Nomenclature, Characteristic and Epidemiology of Tumour

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Learning outcome

- Define **neoplasia**
- **Classify** tumours based on its' nomenclature
- Describe **tumour behaviour and differences** benign & malignant
- Describe different **modes of tumour spread**
- Describe the **epidemiology** of tumours

Lecture outline

- Definition of **neoplasia**
- **Nomenclature** of benign and malignant
- **Differentiation** between benign and malignant
- Modes of tumour spreading
- **Epidemiology** of neoplasm

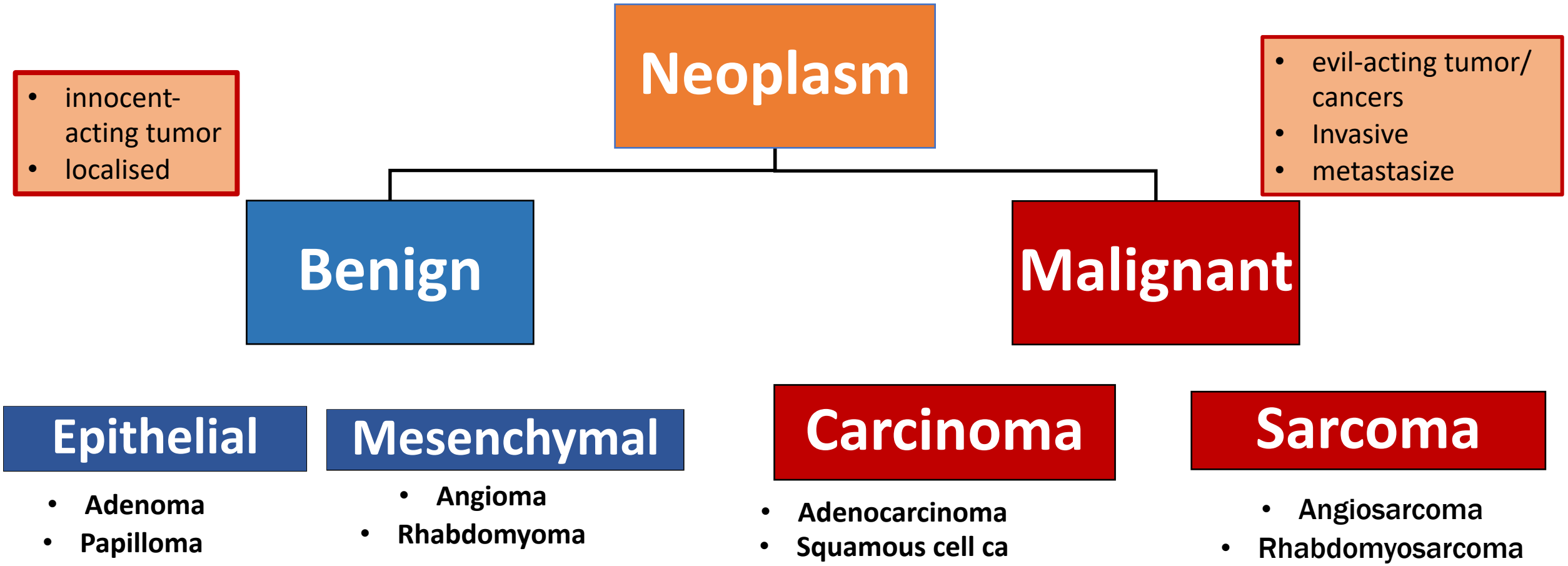
Definition

- **Neoplasia** = new growth
- **Neoplasm** = an abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner after cessation of the stimuli which evoked the change.
- **Tumour** = Neoplasm (interchangeably)

Nomenclature

Tumour are naming according to the **types of tissue they arise from** (cell of origin e.g epithelial, mesenchymal, haematolymphoid

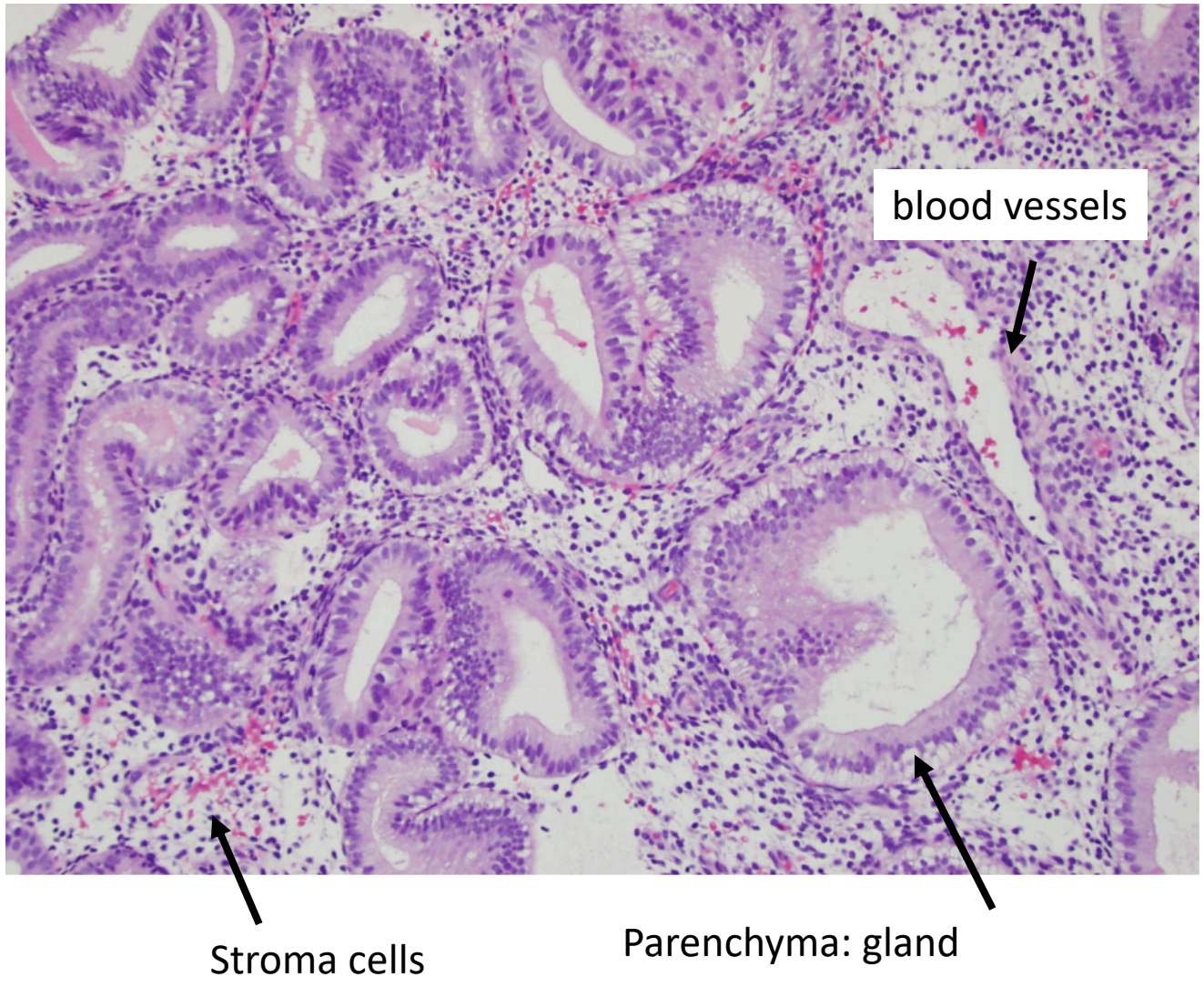
Nomenclature



Nomenclature

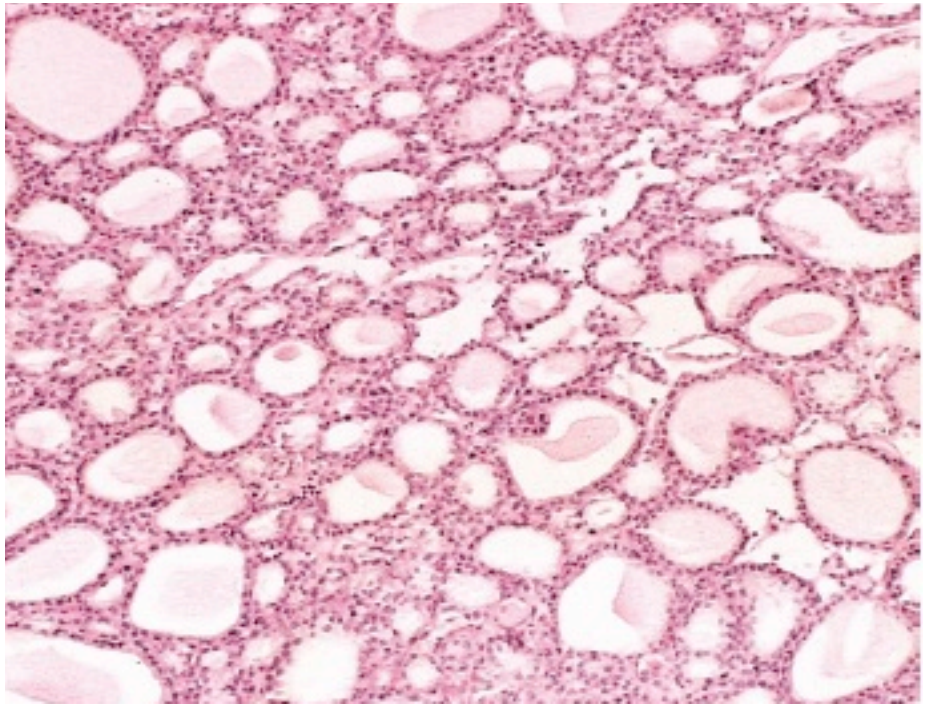
All neoplasm are composed of 2 components:

- **Parenchyma**-a functioning tissue of an organ e.g glands
- **Stroma**-made up of connective tissue, blood vessels, cells of the adaptive and innate immune system.
  - *It provides the structural framework and stromal blood supply which essential for the growing cells*



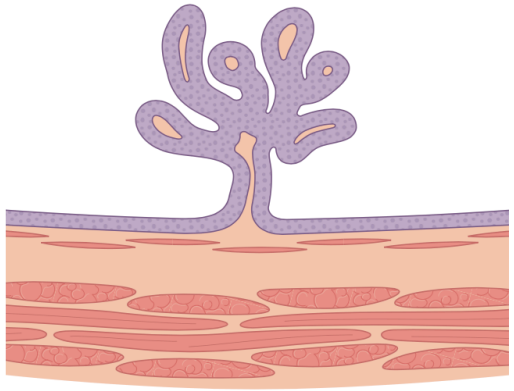
Nomenclature: Benign

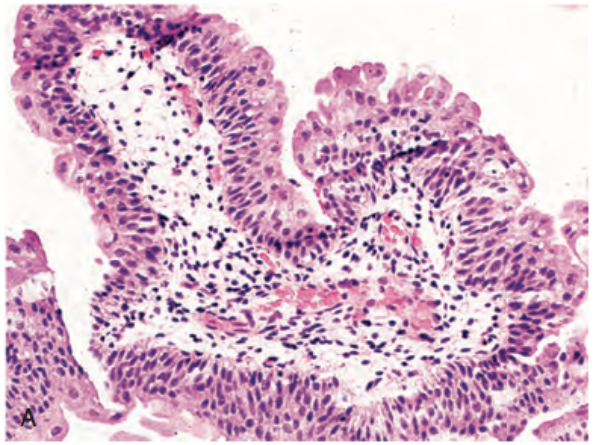
- Designated by the suffix "**oma**" to the cell of origin
- **Benign epithelial tumours**
  - **Cell of origin-**eg: tumour arise from glands- Adenoma
  - **Microscopic** appearance -eg: epithelial neoplasms on the surface with finger-like processes- Papillomas
  - **Macroscopic** architecture (gross):mass projecting from body surface, external (skin) or internal (mucosal)- Polyp



Cell of origin-e.g follicular adenoma of the thyroid

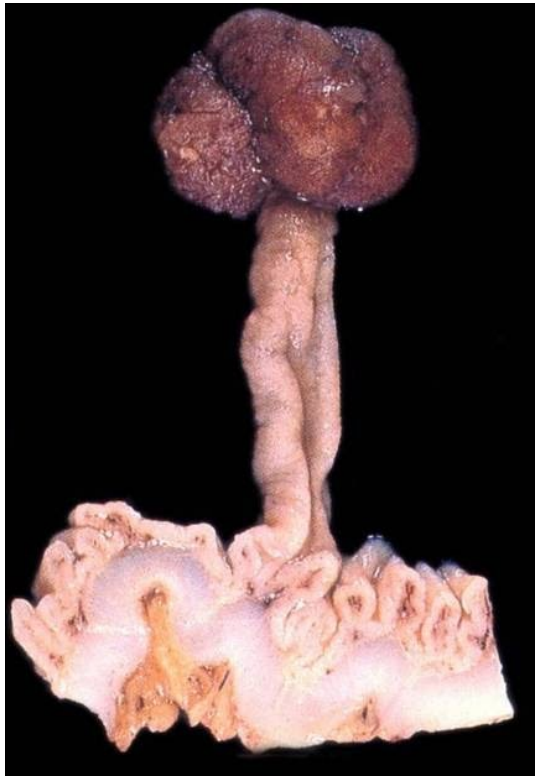
Microscopic appearance

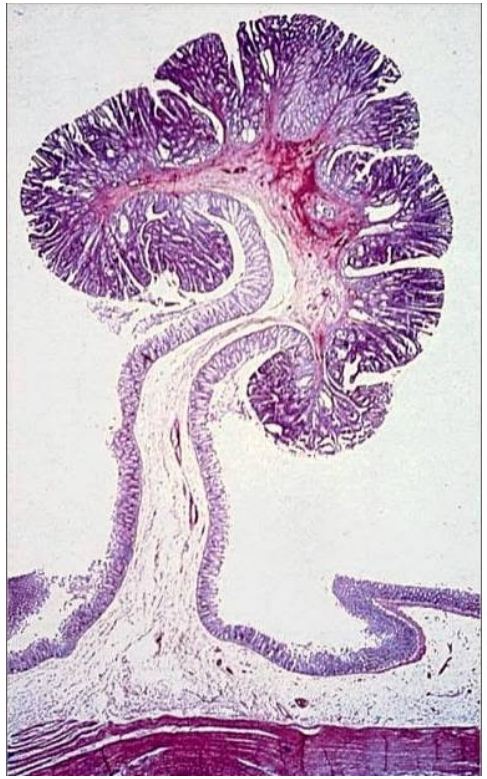




Papilloma consisting of small papillary fronds lined by normal-appearing urothelium

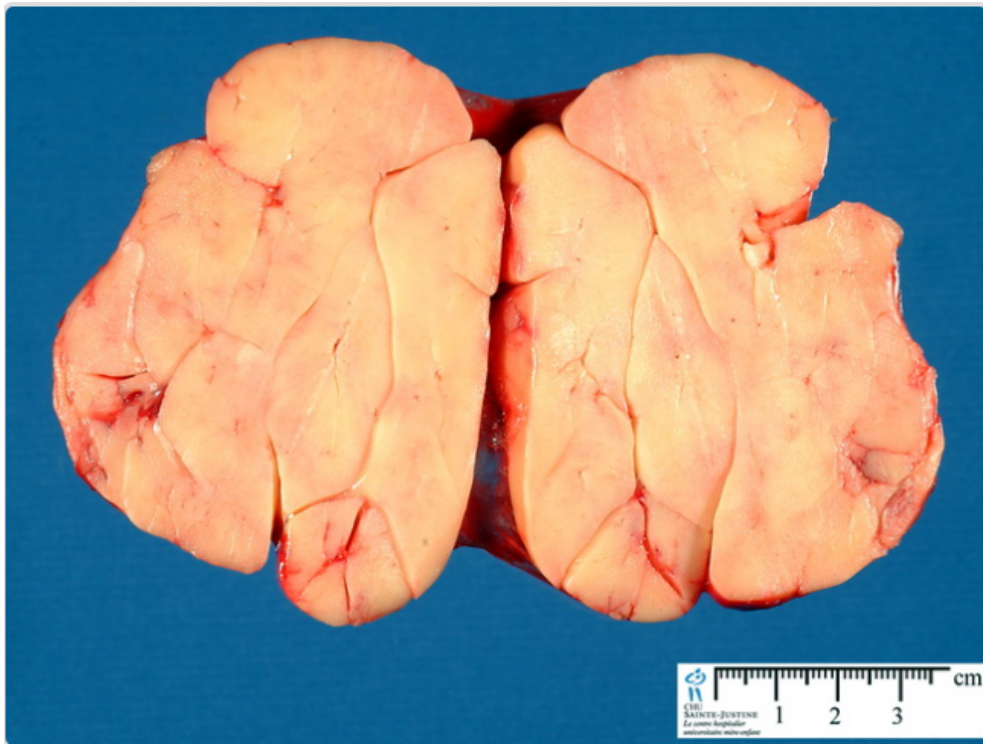
Macroscopic architecture (gross):

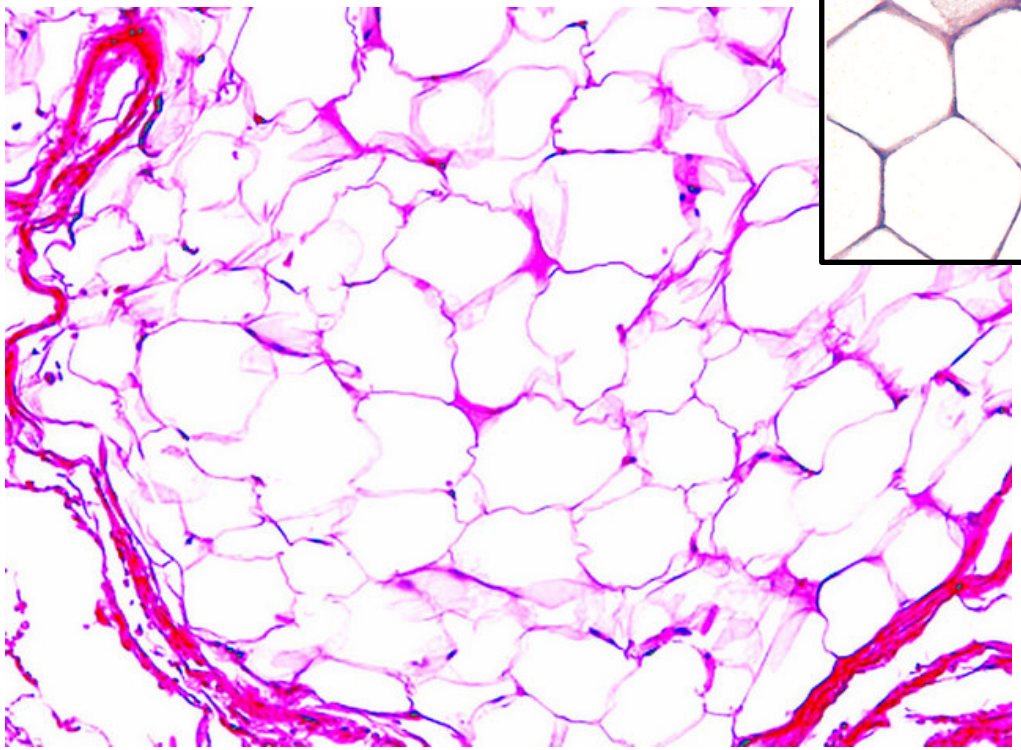


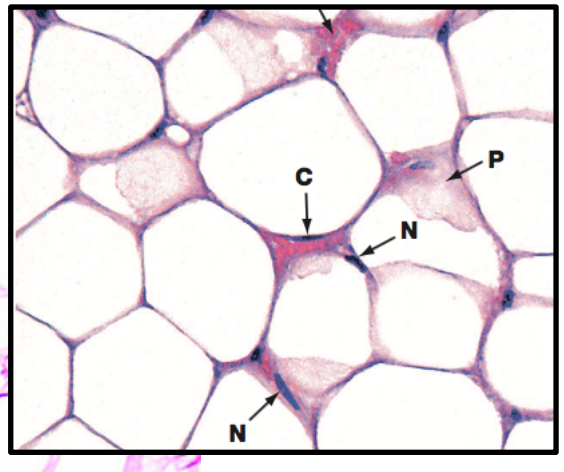


Colonic polyp

- Benign **mesenchymal tumour-**the suffix-oma is added to the name of the cell type from which area the tumour arises.
  - **Fibroma**- derived from fibroblast
  - **Chondroma**- derived from cartilage
  - **Lipoma**- derived from adipocytes







Lipoma - resemble normal adipocytes

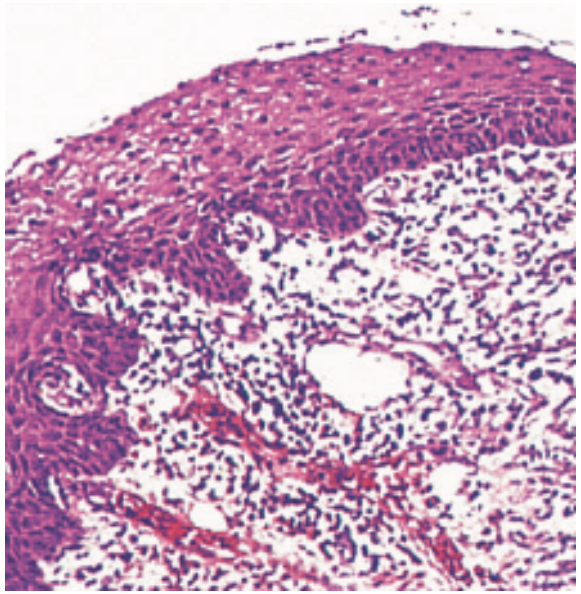
Nomenclature: Malignant

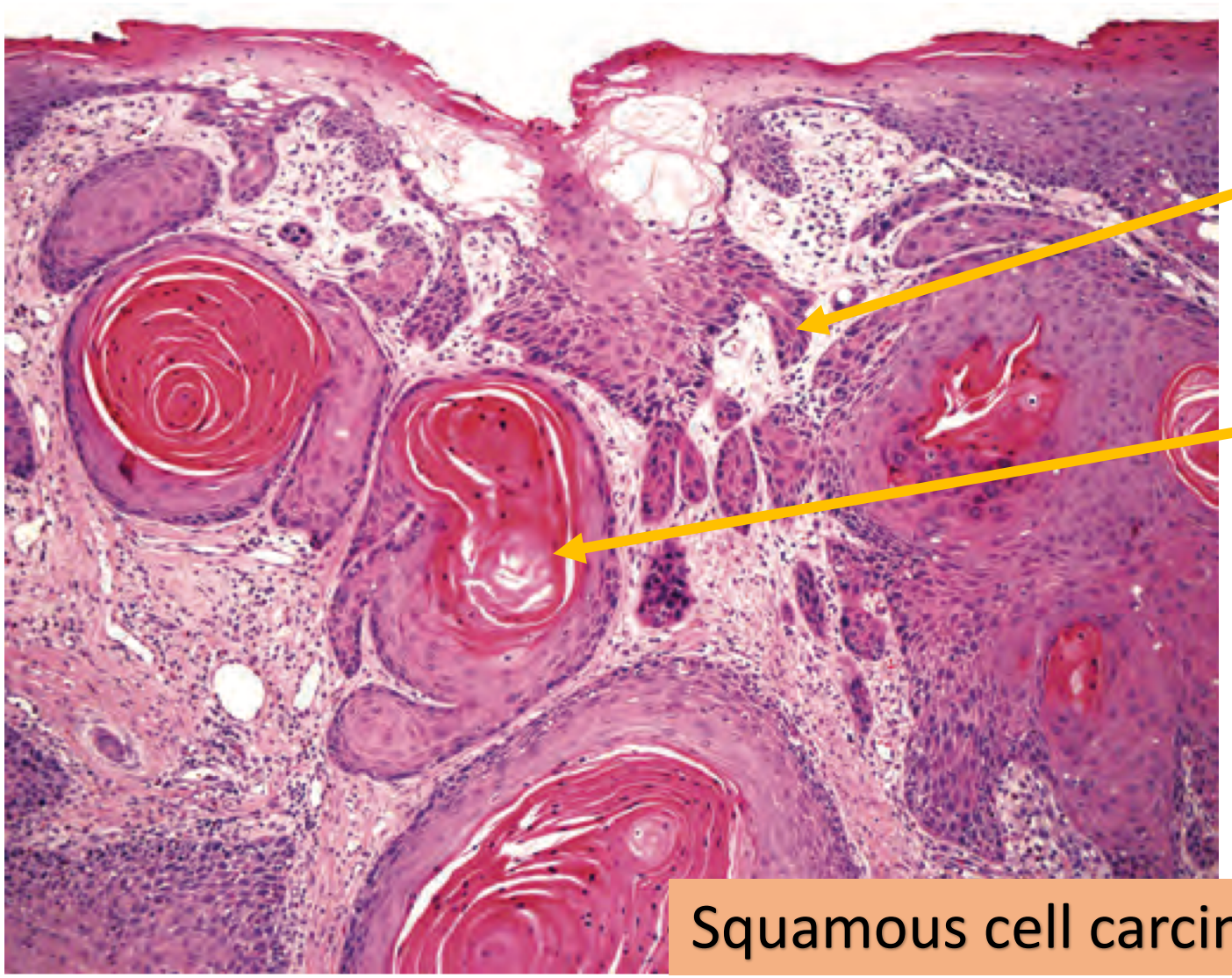
Malignant tumors = cancers

- **Carcinomas:** malignant tumours arising from epithelial cells lining the parenchymal organs.
  - Squamous cell carcinoma-resemble stratified squamous epithelium.
  - Adenocarcinoma-grow in a glandular pattern

- **Sarcomas**: malignant tumours arising in mesenchymal tissue
  - Fibrous tissue- fibrosarcoma
  - Adipocytes/fatty tissue-Liposarcoma
  - Bony tissue (osteoid)- Osteosarcoma

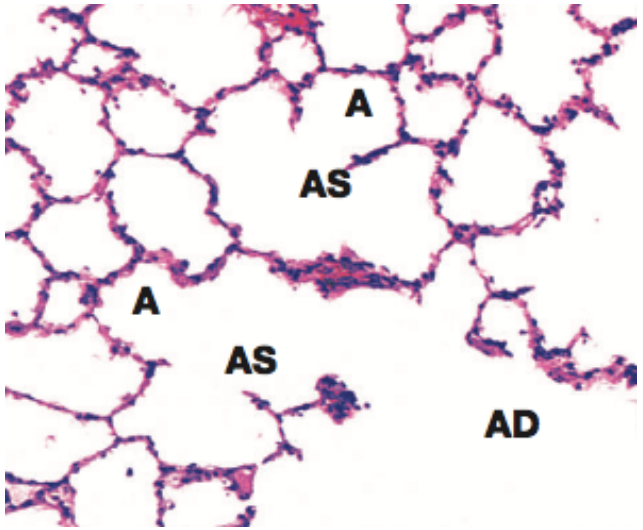
Malignant- Carcinomas

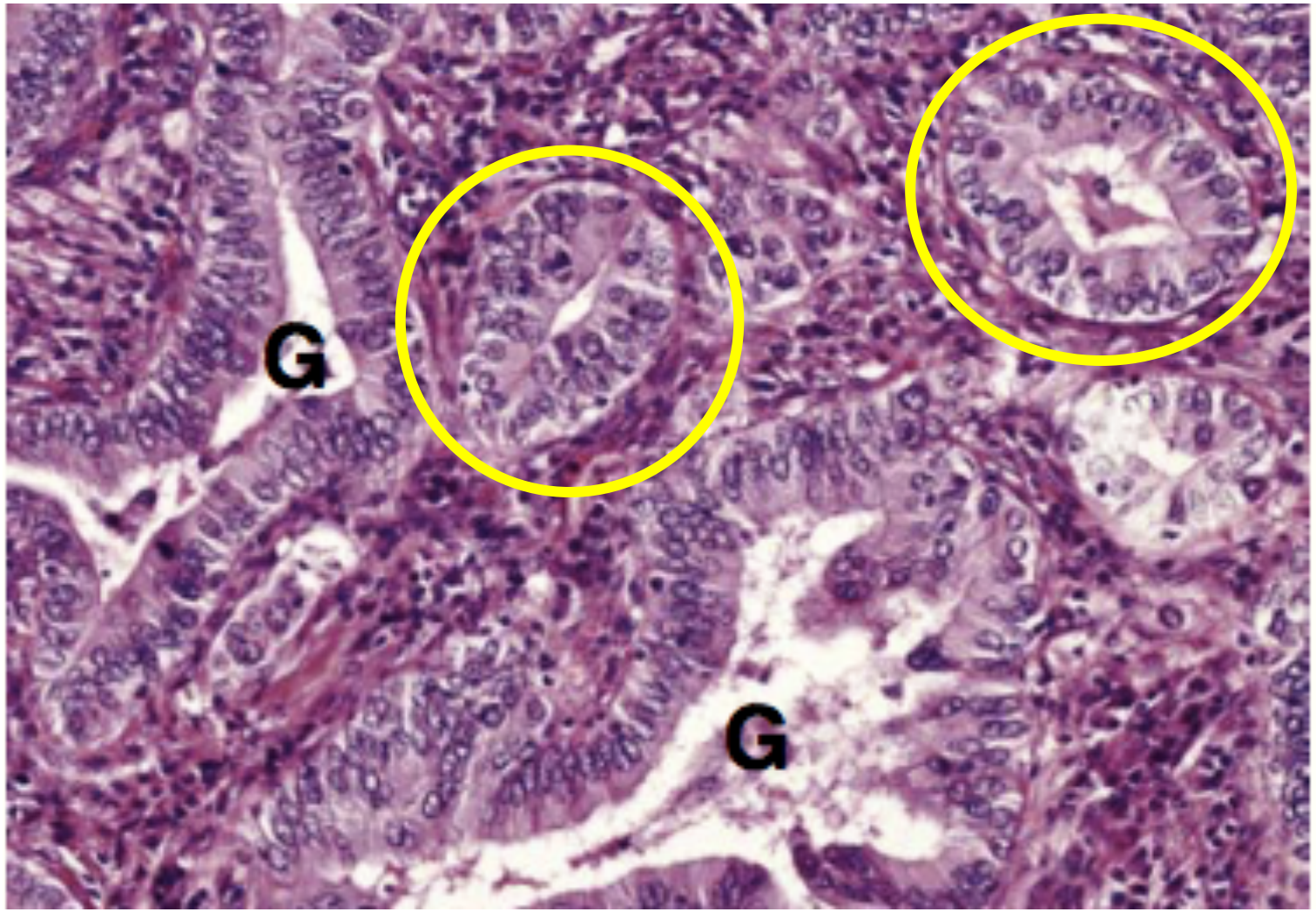




Squamous cell carcinoma of cervix

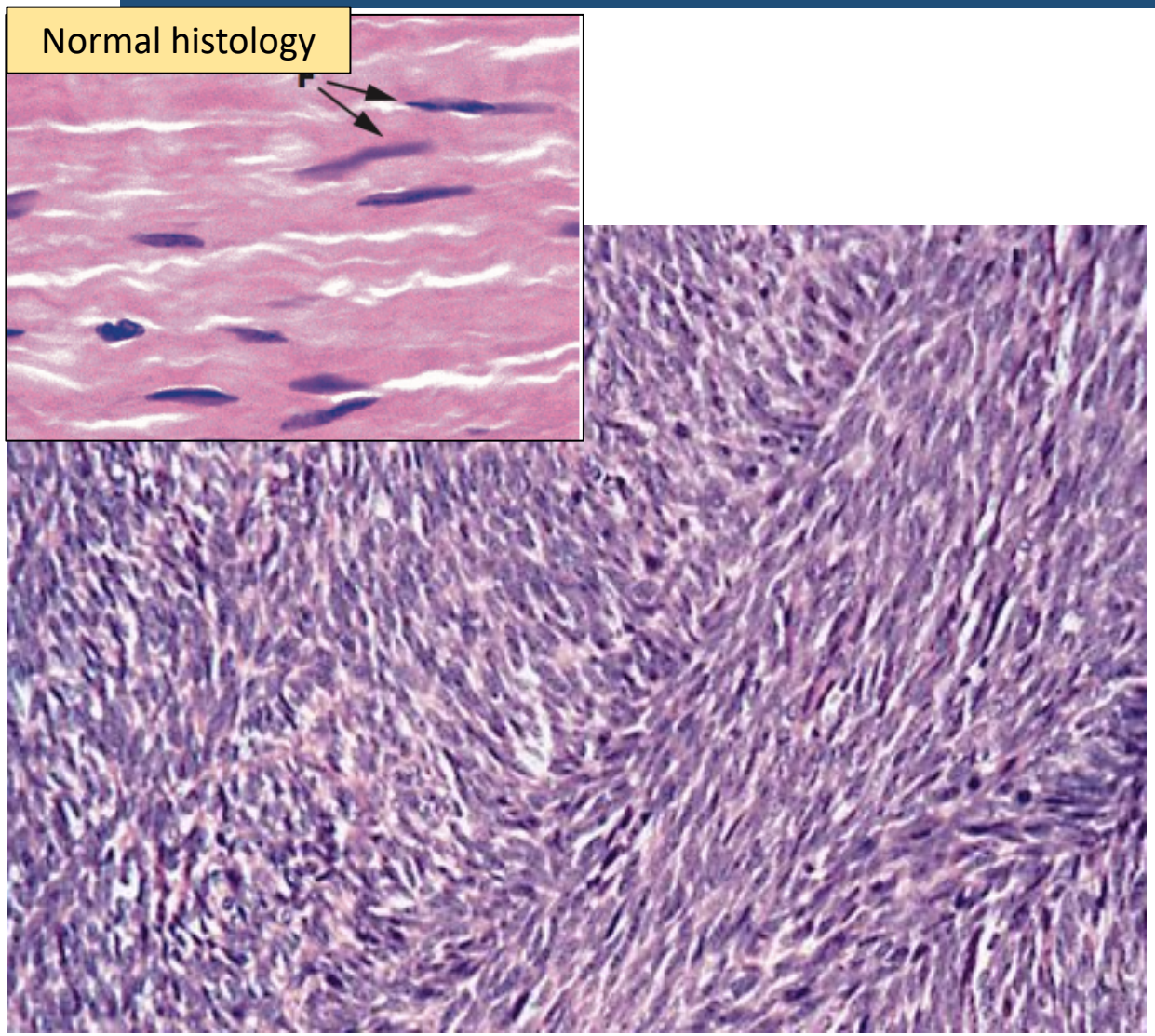
Normal histology



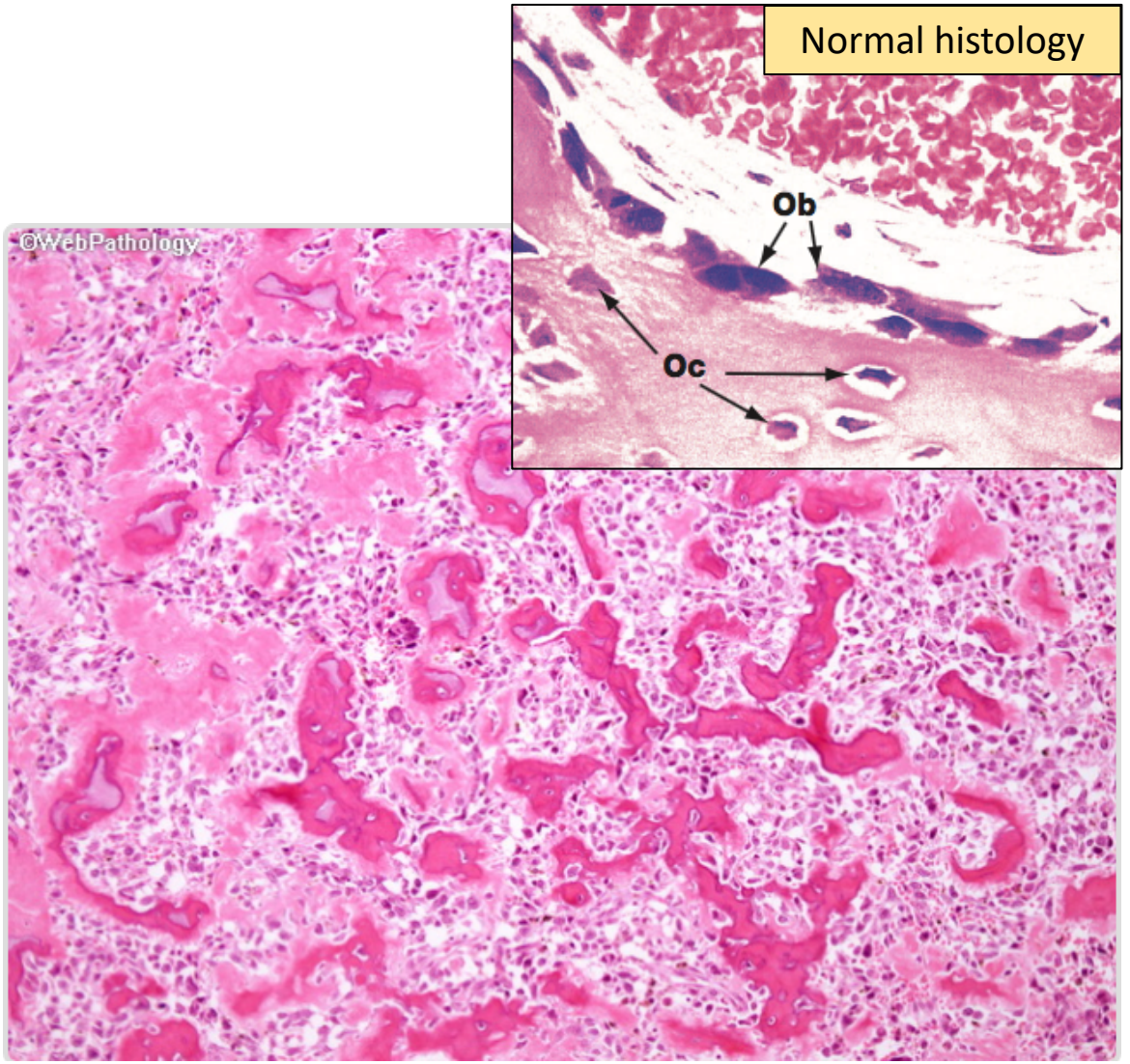


Adenocarcinoma of lung

Malignant-Sarcomas



Fibrosarcoma



Osteosarcoma

Some malignant misnomer

Melanoma-melanocytes

Lymphoma-lymphoid cells

Hepatoma

Seminoma and etc.

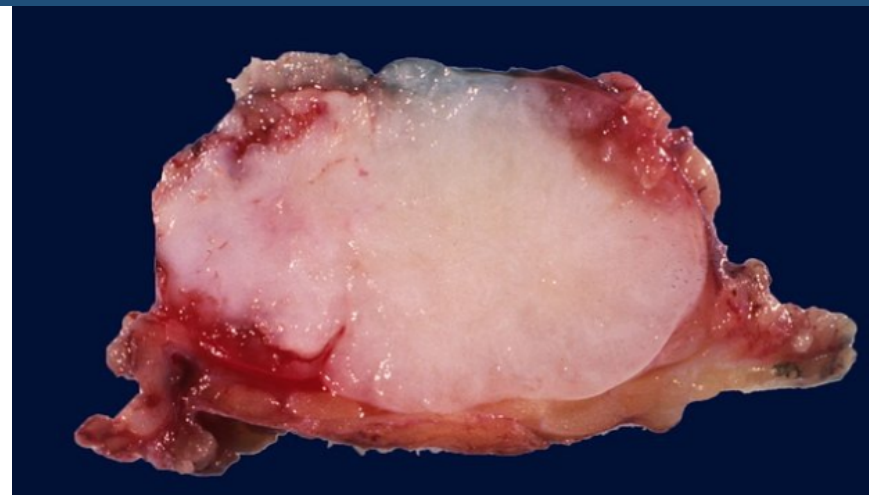
Neoplasms ending in "-**blastoma**" resemble primitive embryonic tissues, which are often pediatric neoplasms:

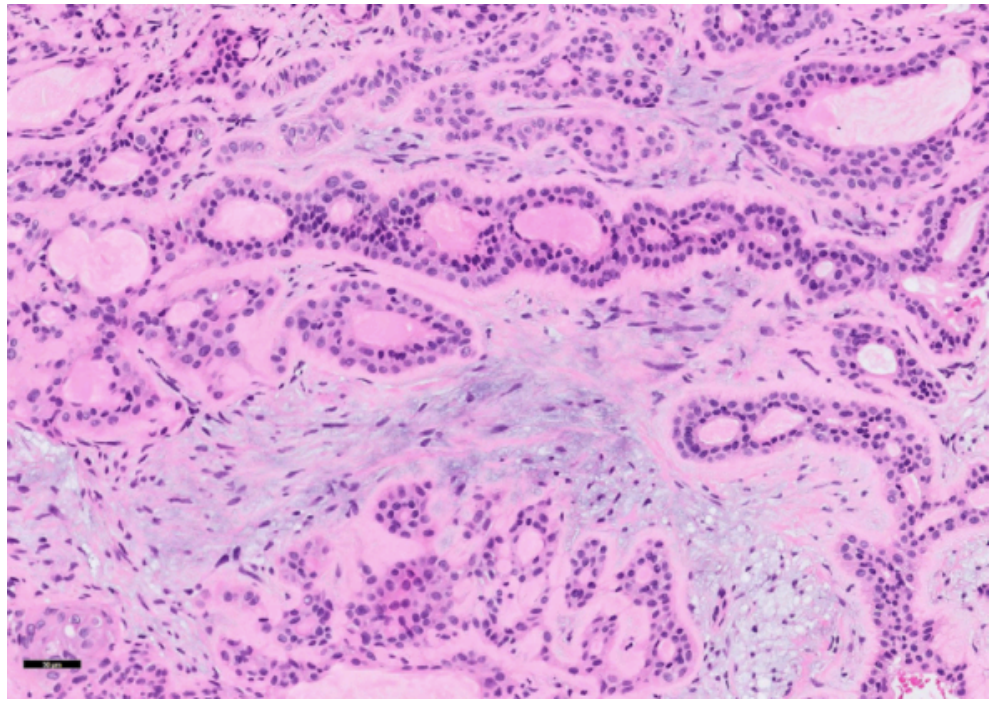
- Retinoblastoma
- Neuroblastoma-immature nerve cells, adrenal gland
- Hepatoblastoma
- Medulloblastoma
- Nephroblastoma/ Wilms’ tumour

Nomenclature: Special categories tumours

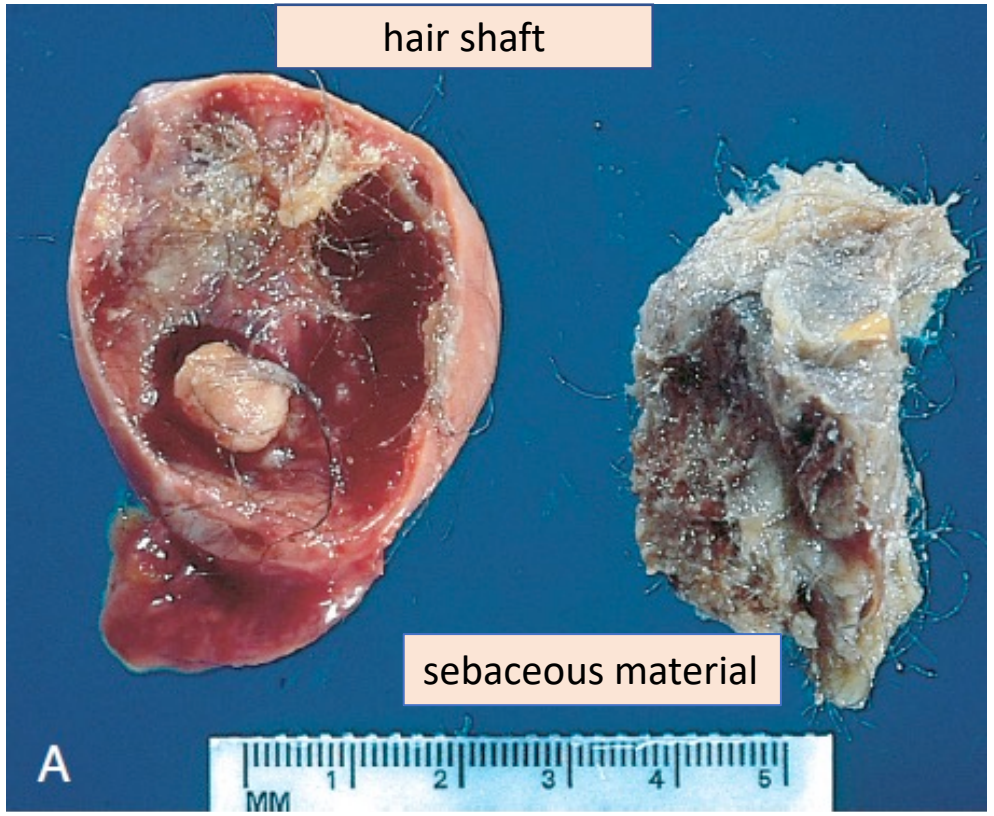
Mixed tumour

- Tumours arise from single neoplastic clone that capable of producing both epithelial and mesenchymal cells.
- E.g.: Pleomorphic adenoma → contains epithelial components, scattered within a myxoid stroma with cartilage or bone.



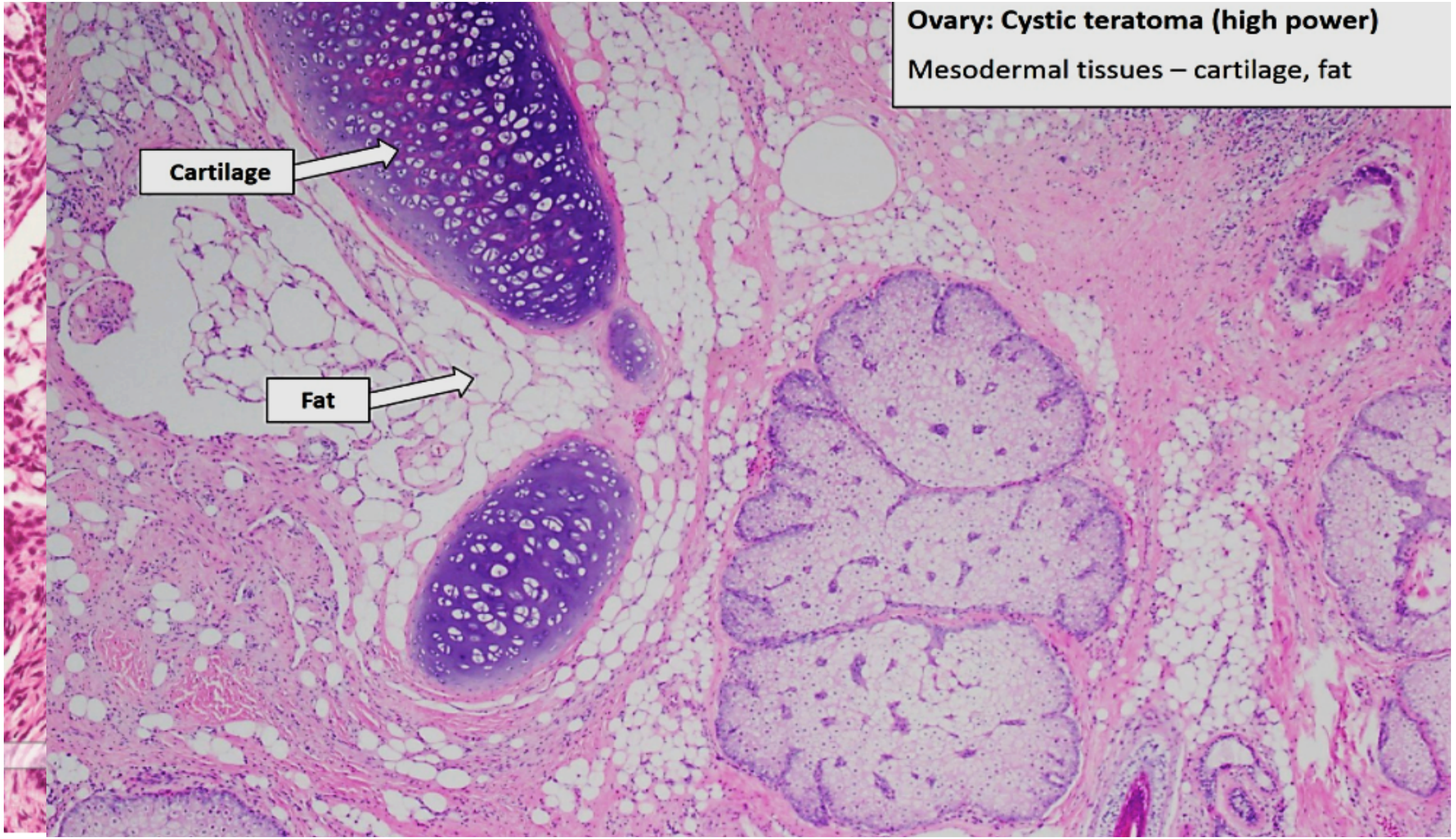


Nomenclature: Special categories tumours



Teratoma

- Contains mature or immature cells arise form the > one germ cell layer (ectoderm, mesoderm, endoderm).
- The tumour originate from **totipotential germ cells** that normally present in the ovary and testis.
- It able to differentiate into any of the cell types found in adult body-skin, glands, bone, cartilage etc.


Ovary: Cystic teratoma (high power)
Mesodermal tissues – cartilage, fat
Cartilage
Fat

Origin	Benign	Malignant
Tumors of Epithelial Origin		
Stratified squamous	Squamous cell papilloma	Squamous cell carcinoma
Basal cells of skin or adnexa		Basal cell carcinoma
Melanocytes	Nevus	Malignant melanoma
Epithelial lining of glands or ducts	Adenoma Papilloma Cystadenoma	Adenocarcinoma Papillary carcinomas Cystadenocarcinoma
Respiratory passages	Bronchial adenoma	Bronchogenic carcinoma
Renal epithelium	Renal tubular adenoma	Renal cell carcinoma
Liver cells	Hepatic adenoma	Hepatocellular carcinoma
Urinary tract epithelium (transitional epithelium)	Transitional cell papilloma	Transitional cell carcinoma
Placenta epithelium	Hydatidiform mole	Choriocarcinoma
Testicular epithelium (germ cells)		Seminoma Embryonal carcinoma

Origin	Benign	Malignant
Composed of One Parenchymal Cell Type		
Tumors of Mesenchymal Origin		
Connective tissue and derivatives	Fibroma Lipoma Chondroma Osteoma	Fibrosarcoma Liposarcoma Chondrosarcoma Osteogenic sarcoma
Vessels and Surface Coverings		
Blood vessels	Hemangioma	Angiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma
Mesothelium	Benign fibrous tumor	Mesothelioma
Brain coverings	Meningioma	Invasive meningioma
Blood Cells and Related Cell Types		
Hematopoietic cells		Leukemias
Lymphoid tissue		Lymphomas
Muscle		
Smooth	Leiomyoma	Leiomyosarcoma
Striated	Rhabdomyoma	Rhabdomyosarcoma

Need to know this!

MCQ

The following tumours are benign:

A. Lymphangioma T

B. Liposarcoma F

C. Lymphoma F

D. Seminoma F

E. Osteoma T

Tumour behaviour-differences benign & malignant

General characteristics of tumour based in Clinical features/Behavior

Benign Tumours

- Small size
- Slow-growing
- Non-invasive
- Stay localized
- Rarely fatal, but can cause serious effect/death eg: meningioma

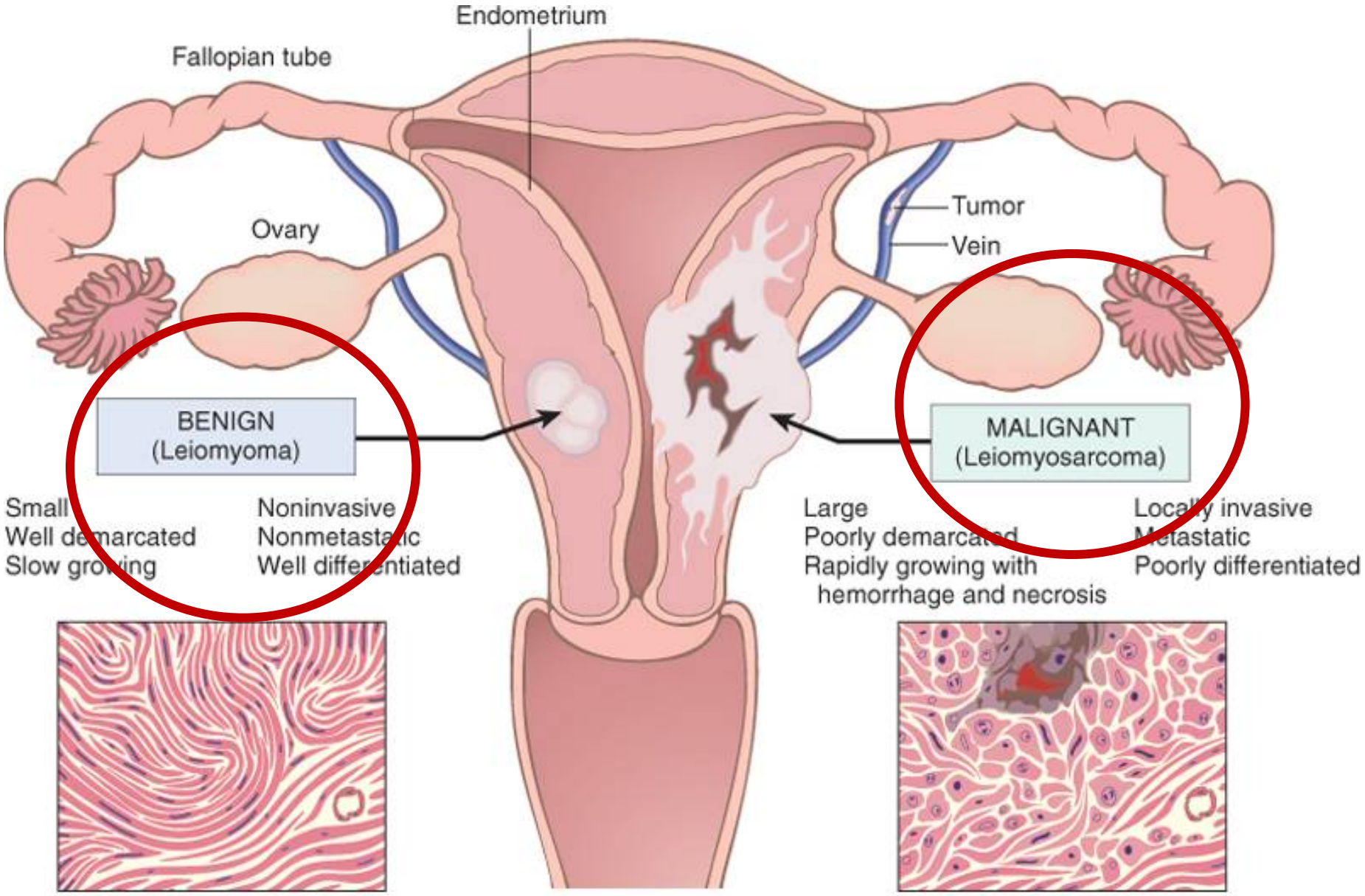
Malignant Tumours

- Large
- Fast-growing
- Invasive
- Metastasize
- Usually fatal if untreated

General characteristics of tumour based in Gross Appearance

Benign	Malignant
• Well circumscribed • Encapsulated but not always e.g. Follicular adenoma of thyroid • Rounded –leiomyoma of uterine • Not much hemorrhage • No necrosis	• Irregular, some are well demarcated • Non encapsulated • Hemorrhage or necrosis (pallor area within a fleshy tumour) • Lymph nodes metastasis

Benign vs. Malignant



Why is it so important to differentiate benign and malignant tumour?

For patient management
treatment
prognosis

Clinical features only is not enough!

Histopathological examination is crucial

Characteristic of BENIGN and MALIGNANT tumours

Degree of differentiation & anaplasia (morphology/microscopic appearance)

Rate of growth

Local invasion/direct spread

Metastasis/distant spread

Degree of differentiation & anaplasia

Differentiation: How much the tumour cells resemble their cells of origin morphologically and functionally.

- Benign tumours generally are well differentiated-e.g lipoma
- Malignant tumours-ranging from well differentiated to undifferentiated

Anaplasia: Lack of differentiation

Tumour differentiation

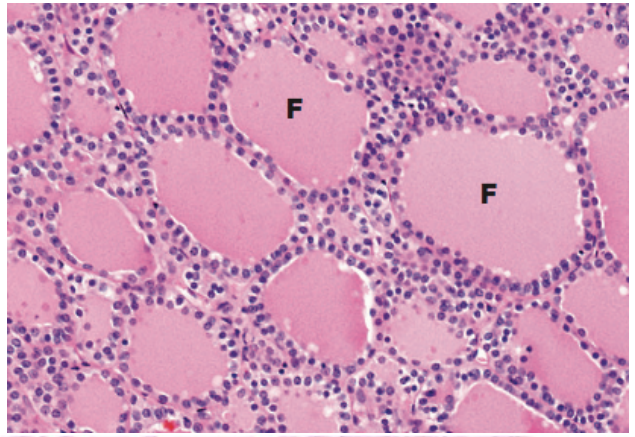
How much the tumour cells resemble their cells of origin morphologically and functionally

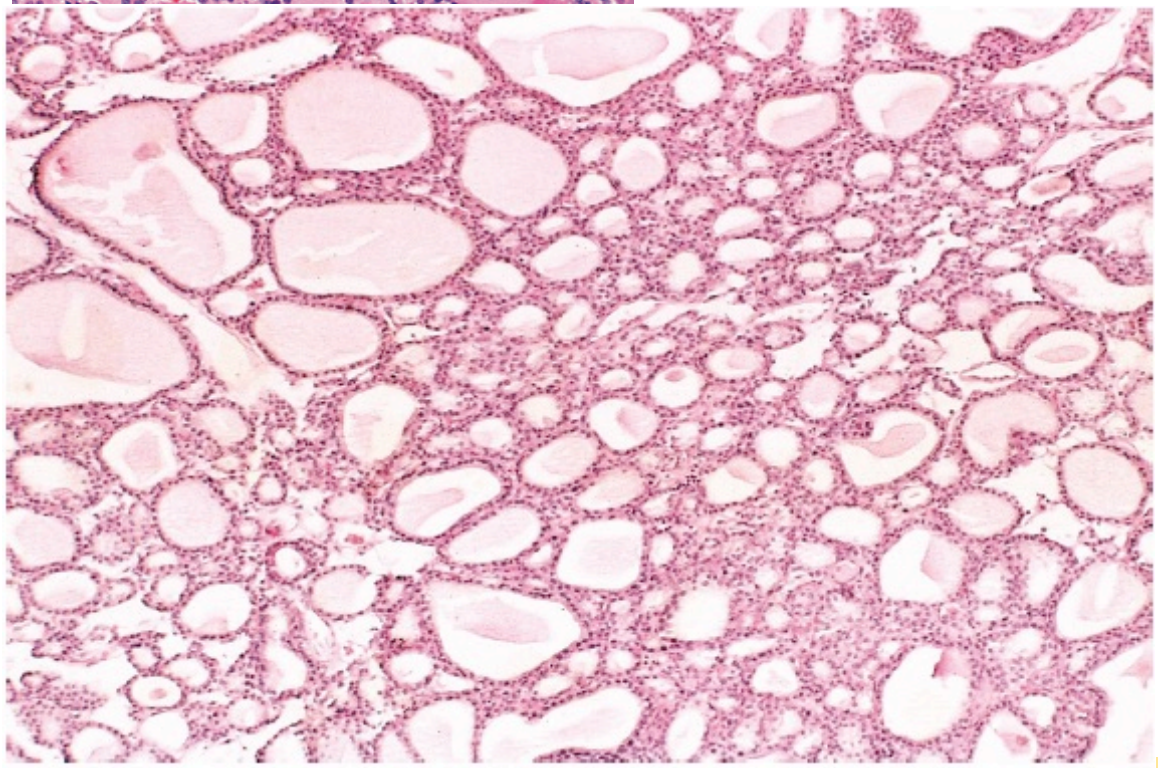
Well-differentiated – closely resembles normal counterpart

Moderately-differentiated – somewhere in between.

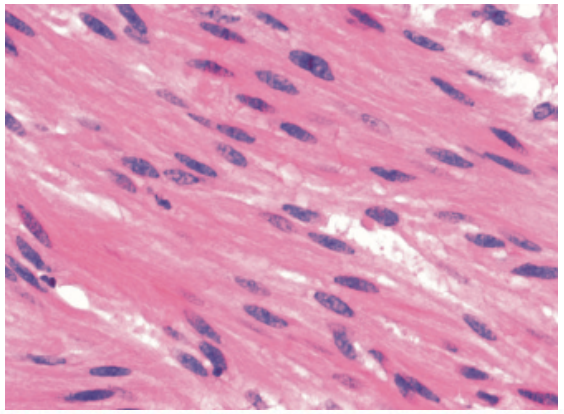
Poorly-differentiated –refers to tumors that show only minimal resemblance to the normal parent tissue they are derived from.

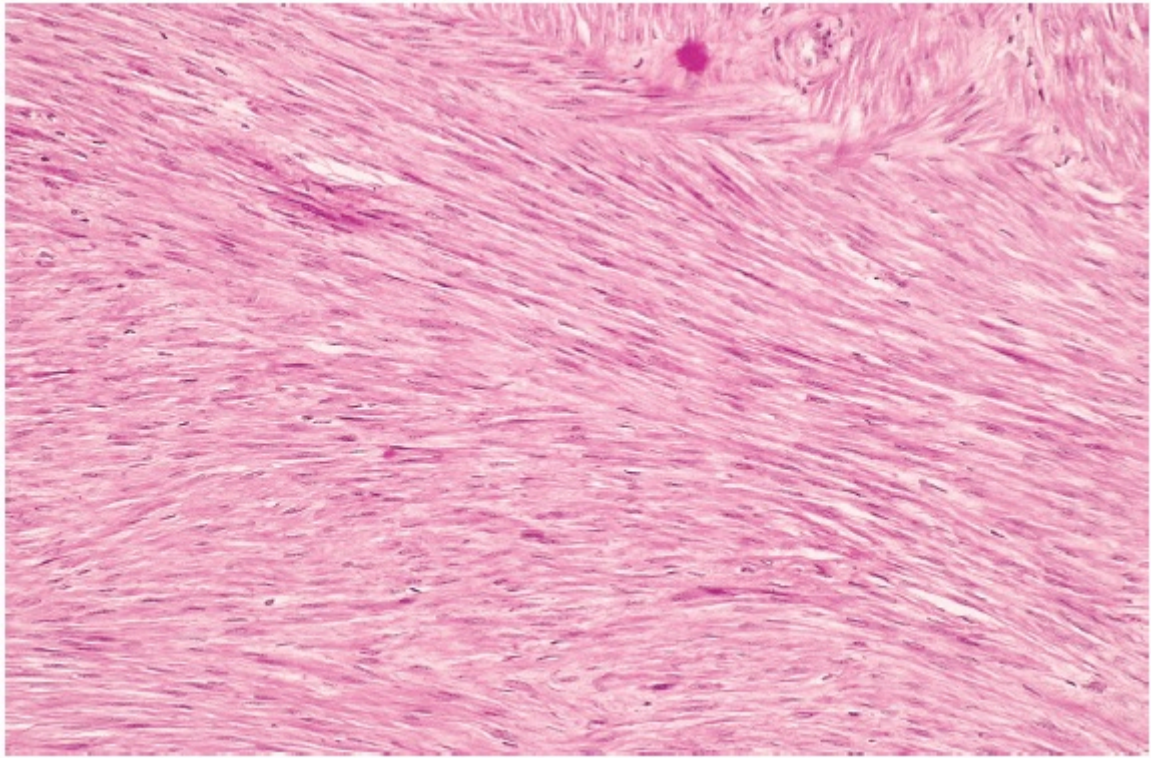
Anaplastic-means the tumour shows no obvious similiarity to it's cell of origin



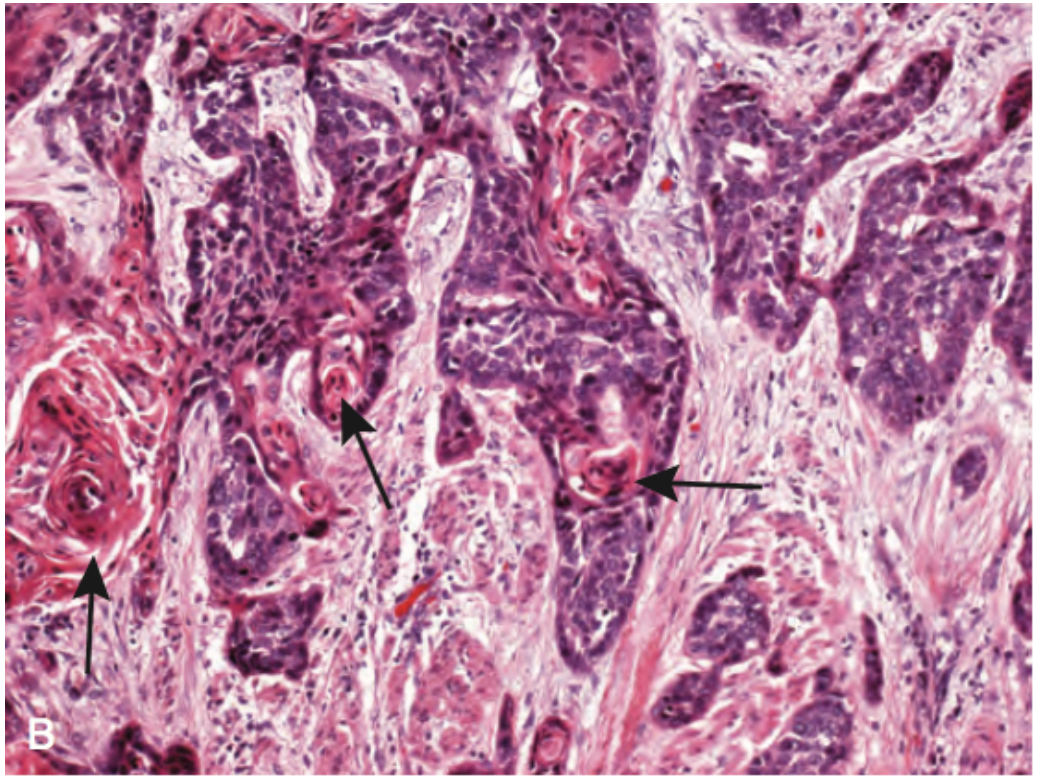


Follicular adenoma of the thyroid- well differentiated



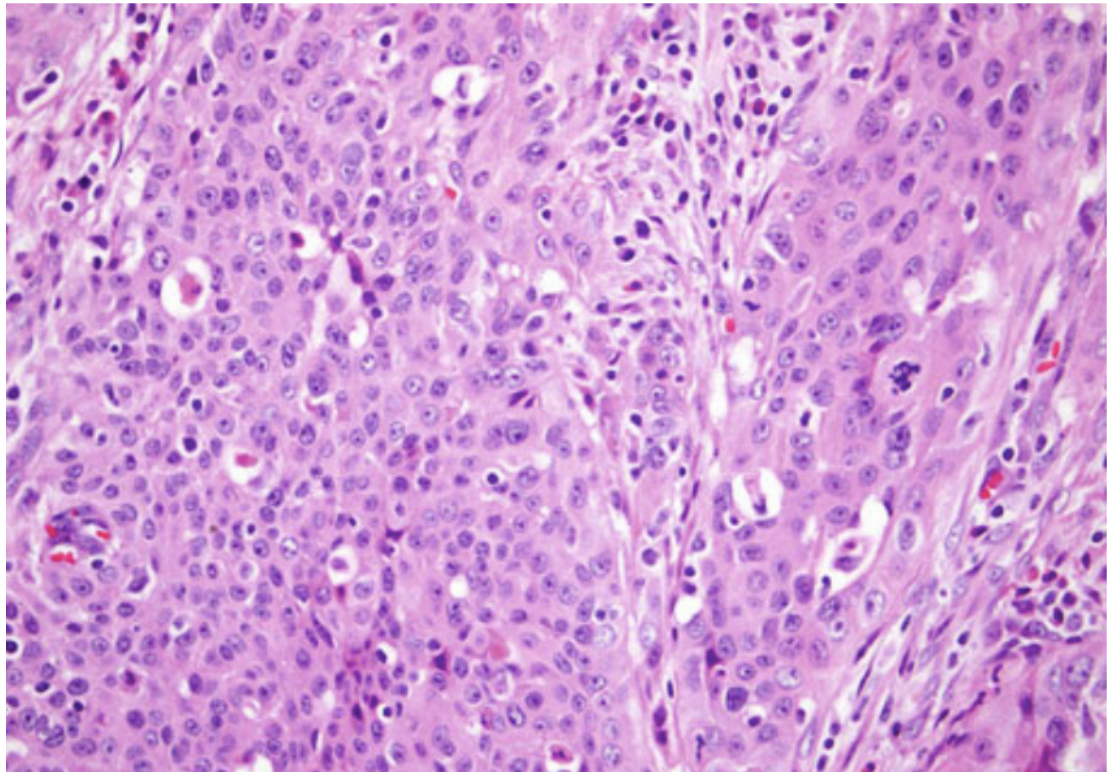


Leiomyoma of the uterus, well-differentiated tumor closely resemble smooth muscle cells



Well-differentiated squamous cell carcinoma

-Abundant keratin (keratin pearls)
-Individual cell keratinization (intense cytoplasmic eosinophilia)
-Wells & tightly packed cells & intercellular bridges.
-Nuclei are large, irregular, and hyperchromatic.
-Mitotic figures are present.



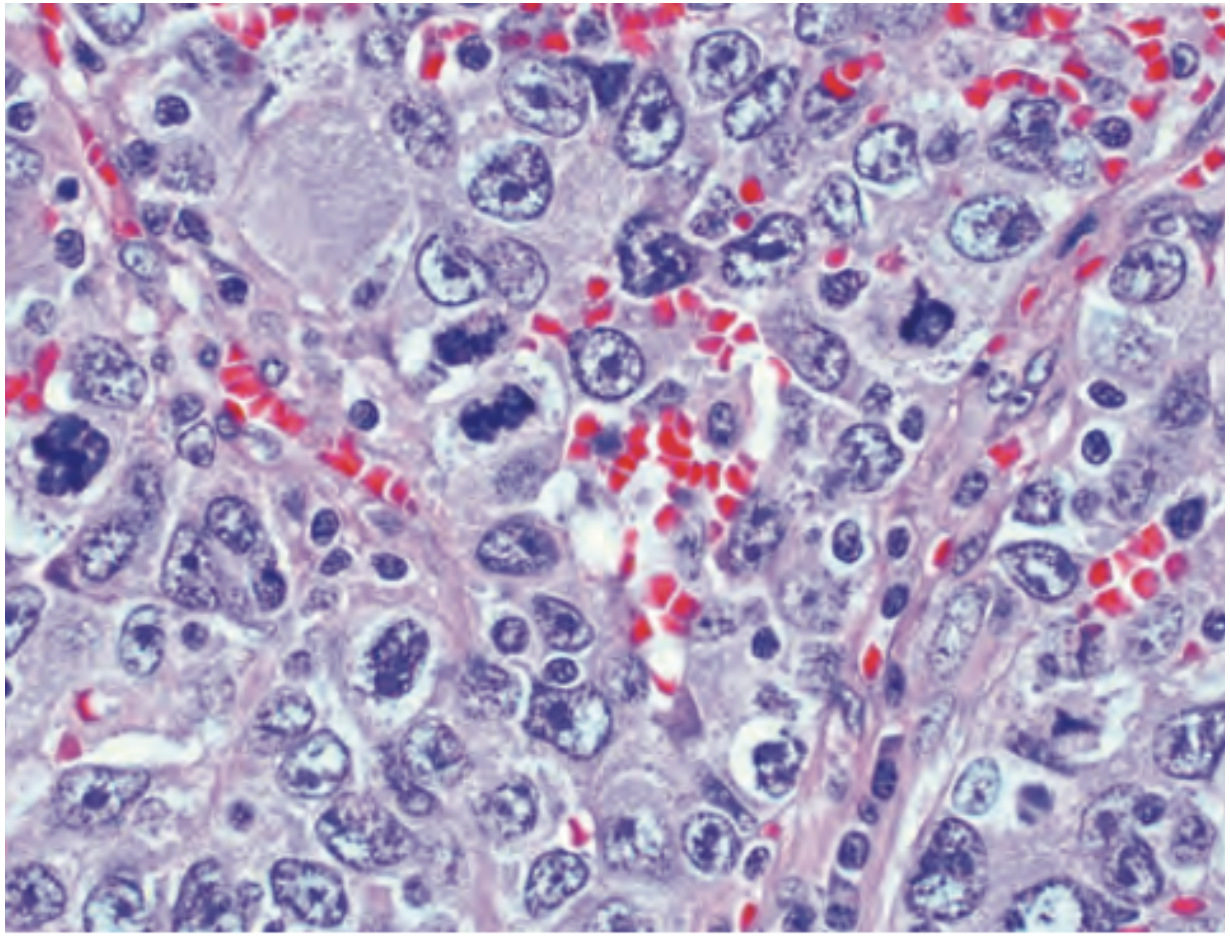
Poorly differentiated squamous cell carcinoma

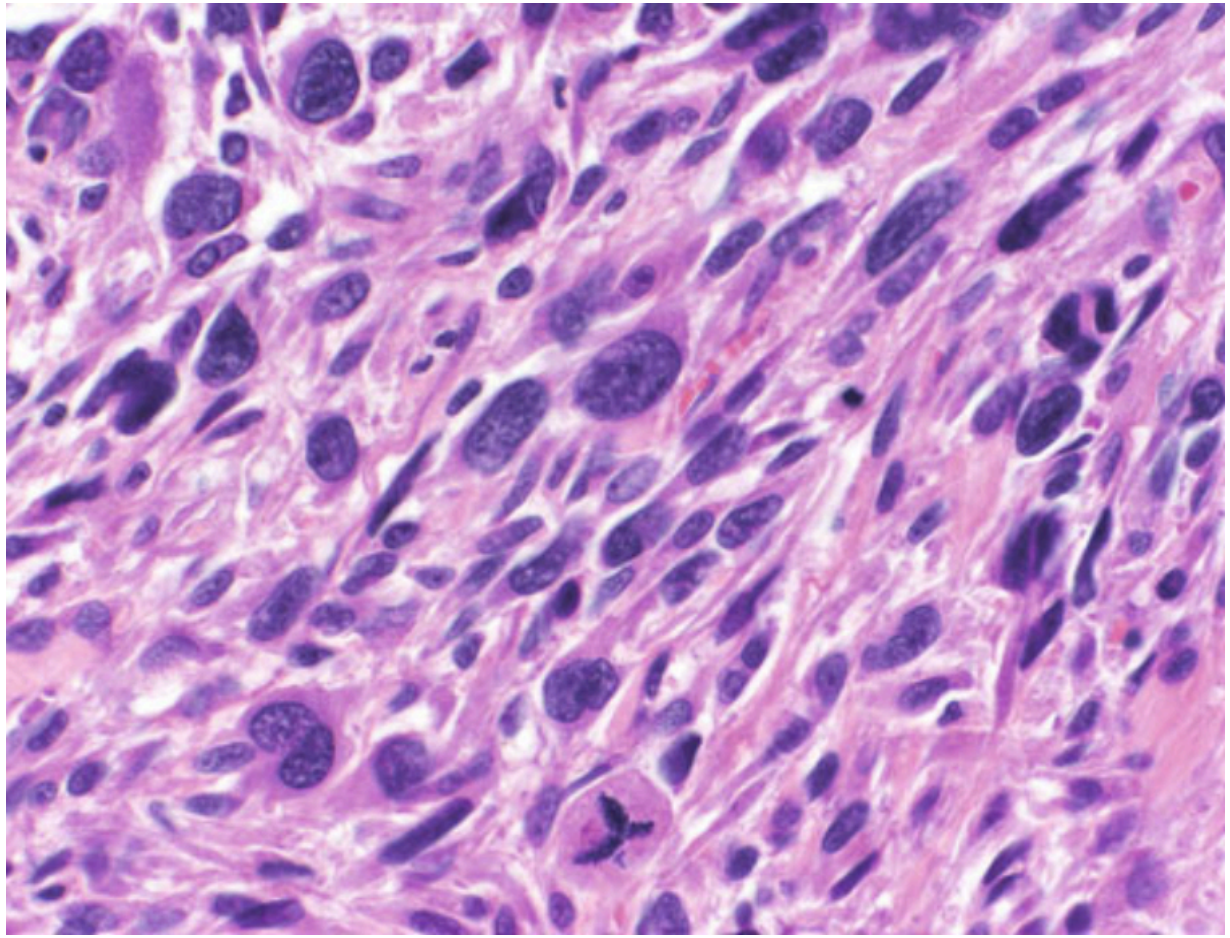
- Keratinization may be difficult to find/absent
- Hyperchromatic oval nuclei and scant indistinct cytoplasm
-Mitoses and areas of necrosis are abundant.
-Occasionally composed of large, pleomorphic cells with giant bizarre cells

Anaplasia- Lack of differentiation

Features of anaplasia:

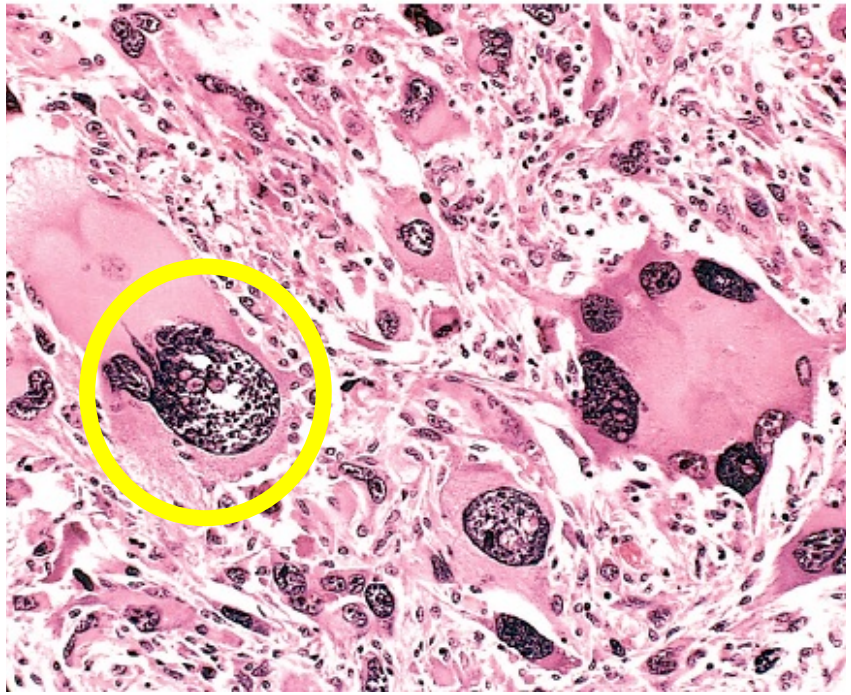
- Pleomorphism
- Abnormal nuclear morphology
- Mitoses
- Loss of polarity
- Other-tumour giant cells



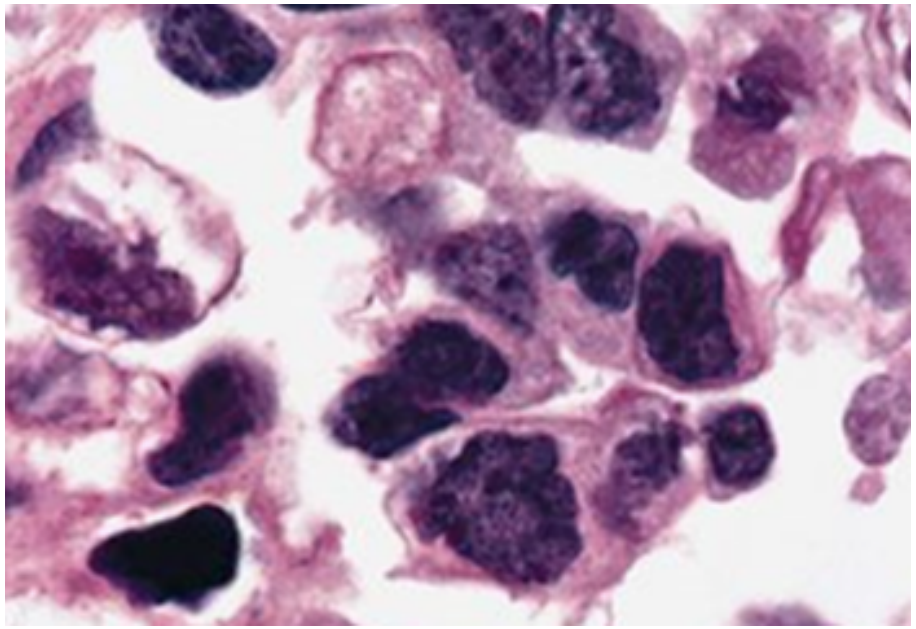


Pleomorphism

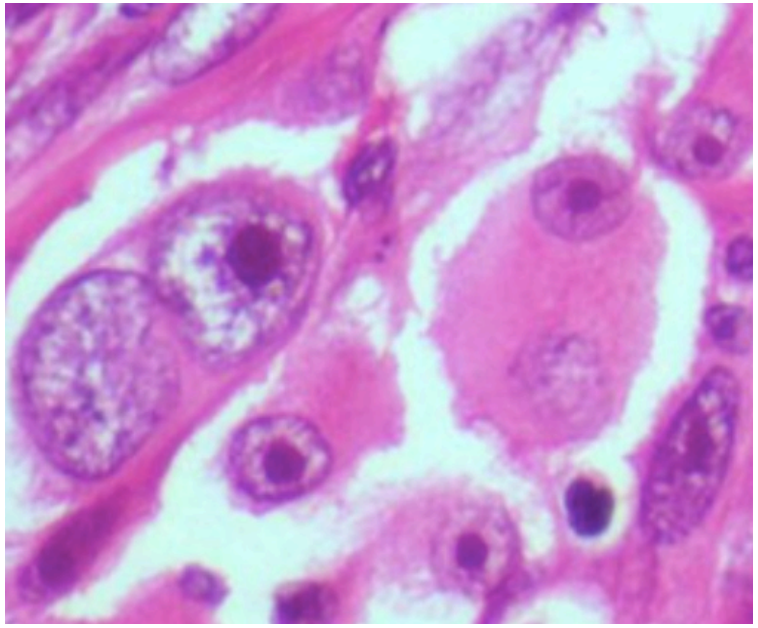
- Variation in **cell** size and shape
- Range from small cells with an undifferentiated to tumor giant cells.



Variable **nuclear** shape, irregular



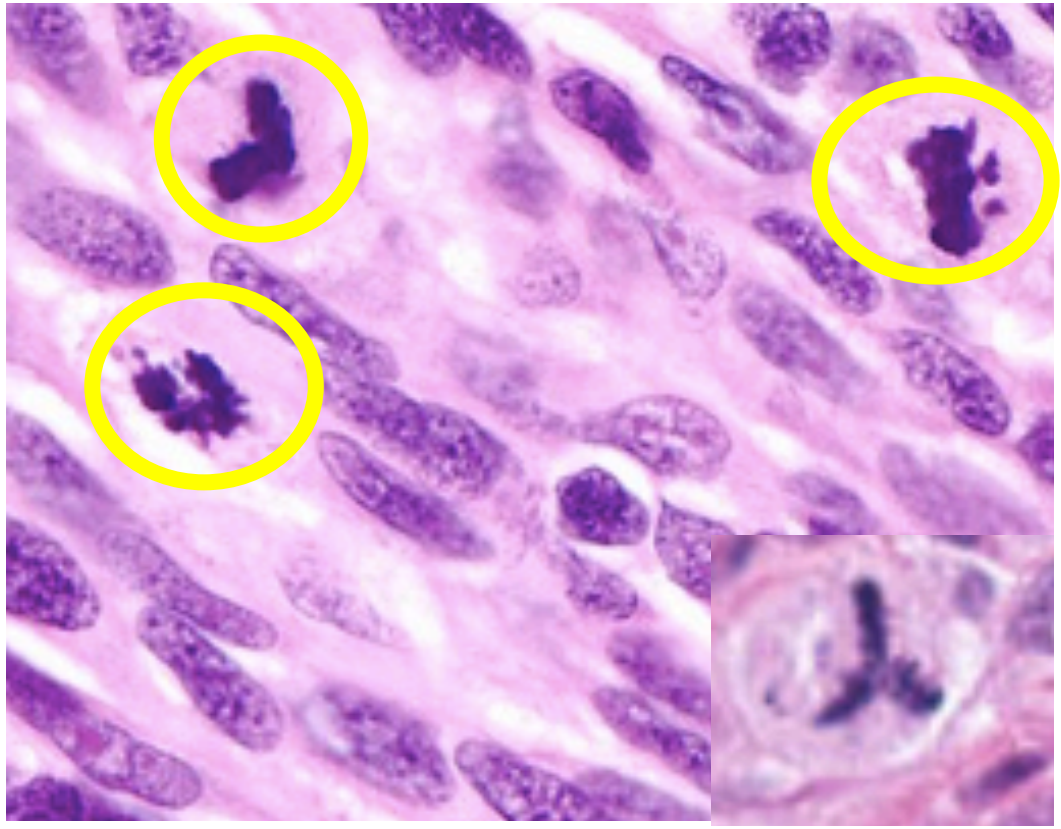
Hyperchromatic, irregular, enlarged nuclei

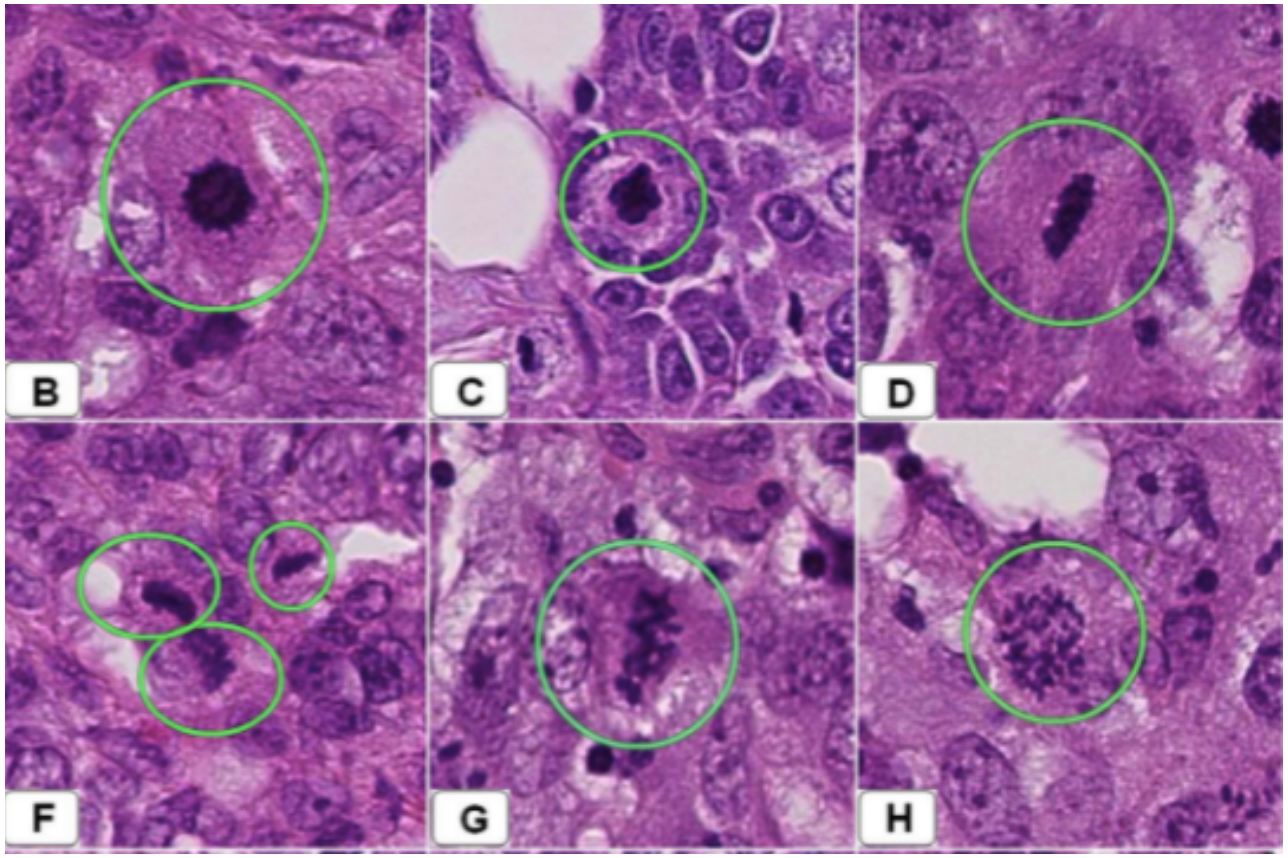


Prominent nucleolus

Abnormal nuclear morphology

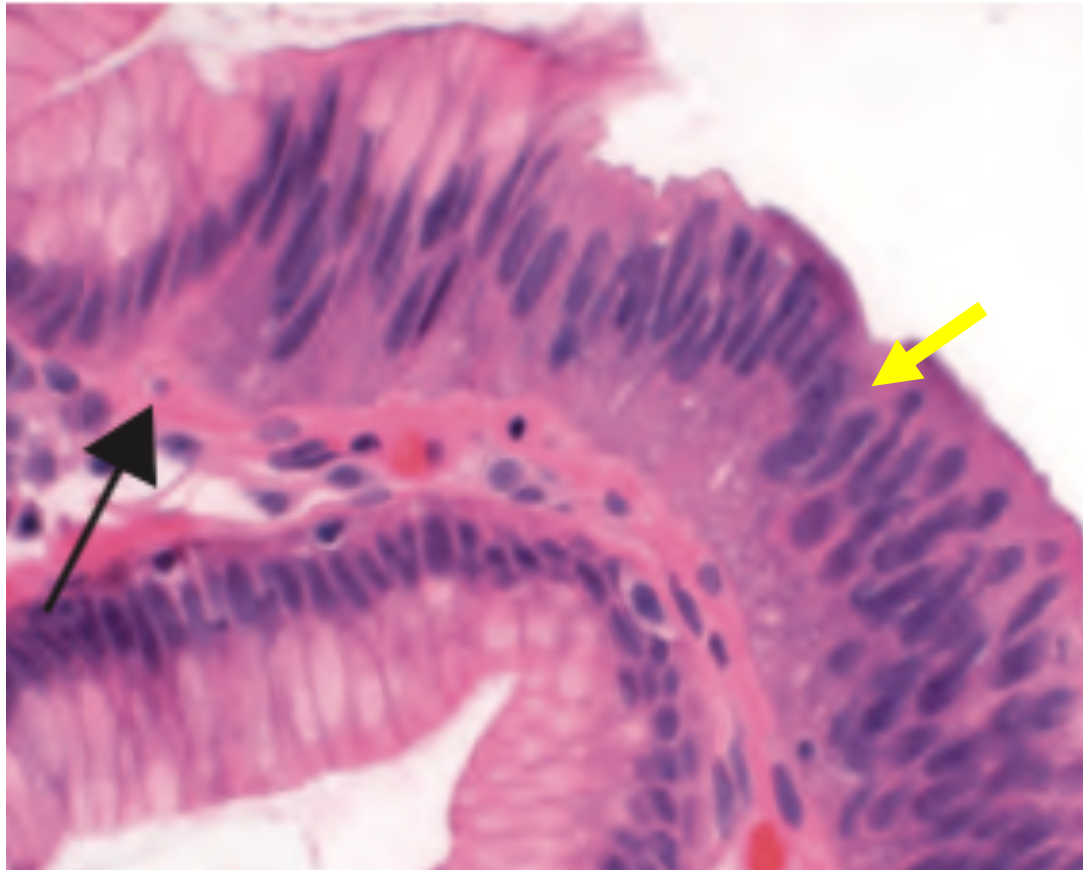
- Increase nuclear-to-cytoplasm ratio (N:C)
- Variable **nuclear** shape, irregular
- Hyperchromatic: Chromatin more darkly stained
- Chromatin coarsely clumped and distributed along the nuclear membrane
- Abnormally large nucleoli

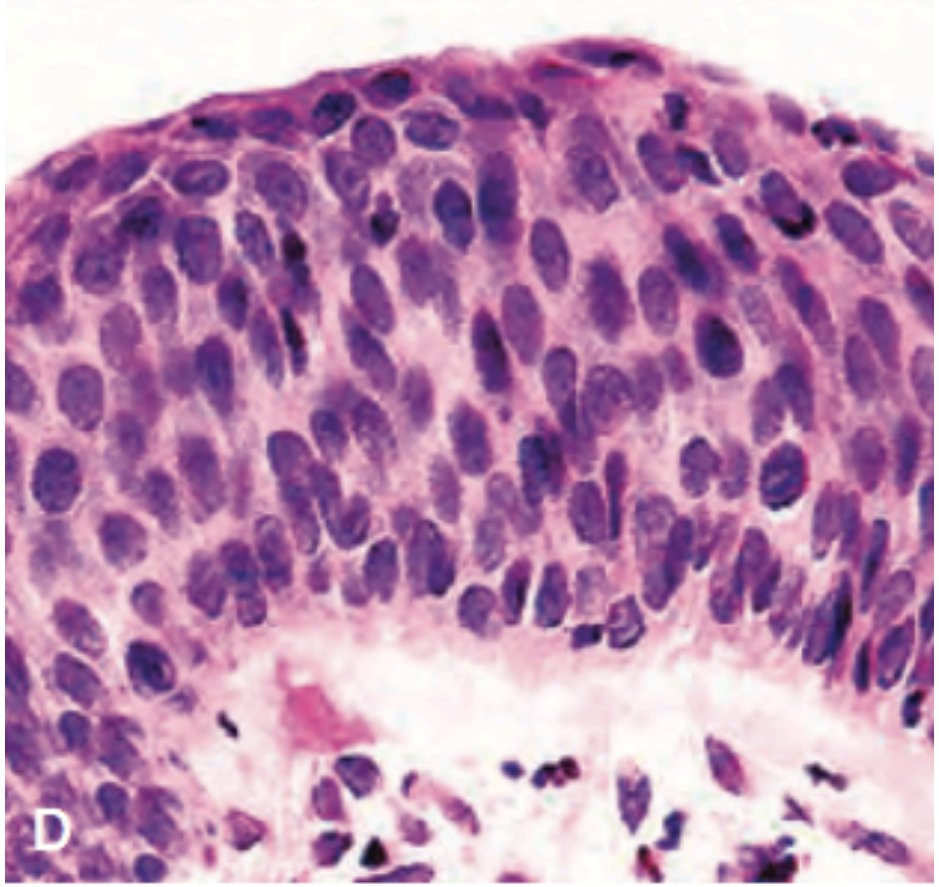




Mitoses.

- Increase mitosis, reflecting high rate of proliferation.
- Presence of mitoses not equal to malignancy. Eg: mitosis in epithelial lining of the gut cells of normal tissues exhibiting rapid turnover.





Loss of polarity.

- Orientation of anaplastic cells with respect to each other or to supporting structures like basement membranes is markedly disturbed/cells grow in a **disorganized fashion**.

Metaplasia vs Dysplasia vs Carcinoma in situ

Metaplasia: replacement of one type of cell with another type

- a/w tissue damage, repair, and regeneration. The replacing cell type is more suited to a change in environment.

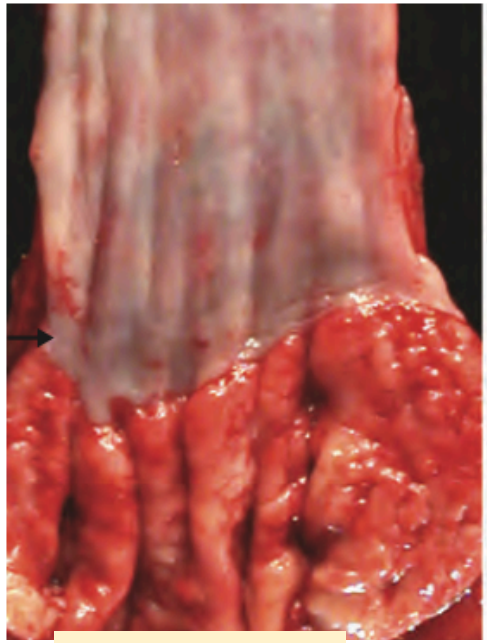
Dysplasia: disordered growth, loss architecture orientation

- Dysplastic cells exhibit considerable pleomorphism-large hyperchromatic nuclei, N : C, increased mitosis. Can be reversible.

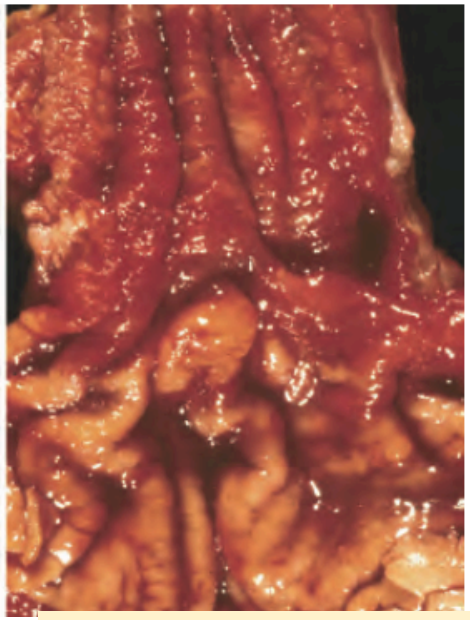
Carcinoma in situ (CIS)-Preinvasive stage of cancer

- Marked dysplasia and involved the full thickness BUT do not invade the basement membrane.
- Display all the cytologic features of malignancy, and have high probability progress to invasive ca if untreated.
- Often seen in – skin, breast, bladder, oropharynx, & uterine cervix.

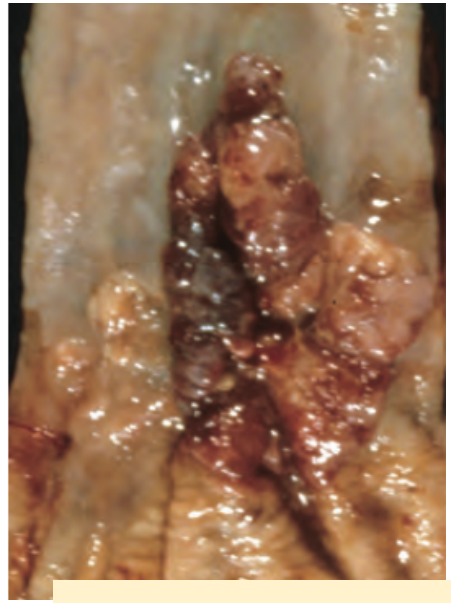
Long standing gastric reflux, replace the gastric mucosa to intestinal mucosa (Barrett esophagus) → Dysplasia → Adenocarcinoma



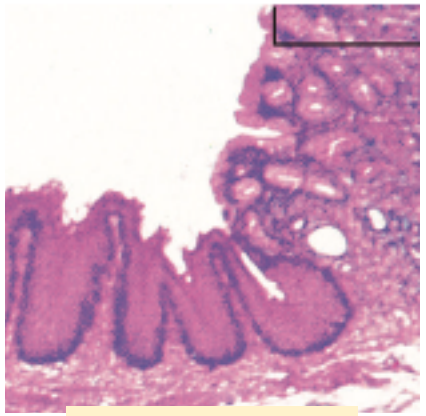
Normal GEJ



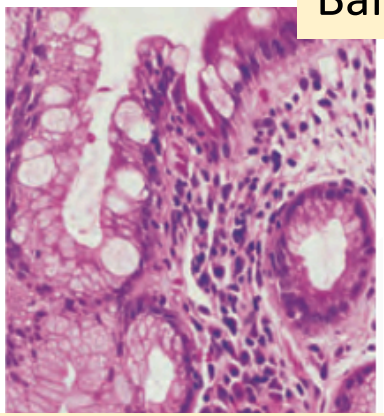
Barrett esophagus



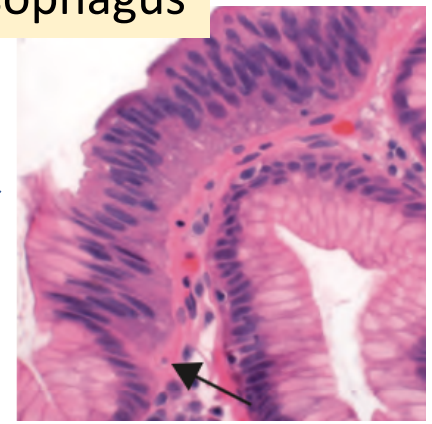
Adenocarcinoma



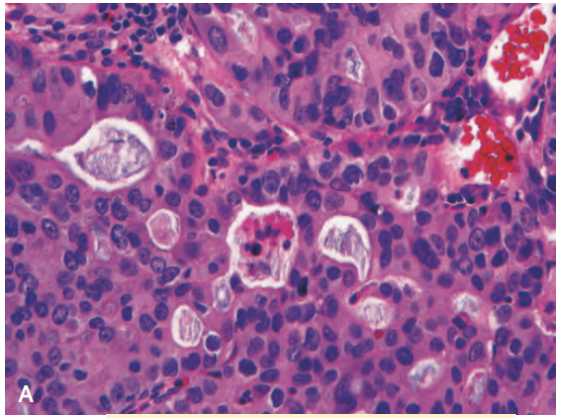
Normal GEJ



Intestinal metaplasia

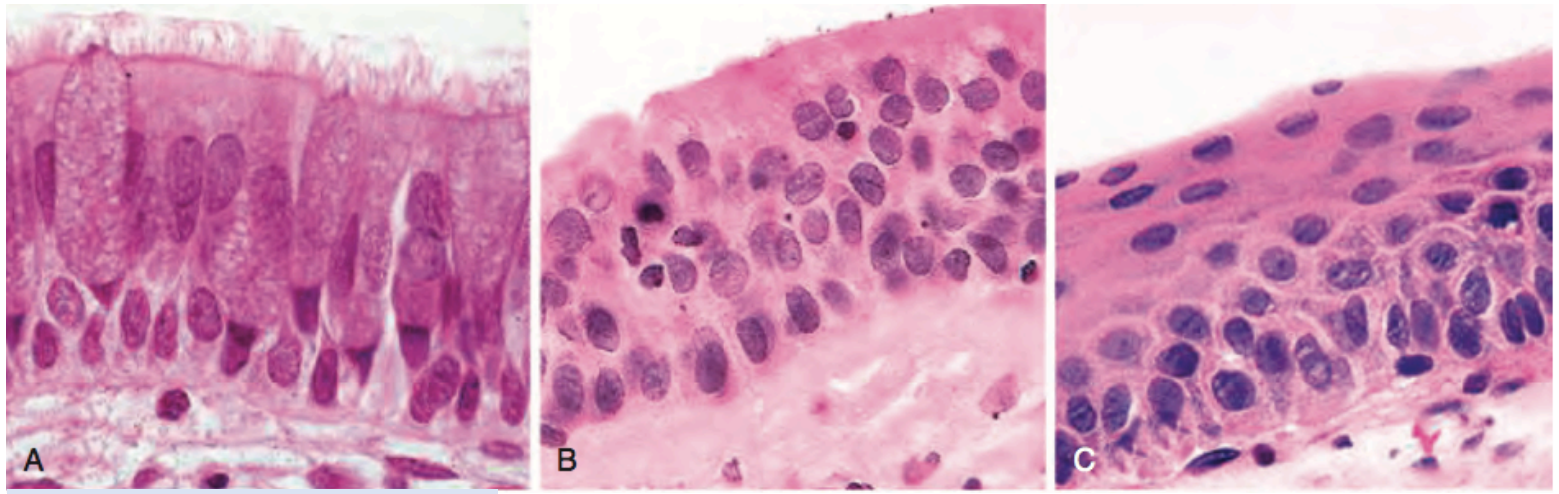


Dysplasia

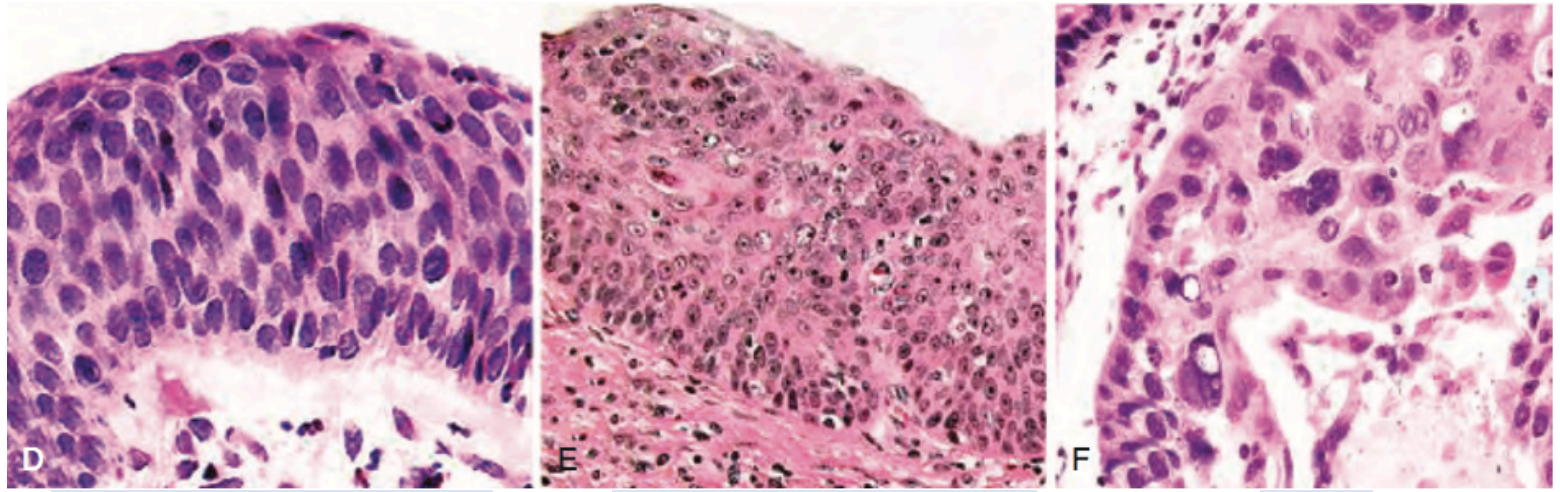


Adenocarcinoma

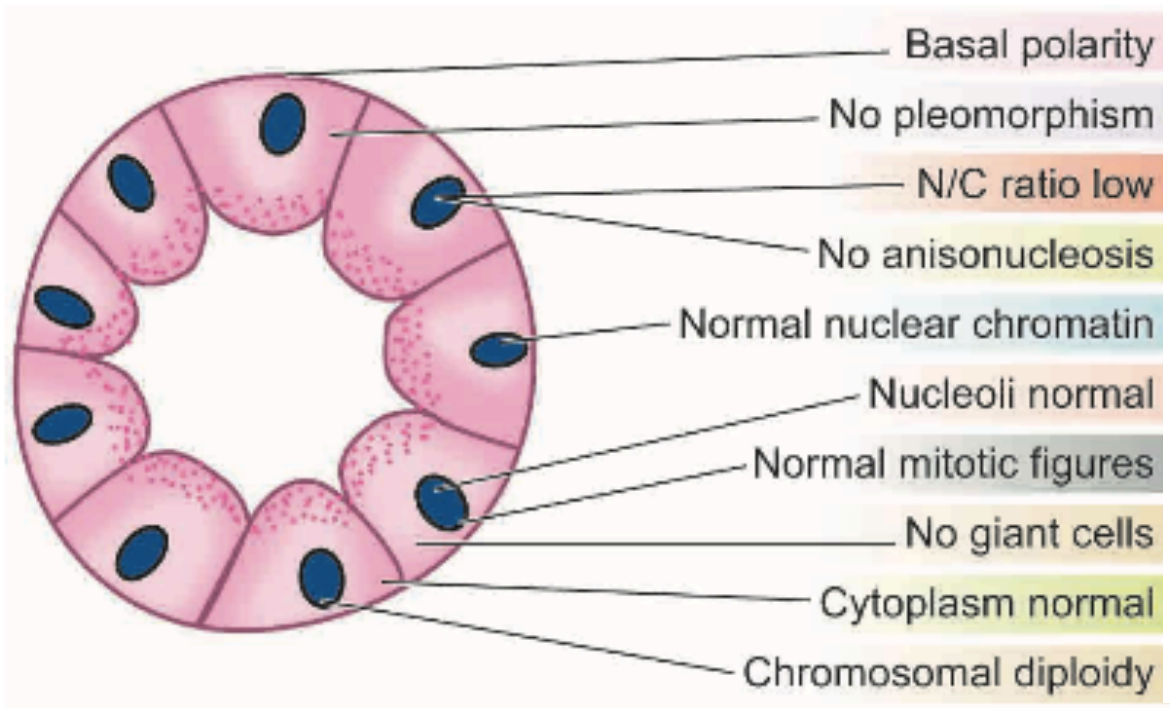
Chronic smoker (respiratory epithelium → squamous metaplasia→ Dysplasia → SCC



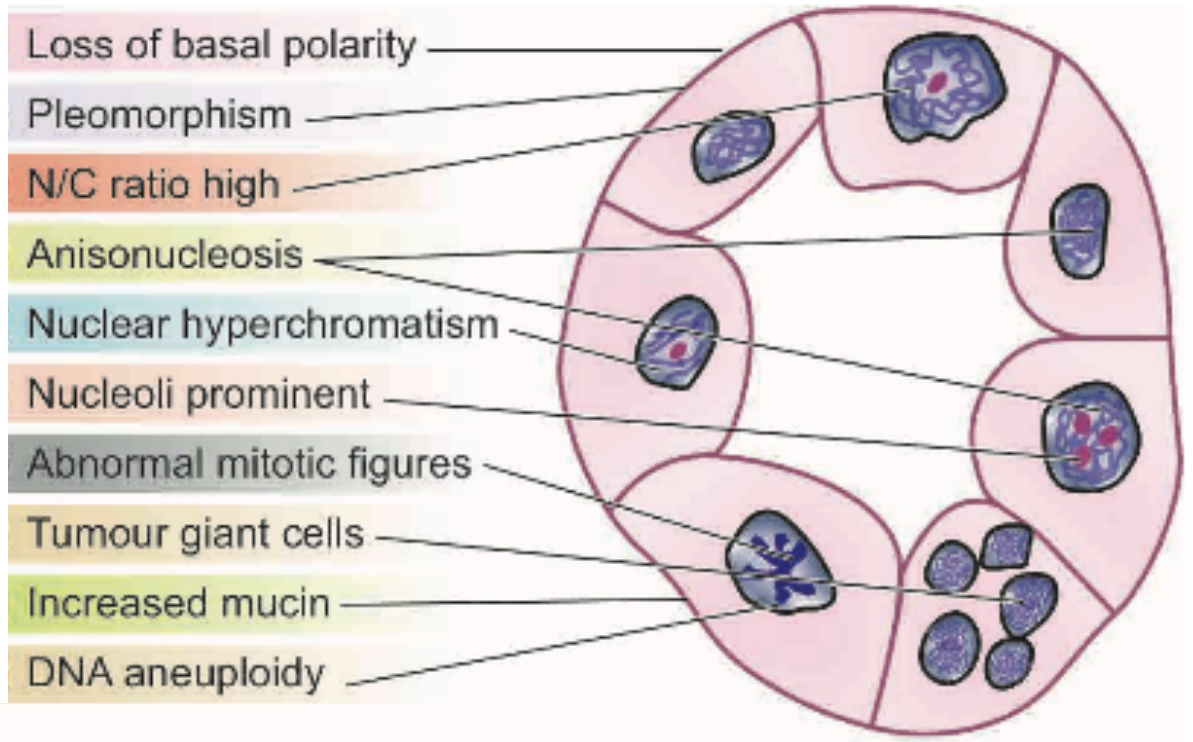
goblet cell hyperplasia → basal cell hyperplasia → squamous metaplasia →



→ squamous dysplasia → Carcinoma in situ → SCC



A, NORMAL MORPHOLOGY



B, CYTOMORPHOLOGY IN CANCER

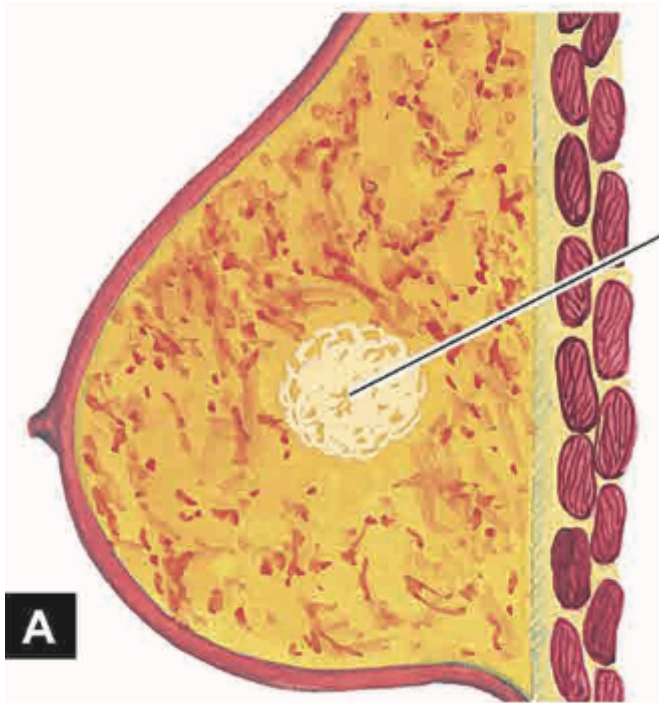
Rate of growth

- Tumour cells generally proliferate more rapid than the normal cells.
- Generally, benign tumours grow slowly as compare with malignant tumors
- But some cancers tend to grow slowly & a/w survival for many years, often without treatment, some of them rapidly growing that may be lethal within months or weeks.
- Rate of growth of a tumour depends upon 3 important parameters:
  - doubling time of tumour cells
  - number of cells remaining in proliferative pool (growth fraction)
  - rate of loss of tumour cells by cell shedding.

Modes of tumour spread
-Local Invasion/direct spread

Benign tumors grow as:

- Cohesive, expansile masses
- Rimming by fibrous tissue (capsule) consists of extracellular matrix (ECM) deposited by stromal cells such as fibroblasts.
  - makes the tumor discrete, readily palpable, movable (nonfixed), and easily excisable by surgical enucleation.
  - remain localized to their site of origin
  - lack the capacity to invade or metastasize to distant sites.
- e.g exceptions to this rule:
  - eg: hemangiomas-unencapsulated & permeate the site in extensive lesion and may be unresectable.



Modes of tumour spread
-Local Invasion-direct spread

Cancers growth:

- Poorly demarcated and lack well-defined cleavage planes.
- Destruction of surrounding tissue-cancer cells do not recognize normal anatomic boundaries
- Accompanied by invasion-
  - the most reliable discriminator of malignant and benign tumors
  - complete surgical resection difficult or impossible
  - Eg: tumour penetrate the wall of the colon or uterus
- Systemic spread-metastases

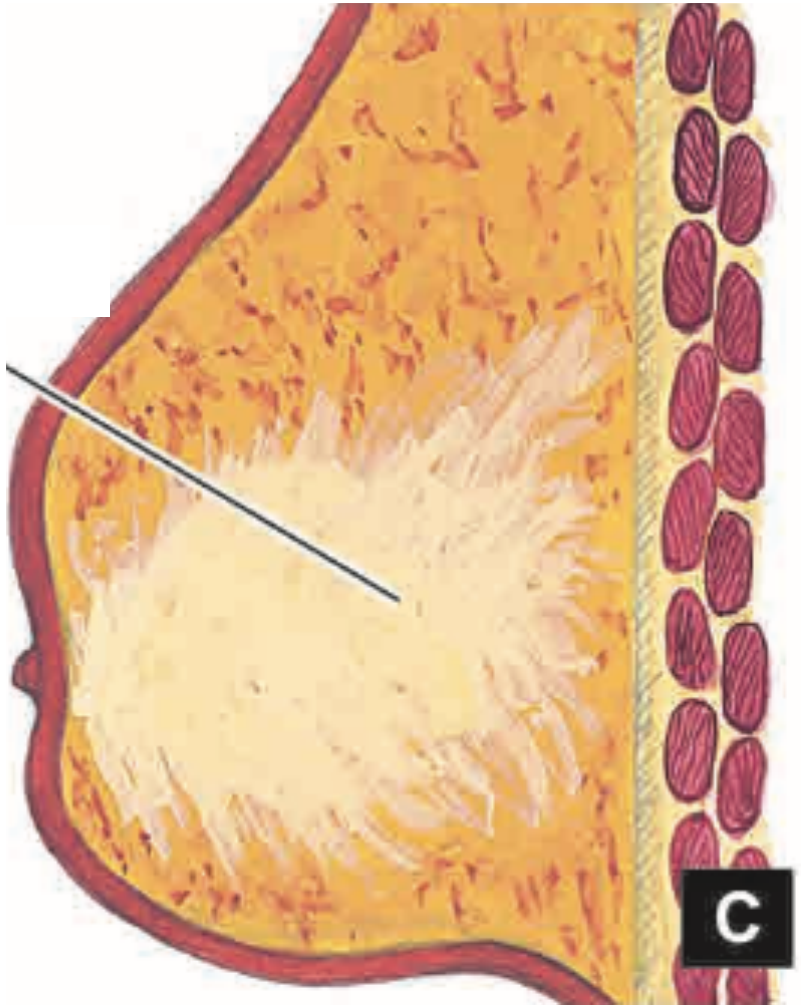
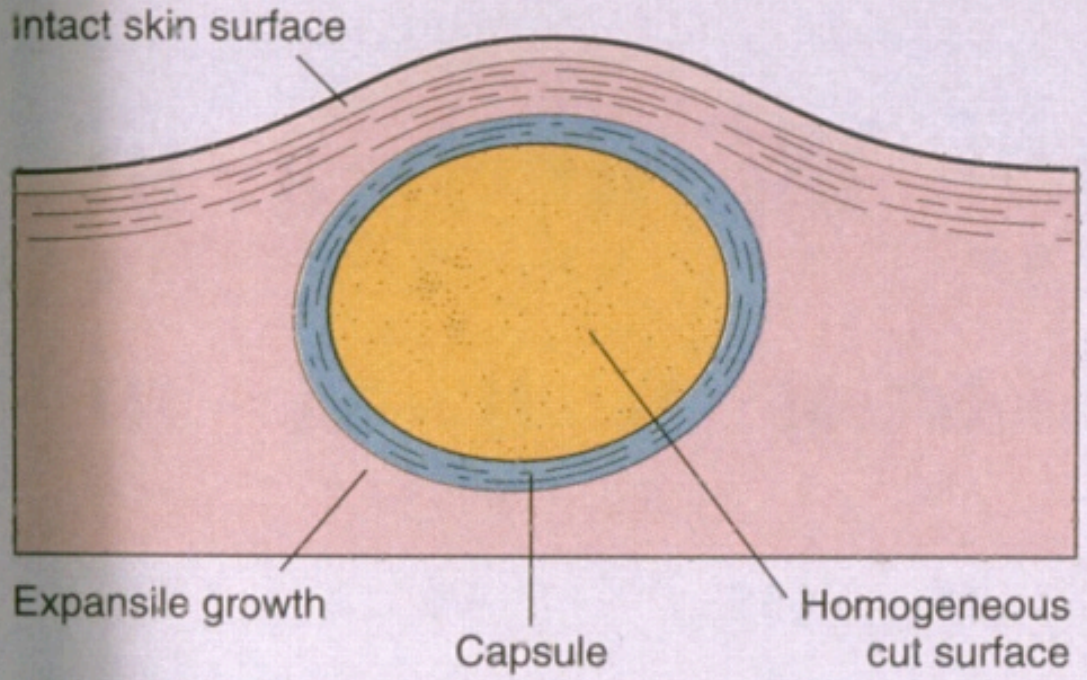
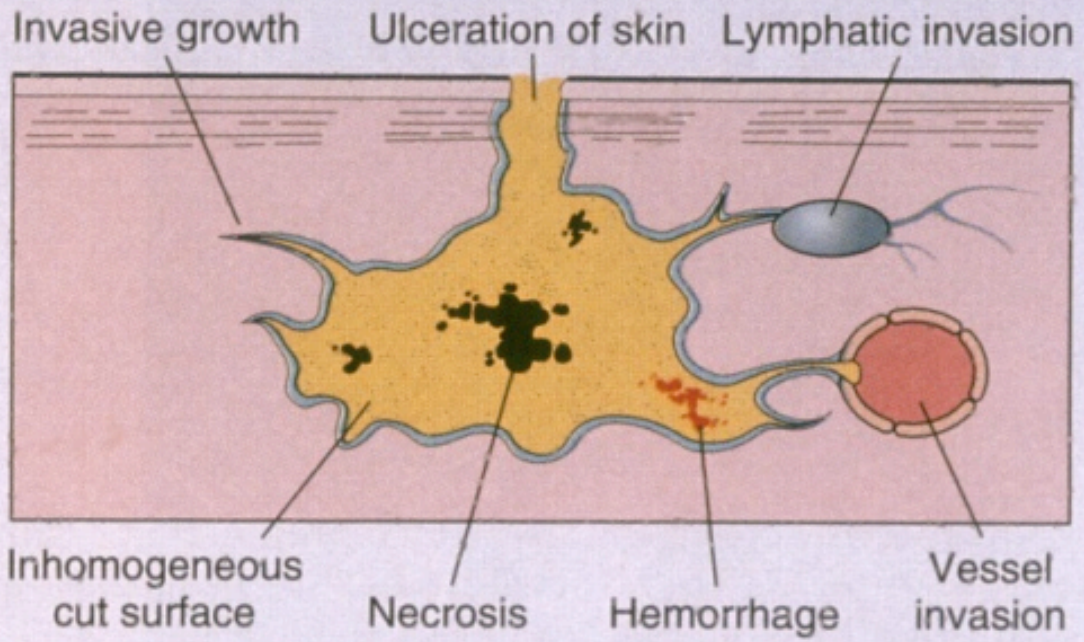


FIGURE 4-1
Gross appearance of benign (A) and malignant (B) tumors.



A BENIGN TUMOR



B MALIGNANT TUMOR

Modes of tumour spread -Metastasis

- Def: Spreading of tumor to sites that are physically discontinuous with the primary tumor
- Metastasis is a complex and unpredictable process that involves many factors relating to both invader and host.
- Metastatic spread strongly reduces the possibility of cure, hence, short of prevention of cancer.
- Cancers cells able to penetrate blood vessels, lymphatics, and body cavities

Modes of tumour spread -Metastasis

- All malignant tumors can metastasize, but some infrequently mets, eg: gliomas and basal cell carcinoma (BCC).

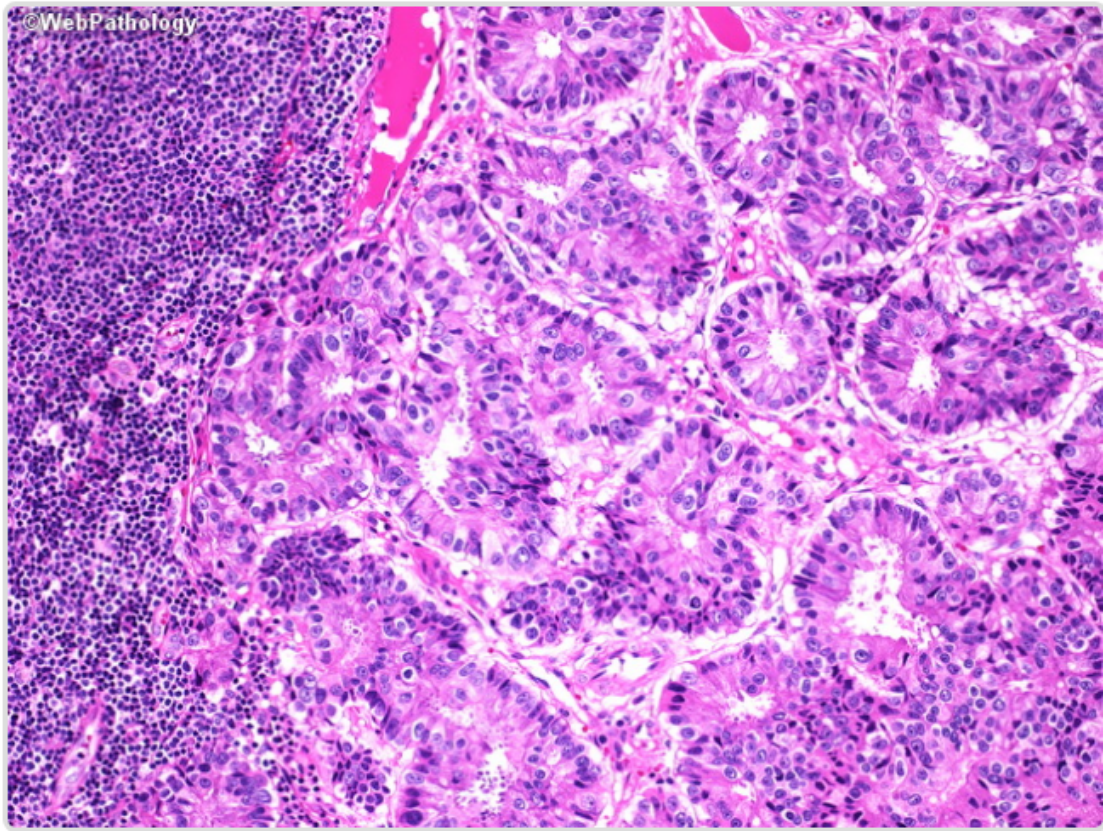
- Three ways tumors metastasize
  1. Direct seeding of body cavities or surfaces
  2. Lymphatic spread
  3. Hematogenous spread

Metastasis- 1. Direct seeding of body cavities or surfaces

- Malignant neoplasm penetrates into a natural "open field" lacking physical barriers→peritoneal cavity, pleural, pericardial, subarachnoid, and joint spaces.
- Ovarian carcinoma spread to peritoneal surfaces
- Appendiceal carcinomas or ovarian carcinomas fill the peritoneal cavity with mucus-secreting OR forming gelatinous mass known as pseudomyxoma peritonei

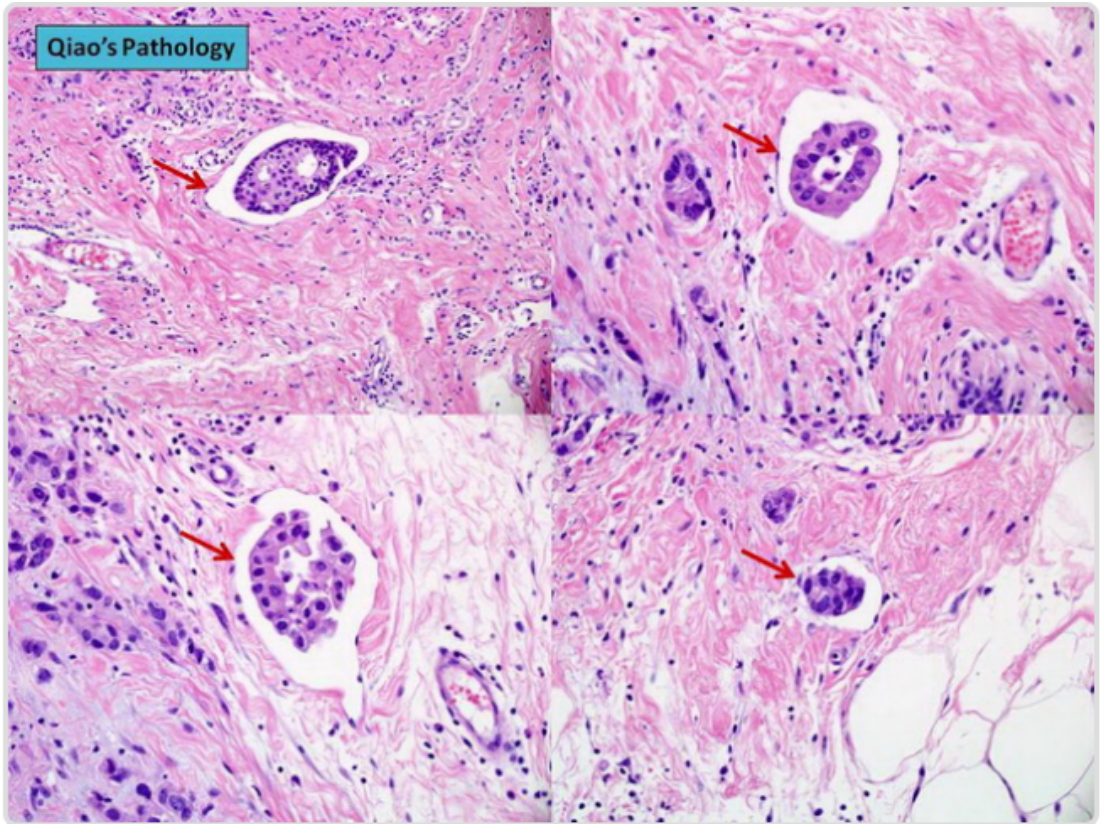
Metastasis-2.Lymphatic Spread

- Typical for carcinomas but also seen for sarcomas.
- Tumour cells spread to lymphatic vessels located at the margins of invading cancers
- The pattern of spread follows the natural routes of lymphatic drainage.
- Breast ca located at UOQ→ disseminate first to the axillary lymph nodes →infraclavicular and supraclavicular lymph nodes.

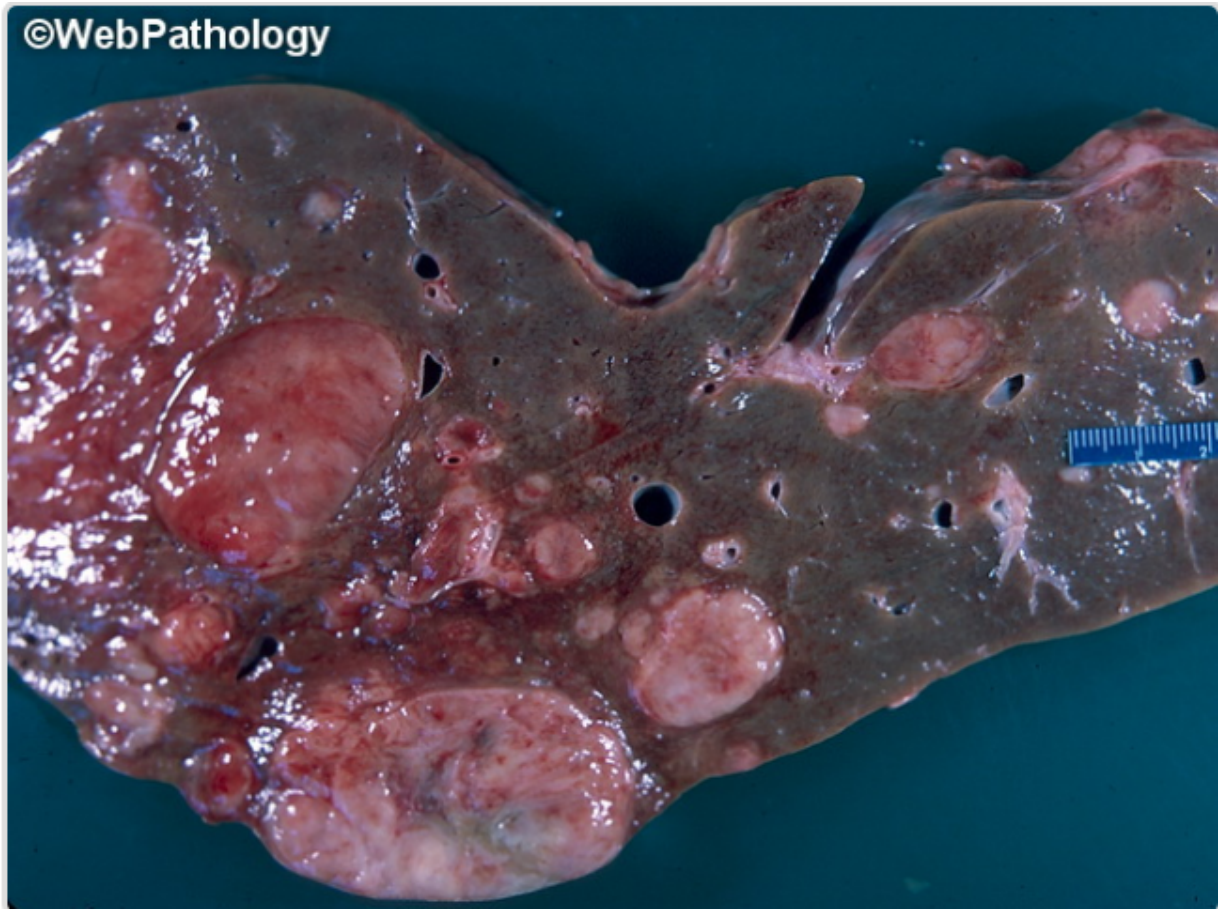


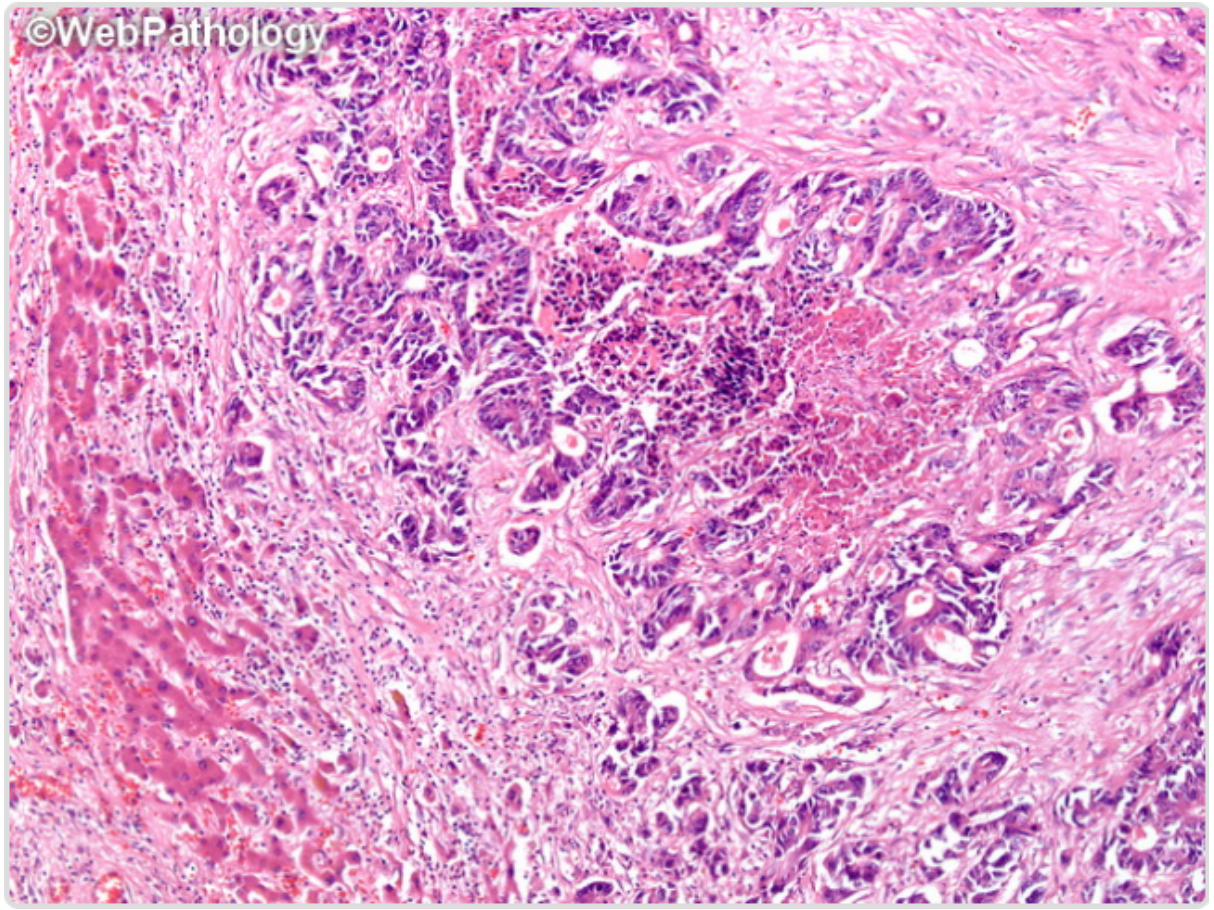
Metastasis-3. Hematogenous Spread

- Typical of sarcomas but is also seen with carcinomas.
- The malignant cells penetrate the small vessels (vein or arteries) at the site of the primary neoplasm.
- Cancers that have propensity growth within the large veins:
  - RCC -renal vein branches→ renal vein→IVC→ right side of heart.
- Liver and the lungs are most frequently involved by hematogenous dissemination.
  - All portal area drainage flows to the liver.
  - All caval blood flows to the lungs.



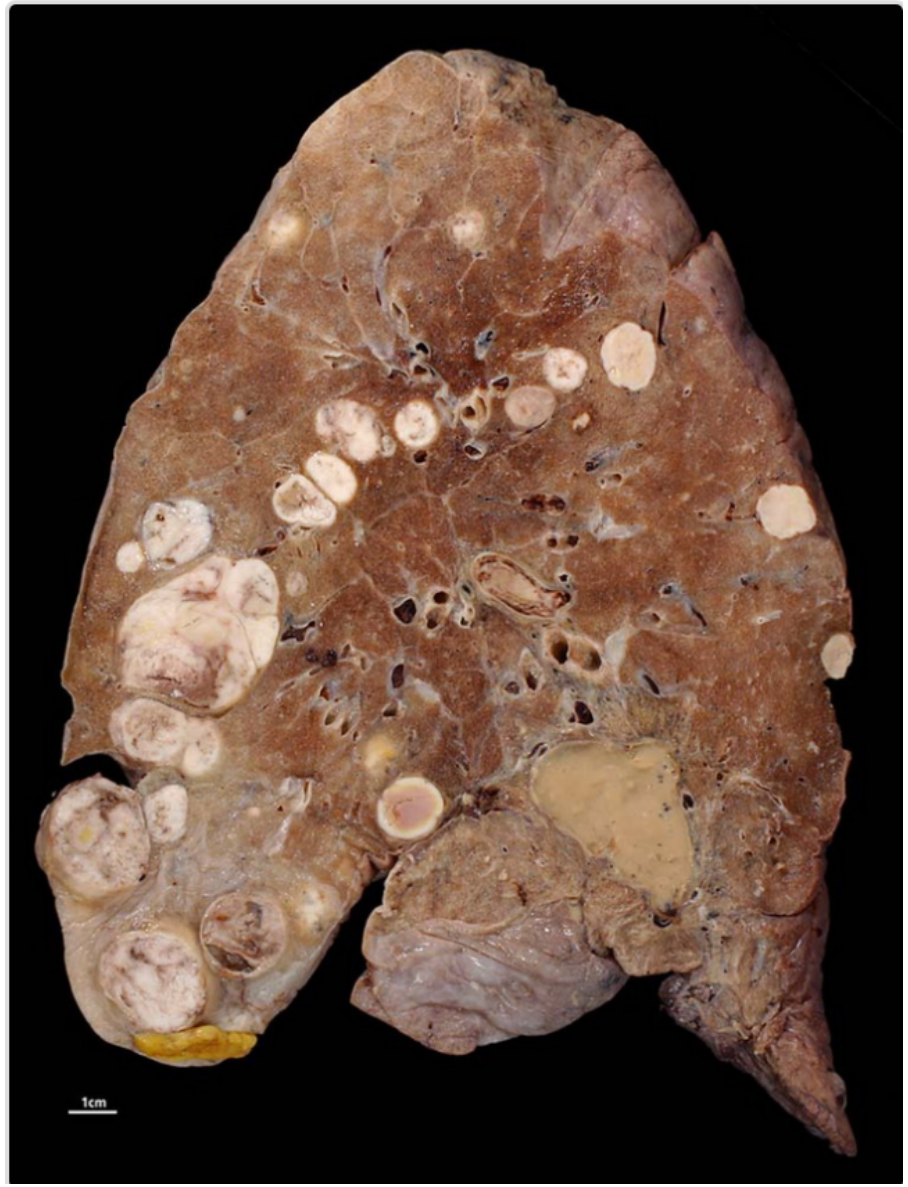
Metastasis to liver

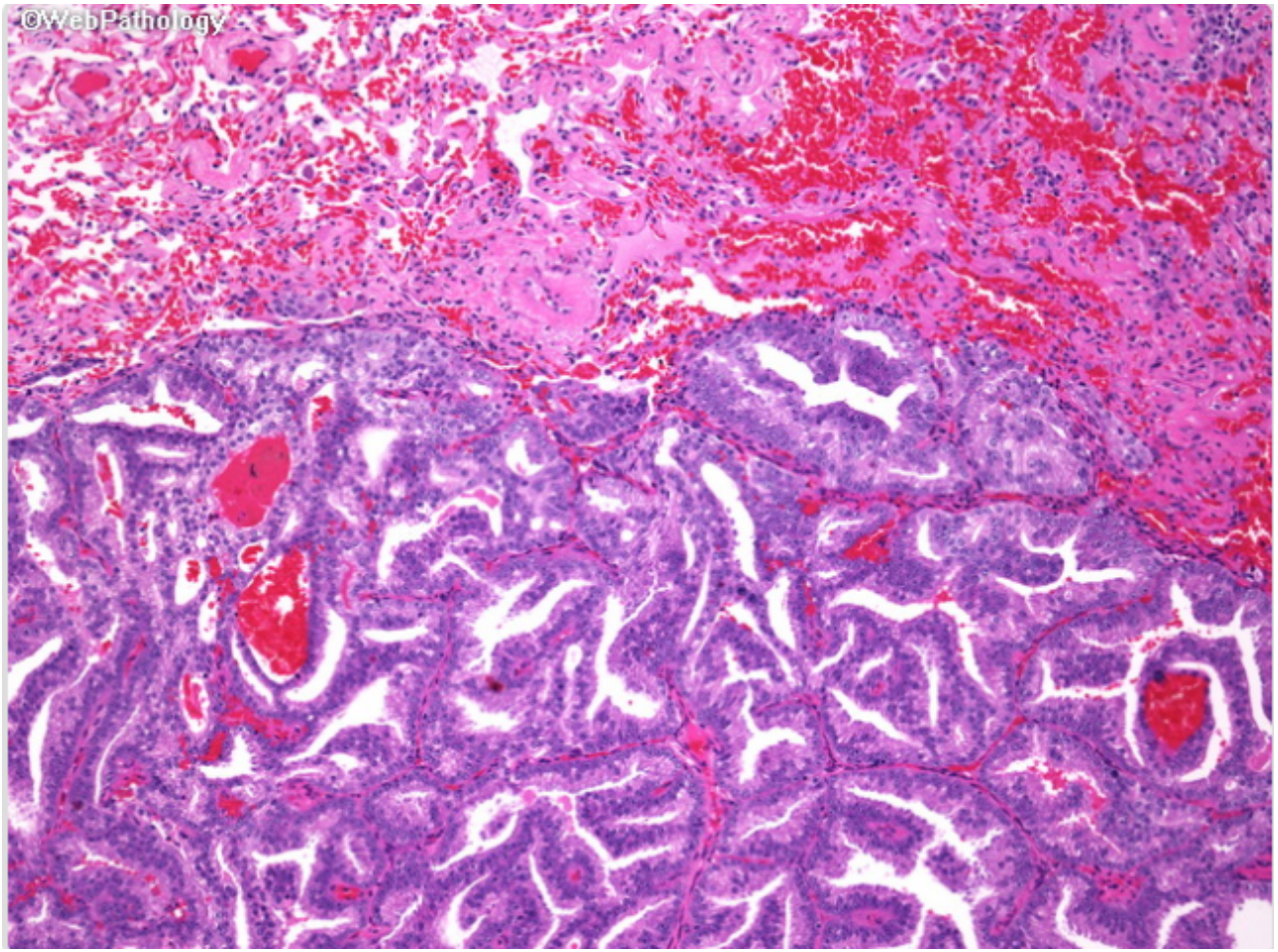




Metastatic colorectal adenocarcinoma

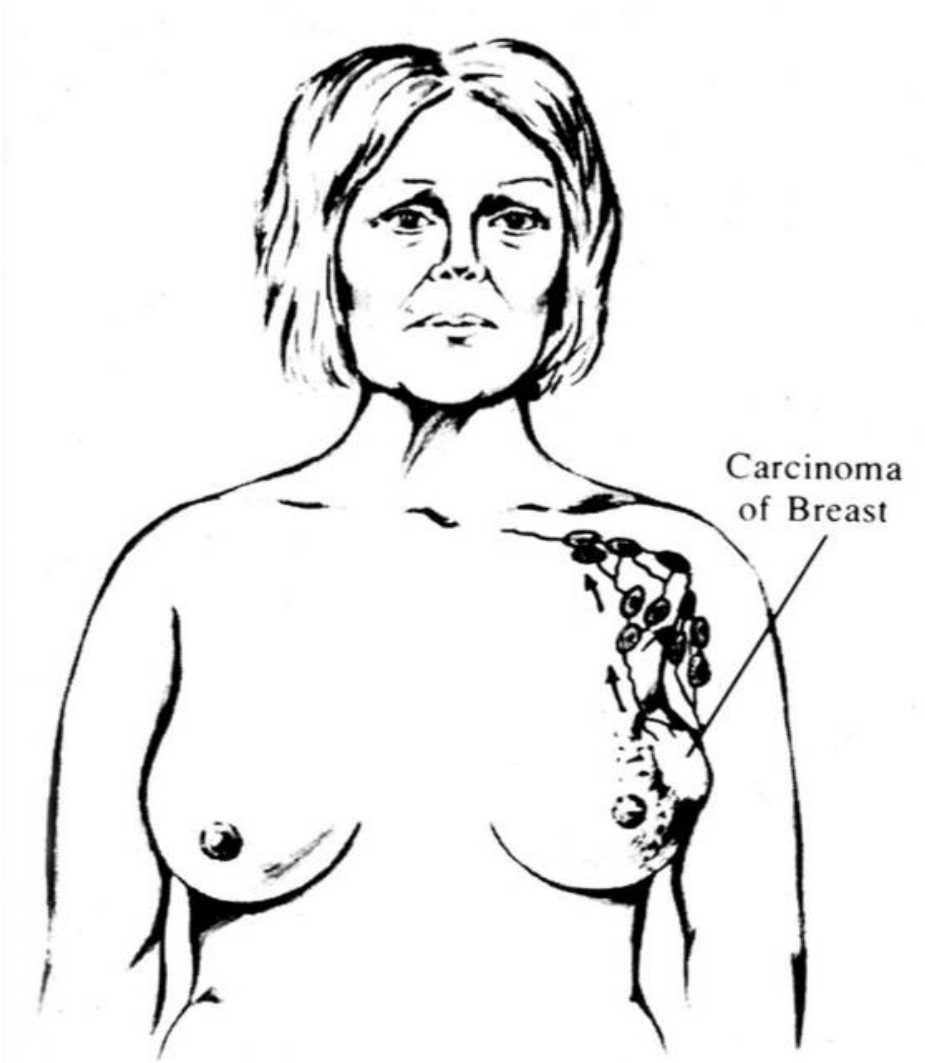
Metastasis to lung





Metastatic prostatic carcinoma

Metastasis (Lymphatic spread)



Metastasis (Hematogenous spread)

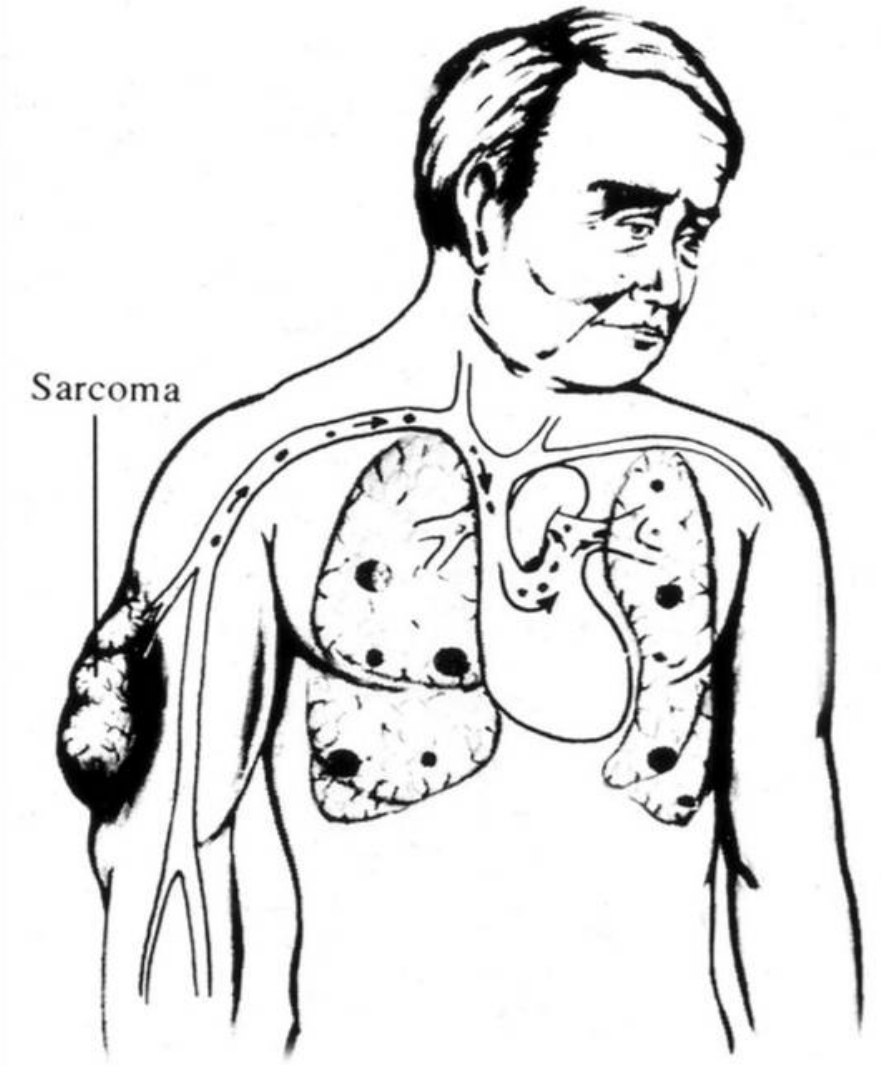


Table 7-2 Comparisons Between Benign and Malignant Tumors

Characteristics	Benign	Malignant
Differentiation/ anaplasia	Well differentiated; structure sometimes typical of tissue of origin	Some lack of differentiation (anaplasia); structure often atypical
Rate of growth	Usually progressive and slow; may come to a standstill or regress; mitotic figures rare and normal	Erratic, may be slow to rapid; mitotic figures may be numerous and abnormal
Local invasion	Usually cohesive, expansile, well-demarcated masses that do not invade or infiltrate surrounding normal tissues	Locally invasive, infiltrating surrounding tissue; sometimes may be misleadingly cohesive and expansile
Metastasis	Absent	Frequent; more likely with large undifferentiated primary tumors

Benign		Malignant (cancer)
• Gross & microscopic appearances are relatively innocent • Remains localized, do not invade • Generally do not spreads	**Appearance/ behavior**	• Gross and microscopic appearance more abnormal • Locally invades organ, adjacent structure • Metastasize
Amendable to local surgical removal	**Treatment**	• Surgical resection, chemotherapy or radiation
Generally patient survives	**Prognosis/ outcome**	• Able to cause death from local or distant spread, cancer cachexia (progressive loss of fat body mass due to proteolysis induce factor)

Grading and Staging of Tumors

Grade

- The **degree of abnormality** of tumour cells base on **morphology /microscopic** findings
- E.g nuclear pleomorphism, mitotic count, tumour pattern /degree differentiation
  - Well: grade 1
  - Moderately: grade 2
  - Poorly: grade 3

Stage

- A proses of determining the **EXTENT of tumour** within the body
- American Joint Committee (AJC) on Cancer Staging (pTNM):
  - "T" stage: Tumor size, degree of penetration of surrounding tissue.
  - "N" : Presence of lymph node involvement .
  - "M“: The existence of metastases

Epidemiology

Epidemiology

- Greek words (**epi-**on or upon), (**demos-**people), **logos** (the study of…)
- Epidemiology is the **study** of the **distribution (frequency)** and **determinants** of **health-related states or events** in **specified populations.**
- Cancer epidemiology study, is used to determine :
  - **Incidence:** frequency new cases of cancer diagnosed in a year
  - **Prevalence**: existing cases of cancer
  - **Mortality:** deaths due to cancer.
  - **Morbidity**: Diseased condition or state.

Cancer incidence and mortality

Numbers at a glance

Total population

7 794 798 844

Number of new cases

19 292 789

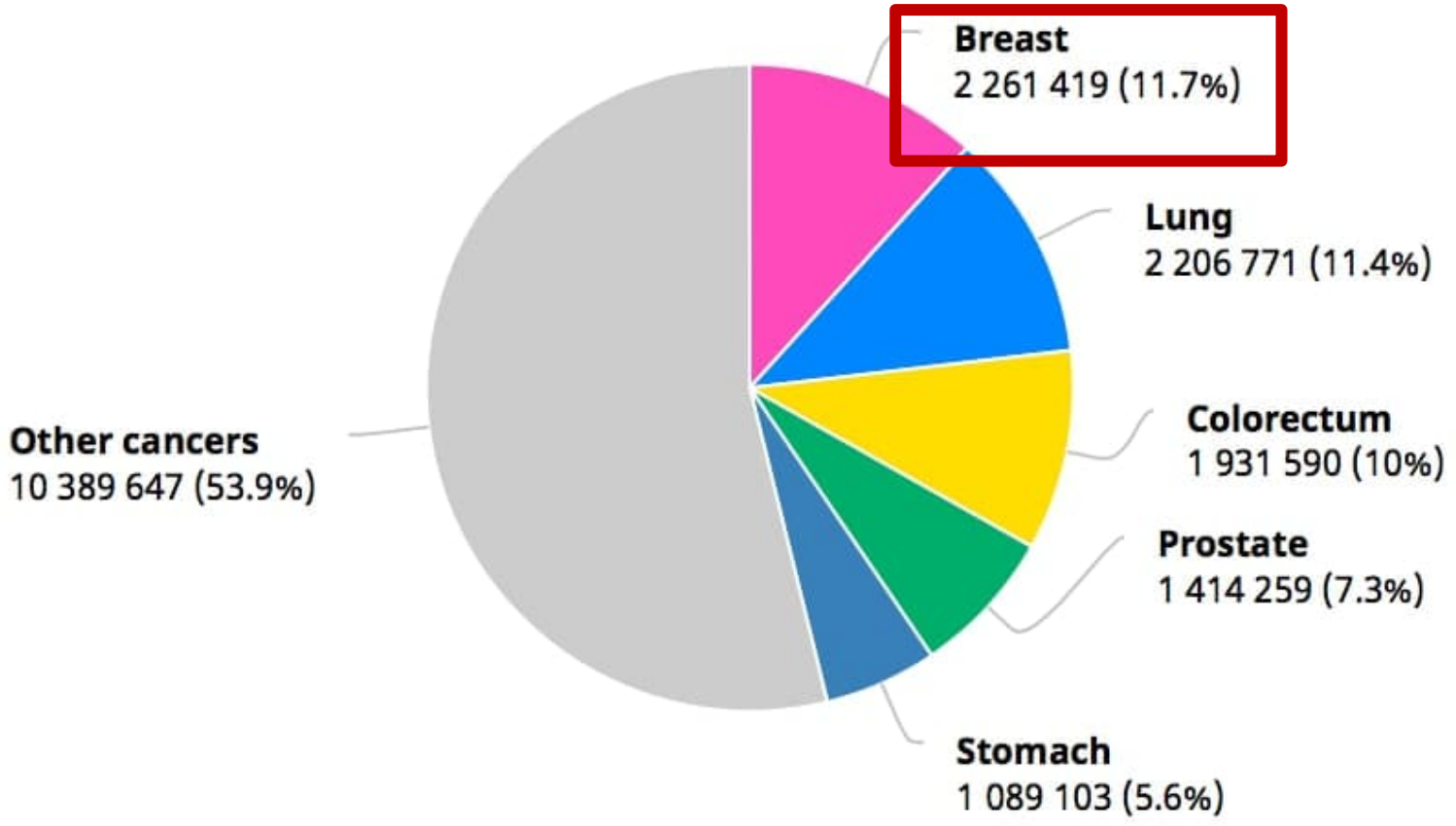
Number of deaths

9 958 133

Number of prevalent cases (5-year)

50 550 287

Number of new cases in 2020, both sexes, all ages



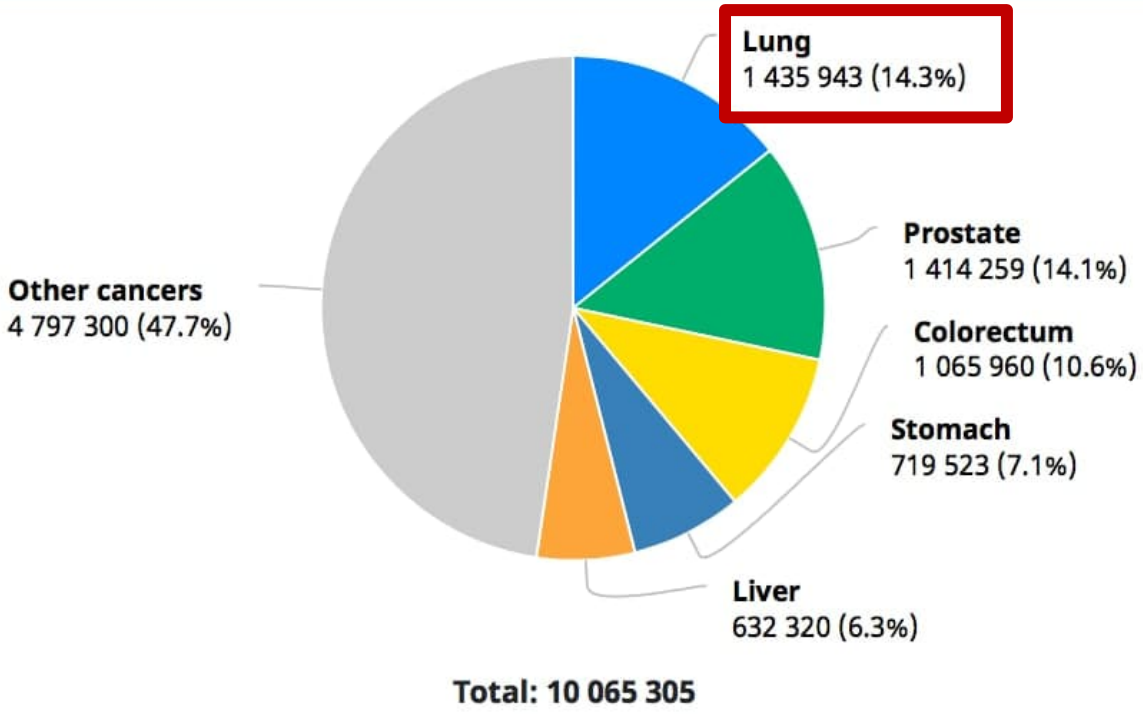
International Agency for Research on Cancer
World Health Organization

GLOBAL CANCER OBSERVATORY

Cancer incidence and mortality

Males

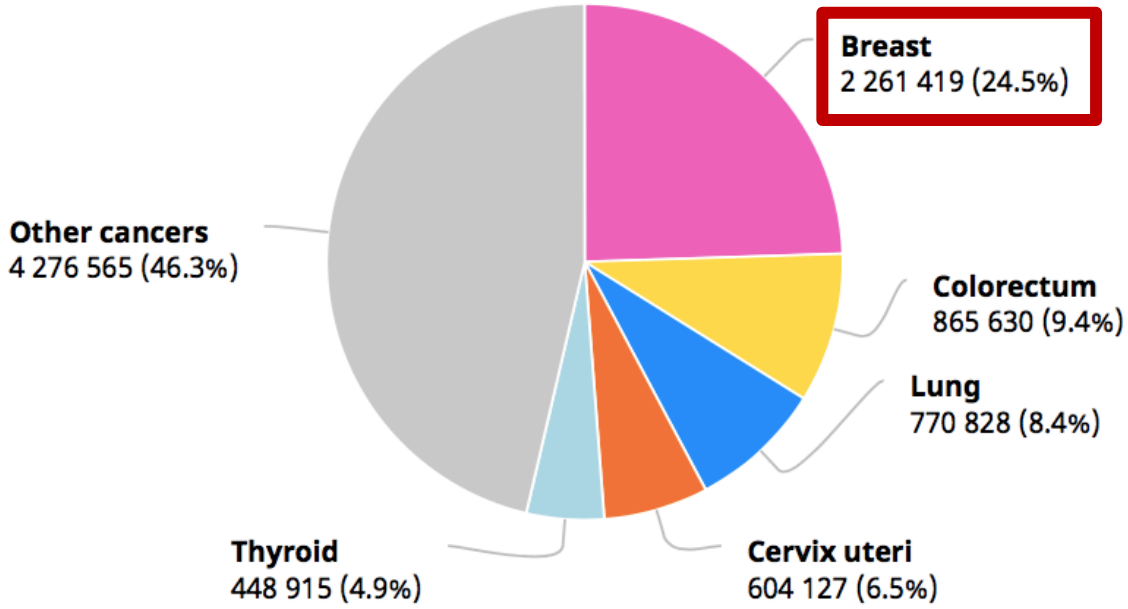
Number of new cases in 2020, males, all ages



Total: 10 065 305

Females

Number of new cases in 2020, females, all ages



Total: 9 227 484

International Agency for Research on Cancer
World Health Organization

GLOBAL CANCER OBSERVATORY

Epidemiology - Malaysia National Cancer Registry Report 2012-2016

A total of **115,238 new cancer cases** were diagnosed in Malaysia for the period of 2012-2016.

Table 7. Ten most common cancers by sex, all residents, Malaysia, 2012-2016

ICD - 10	Sites	No.	%	CR	ASR
Male					
C18-21	Colorectal	8,701	16.9	12.7	14.8
C33-34	Trachea, bronchus and lung	7,686	14.9	11.3	13.2
C61	Prostate	4,189	8.1	6.1	7.7
C81-85,C96	Lymphoma	3,412	6.6	5.0	5.3
C11	Nasopharynx	3,359	6.5	4.9	5.2
C22	Liver	2,949	5.7	4.3	4.9
C91-95	Leukaemia	2,414	4.7	3.5	3.8
C16	Stomach	1,818	3.5	2.7	3.1
C44	Other skin	1,797	3.5	2.6	3.1
C67	Bladder	1,715	3.3	2.5	3.0
	Others	13,465	26.1		
	Total	**51,505**	**100.0**	**75.4**	**86.1**

Table 7. Ten most common cancers by sex, all residents, Malaysia, 2012-2016

ICD - 10	Sites	No.	%	CR	ASR
Female					
C50	Breast	21,634	33.9	32.5	34.1
C18-21	Colorectal	6,814	10.7	10.3	11.1
C53	Cervix uteri	3,981	6.2	6.0	6.2
C56	Ovary	3,575	5.6	5.4	5.6
C33-34	Trachea, bronchus and lung	3,570	5.6	5.4	5.9
C54	Corpus uteri	2,898	4.5	4.4	4.6
C81-85,C96	Lymphoma	2,418	3.8	3.6	3.8
C73	Thyroid	2,137	3.4	3.2	3.2
C91-95	Leukaemia	1,859	2.9	2.8	3.0
C44	Other skin	1,395	2.2	2.1	2.3
	Others	13,452	21.1		
	Total	**63,733**	**100.0**	**95.8**	**101.6**

Risk factors

- **Geographic factors:** Death rate of cancer stomach in Japan > US
- **Age**-Most carcinomas occur in adults older than 55 years of age.
- **Environmental factors:**
  - Cigarette smoking -Ca Lung, Ca of mouth, pharynx
  - Alcohol-Ca esophagus, Ca liver
  - Reproductive history- Ca cervix (a/w multiple partner, age at 1st intercourse, HPV infection

- **Occupational factors:**
  - Arsenic-skin hemangiosarcoma
  - Asbestosis-lung mesothelioma
  - Benzene (paints)-leukemia, Hodgkin lymphoma
  - Nickel (welding)- Ca nose, Ca lung

- **Genetic predisposition of cancer**
  - Autosomal dominant inherited cancer (single inherited mutation of tumour suppressor genes)
    - *RB* - retinoblastoma
    - *P53*- Li- Fraumeni syndrome
    - *APC*- Familial adenomatous polyposis, colon cancer
    - *BRACA1,BRACA2* –Breast & ovarian tumours
  - Autosomal recessive inherited cancer (2 copies of mutated genes)
    - Xeroderma pigmentosum
    - Ataxia-telangietasia
    - Fanconi anemia

- **Acquired predisposing conditions-**
  - Cancers a/w chronic inflammatory: silica/smoking→ lung Ca
  - Cancers a/w infectious agents: HepatitisB/C→Hepatocellular carcinoma
  - Precursor lesions: endometrial hyperplasia → Endometrioid carcinoma
  - Immune deficiency states: T-cell immunity deficits→ susceptible to oncogenic viruses → lymphomas, certain carcinomas

Reference

- Robbins and Cotran, Pathologic Basic of Disease,9th & 10th Edition.
- Web pathology

Epidemiology, Nomenclature & Characteristic of Tumour

Tue 11 Jan 2022 2:30PM - 3:30PM

Student password: oqklhm