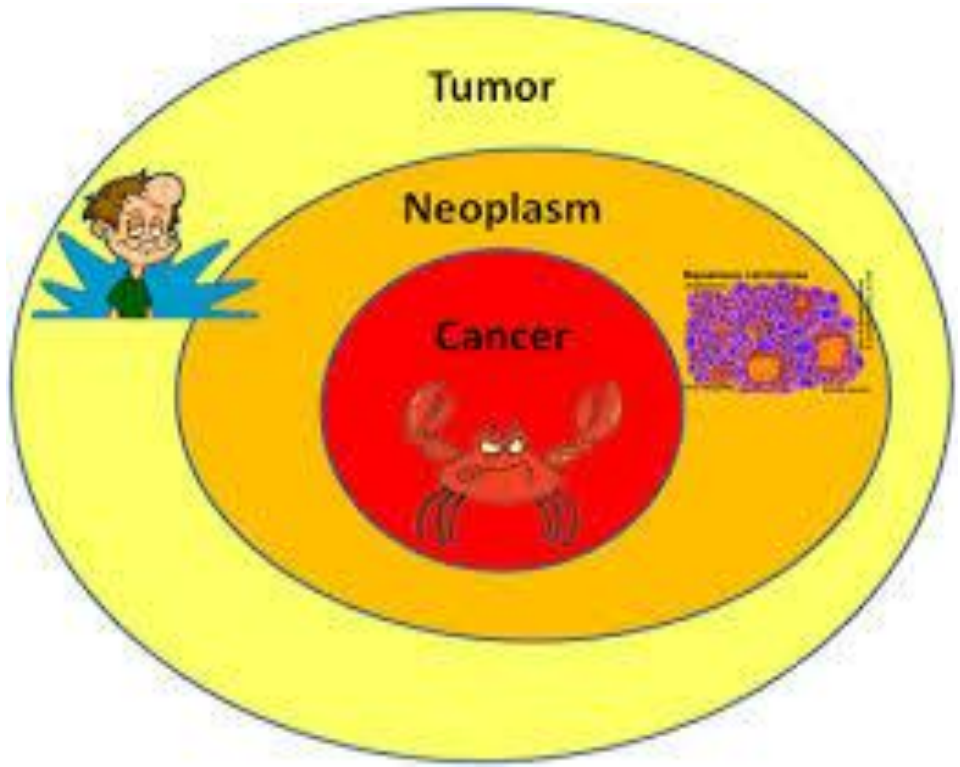
NEOPLASIA LECTURES 1&2

Dr Heyam Awad

FRCPath

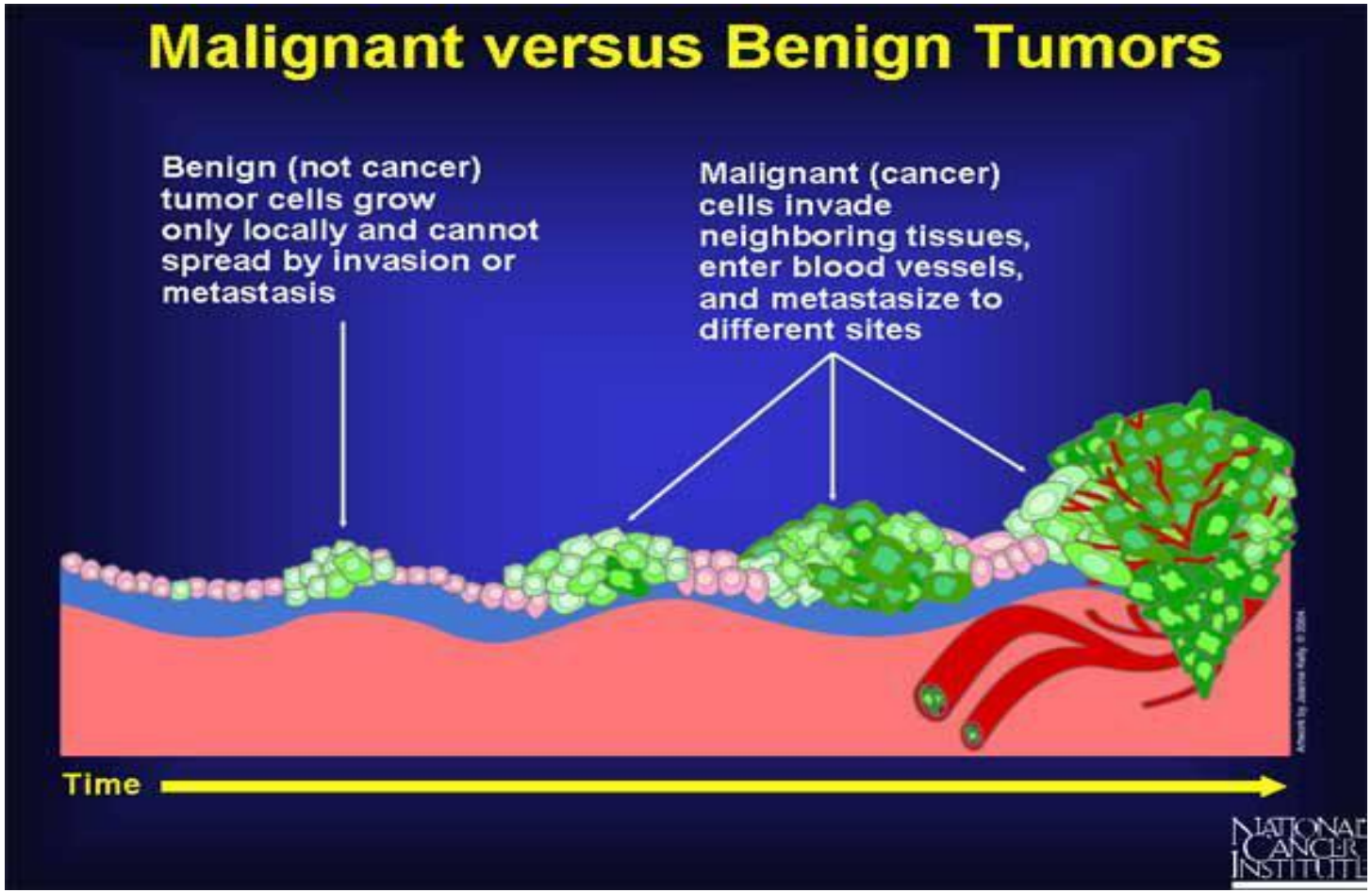
The language

- **Neoplasm:** new growth
- **Neoplastic cells= transformed cells = tumor cells**
- **Tumor = mass, swelling (neoplastic or non-neoplastic)**
- Neoplasms can be **benign or malignant**
- **Cancer = malignant tumors**


Tumor
Neoplasm
Cancer

Tuna vs crab!!!

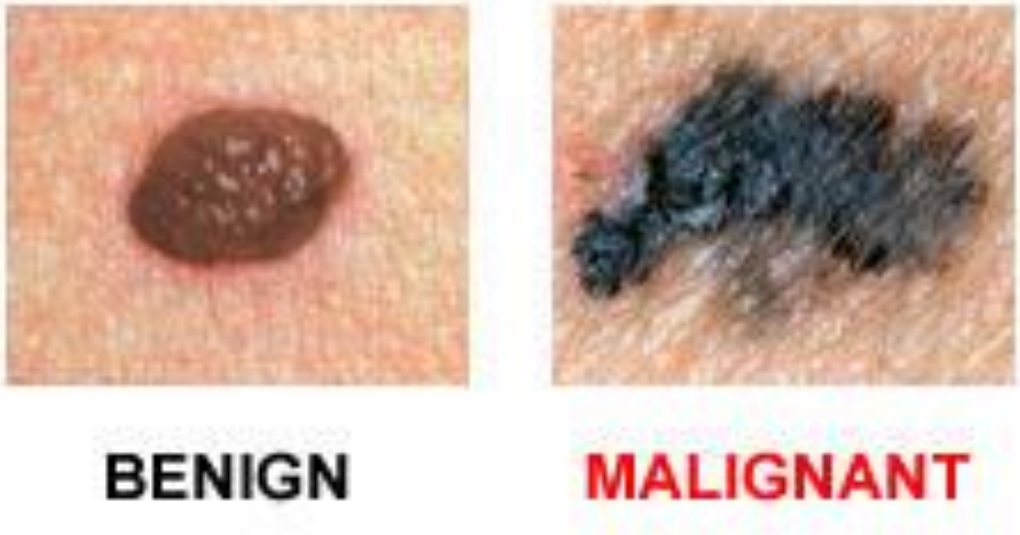

IT'S OKAY, IT'S JUST A BENIGN TUNA.
CARTOONSTOCK .com
Search ID: jml0004


Malignant versus Benign Tumors
Benign (not cancer) tumor cells grow only locally and cannot spread by invasion or metastasis
Malignant (cancer) cells invade neighboring tissues, enter blood vessels, and metastasize to different sites
Time
NATIONAL CANCER INSTITUTE

BENIGN VS MALIGNANT TUMOR

- **Benign**: innocent, localized, local surgical excision possible, patient survives
- **Malignant**: can invade and destroy adjacent structures and can metastasize (spread to distant sites)

Nevus vs malignant melanoma



note

- Some benign neoplasms can be dangerous (like brain tumors)
- Some malignant tumors are highly curable , e:g Hodgkin lymphoma

The language , again!

- Autonomy: neoplasms are autonomous: they keep growing regardless of normal growth regulatory mechanisms.
- This autonomy is incomplete because they need host blood supply, hormones etc

- Neoplasms keep growing like Suzan!

Language, yet again

- Clonality: neoplasms are clonal = they originate from one parent mutated cell.

- However, tumor cells are not carbon copies, and they accumulate different mutations as the tumor progresses, will come to this later!

- **All tumors have two components:**
- **Parenchyma: transformed, neoplastic cells**
- **Stroma: supportive, host derived, non-neoplastic connective tissue, blood vessels, inflammatory cells.**
- **Tumors' behavior depends on the parenchyma but the stroma also pays a role because it is important for tumor growth**

Some Histology

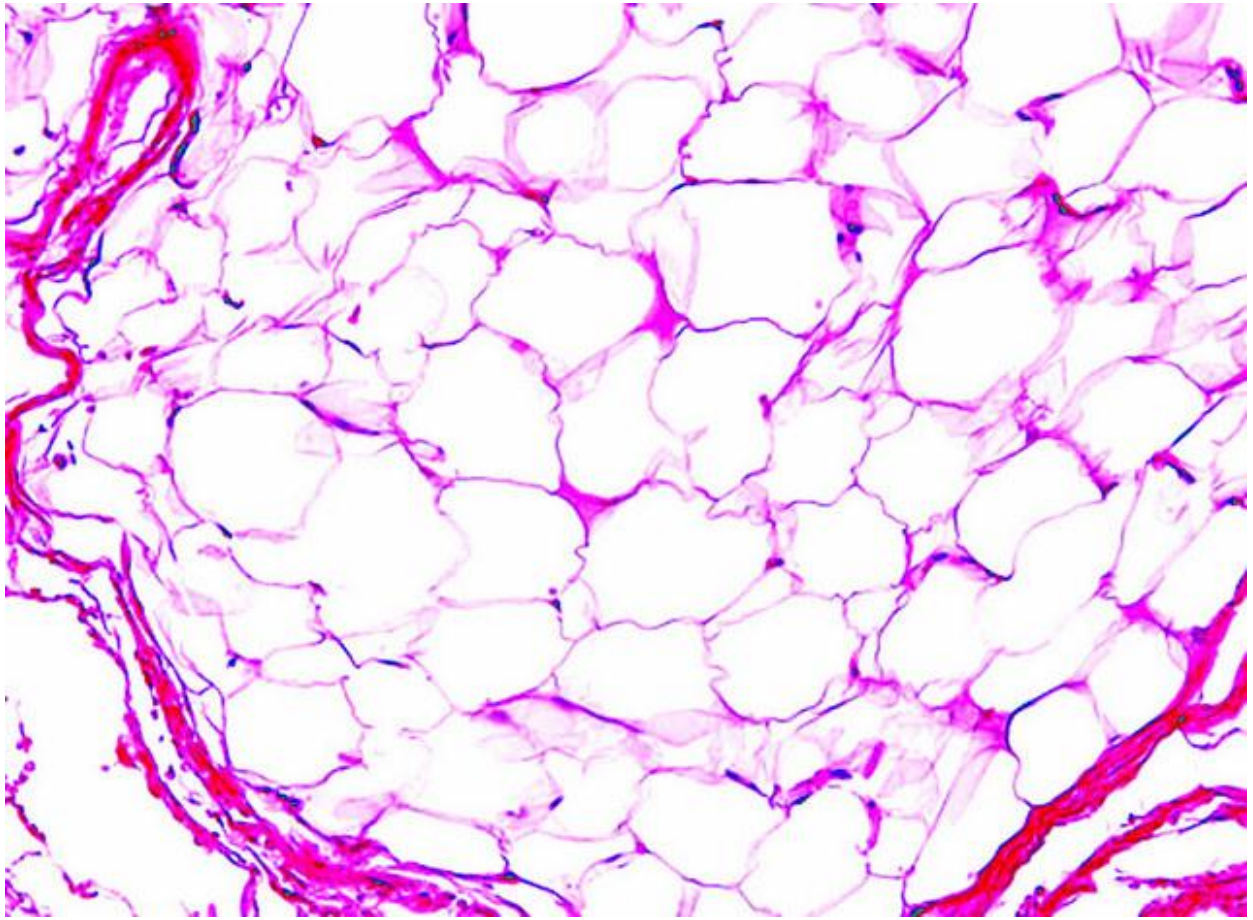
Prostate tissue

Parenchymal cells synthesize *angiogenic factors* that induce the host to supply supportive stromal tissue for it, including fibroblasts and vascular cells

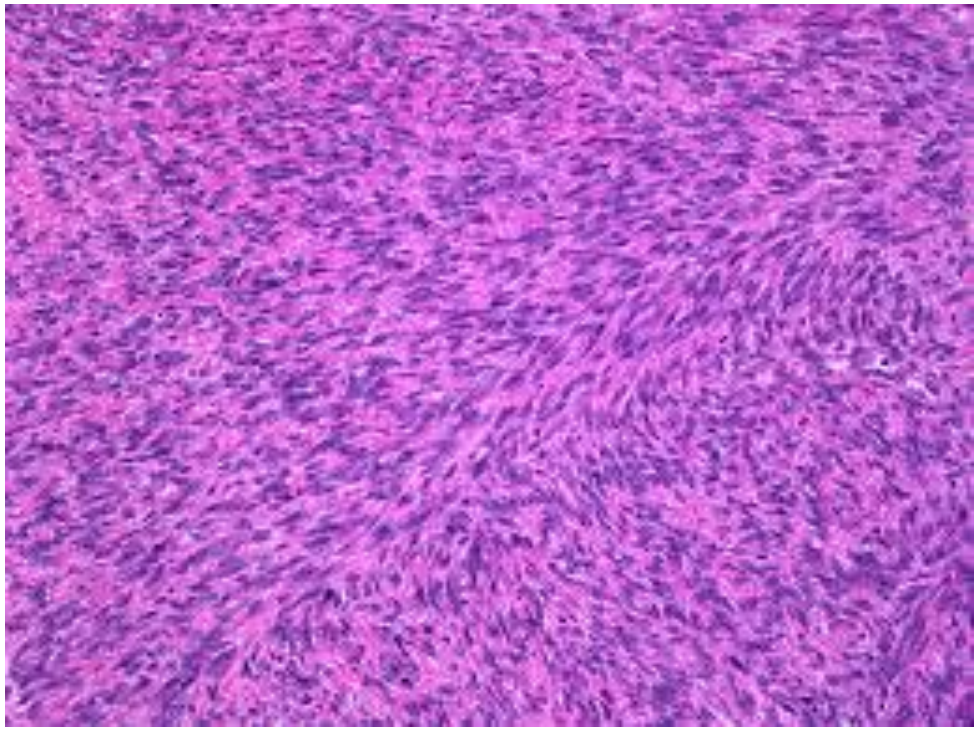
Nomenclature of benign tumors

- Usually named by adding the suffix oma (Fibroma, chondroma, osteoma)

lipoma

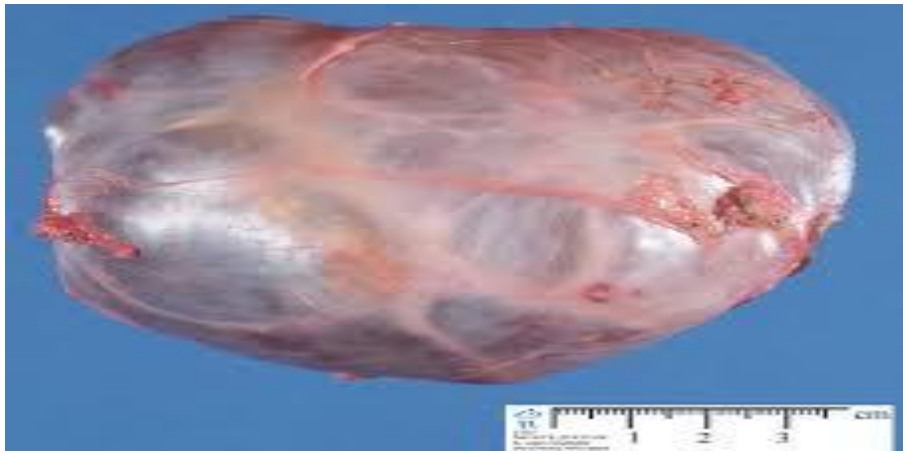


leiomyoma



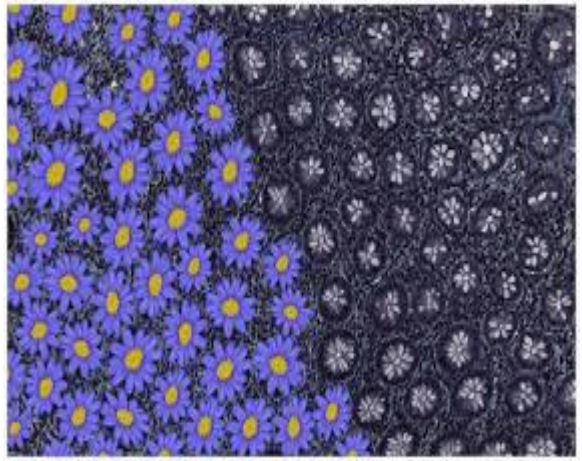
- Adenoma= benign epithelial neoplasm producing glands or neoplasm derived from glands even if it doesn’t produce glands

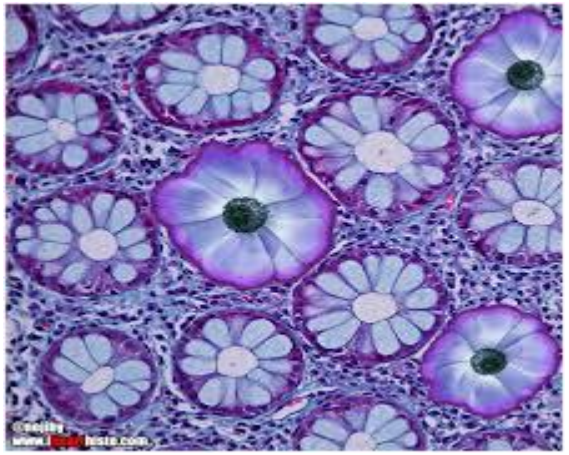
- Cystadenoma: cystic masses usually in the ovary.



Glandular epithelium

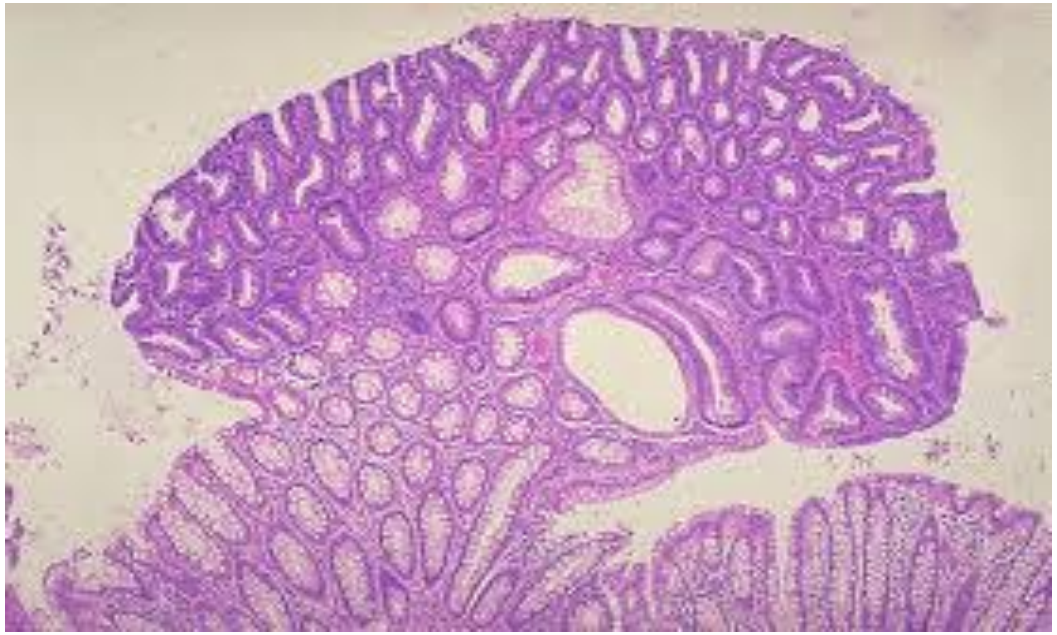
- True gland: cells surrounding a cavity and have secretory action
- E:g coloic glands (beautiful glands that look like daisy flowers)





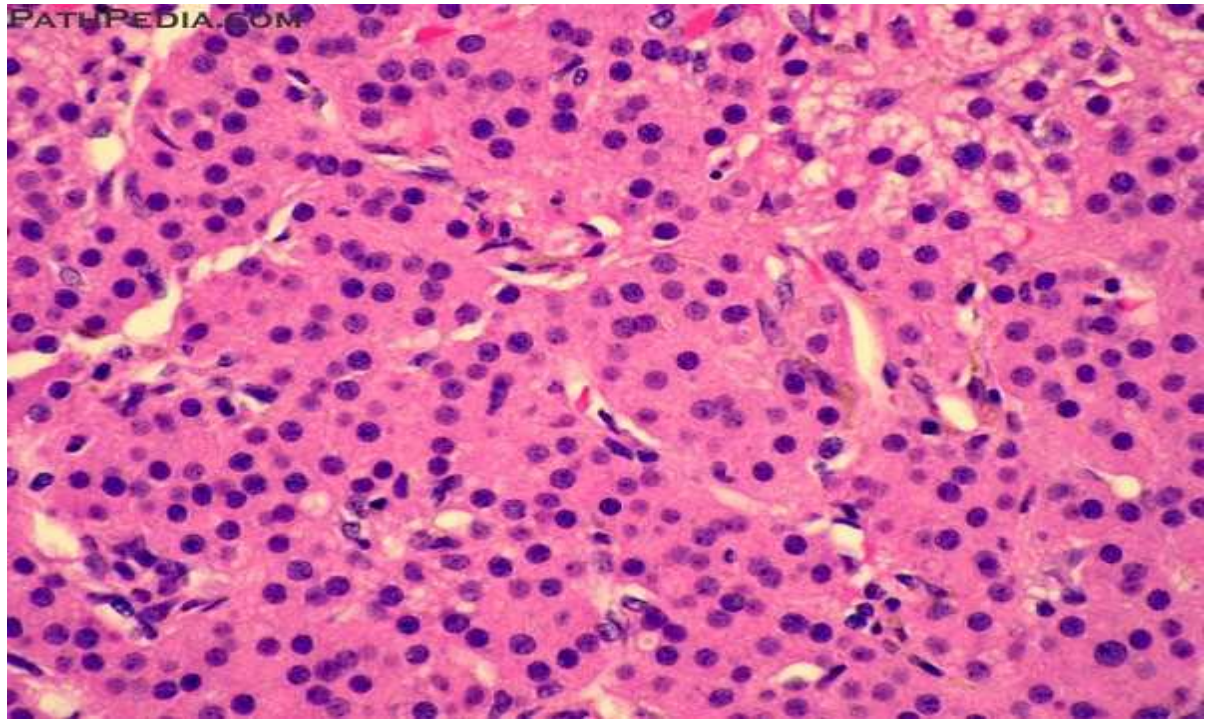
Adenoma/ colon

- Note : this is also called a polyp (used more for macroscopic (gross) appearance)



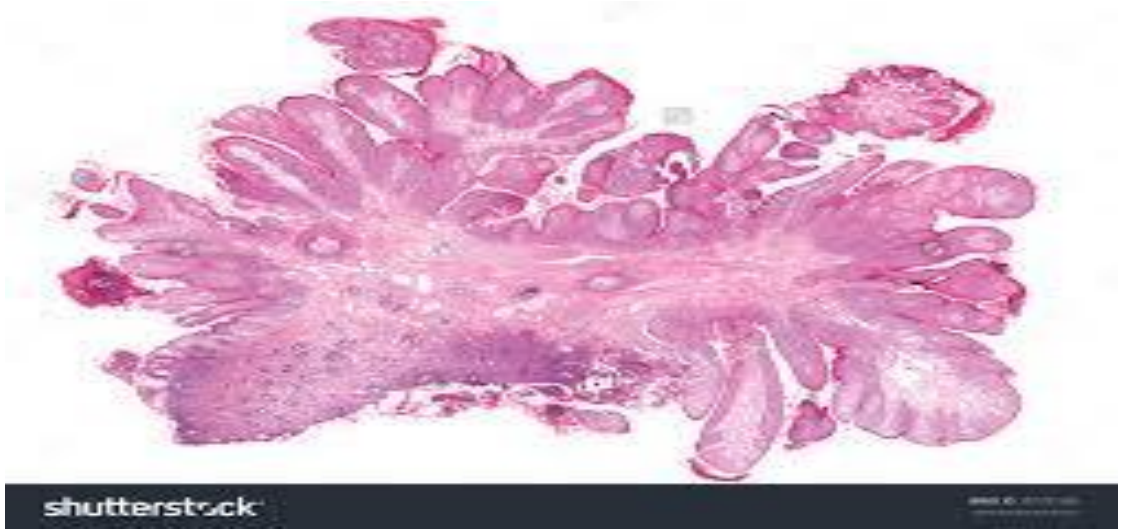
Adenoma/ adrenal gland

- In this example the tumor is derived from glandular epithelium (a gland) but it is not forming glandular structures
-



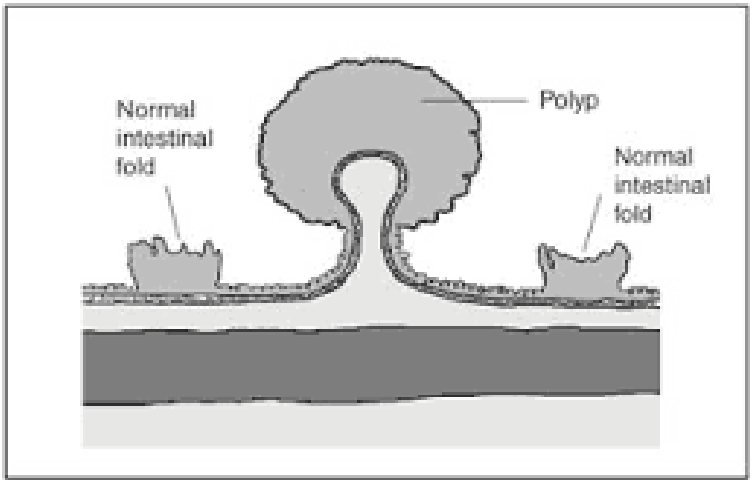
Papilloma

- Papilloma= benign epithelial neoplasm producing macroscopic or microscopic finger like projections



polyp

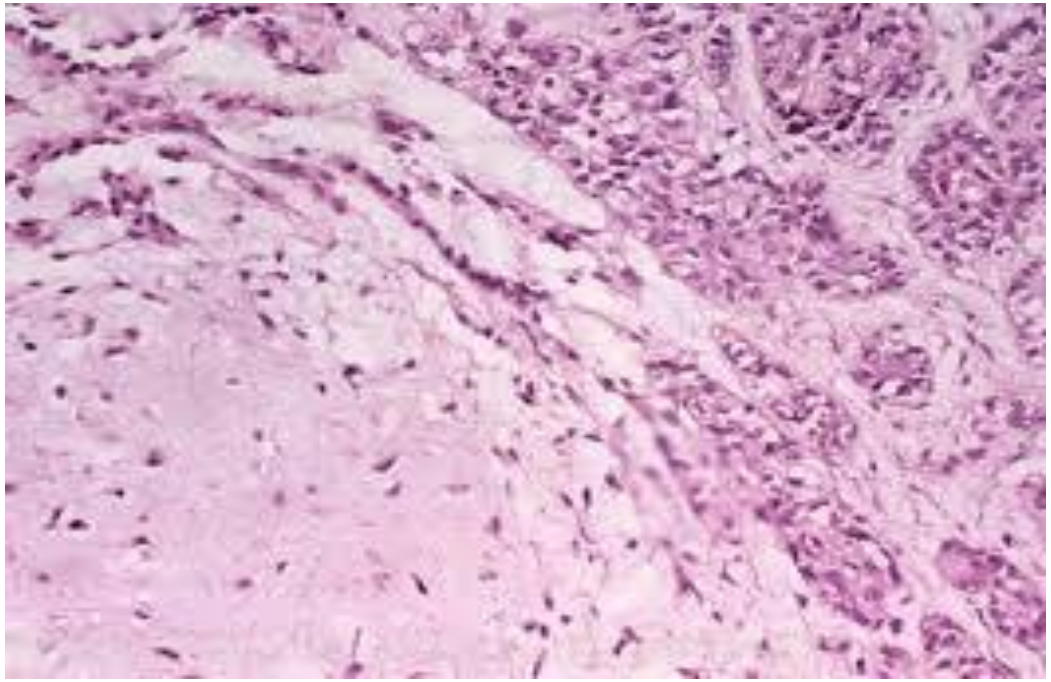
- Polyp: mass projecting above mucosal surface.
- Usually benign but some malignant tumors can be polypoid.
- The term polyp also is used for non-neoplastic conditions like nasal polyps (inflammatory in nature



- Mixd tumors: tumor with divergent differentiation, like salivary gland mixed tumor, pleomorphic adenoma.. you see epithelial elements in a fibromyxoid stroma. Both (epithelial and stromal) derived from epithelial and/ or myoepithelial cells
- Fibroadenoma of the breast also mixed, epithelial glands in fibrous stoma. Only stroma clonal

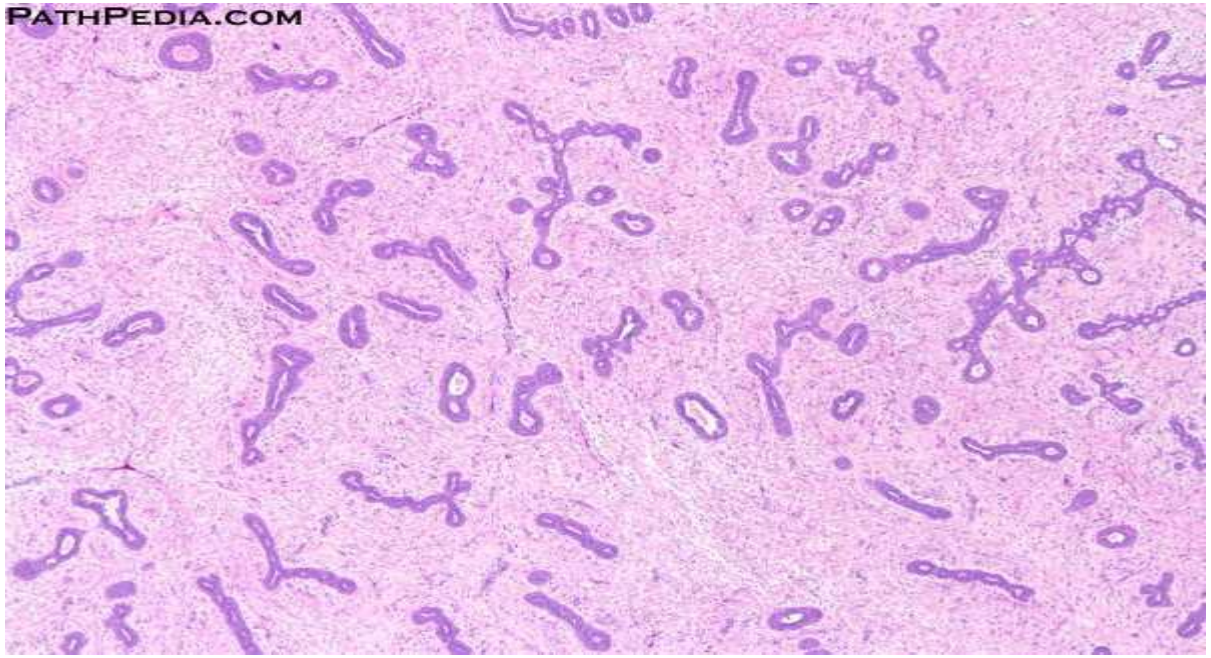
Pleomorphic adenoma/ salivary gland

- This is an example of a benign mixed tumor



Fibroadenoma/ breast

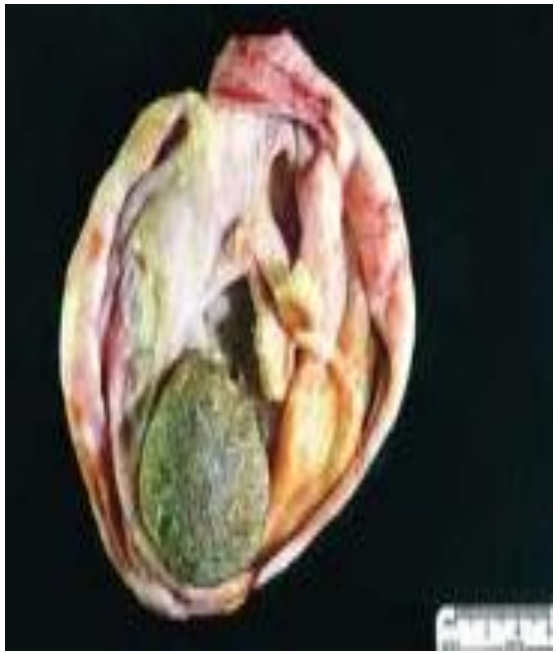
- This is another example of benign mixed tumor. Note the benign glands surrounded by the benign stroma. The stroma only is clonal



teratoma

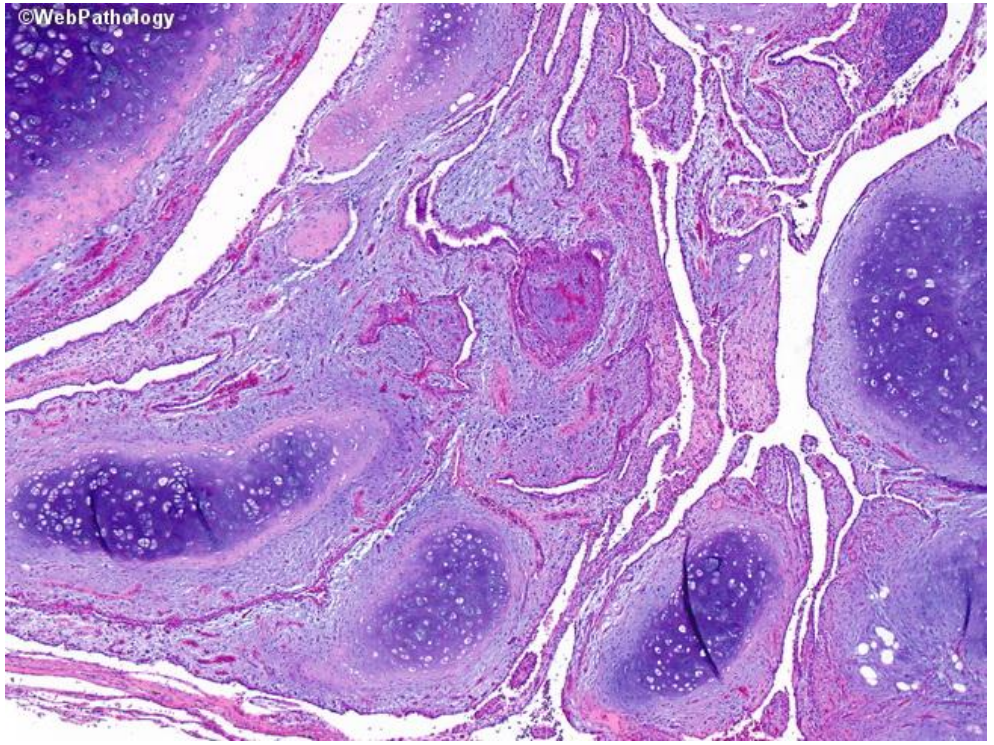
- A type of mixed tumor containing elements of more than one germ cell layer.
- They originate from totipotential germ cells (in ovary or testis or sequestered midline embryonic rests.
- If all elements in the tumor are mature= benign teratoma = mature teratoma
- If some are immature: immature teratoma = malignant teratoma

teratoma



hamartoma

- Mass of disorganized tissue indigenous to a particular site
- In this example: pulmonary hamartoma, there are tissues normally found in the lung (alveoli, cartilage..) but are not in the normal organization



NOTE

- Hamartomas were traditionally thought to be developmental malformations however, genetic studies demonstrated the presence of some acquired translocations suggesting a neoplastic nature

choristoma

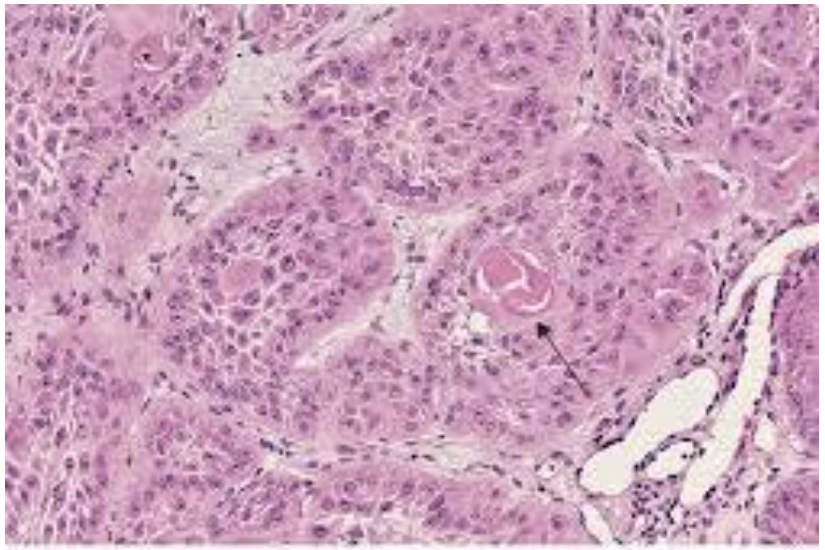
- Heterotopic rests of cells, normal in appearance but present in an abnormal location
- Example: well organized pancreatic tissue present in the stomach.
- These are congenital anomalies, not neoplasms.

- **<u>Nomenclature of malignant tumors</u>**
- -malignant tumors arising in solid mesenchymal tissue: **sarcoma** .
- -sarcomas subdivided according to cell of origin: fibrosarcma, chondrosarcoma, leiomyosarcoma..

- in mesenchymal cells of blood: leukemias and lymphoma (NOTE: lymphoma , although ends with oma is malignant)

- -- malignant tumors of epithelial cells: **carcinomas**.
- -carcinoma subdivided to adenocarcinoma (from glandular structures) and squamous cell carcinoma.. and other types
- - poorly differentiated or undifferentiated carcinoma: if tumor shows little differentiation

Squamous cell carcinoma

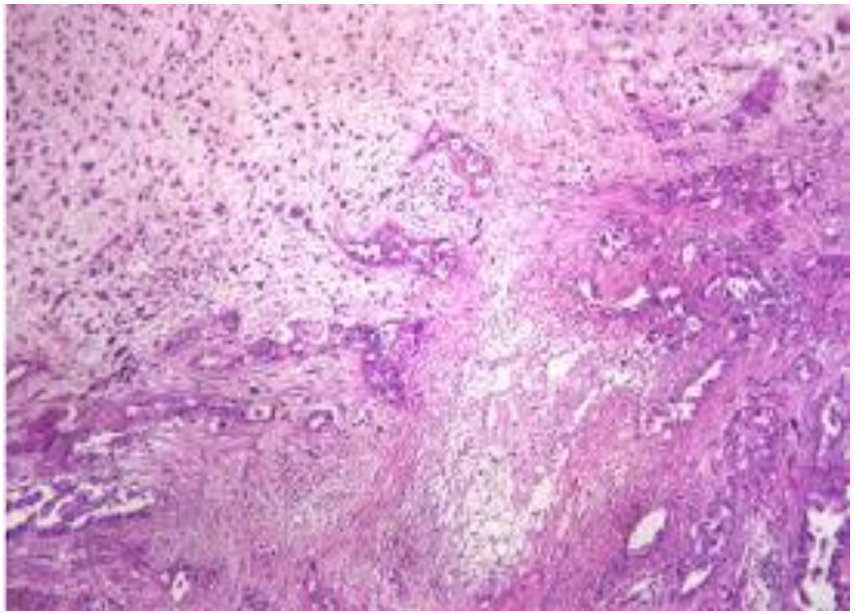


Well-differentiated squamous cell carcinoma of the skin. The tumor cells are strikingly similar to normal squamous epithelial cells, with intercellular bridges and nests of keratin pearls

- The nomenclature doesn’t depend on cell lineage, epithelium derived from the three germ lines (skin from ectoderm, GI from endoderm and renal epithelium from mesoderm) but all are carcinomas

Malignant mixed tumors

- As in benign neoplasms, some malignant tumors can have malignant epithelial and stromal elements
- Example : carcinosarcoma



The exceptions!!

- Melanoma
- Seminoma
- Lymphoma
- Mesothelioma
- Multiple myeloma

- These are malignant OMAs

- ***NOTE:***

Because benign tumors are genetically stable, their genotype change over time is limited, that's one reason why benign tumors; in general , stay as benign and do not transform to malignant neoplasms.

This means a firboadenoma of the breast for example carries minimal risk, if any, to become breast carcinoma.

Characteristics of neoplasms

- 1. differentiation and anaplasia
- 2. rate of growth
- 3. local invasion
- 4. metastasis

Differentiation and anaplasia

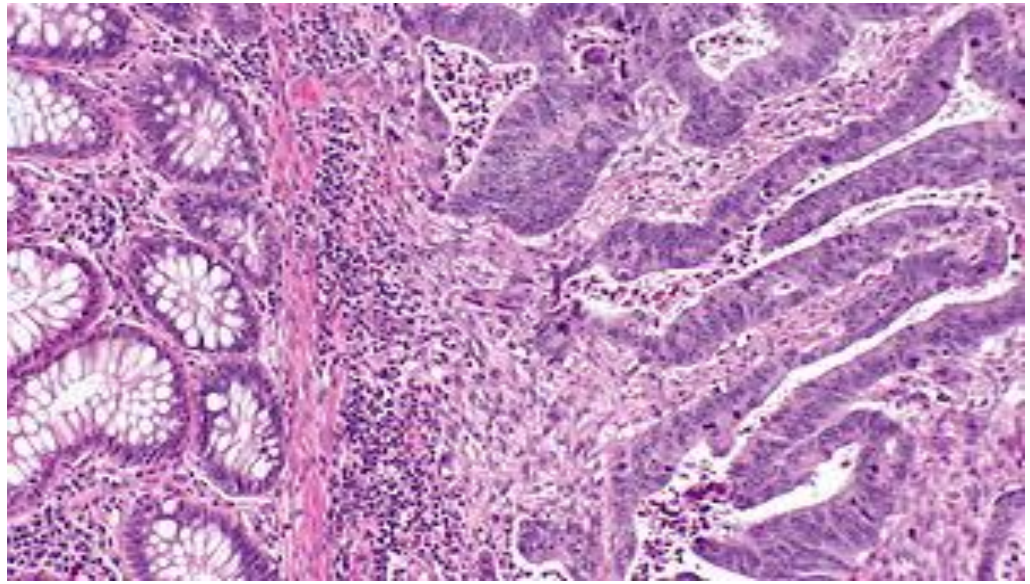
- This is a character of parenchymal , transformed cells only (not the stroma)
- Differentiation: the extent to which neoplastic cells resemble the cells they originated from, both morphologically and functionally.

Benign tumors : well differentiated

- Benign tumors resemble their parent cells
- Pituitary adenoma can look exactly like normal pituitary gland and can secrete hormones secreted from that gland

Malignant neoplasms: less differentiated

- Malignant neoplasms have a wide range of differentiation.. From well to poorly differentiated.

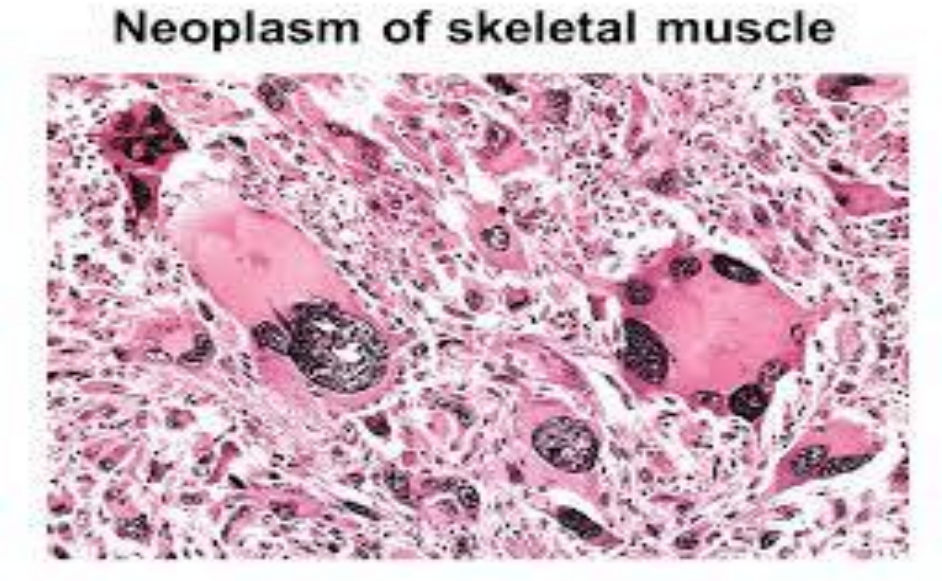


- Supportive stroma cannot help differentiating benign from malignant neoplasms.
- However, malignant tumors can produce dense abundant stroma (desmoplastic stroma) that makes the tumor solid and scirrhous.

- SO: stroma determines consistency of the tumor.. More dense stroma means solid fixed tumor.

anaplasia

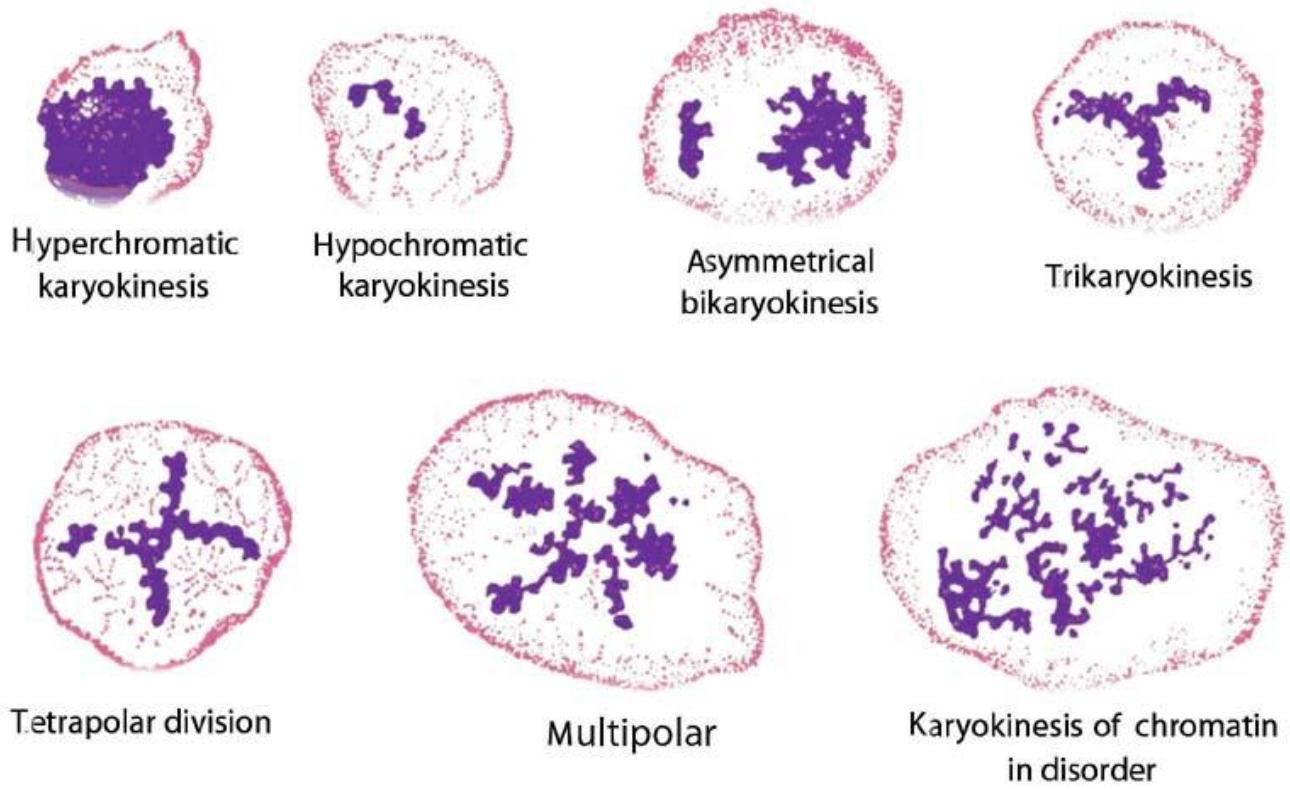
- = lack of differentiation



- Anaplasia is a hallmark of malignancy.
- Anaplasia= backward formation, implying dedifferentiation
- However: some tumors arise from stem cells that fail to differentiate, others originate from mature cells that lost differentiation!

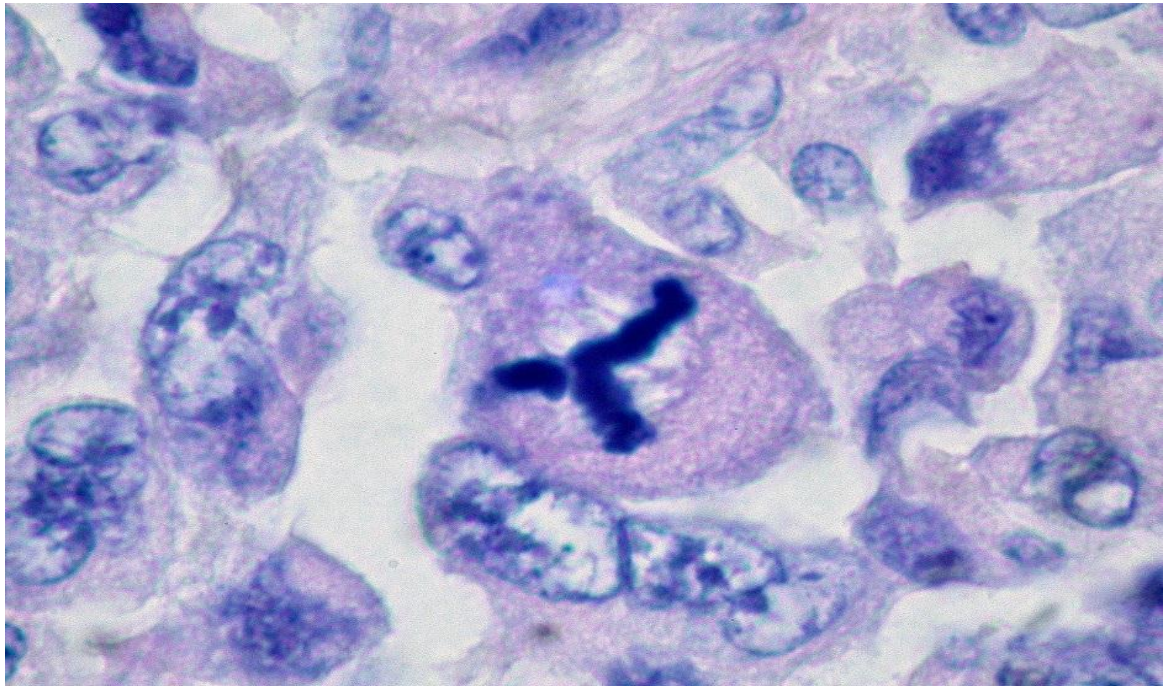
Features of anaplastic cells

- Pleomorphism: variation in size and shape
- Hyperchromatic, dark nuclei
- Bizarre abnormal nuclei with coarse chromatin
- Large nuclei with high nucleo-cytoplasmic ratio (N/C ratio). Note: normal N/C ratio is 1:4 or 1:6
- Presence of large giant cells, with multiple nuclei
- Prominent nucleoli.
- Increased mitotic activity with abnormal appearance: tripolar or quadripolar
- Cells abnormally oriented with loss of polarity

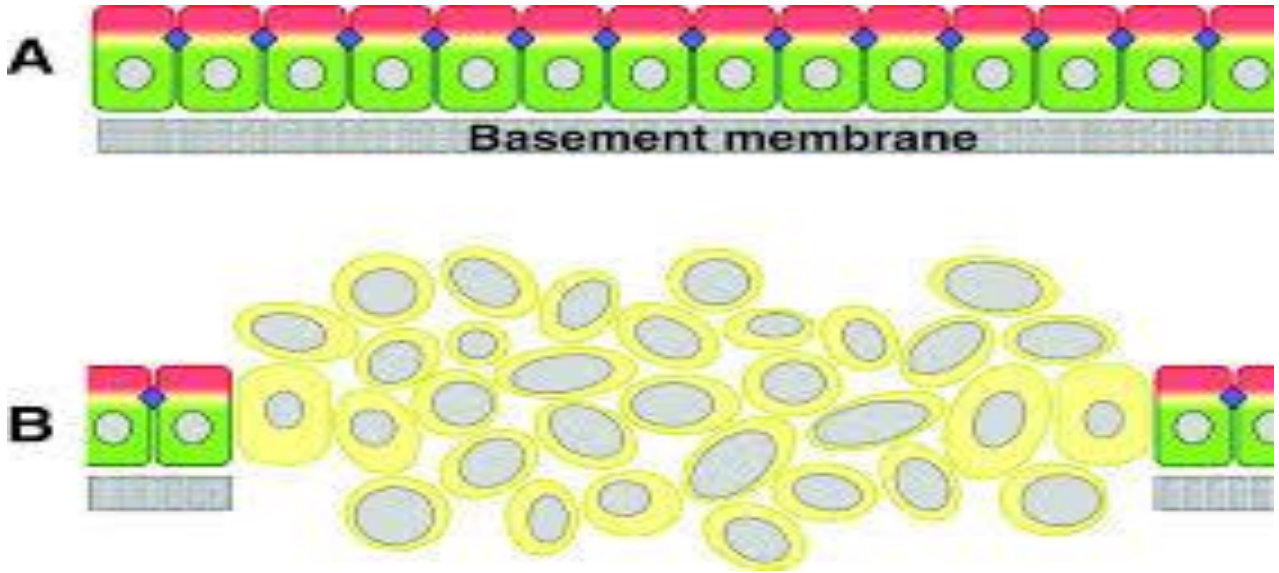


abnormal mitotic figures in malignant tumors

Tripolar mitosis



Loss of polarity= loss of normal organization



Rate of growth

- Most benign tumors: slow growing
- Most malignant: fast growing, more mitotically active

exceptions

- Leiomyoma of uterus: can grow rapidly during pregnancy due to high strong level

- What do you expect to happen to leiomyomas during menopause?

- Rate of growth of malignant tumors usually correlates irreversibly with the level of differentiation.
- Anaplastic, undifferentiated tumors grow rapidly
- Most if not all cancers take years or decades to become clinically apparent

Rate of growth of tumors

- Some grow slowly then rate of growth increases suddenly… due to a new aggressive subclone.
- Some slow and steady
- Some necrotize and leave only mets (choriocarcinma)

- Rapidly growing tumors usually have central necrosis
- This is because the blood supply of the tumor cannot meet the demands of the quickly growing mass of transformed cells

Local invasion

- Benign neoplasms: remain localized
- Encapsulated: the capsule is derived from 1. stroma of the host tissue and 2. parenchymal cell atrophy under the pressure of the expanding tumor.

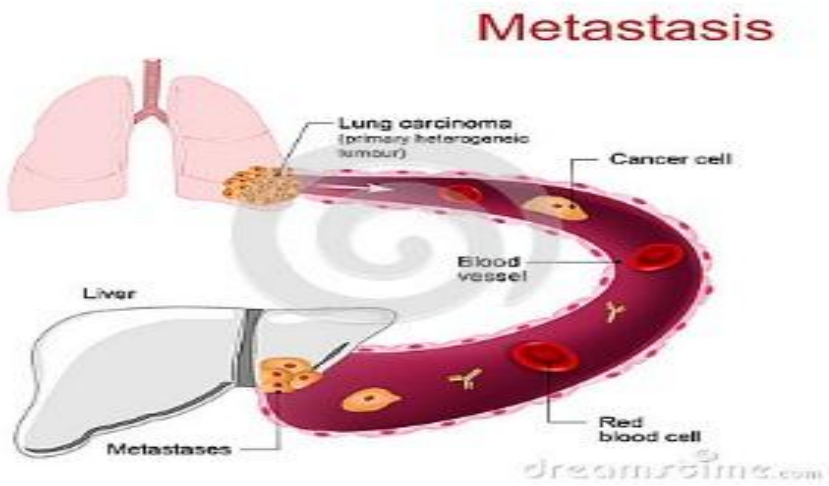
- However, not all benign tumors are encapsulated but even the un-encapsulated ones have line of cleavage in the majority of cases (e:g uterine leiomyoma)

Invasion In malignant tumors

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

Metastasis (mets)

- Metastais= 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.



mets

- Cancers differ in their ability to metastasize
- 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

The more anaplastic and the larger the tumor.. Metastasis is more likely

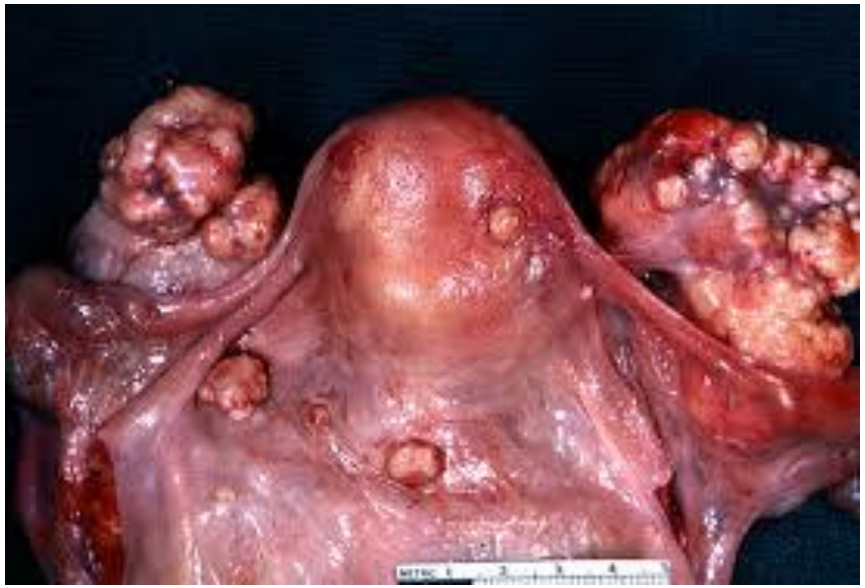
Of course there are exceptions!

Routes of metastatic spread

- 1. seeding within body cavities
- 2. lymphatic spread
- 3.hematogenous spread

Seeding through body cavities

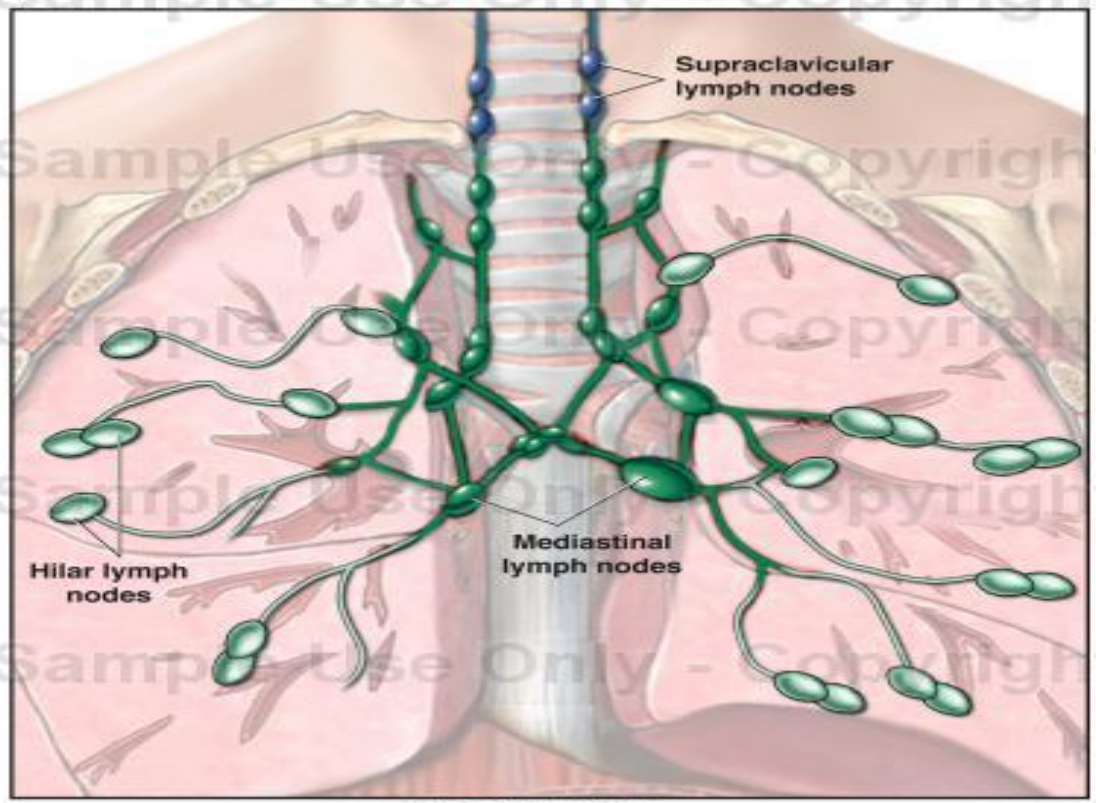
- Ovarian cancer.. Covers peritoneal cavity



Lymphatic spread

- More in carcinoma , rare in sarcoma
- Pattern of lymph nodes affected depends on the site of primary tumor
- Tumors metastasize to regional lymph nodes first, however skip metastases can occur
- Regional nodes= nodes naturally draining that area
- Skip mets: spread to distant nodes skipping the regional ones!

Lymph Nodes of the Thorax



Anterior Cut-away View

Hematogenous spread

- Sarcomas spread mainly by hematogenous route
- Carcinomas can also spread by this route

- Liver and lungs are the most common sites of spread (most common recipients)

Benign vs malignant neoplasms

	Benign	malignant
genetics	Few mutations, clonal but genetically more stable	Genetically unstable
Macroscopic/ gross appearance	Soft, mobile, encapsulated	Hard, fixed, infiltrative
differentiation	Well differentiated	Well o poor , anaplastic
Mitosis/ rate of growth	low	High, abnormal mitoses
Local invasion	localized	invasive
metastasis	no	yes