Neoplasia 2
CHARACTERISTICS OF BENIGN AND MALIGNANT NEOPLASMS

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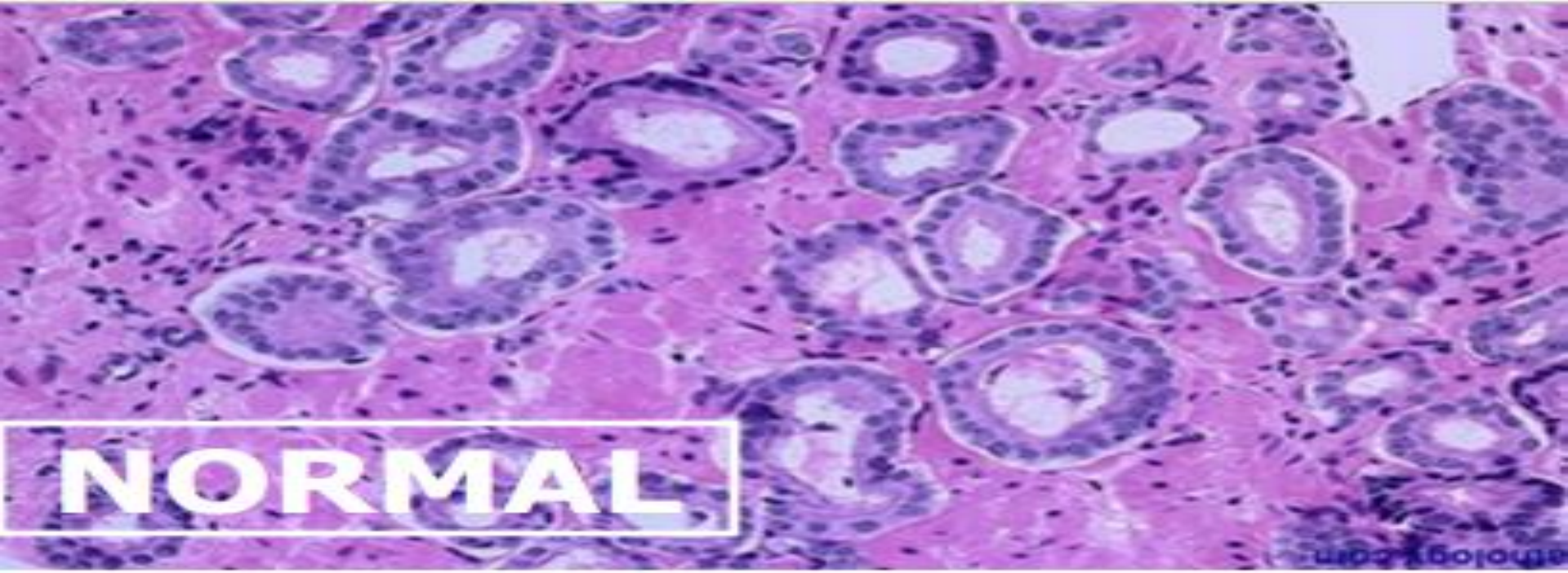
How do benign & malignant tumors differ?

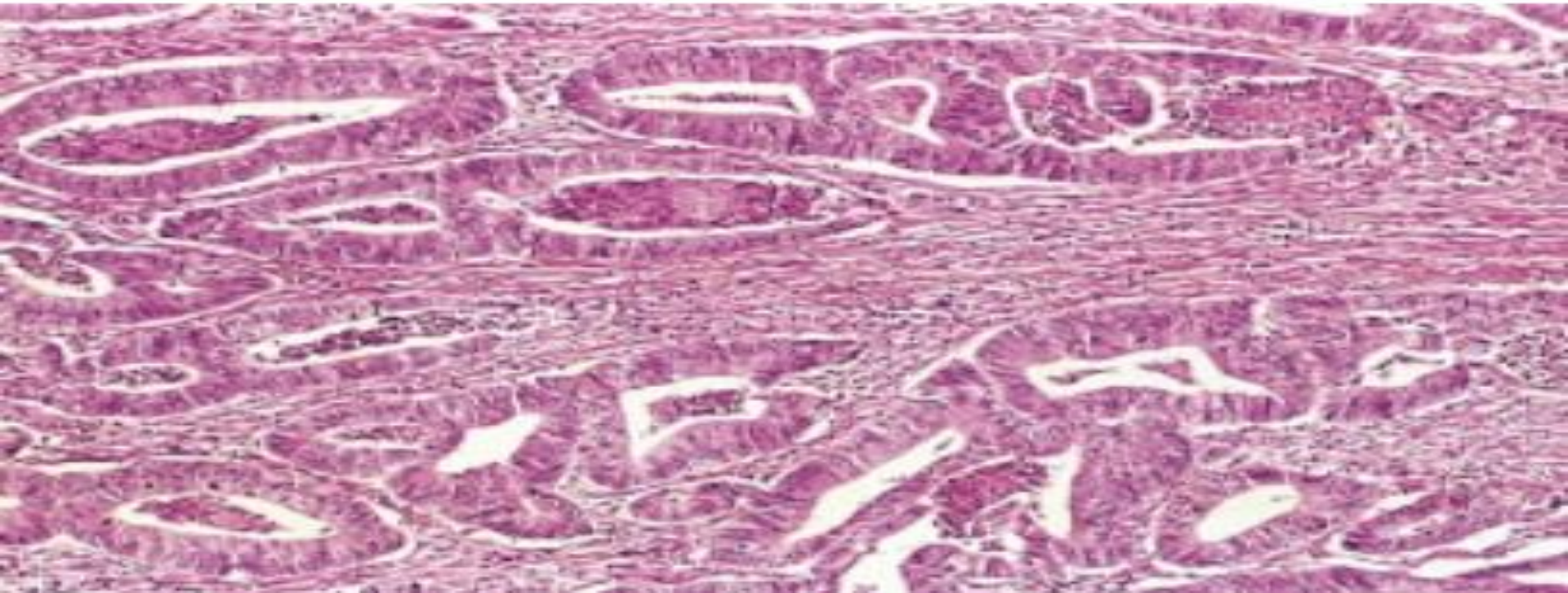
- There are fundamental features by which most benign and malignant tumors can be distinguished:

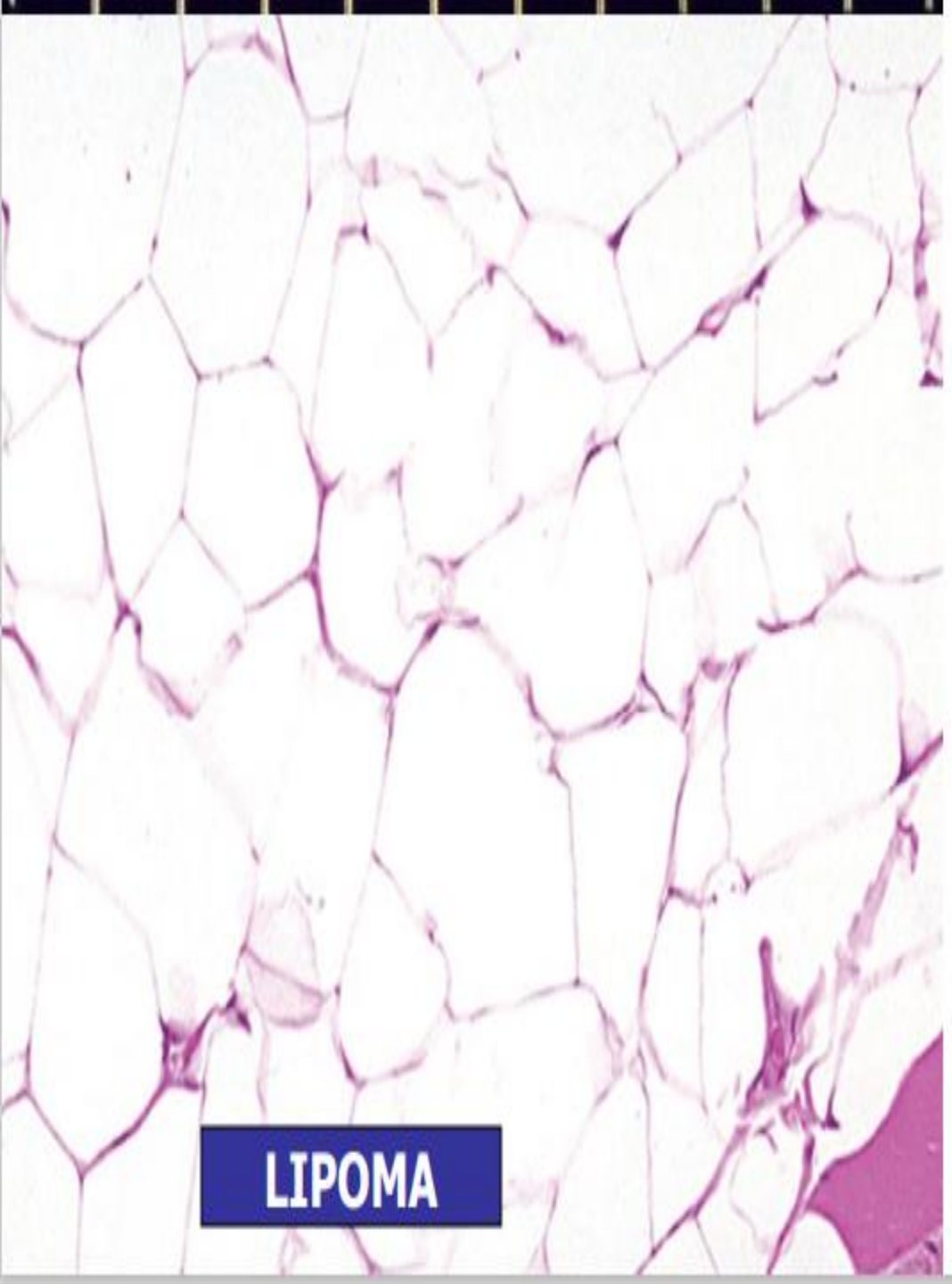
- **Differentiation & anaplasia**
- **Rate of growth**
- **Presence of capsule**
- **Local invasion**
- **Distant metastasis**

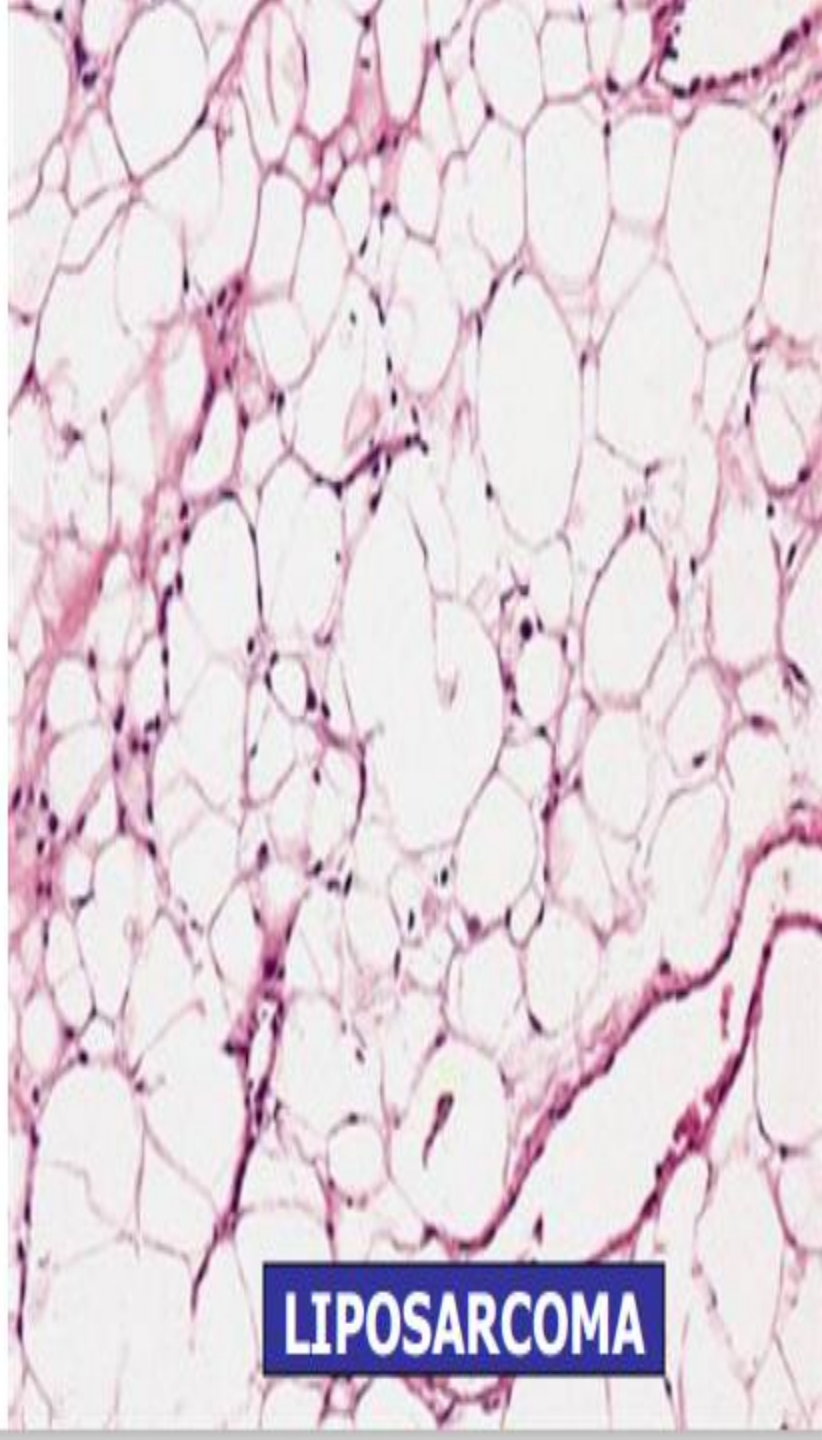
1. Differentiation and Anaplasia

- **Differentiation refers to the extent to which neoplasms resemble their parenchymal cells of origin, both morphologically and functionally.**

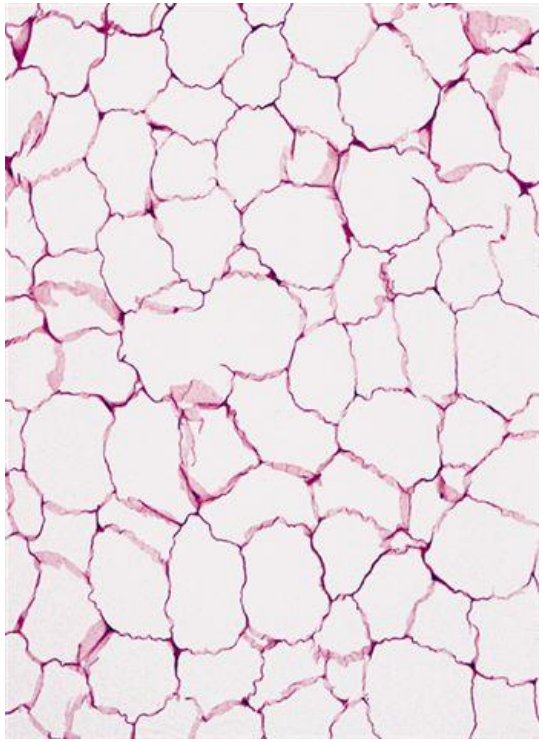

NORMAL



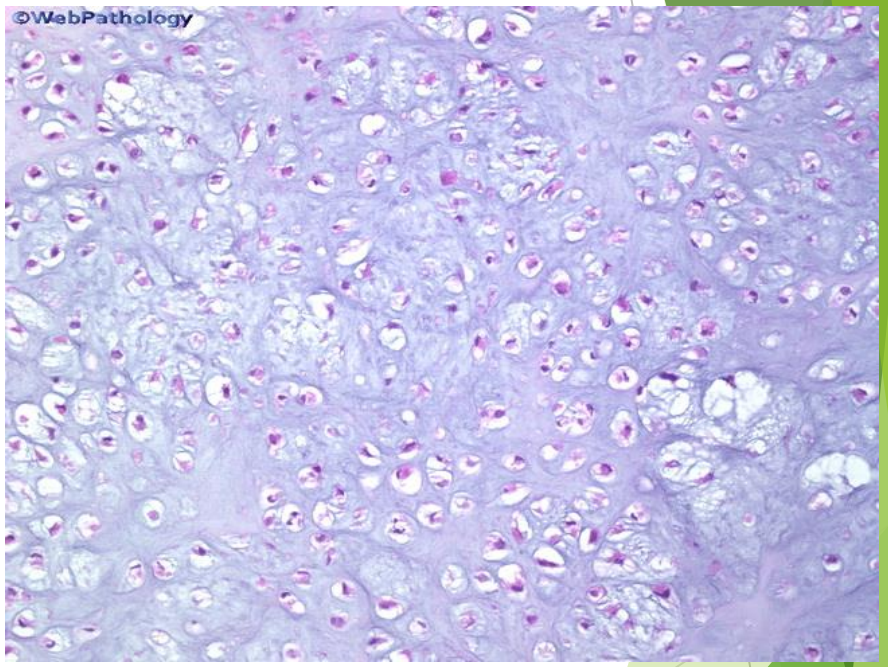

LIPOMA


LIPOSARCOMA

In benign neoplasms



lipoma



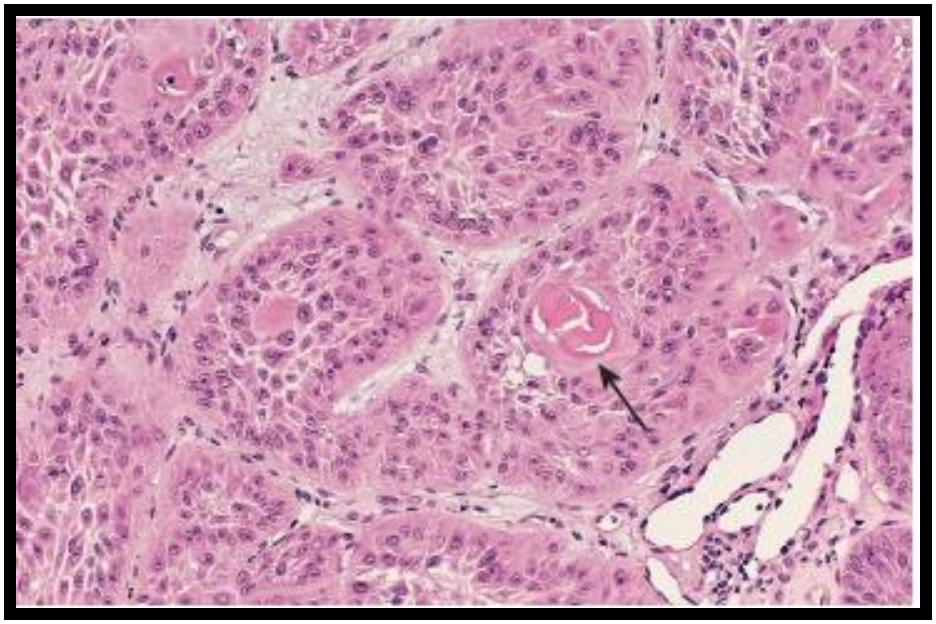
chondroma

Anaplasia

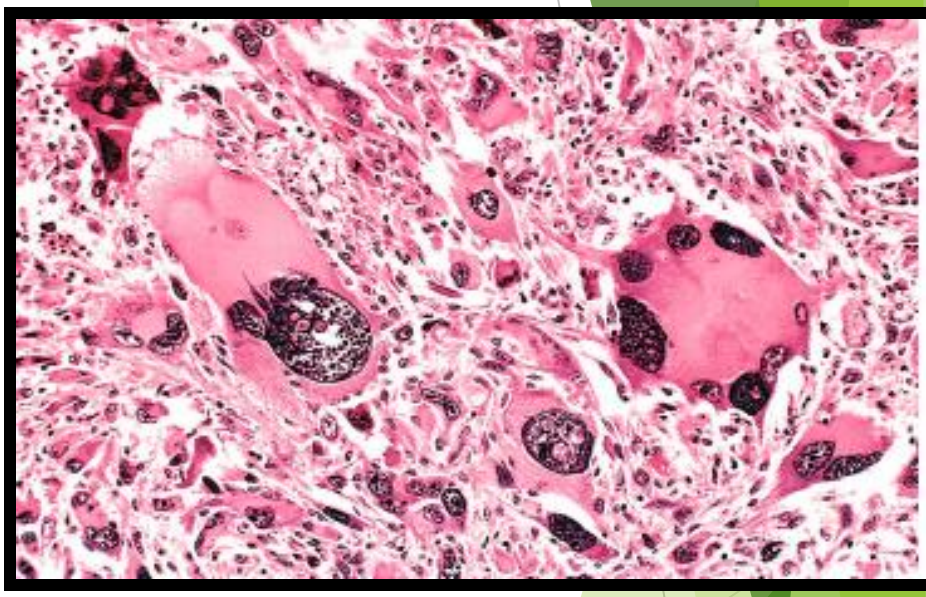
- Tumors composed of undifferentiated cells are said to be anaplastic, a feature that is a reliable indicator of malignancy.

- The term anaplasia literally means “backward formation”—implying dedifferentiation, or loss of the structural and functional differentiation of normal cells.

In malignant neoplasms

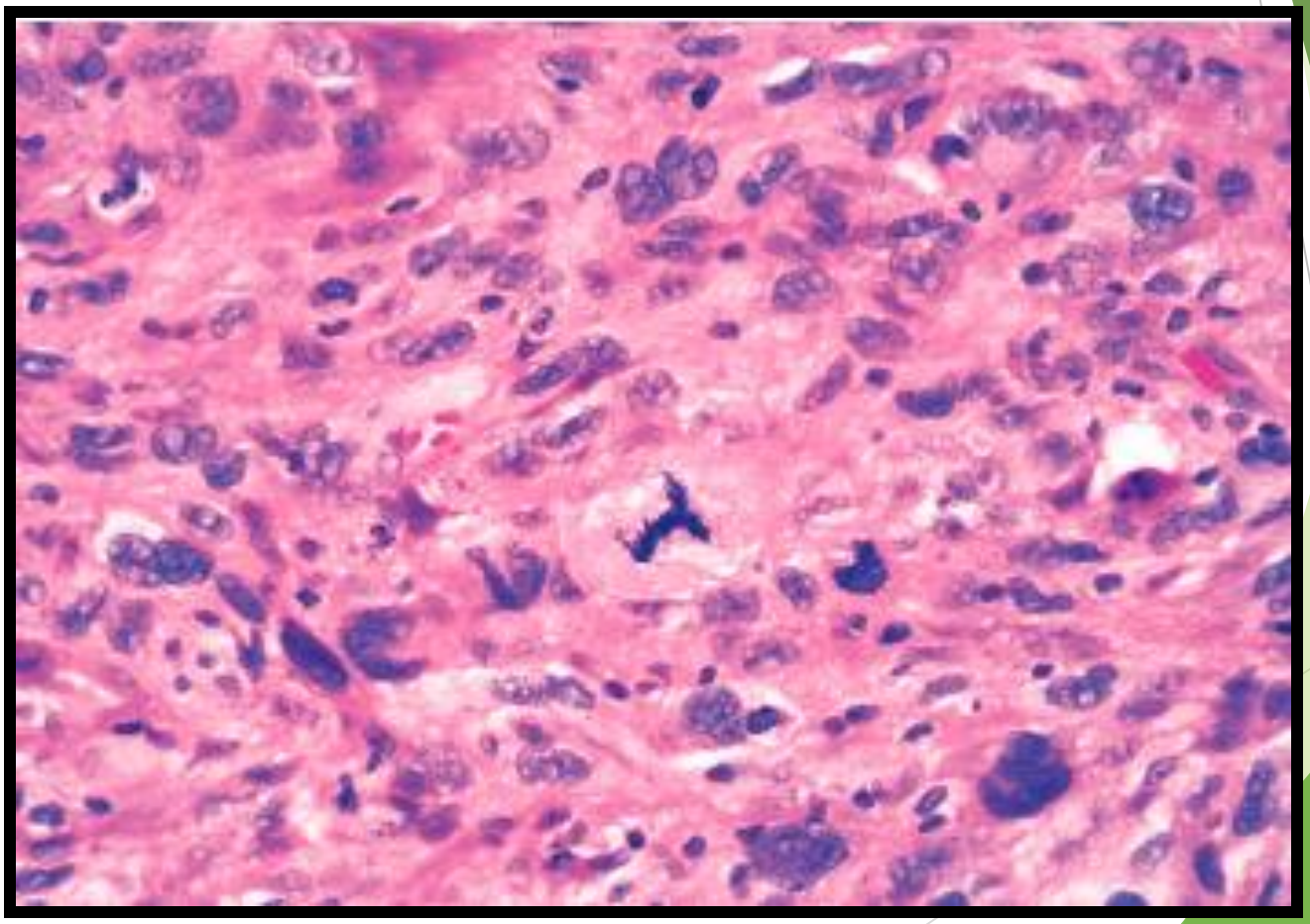


Well-differentiated squamous cell carcinoma



Pleomorphic malignant tumor

Anaplastic cells



Anaplastic cells often display the following morphologic features:

- Pleomorphism (variation in size and shape).
- Nuclear abnormalities:

a. hyperchromatism (dark-staining).

b. variation in nuclear size and shape

c. prominent single or multiple nucleoli.

d. Enlargement of nuclei (increased nuclear-to-cytoplasmic ratio).

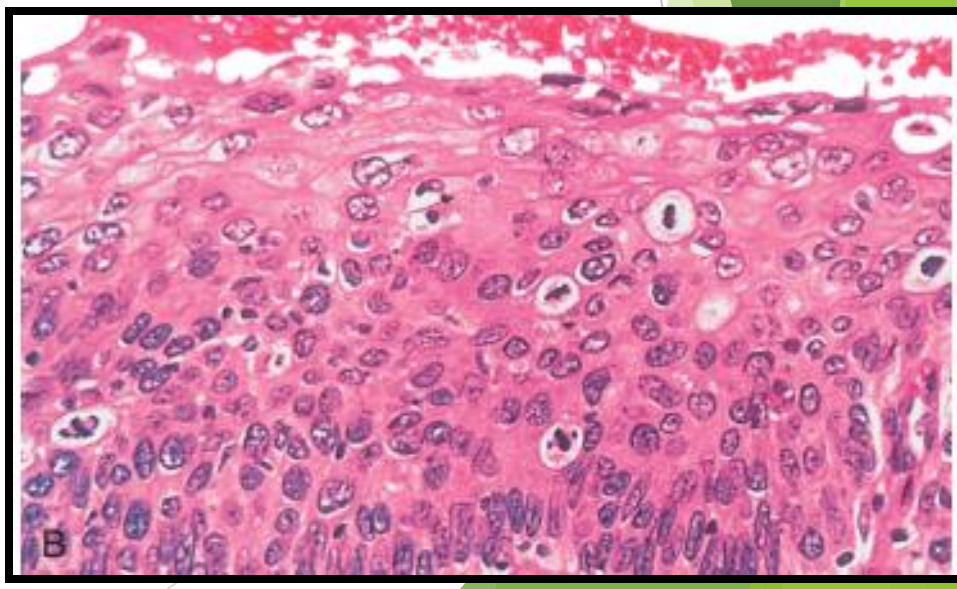
- Tumor giant cell formation.
- Atypical mitoses, which may be numerous.

Anarchic multiple spindles may produce tripolar or quadripolar mitotic figures

- Loss of polarity.

Dysplasia

- Dysplasia referring to disorderly proliferation.
- Dysplastic epithelium is recognized by a loss in the uniformity of individual cells and in their architectural orientation.



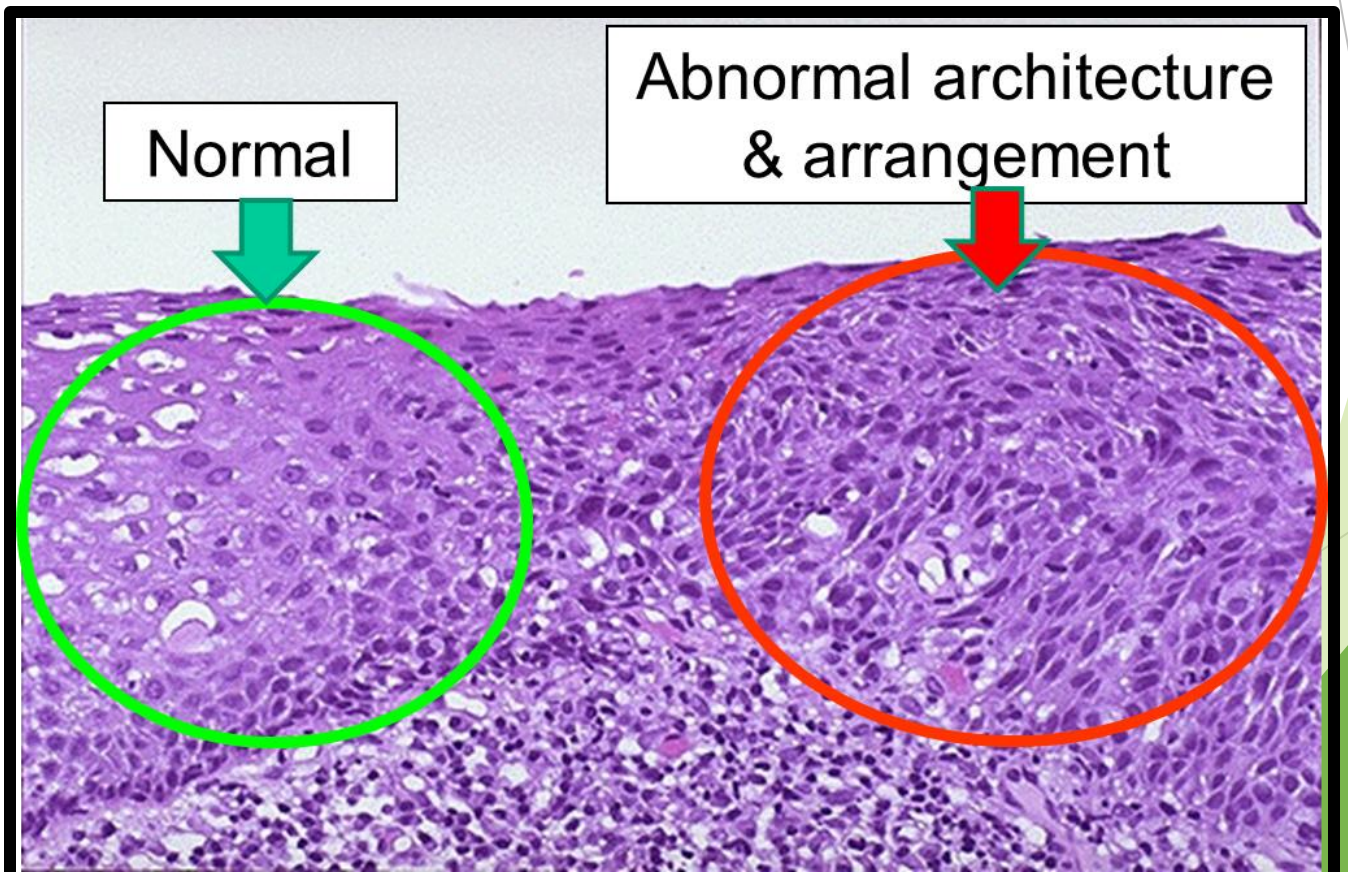
Dysplasia

- When a tumor cell loses differentiation, it gradually gains features of DYSPLASIA
- Dysplasia is a disorderly, non-neoplastic proliferation of cells with loss of architectural orientation
- Cells are either tumor stem cells or there is a process of gradual loss of differentiation of mature cells
- It may precede malignancy

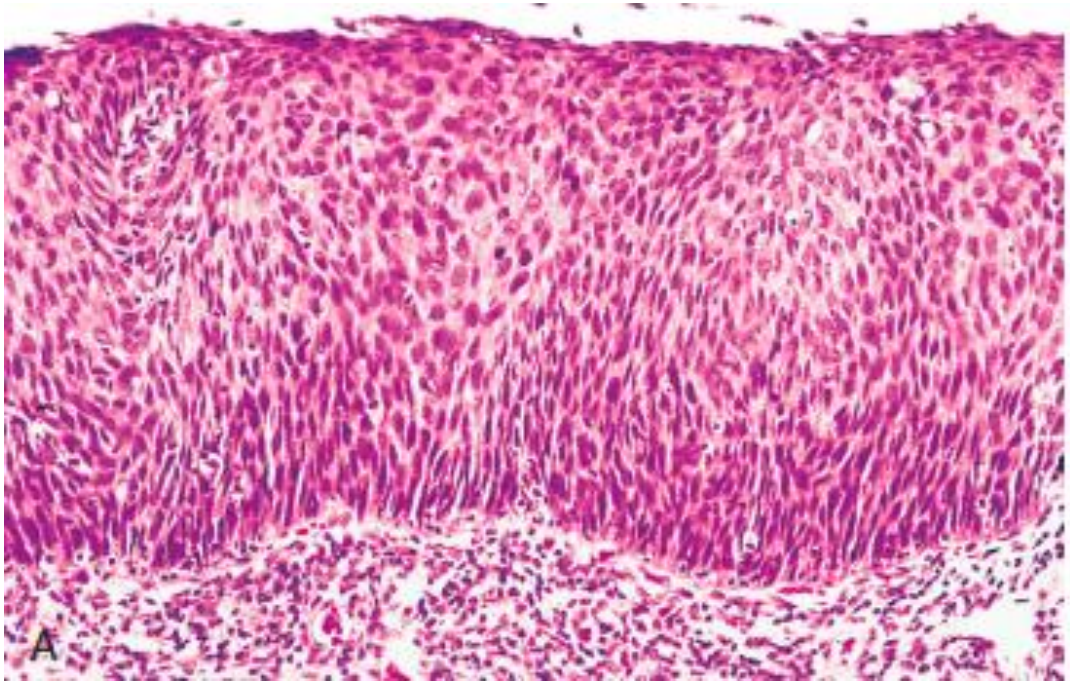
- Dysplastic cells exhibit:

- Pleomorphism.

- Hyperchromatic nuclei.



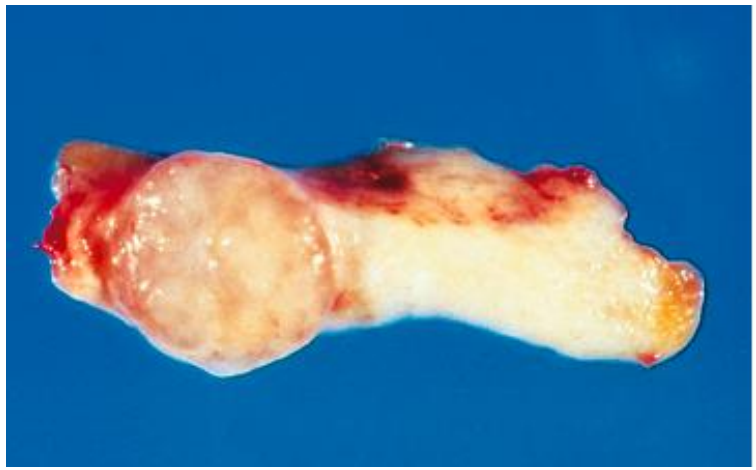
- When dysplastic changes are severe and involve the entire thickness of the epithelium, the lesion is referred to as carcinoma in situ.

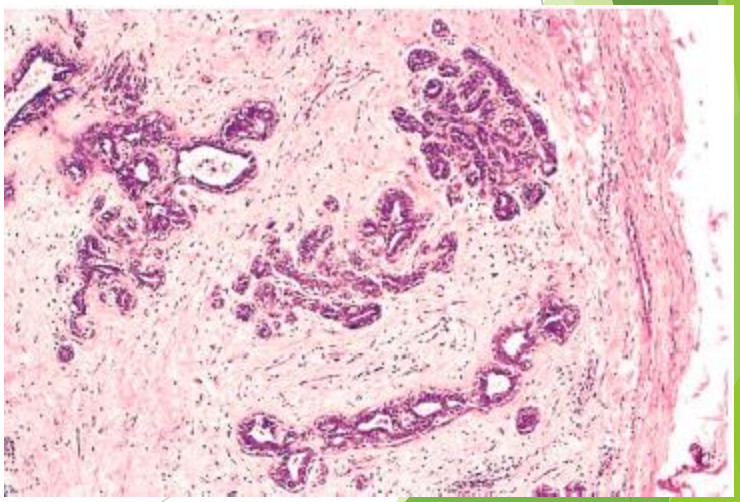


The presence of dysplasia marks a tissue as being at increased risk for developing an invasive cancer.

2. Local Invasion

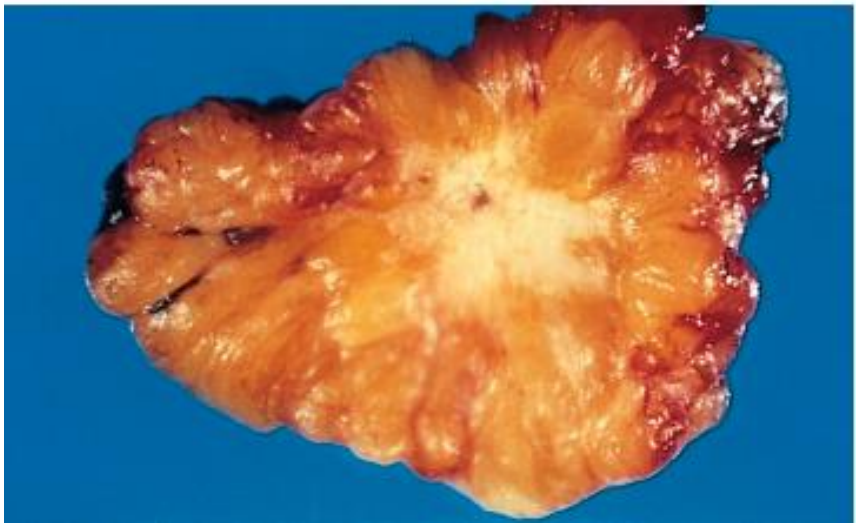
- Most benign tumors grow as cohesive expansile masses that remain localized to their sites of origin.
- encapsulation is the rule in benign tumors, but?

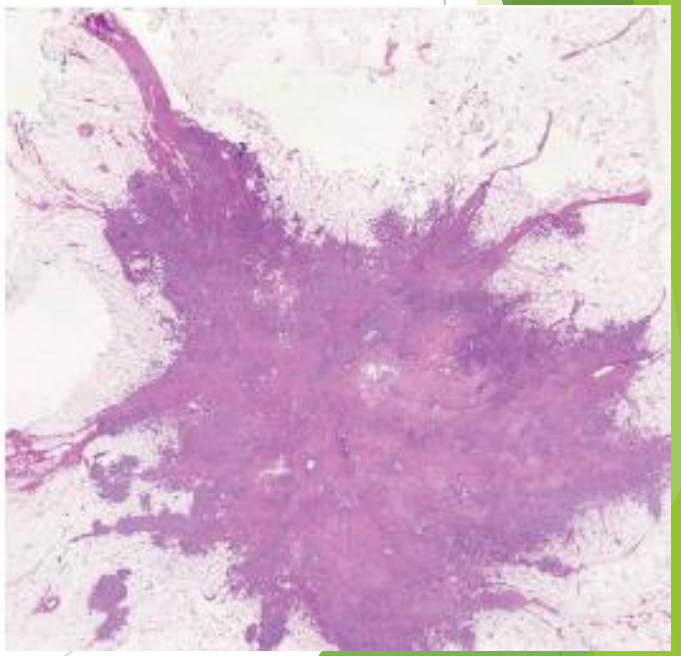




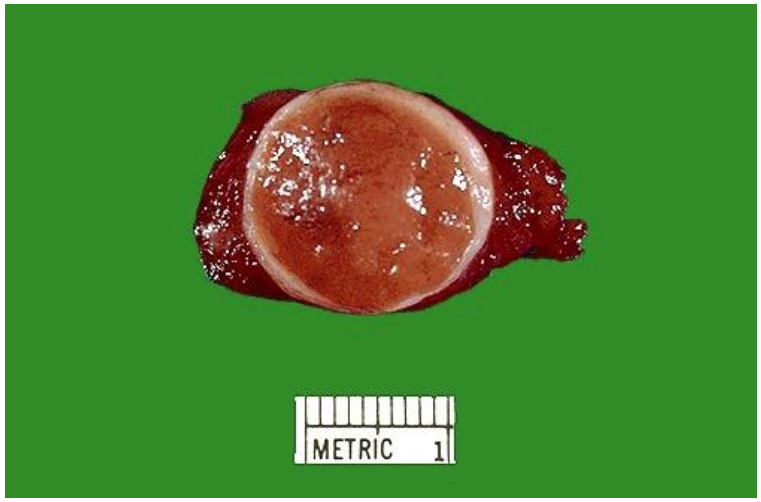
- The growth of cancers is accompanied by progressive infiltration, invasion, and destruction of surrounding tissues.

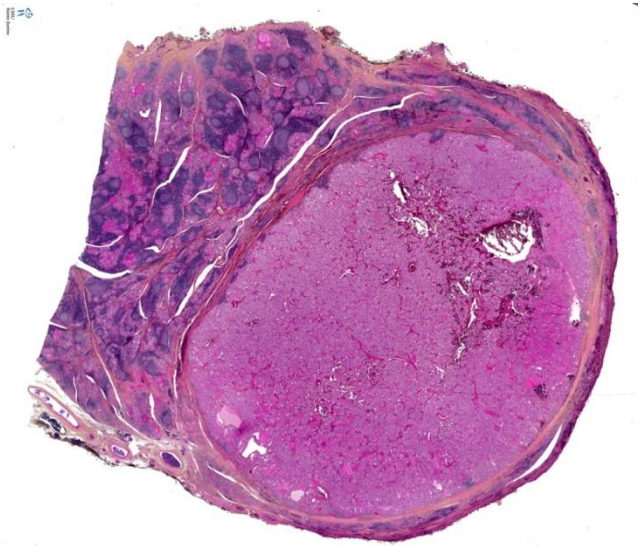
- Cancers lack well-defined capsules

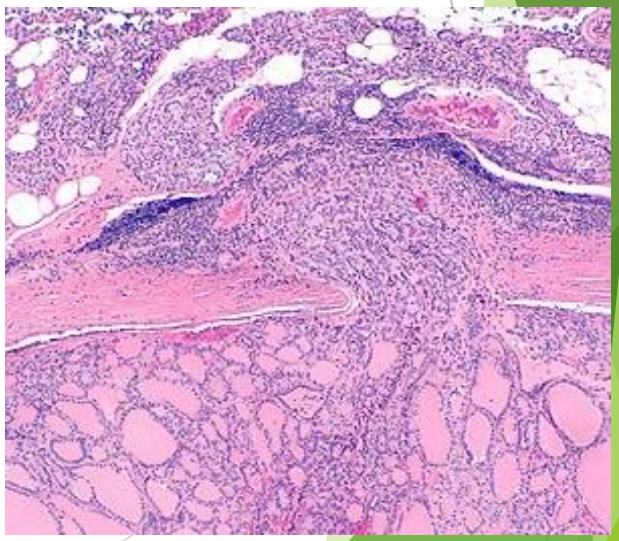




Thyroid nodule





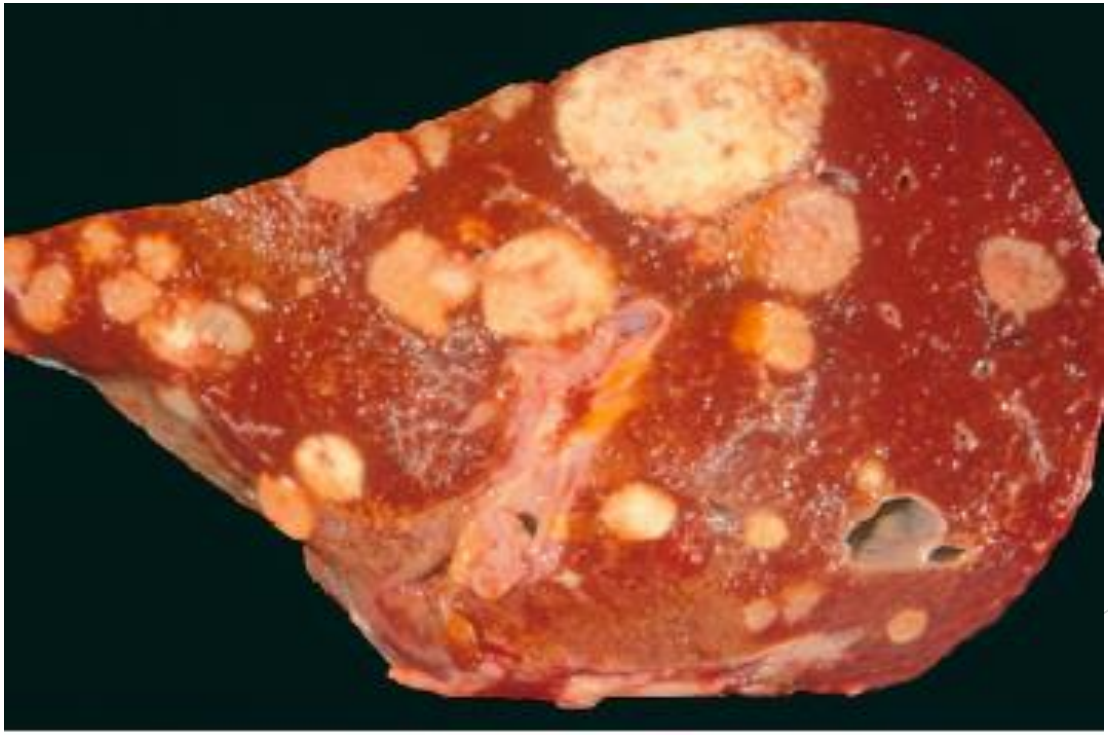


Follicular adenoma Follicular carcinoma

3. Metastasis

- Spread of a tumor to sites that are physically discontinuous with the primary tumor.
- Remember: by definition benign neoplasms do not metastasize.
- In general, the more anaplastic and the larger the primary neoplasm, the more likely is metastatic spread.

The invasiveness of cancers permits them to penetrate into blood vessels, lymphatics, and body cavities, providing opportunities for spread.

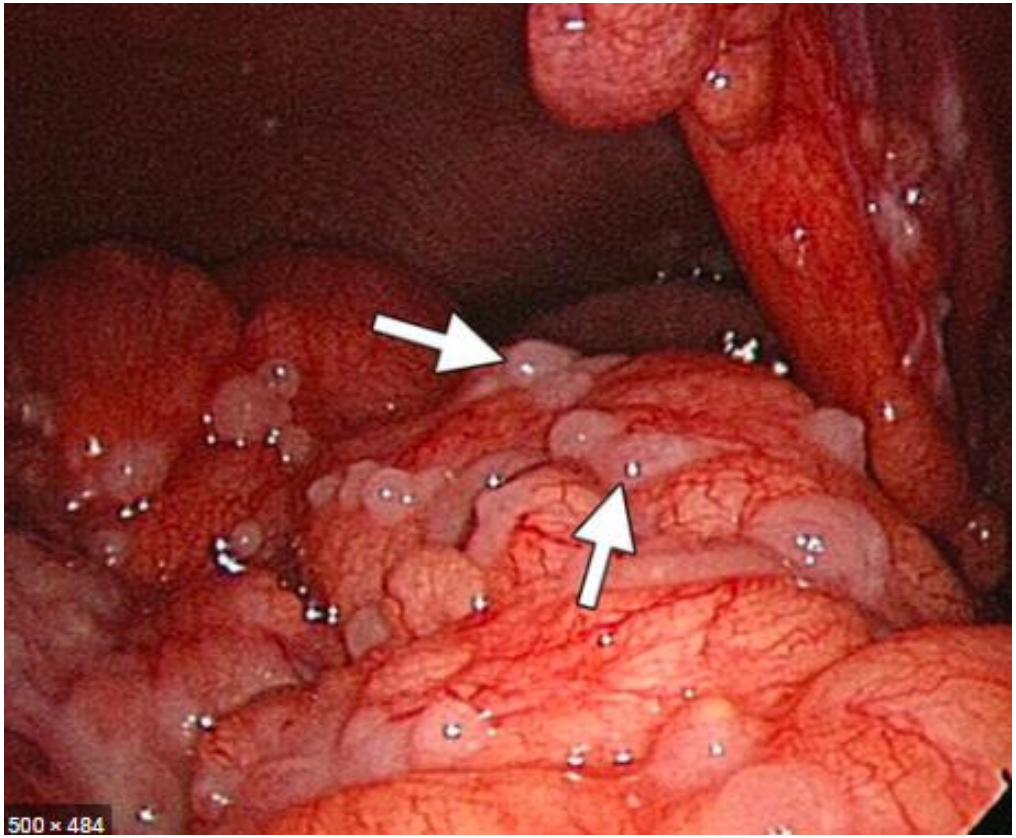


- **Malignant neoplasms disseminate by one of three pathways:**

- **(1) seeding within body cavities*.**

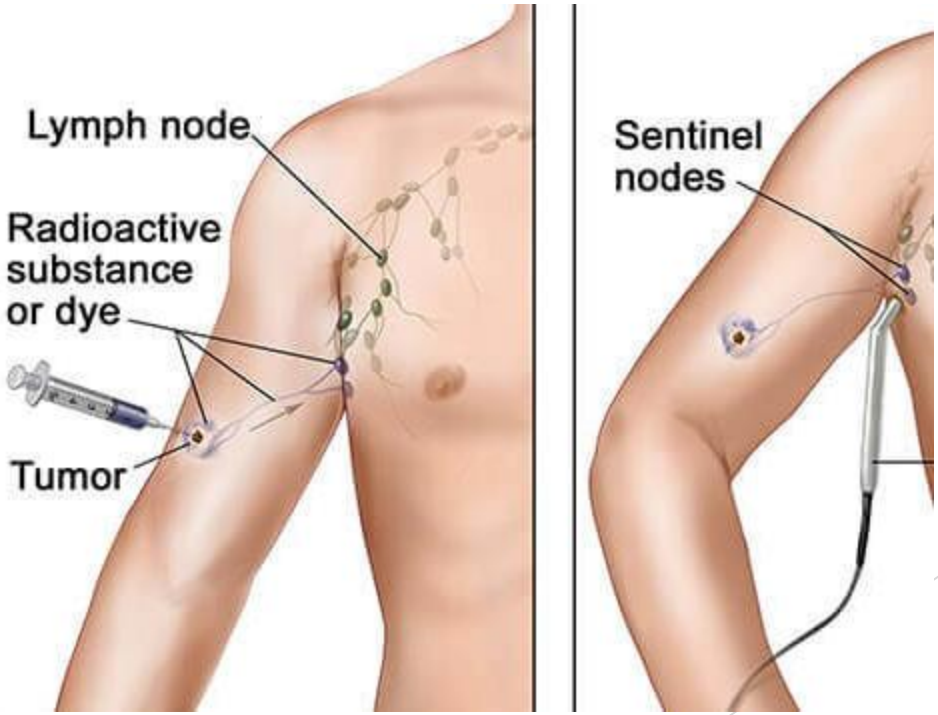
- **(2) lymphatic spread: typical of carcinomas.**

- **(3) hematogenous spread: favored by sarcomas.**

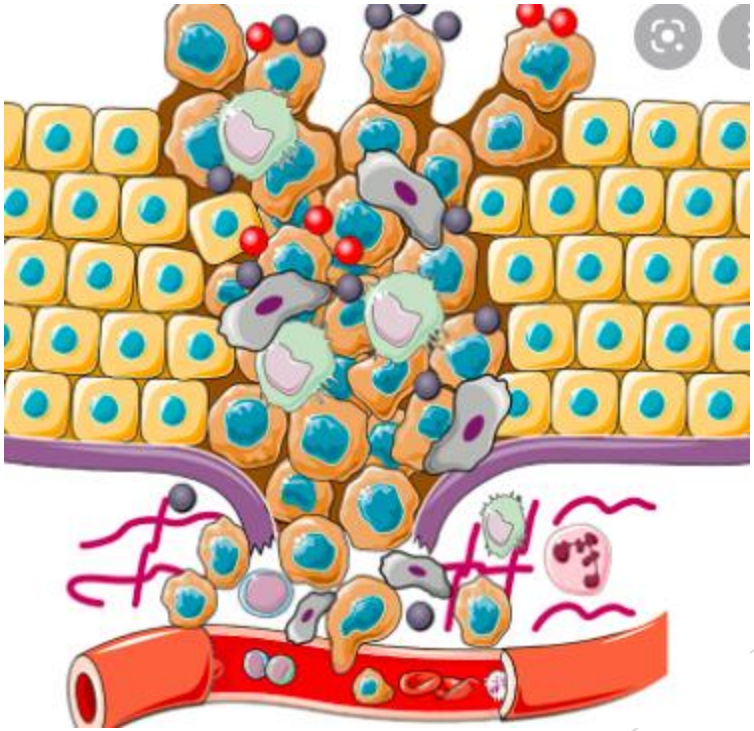


Seeding of ovarian cancer in peritoneal surface.

- A “sentinel lymph node” is the first regional lymph node that receives lymph flow from a primary tumor.



- Since all portal area drainage flows to the liver, and all caval blood flows to the lungs, the liver and lungs are the most frequently involved secondary sites in hematogenous dissemination



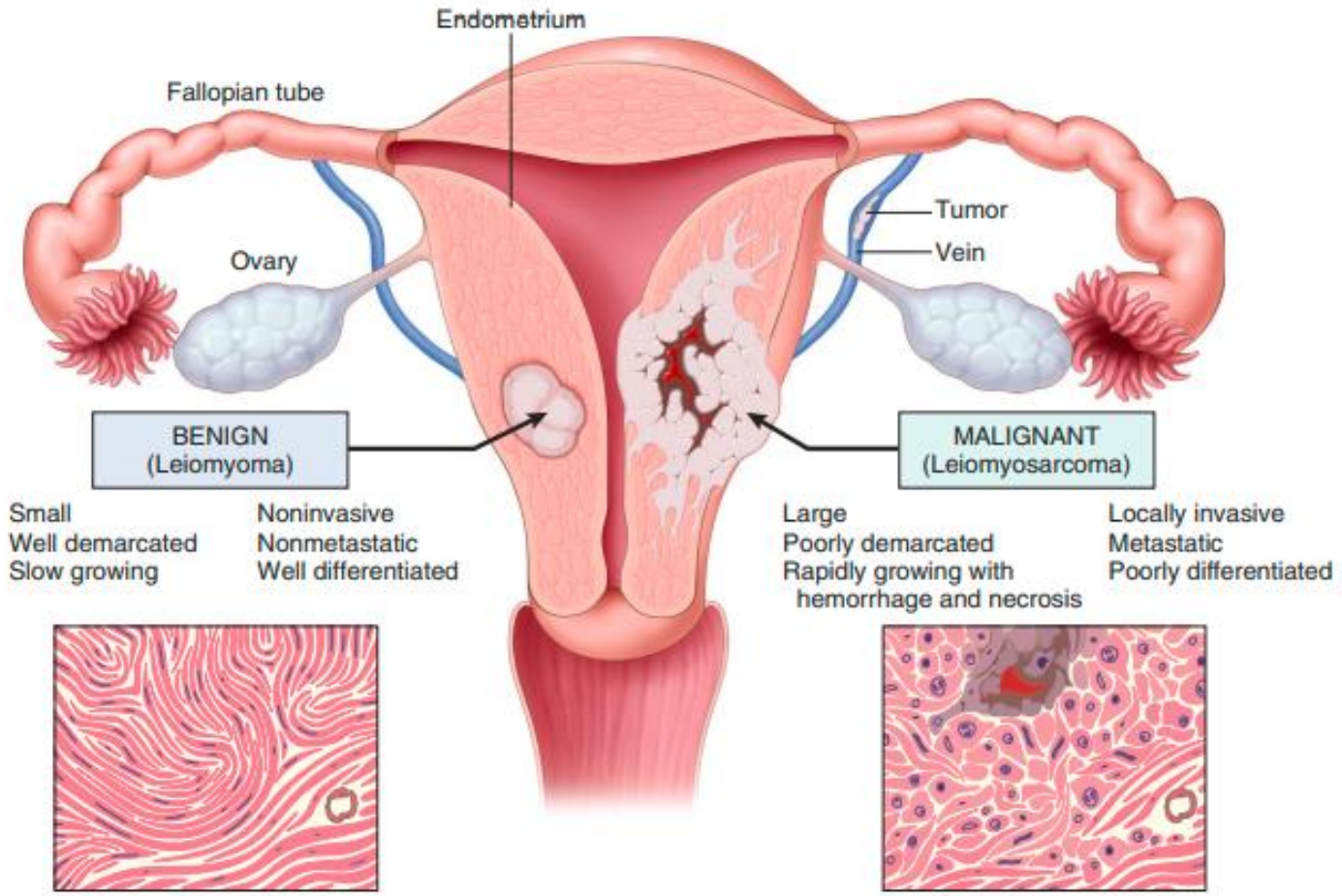


Fig. 6.12 Comparison between a benign tumor of the myometrium (leiomyoma) and a malignant tumor of similar origin (leiomyosarcoma).

EPIDEMIOLOGY

- Study of cancer occurrence in populations has contributed to knowledge about its origins, e.g:

- Cigarette smoking is associated with lung cancer.

- Colon cancer and dietary patterns

Factors that influence the predisposition to cancer

- 1. **Environmental Factors:**

- **A. Diet.**
- **B. Smoking: in cancer of lung and upper airway.**
- **C. Alcohol consumption.**
- **D. Reproductive history: with cancers of the endometrium and breast**
- **E. Infectious agents.**

- 2. **Age and Cancer:**

- **The frequency of cancer increases with age.**

- **The rising incidence with age explained by the accumulation of somatic mutations that drive the emergence of malignant neoplasms and the decline in immune competence.**

3. Acquired Predisposing Conditions:

- Acquired conditions that predispose to cancer include :
- 1. Disorders associated with chronic inflammation, e.g Inflammatory bowel disease and Colorectal carcinoma.
- 2. Immunodeficiency states predispose to virus-induced cancers.
- 3. Precursor lesions:
- are localized disturbances of epithelial differentiation that are associated with an elevated risk for developing carcinoma.

Table 6.3 Chronic Inflammatory States and Cancer

Pathologic Condition	Associated Neoplasm(s)	Etiologic Agent
Asbestosis, silicosis	Mesothelioma, lung carcinoma	Asbestos fibers, silica particles
Inflammatory bowel disease	Colorectal carcinoma	
Lichen sclerosis	Vulvar squamous cell carcinoma	
Pancreatitis	Pancreatic carcinoma	Alcoholism, germ line mutations (e.g., in the trypsinogen gene)
Chronic cholecystitis	Gallbladder cancer	Bile acids, bacteria, gallbladder stones
Reflux esophagitis, Barrett esophagus	Esophageal carcinoma	Gastric acid
Sjögren syndrome, Hashimoto thyroiditis	MALT lymphoma	
Opisthorchis, cholangitis	Cholangiocarcinoma, colon carcinoma	Liver flukes *(Opisthorchis viverrini)*
Gastritis/ulcers	Gastric adenocarcinoma, MALT lymphoma	*Helicobacter pylori*
Hepatitis	Hepatocellular carcinoma	Hepatitis B and/or C virus
Osteomyelitis	Carcinoma in draining sinuses	Bacterial infection
Chronic cervicitis	Cervical carcinoma	Human papillomavirus
Chronic cystitis	Bladder carcinoma	Schistosomiasis

Many different precursor lesions have been described:

- Squamous metaplasia and dysplasia of bronchial mucosa a risk factor for lung carcinoma
- Endometrial hyperplasia and dysplasia a risk factor for endometrial carcinoma
- Leukoplakia of the oral cavity, vulva, and penis, which may progress to squamous cell carcinoma
- Villous adenoma of the colon, associated with a high risk for progression to colorectal carcinoma

CANCER GENES

- Cancer genes can be defined as genes that are recurrently affected by genetic aberrations in cancers, presumably because they contribute directly to the malignant behavior of cancer cells.

- Causative mutations that give rise to cancer genes may be:
  - acquired by the action of environmental agents
  - inherited in the germ line

- 1. Oncogenes:
- are genes induce a transformed phenotype when expressed in cells by promoting increased cell growth.

- They are overexpressed versions of normal cellular genes, which are called proto-oncogenes.

- Most oncogenes encode :
- pro-growth signaling pathways.
- factors that enhance cell survival.

- 2. Tumor suppressor genes :

- are genes that normally prevent uncontrolled growth and, when mutated or lost from a cell, allow the transformed phenotype to develop.

- 3. Genes that regulate apoptosis :

- primarily act by enhancing cell survival, rather than stimulating proliferation per se.
- Normally these genes protect against apoptosis are often overexpressed in cancer cells.

- 4. genes that regulate interactions between tumor cells and host cells:
- these genes are recurrently mutated or functionally altered in certain cancers.
- Particularly important are genes that inhibit recognition of tumors cells by the host immune system.

Table 6.4 Inherited Predisposition to Cancer

Inherited Predisposition	Gene(s)
Autosomal Dominant Cancer Syndromes	
Retinoblastoma	*RB*
Li-Fraumeni syndrome (various tumors)	*TP53*
Melanoma	*CDKN2A*
Familial adenomatous polyposis/colon cancer	*APC*
Neurofibromatosis 1 and 2	*NF1*, *NF2*
Breast and ovarian tumors	*BRCA1*, *BRCA2*
Multiple endocrine neoplasia 1 and 2	*MEN1*, *RET*
Hereditary nonpolyposis colon cancer	*MSH2*, *MLH1*, *MSH6*
Nevoid basal cell carcinoma syndrome	*PTCH1*
Autosomal Recessive Syndromes of Defective DNA Repair	
Xeroderma pigmentosum	Diverse genes involved in nucleotide excision repair
Ataxia-telangiectasia	*ATM*
Bloom syndrome	*BLM*
Fanconi anemia	Diverse genes involved in repair of DNA cross-links

The End

Q??