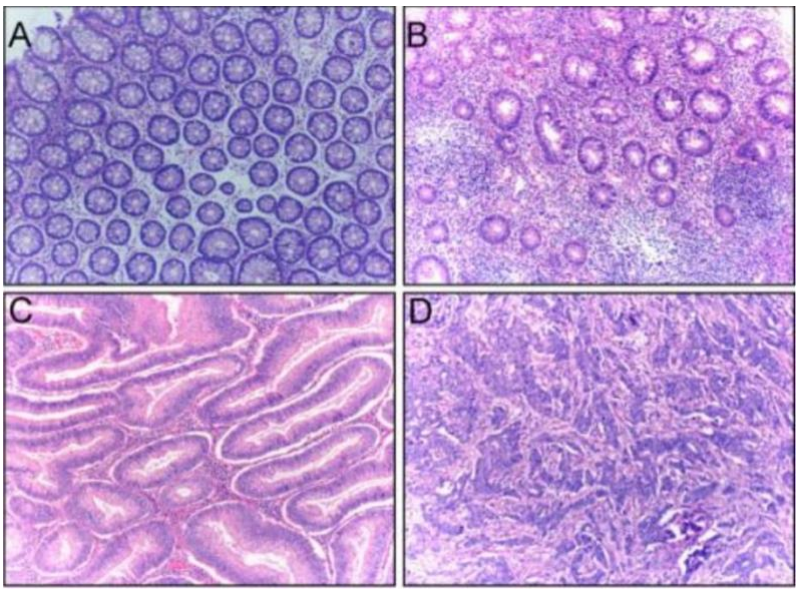
A. *Normal mucosa of the colon:* **daisy round flower.**

B. *Well-differentiated tumors:* **still have some similarity to their cell of origin.**

C. *Moderately differentiated*: **less resemblance to cell of origin.**

D. *Poorly differentiated*: **almost no similarity to cell of origin.**

✓ These stages of differentiation are referred to as: tumor grades. well, is **grade 1, moderate is grade 2, poor is grade 3.**



✓ **The more we go from grade 1 to grade 3 the worse the prognosis, which mean that poorly differentiated tumor is less functional and it's behaviour is worse than well differentiated malignant tumor.**

Tumor Grade & Tumor Stage

- For each tumor, there is a grade and a stage.

➢ ***Grade:*** refers to the **morphology**: to what we see under the microscope

➢ ***Stage:*** refers to the **extent of tumor spread, presence of metastasis.**

✓ Both grade and stage **are important for prognosis**. BUT **the stage** is much **more important.**

Notes about the differences between malignant and tumor (recap from last lecture).

Tumor stage is the single most important prognostic factor.

Malignant tumors have higher rate of growth than benign tumors (more cells undergoing mitotic activity).

- Benign tumors are circumscribed and don't invade around tissue, while malignant is invasive.
- Malignant metastasis to other regions and organs. (Through lymphatic vessels & blood vessels, etc).

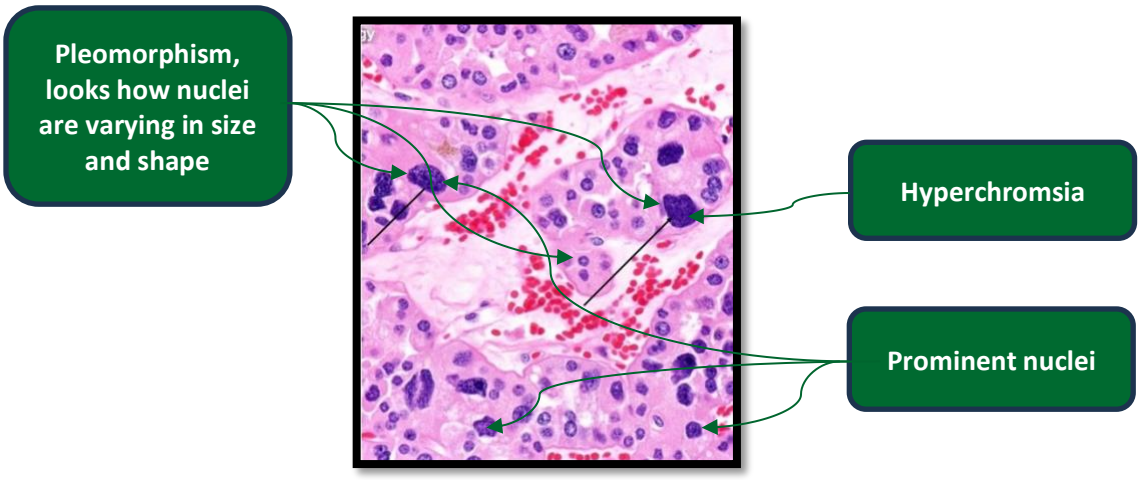
Anaplasia

Lack of differentiation. So, we have almost **complete loss of differentiation.**

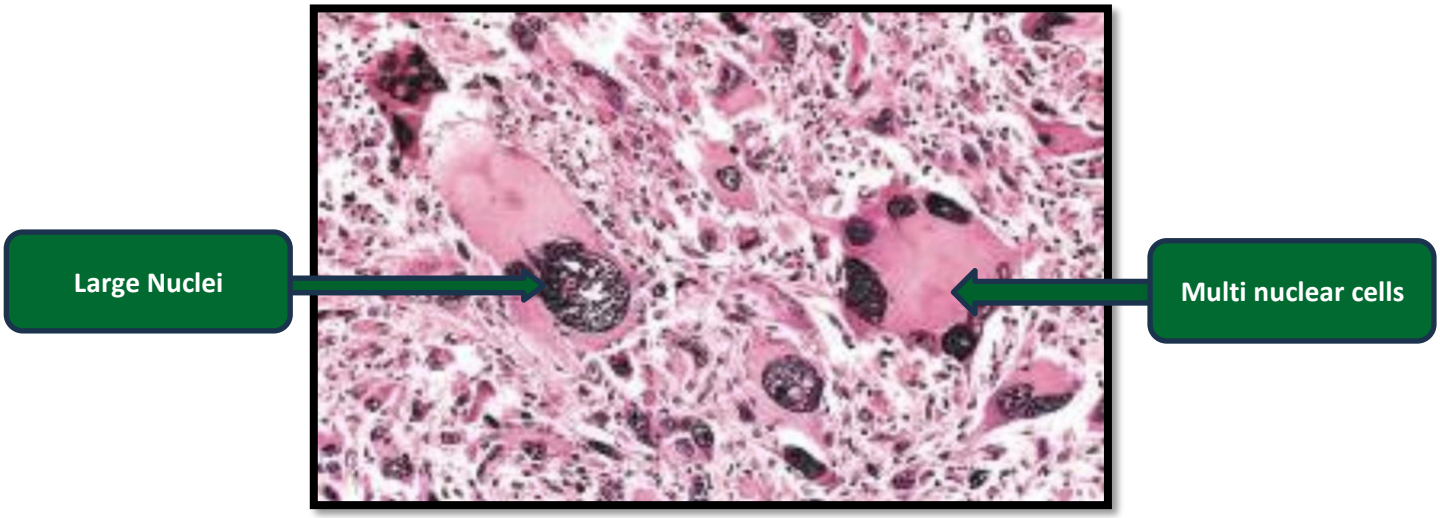
Anaplasia is a hallmark for cancer.

❖ **Features of anaplastic cells :**

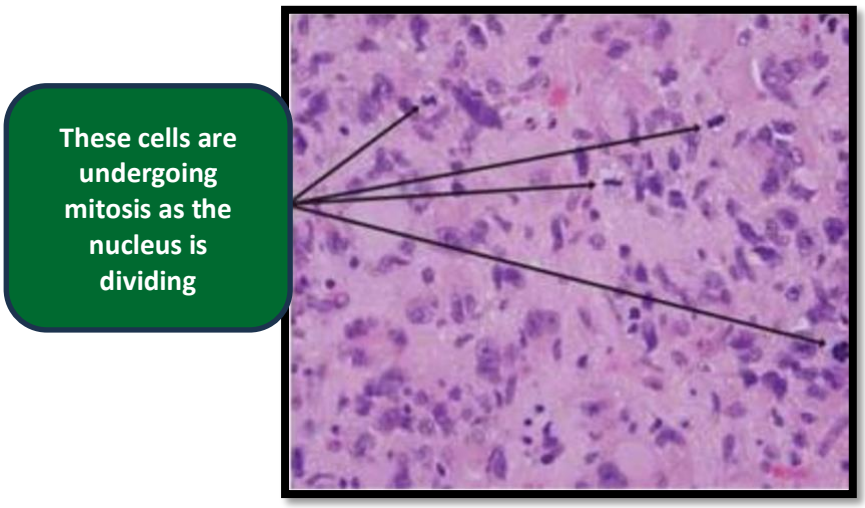
- **Differentiation :**
  - **Pleomorphism:** variation in nuclear size and shape (variability in the morphology).
  - **Hyperchromasia: dark** nuclei.
  - **Prominent nucleoli.**



- **Large nuclei with high nuclear-cytoplasmic ratio (N/C ratio).**
  Note: **normal N/C ratio is 1:4 or 1:**
- Presence of **large giant cells,** with **multiple nuclei.**



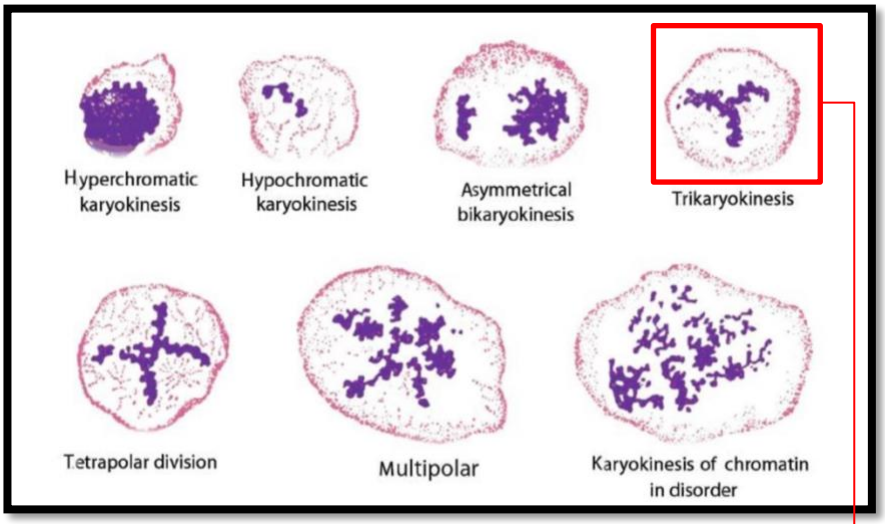
- **Increased mitotic activity**



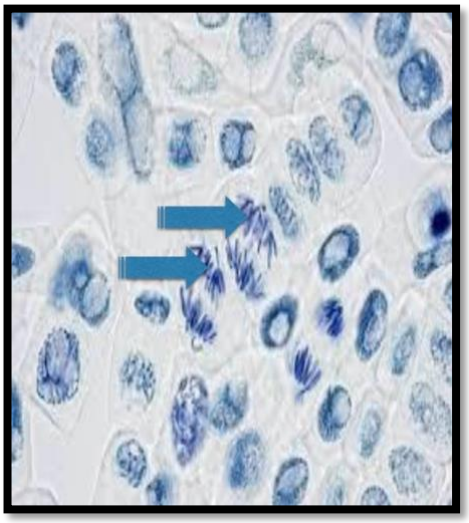
Atypical mitoses, which may be numerous (increased) Anarchic multiple spindles may produce tripolar or quadripolar mitotic figures (shown in next point).

In healthy adult tissues (with some exceptions like skin or gut lining), cells do not divide frequently. When a pathologist sees many cells dividing in a small area (as shown by the arrows), it indicates that the tissue is growing rapidly. This is a hallmark of tumors.

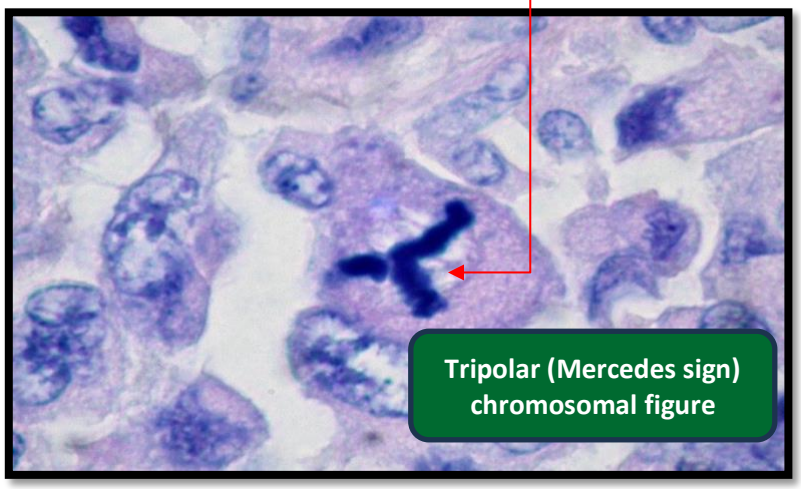
➢ **abnormal appearance of chromosomes during mitosis**: **tripolar (Mercedes sign) or quadripolar, multipolar** (Means that chromosomes and chromatin are not arranged as normal mitosis).



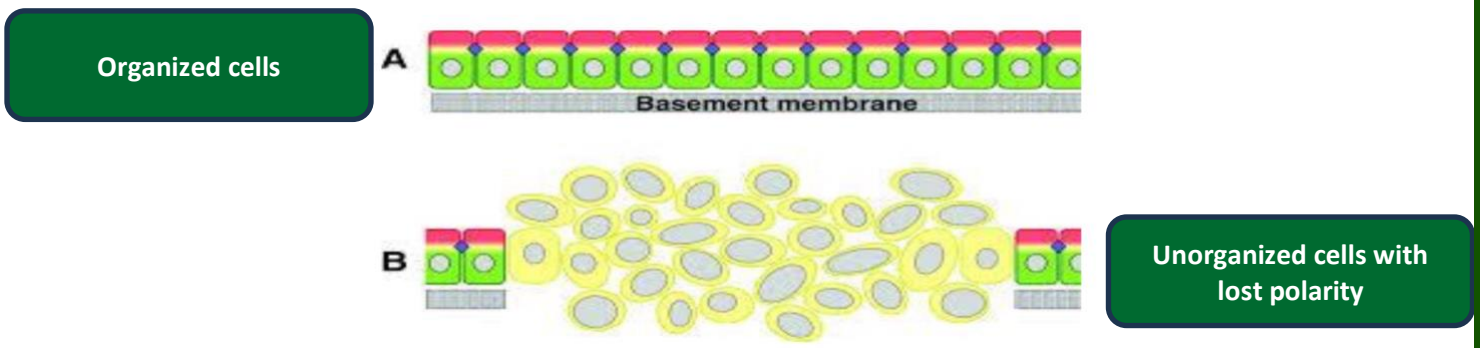
Abnormal mitotic figures in malignant cells



Normal mitotic spindle formation.



➢ **Cells abnormally oriented with loss of polarity** (loss of normal organization).



- **Increased growth rate**
  - **Most benign tumors: slow growing.**
  - **Most malignant: fast growing, more mitotically active.**
- **Local invasion**

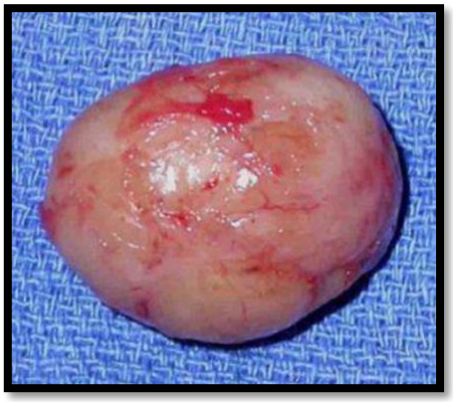
Benign neoplasms: **remain localized, well circumscribed and do not invade.**

This is because they **are encapsulated**: the capsule is derived from :

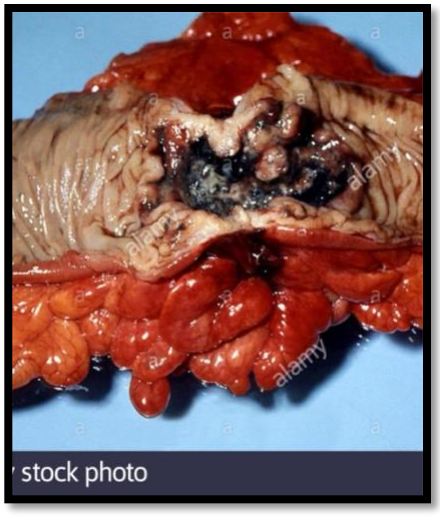
1. **Stroma of the host tissue and**
2. **Parenchymal** cell atrophy under the pressure of the expanding tumor.

*Parenchymal cells are cells that constitute most of the organs volume.

- However, not all **benign tumors are encapsulated** but even the **unencapsulate ones have a line of cleavage in the majority of cases** (e.g. uterine leiomyoma).



Invasion In malignant tumors

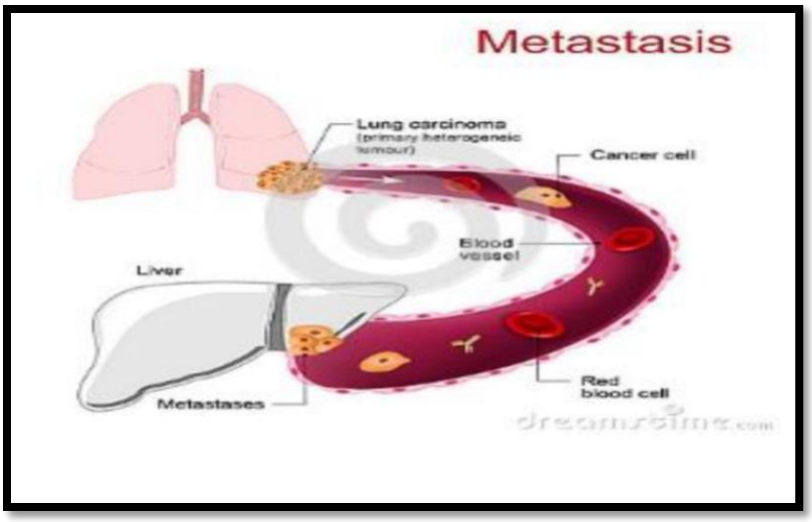


- Cancer: **progressive infiltration and invasion.**
- Usually there are **no well-defined capsules.** So must be removed with a wide margin
- **Local invasion** is the second most important feature **to differentiate benign from malignant neoplasms; metastasis is the most important feature.**

Metastasis

Secondary implants of the tumor **which are discontinuous with the primary tumor and located in distant sites.**

- Metastasis is the **most important feature of malignancy**.

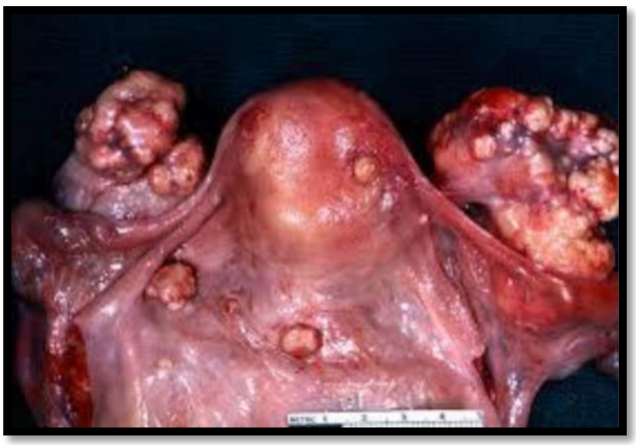


<u>Cancers differ in their ability to metastasize</u>

- Basal cell carcinoma of skin **doesn't metastasize**
- CNS tumors **rarely metastasize.**
- Bone =osteogenic sarcoma **usually found to be metastasized before discovering the primary tumor.**

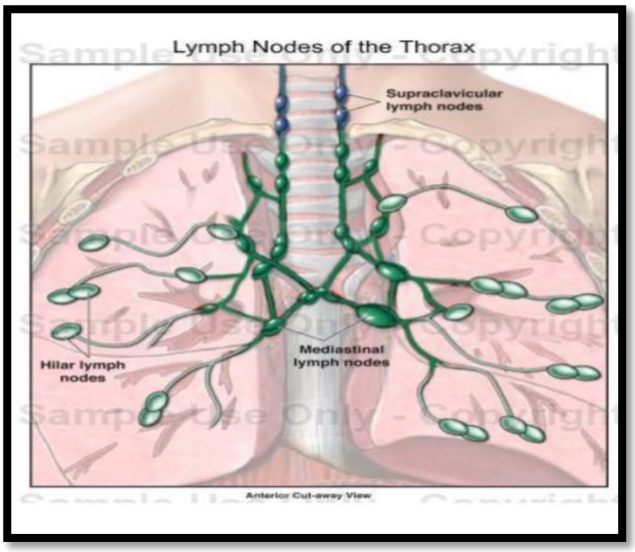
Routes of metastasis spread

1. Seeding within body cavities



- **occurs when a tumour in a site in close proximity to a peritoneal surface, usually the ovary or appendix, seeds the surface.**
- Ex. Ovarian cancer, tumor cells move through the peritoneal cavity and fill it with metastatic deposits.

2. Lymphatic spread



- Carcinomas spread first by this route (through lymphatic vessels).
- Sarcomas **rarely** spread by lymphatics.
- **More in carcinoma, rare in sarcoma**
- Pattern of lymph nodes **affected depends on the site of primary tumor.**

3. Hematogenous spread

- **Sarcomas** spread **mainly by** hematogenous route.
- Carcinomas also spread by this route, but they **metastasize to lymph nodes first (via lymphatic route).**
- Liver and lungs are the most common **sites of spread (most common recipients),** because they receive a large amount of blood, so metastatic deposits can colonize these sites.

Benign vs. malignant neoplasms (Recall from last lecture)

	benign	Malignant
genetics	Few mutations, clonal but genetically more stable	Genetically unstable
Macroscopic appearance	Soft, mobile, encapsulated	Hard, fixed, infiltrative
differentiation	Well differentiated	Well or poor Anaplastic
mitosis	low	High and abnormal
Local invasion	localized	Invasive
metastasis	no	yes

Two important terms: dysplasia and carcinoma in situ.

• These two are precancerous lesions, occurring mainly on epithelium, specifically on mucosal surfaces. They are preneoplastic (premalignant) and with time they can progress to neoplasia (malignancy) if not treated.

Dysplasia (خلل في النسيج)

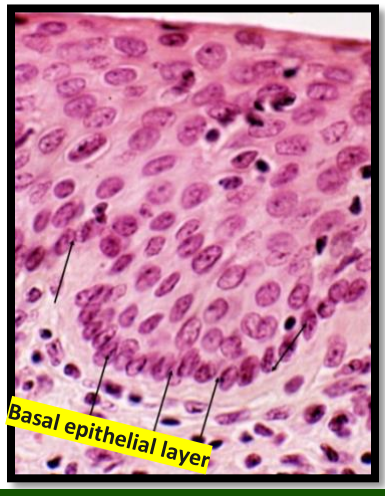
Dysplasia

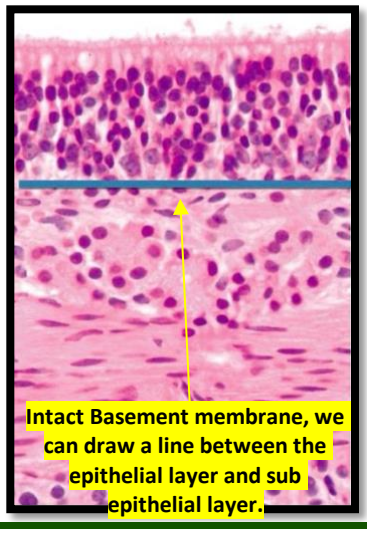
Dys = Bad or difficult

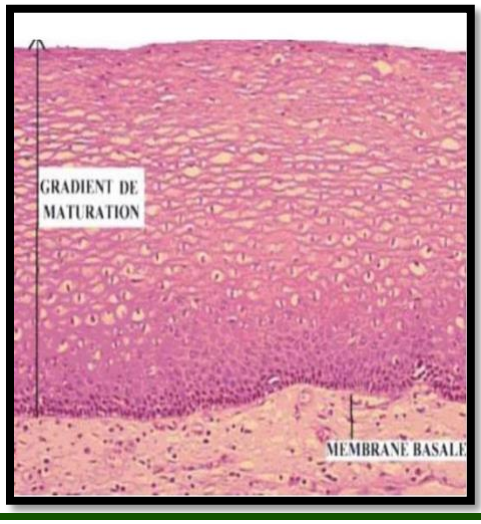
Plasia = Formation or division

Ground info

- Normal epithelium is **well organized** and cells approximately **have the same shape**. Does not contain recurrent mutations.
- It is composed of layers of cells that **mature as we go up: towards the surface.**
- Epithelial tissue **regenerates all the time**, so cells **originate from the base of the** epithelium and **grow upwards (the cells of the base regenerate and the new cells migrate upwards).**
- During this growth they mature and when they reach the surface, they spend **the rest of their lifespan as fully mature cells then they die by apoptosis or cell senescence** – normally mitotic figures are only seen in the lower third of the epithelium because the basal cells are the only cells that undergo mitosis normally.







- There is an **intact, non-invaded, basement membrane. (Which means that the regeneration will not metastasise the basement membrane.**

The basement membrane separate epithelium from subepithelia tissue

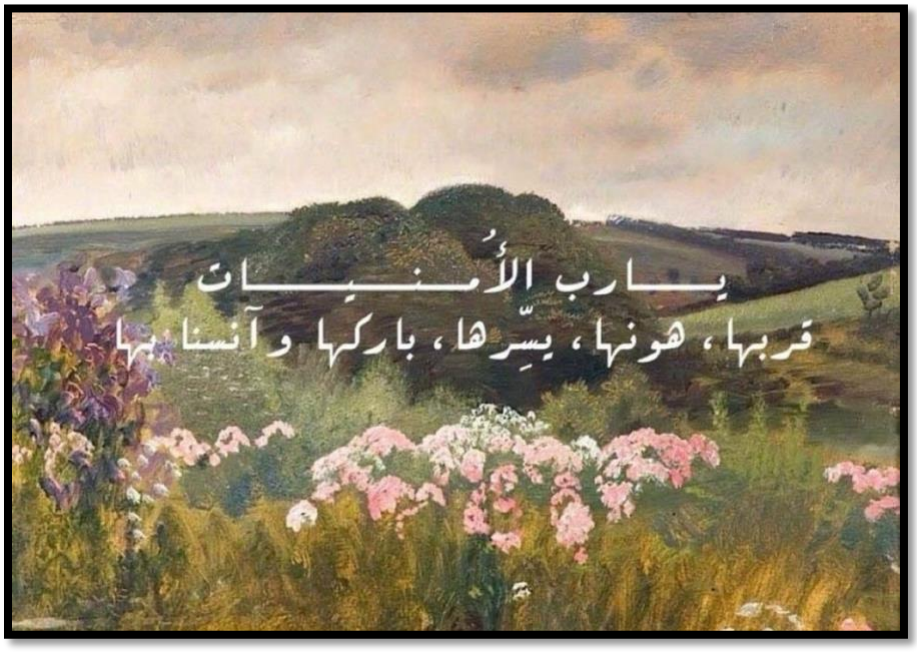
Definition (Dysplasia)

- **Disordered but non-neoplastic proliferation confined to the mucosa without affecting the underlying tissue.** (because dysplasia **is confined to the epithelium,** it **doesn't disrupt the basement membrane).**

- Loss of uniformity of individual cells and in their architectural orientation, tissue loses its organization.

- Expansion of immature cells.

- Seen mainly in epithelial lesions.

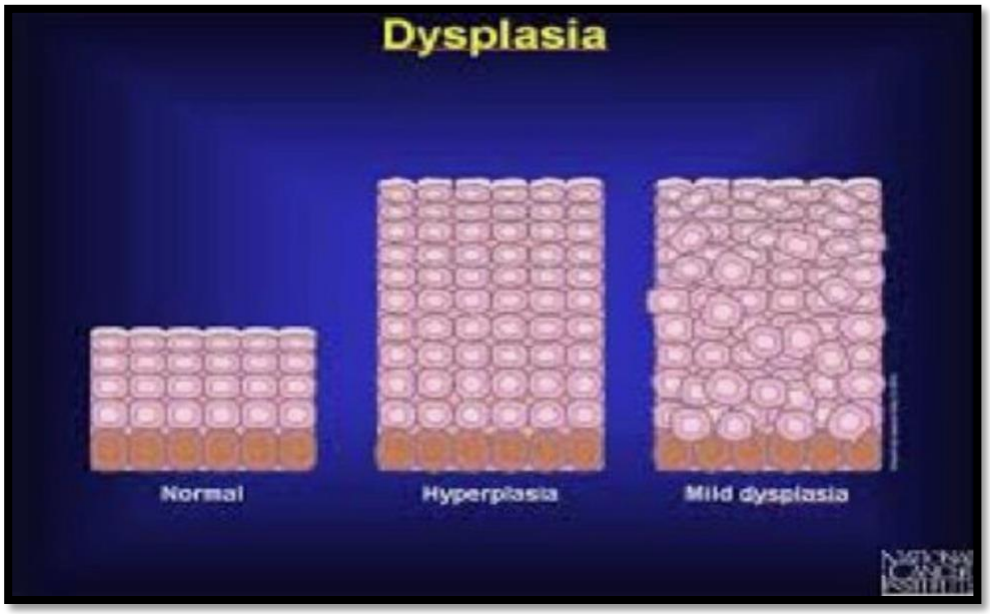


Histologic features of dysplasia

- Loss of orientation.
- Pleomorphism.
- Large cells loss of polarity.
- Hyperchromatic nuclei.
- More mitoses than normal may change skin colour.
- Mitosis in an abnormal location (normal location is at the basal layers of epithelium… abnormal: **mitosis seen in more superficial layers**).

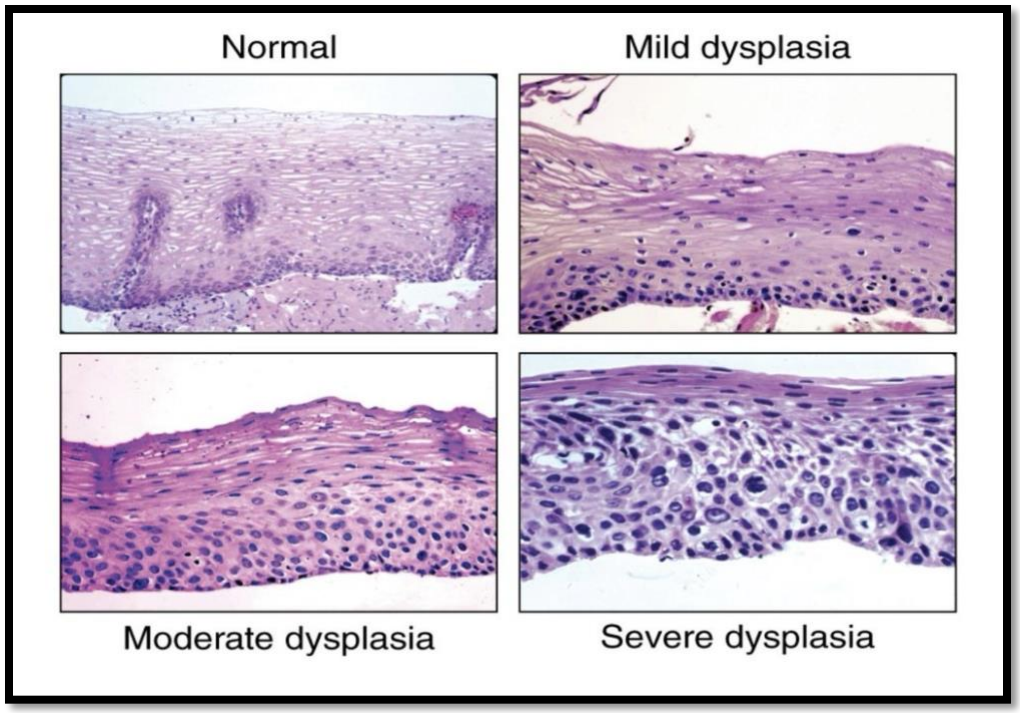
NOTE: **many of these features are similar to those we discussed in anaplasia.** BUT here **these changes are seen only within the epithelium without invading the basement membrane that separates the epithelium from the underlying tissue.**

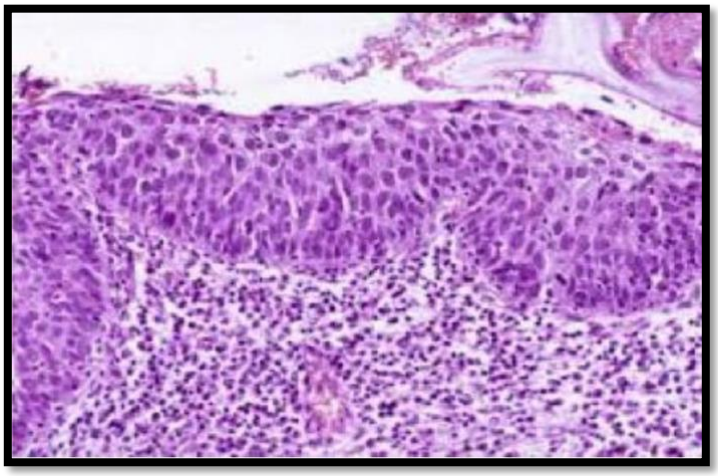
Hyperplasia increases in number of cells but normal (sustain maturation polarity mitosis only in lower third).



Grades of dysplasia

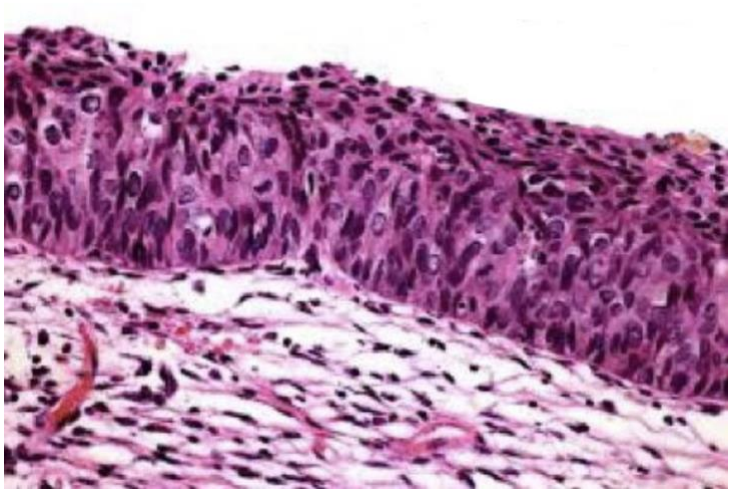
- Dysplasia is divided into **mild, moderate and severe**
- This depends on the **extent of epithelial involvement.**
- *If only the lower third of the epithelium affected:* **mild low probability to proceed to cancer**
- *Two thirds*: **moderate**
- *Full thickness*: **severe high probability to proceed to cancer**



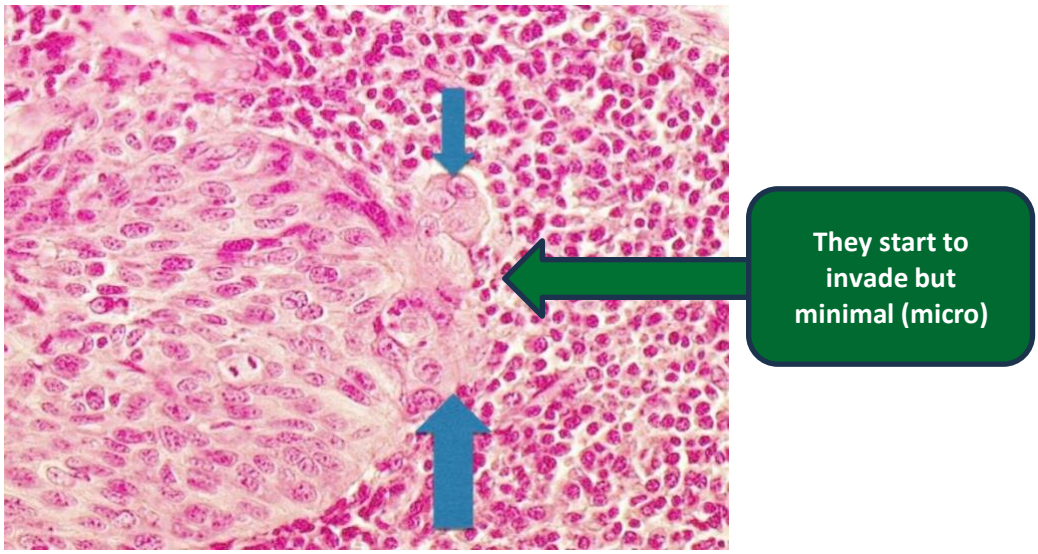


Severe dysplasia has high probability of developing into cancer.

In situ carcinoma: severe dysplasia involving the whole thickness of the epithelium Again: basement membrane intact. That's why it is "in situ"



Micro invasive carcinoma: there is dysplasia, but it is invading the basement membrane worse than in situ carcinoma, **when the invading becomes significant, it is considered malignant neoplasia.**



Behavior of dysplasia

•Although non neoplastic, dysplastic cells can accumulate mutations and transform into malignant lesions. But it's not always and not common.

- **Dysplasia is a precursor of malignancy.** So, we have to make regular screening for cancers that originate from dysplasia to prevent the formation of a tumor – dysplasia progress to cancer **only if mutations accumulate, not all dysplasia proceed to cancer.**

- However, **mild and even moderate dysplasia could regress if initial insult removed.** Mild dysplasia reversible if causative agent removed moderate dysplasia may be reversed if causative agent is removed **severe dysplasia mostly is not reversible.**
- The risk of dysplasia developing to cancer is directly proportional to the severity of the dysplasia (severe is at high risk of developing to cancer than moderate and mild).

✓ Severe > moderate > mild

Summary

- There are certain changes that can affect epithelial tissue before it gets fully carcinomatous.
- Abnormal organization of abnormal cells confined to the mucosa; this is dysplasia
- Dysplasia can be divided into three grades: mild, moderate, and severe.
- Mild dysplasia affects the lower third of the epithelium
- Moderate: affects the lower two thirds
- Severe: involves almost the full thickness.
- Carcinoma in site is the worst, severest form of dysplasia. It involves the entire thickness, and the individual cells are very pleomorphic and anaplastic.
- The basement membrane is intact in all these stages
- If the abnormal cells invade the basement membrane, then the lesion has transformed into micro-invasive carcinoma.
- Microinvasive carcinoma can spread further to become an invasive carcinoma

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Benign tumors tend to be well differentiated, encapsulated, non-invasive, slowly growing, and they do not metastasize.

Malignant tumors are anaplastic, rapidly growing, invading masses, and they do metastasize.

Metastasis occurs via three routes: 1. lymphatic spread where the tumor cells invade lymphatics and colonize lymph nodes. Carcinomas spread first by this route. Sarcomas rarely spread by lymphatics.

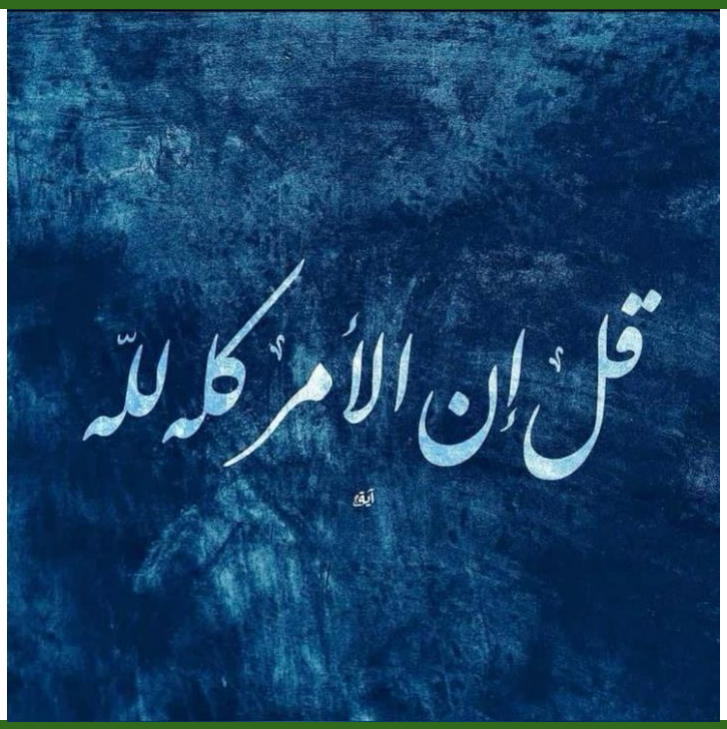
2. Hematogenous: tumor cells invade blood vessels and reach distant organs. Sarcomas spread by this route. Carcinomas also use it.

3. Peritoneal seeding: occurs when a tumor in a site in close proximity to a peritoneal surface, usually the ovary or appendix, seeds the surface.

- Dysplasia means disorganized growth confined to a mucosal surface. It is not neoplastic but can progress to neoplasia.
- Carcinoma in situ is full of atypia, not invading the underlying tissue.
- Microinvasive carcinoma occurs when the carcinoma in situ cells penetrate the basement membran

Additional Resources

رسالة من الفريق العلمي:



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