



# NOVA

Charting New Horizons in Education

Introduction to Neoplasia I

# 16

Pathology



# VA Introduction from robbins



- **Cancer's Impact:**

- ✓ Cancer is the second leading cause of death in the United States, after cardiovascular diseases.
- ✓ Cancer is not a single disease but a group of diseases with similar characteristics, including abnormal cell growth.
- ✓ Some cancers are curable, while others are almost always fatal.

- **Fundamental Features of All Cancers:**

- Cancer as a Genetic Disorder: Cancer is caused by DNA mutations, which can occur due to exposure to mutagens, errors in cell processes, or inheritance.
- Cancers often show epigenetic alterations, such as changes in DNA methylation and histone modification.
- These genetic and epigenetic changes affect genes regulating growth, survival, and senescence.

# Introduction from Robbins



- **Heritability and Selection of Genetic Alterations:**

- ✓ Mutations in cancer cells are heritable and passed on during cell division.
- ✓ Cancer cells with mutations that give them a growth or survival advantage outcompete surrounding cells, dominating the tumor population.
- ✓ Tumors are clonal (originating from a single cell) at initiation, but they evolve as genetically distinct subclones with more aggressive traits (tumor progression).

- **Cancer Hallmarks:**

- ✓ Mutations and epigenetic changes provide cancer cells with a set of properties known as cancer hallmarks.
- ✓ These hallmarks influence the cancer's natural progression and response to therapies.

# ❖ Nomenclature



- Neoplasia means “new growth,” and a new growth is called a neoplasm.
- Tumor originally applied to the swelling caused by inflammation
- Oncology (Greek oncos = tumor) is the study of tumors or neoplasms.
- Although all physicians know what they mean when they use the term neoplasm, British oncologist Willis came closest: “A neoplasam is 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.”

# Composition



- **All tumors have two main components:**
  1. **Neoplastic Cells:** These form the tumor parenchyma (the functional tissue of the tumor).
  2. **Reactive Stroma:** Made up of connective tissue, blood vessels, and immune system cells (both adaptive and innate).
- **Tumor Classification and Behavior:**
  - ✓ Tumors are classified and their biological behavior is determined primarily by the parenchymal component (neoplastic cells).
  - ✓ However, the growth and spread of tumors heavily depend on their stroma (the supportive tissue).

# Composition

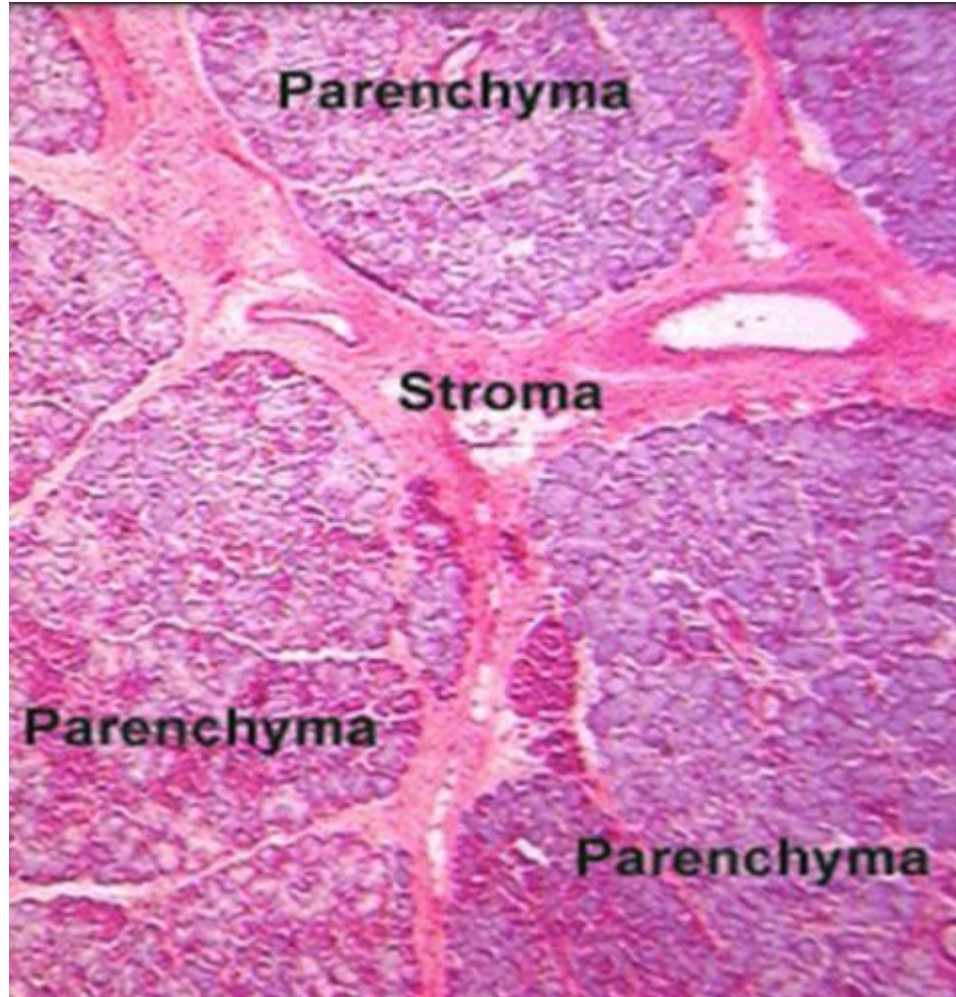


- **Variations in Tumor Stroma:**

- ✓ In some tumors, there is little connective tissue (scant), making the tumor soft and fleshy.
- ✓ In other tumors, neoplastic cells stimulate the formation of abundant collagenous stroma, a process called **desmoplasia**.
- ✓ Some desmoplastic tumors, such as certain cancers of the female breast, can become very hard or **scirrhous (stony hard)**.

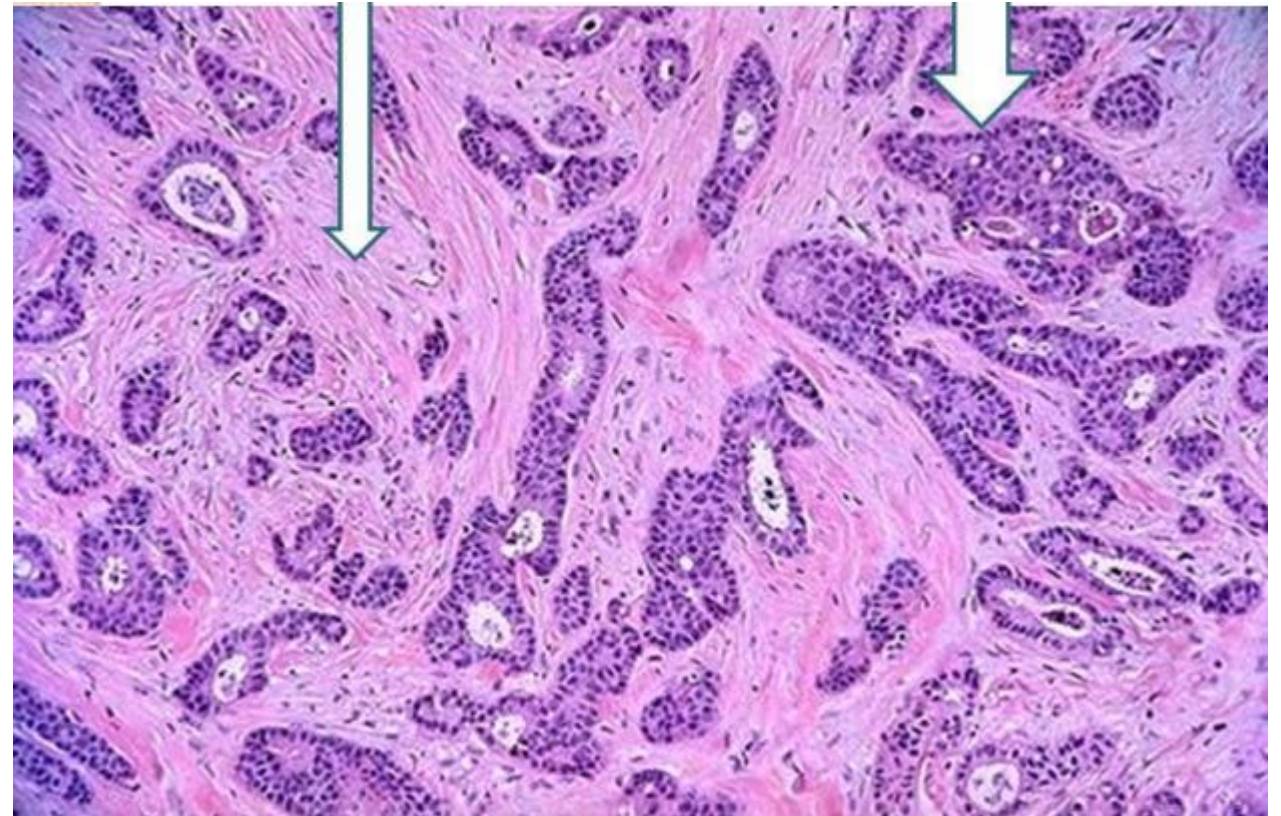


# Composition



stroma

Parenchyma



# ❖ Benign



1. Benign tumors stay localized at their site of origin.
2. They are typically amenable to surgical removal.
3. Patients generally survive after treatment.
4. Exceptions occur when benign tumors are located in critical areas, such as the brain, where they can cause significant morbidity and may be fatal.

❖ **Naming Benign Tumors of Mesenchymal Cells:** Naming is relatively simple: the suffix “-oma” is added to the cell type from which the tumor arises.

- ✓ Example: A benign tumor of fibroblast-like cells is called fibroma.
- ✓ Example: A benign cartilaginous tumor is called chondroma.



# ❖ Benign



❖ **Naming Benign Epithelial Tumors:** The naming of benign epithelial tumors is more complex, based on:

1. The cell of origin.
  2. The microscopic appearance.
  3. The macroscopic architecture.
- ✓ Adenomas: Benign epithelial tumors derived from glandular tissues, even if the tumor cells don't form glandular structures.
1. Example: A benign tumor from renal tubular cells forming tightly clustered glands or a mass of adrenal cortical cells growing as a solid sheet is called adenoma.

# ❖ Benign



## ❖ Other Types of Benign Epithelial Tumors:

- ✓ **Papillomas:** Benign tumors producing fingerlike or warty projections from epithelial surfaces.
- ✓ **Cystadenomas:** Benign tumors forming large cystic masses, such as those in the ovary.
- ✓ **Papillary Cystadenomas:** Tumors producing papillary projections that protrude into cystic spaces.
- ✓ **Polyps:** A polyp is a visible projection above a mucosal surface (e.g., in the gastric or colonic lumen), If the polyp contains glandular tissue, it is referred to as an adenomatous polyp.
- ✓ POLYPS → When a neoplasm—benign or malignant— produces a macroscopically visible projection above a mucosal surface and projects, for example, into the gastric or colonic lumen, it is termed a polyp.
- ✓ If the polyp has glandular tissue, it is called an adenomatous polyp

# va Benign

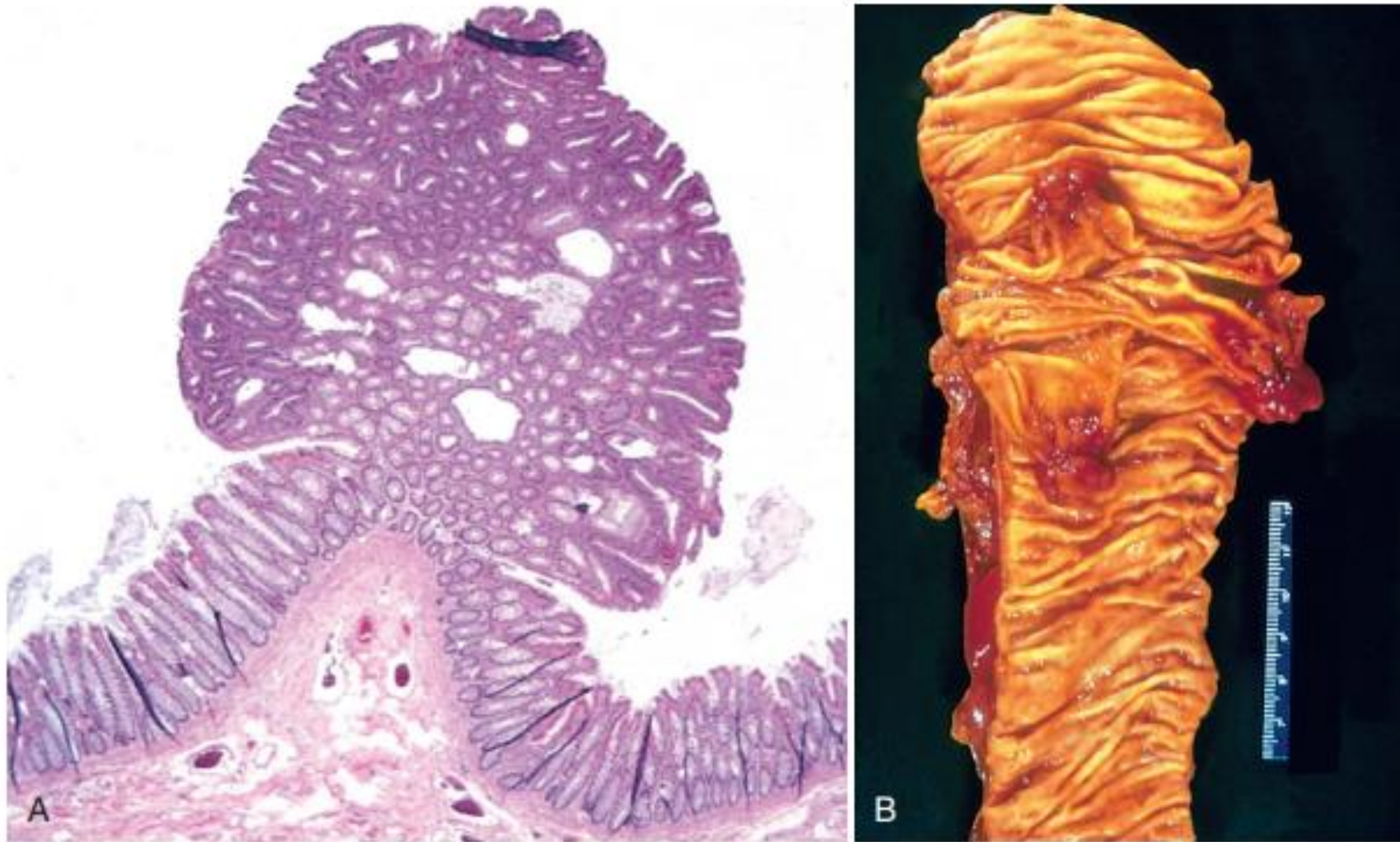
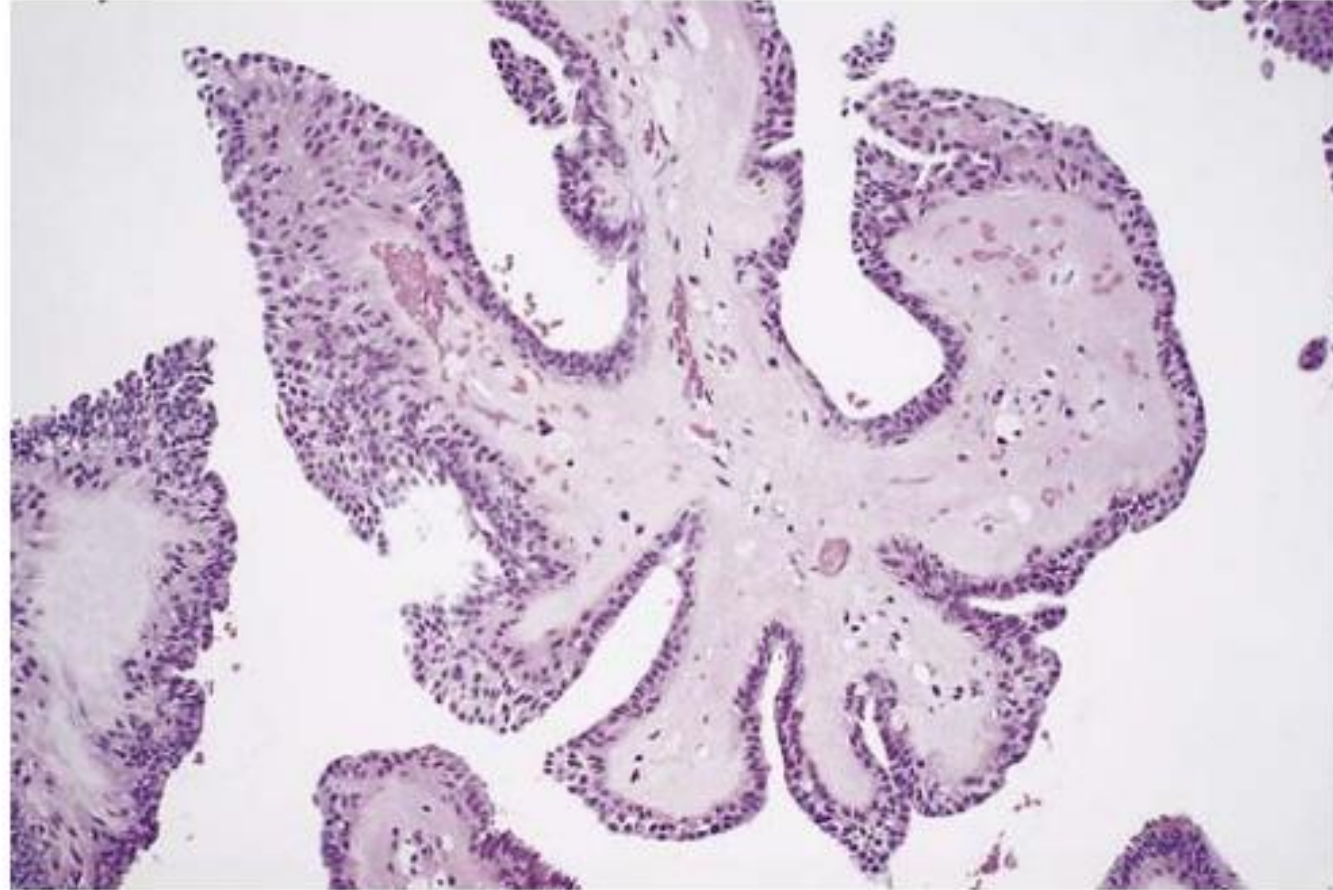


Figure 7.1 Colonic polyp. (A) An adenomatous (glandular) polyp is projecting into the colonic lumen and is attached to the mucosa by a distinct stalk. (B) Gross appearance of several colonic polyps.

# va Benign



**eFIG. 6.1** Intraductal papilloma of breast. The papillary fronds have a fibrovascular core and are lined by epithelium. (From Fletcher CD: *Diagnostic Histopathology of Tumors*, ed 5, Philadelphia, 2021, Elsevier, Fig. 16.24.)

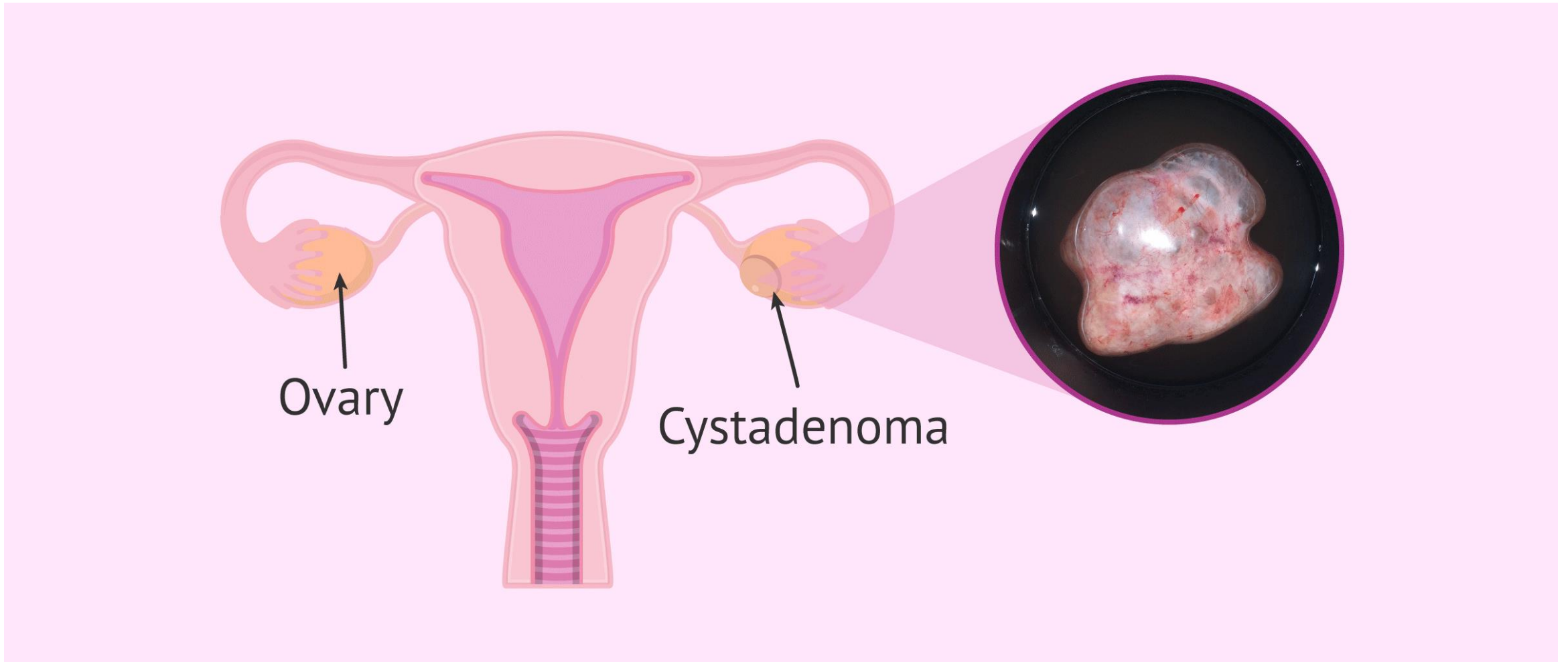


# va Benign



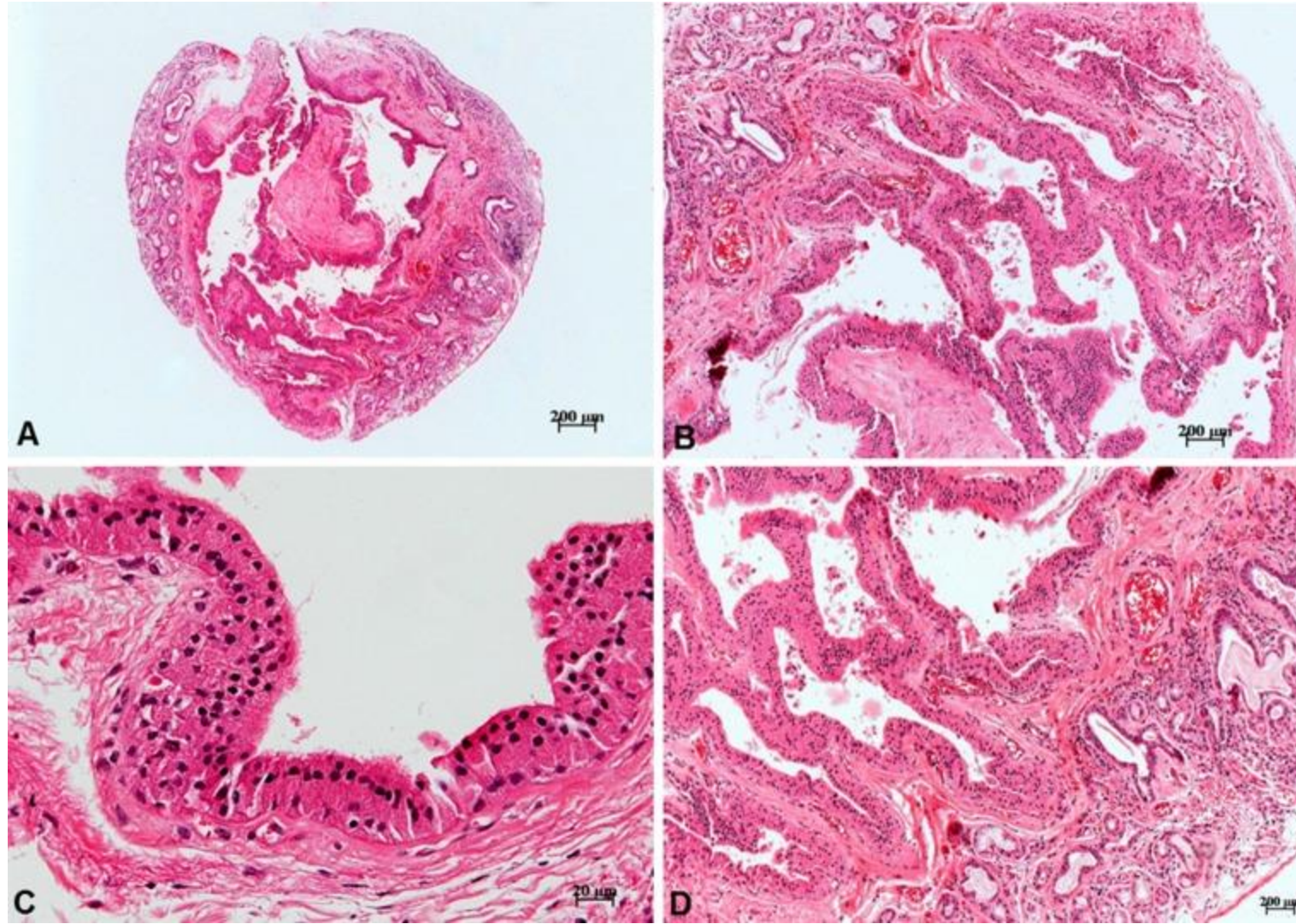
HEPATIC  
ADENOMA

# Benign





# va Benign



a Low magnification showing cystic spaces with papillary projections

# Benign



→ wart



Papilloma

# ❖ Malignant



1. Malignant tumors can invade and destroy adjacent structures.
  2. They have the ability to spread to distant sites (metastasize).
  3. Malignant tumors are collectively referred to as cancers.
  4. The term comes from the Latin word for crab, due to their tendency to adhere to and seize any part in an obstinate manner.
  5. Not all cancers are deadly; some are discovered at early stages and can be treated through surgical excision or systemic drugs/therapeutic antibodies.
  6. Despite potential treatment, the designation “malignant” always signals a serious concern (Red flag).
- Nomenclature of Malignant Tumors: The naming system for malignant tumors is similar to that of benign neoplasms, with specific additions.

# ❖ Malignant



- ❖ **Malignant Tumors in Mesenchymal Tissues:** Malignant tumors arising in solid mesenchymal tissues (connective tissues) are called **sarcomas** (Greek "sar" meaning fleshy).
  - ✓ Examples: fibrosarcoma and chondrosarcoma.
  
- ❖ **Malignant Tumors in Blood-forming Cells:**
  - ✓ Tumors originating from blood-forming cells are called **leukemias** (literally "white blood") or **lymphomas** (tumors of lymphocytes or their precursors).
  
- ❖ **Malignant Tumors of Epithelial Cell Origin:** Malignant tumors arising from epithelial cells are called **carcinomas** → Carcinomas can be further classified:
  - ✓ Squamous cell carcinoma: Tumor cells resemble stratified squamous epithelium.
  - ✓ Adenocarcinoma: Neoplastic epithelial cells grow in a glandular pattern.

# ❖ Malignant



## ❖ Identification of Tissue or Organ of Origin:

- ✓ Sometimes, the tissue or organ of origin can be identified and added as a descriptor, such as:
  - ✓ Renal cell adenocarcinoma (kidney).
  - ✓ Bronchogenic squamous cell carcinoma (lung).

## ❖ Undifferentiated Malignant Tumors:

- ✓ In about 2% of cases, cancers are composed of cells of unknown origin and are classified as undifferentiated malignant tumors.

# VA Malignant



Malignant tumors arising in solid mesenchymal tissues are usually called *sarcomas* (Greek *sar* = fleshy; e.g., fibrosarcoma, chondrosarcoma, leiomyosarcoma, and rhabdomyosarcoma), whereas those arising from blood-forming cells are designated *leukemias* (literally, white blood) or *lymphomas* (tumors of lymphocytes or their precursors).



Malignant neoplasms of epithelial cell origin, derived from any of the three germ layers, are called *carcinomas*. Thus, cancers arising in the ectodermally derived epidermis, the mesodermally derived renal tubules, and the endodermally derived lining of the gastrointestinal tract are all termed carcinomas.

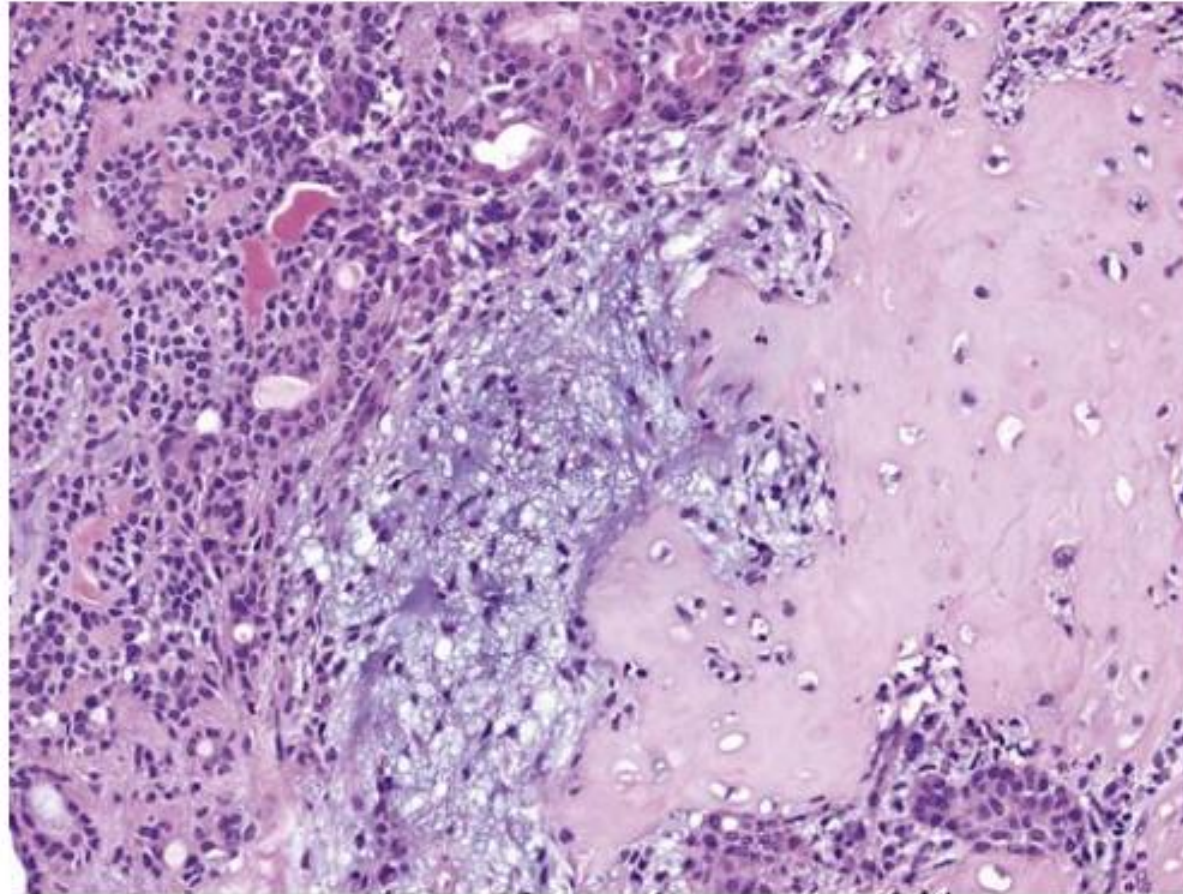


# Neoplasms



- **Neoplastic Cells Resemble Each Other:** Neoplastic cells in a tumor, whether benign or malignant, typically resemble each other because they originate from a single transformed progenitor cell.
- **Mixed Tumors:** In rare instances, tumor cells undergo divergent differentiation, leading to mixed tumors.
- Mixed tumors are clonal, meaning they arise from a single progenitor cell, but that progenitor cell has the ability to differentiate into more than one lineage → An example of a mixed tumor is a mixed tumor of the salivary gland, also called a pleomorphic adenoma → This benign tumor contains epithelial components dispersed throughout a fibromyxoid stroma, and sometimes includes islands of cartilage or bone.

# Neoplasms



**FIG. 6.2** Mixed tumor of the parotid gland. Areas containing nests of epithelial cells (on the left) and myxoid stroma forming cartilage and bone (an unusual feature, on the right) are present in this field. (From Fletcher CD: *Diagnostic Histopathology of Tumors*, ed 5, Philadelphia, 2021, Elsevier, Fig. 7.11.)

# Teratoma



- A teratoma is a special type of mixed tumor that contains recognizable mature or immature cells or tissues derived from more than one germ cell layer.
- Teratomas may contain elements from all three germ layers (ectoderm, mesoderm, and endoderm).
- **Origin of Teratomas:** Teratomas originate from totipotent germ cells, which normally reside in the ovary and testis, or may be found in midline embryonic rests.
- Germ cells have the capacity to differentiate into any of the cell types found in the adult body.
- **Composition of Teratomas:** Because germ cells can differentiate into a variety of cell types, teratomas can give rise to neoplasms containing elements such as bone, epithelium, muscle, fat, nerve, and other tissues, all mixed together in an unorganized fashion.

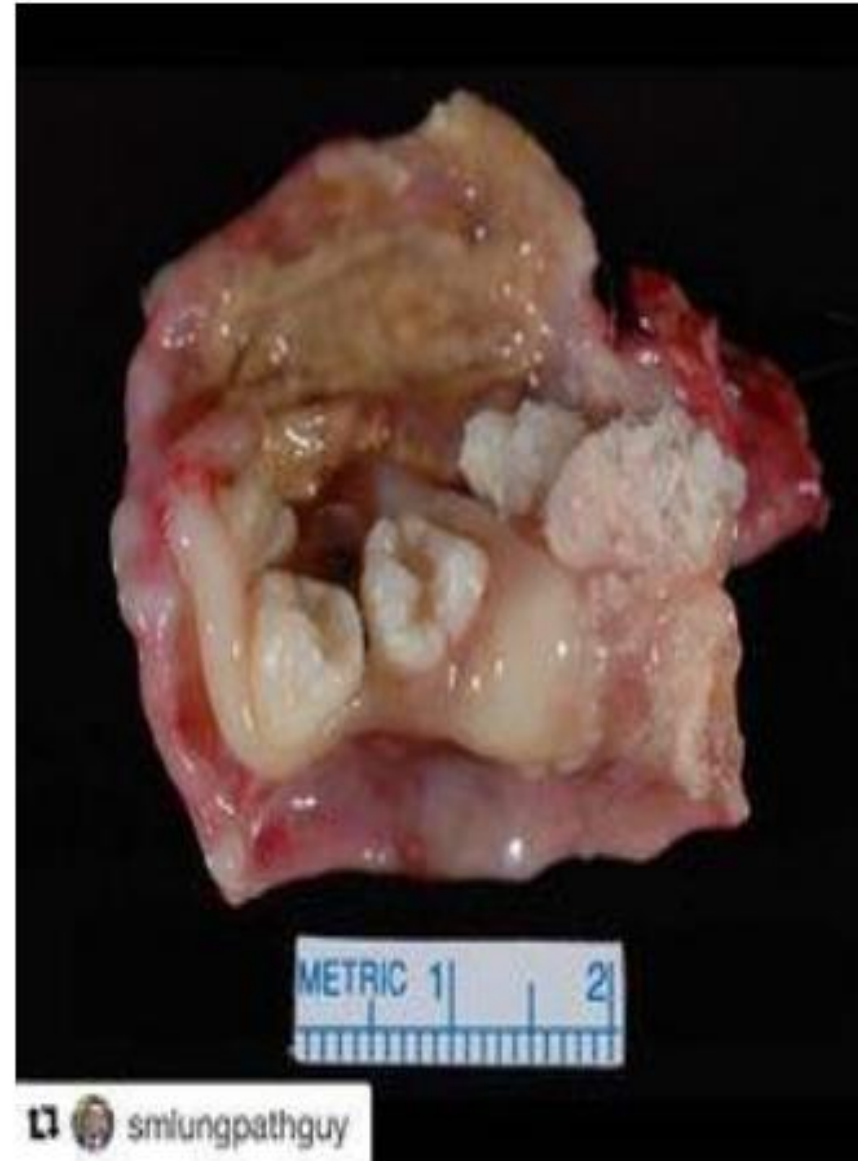
# Teratoma



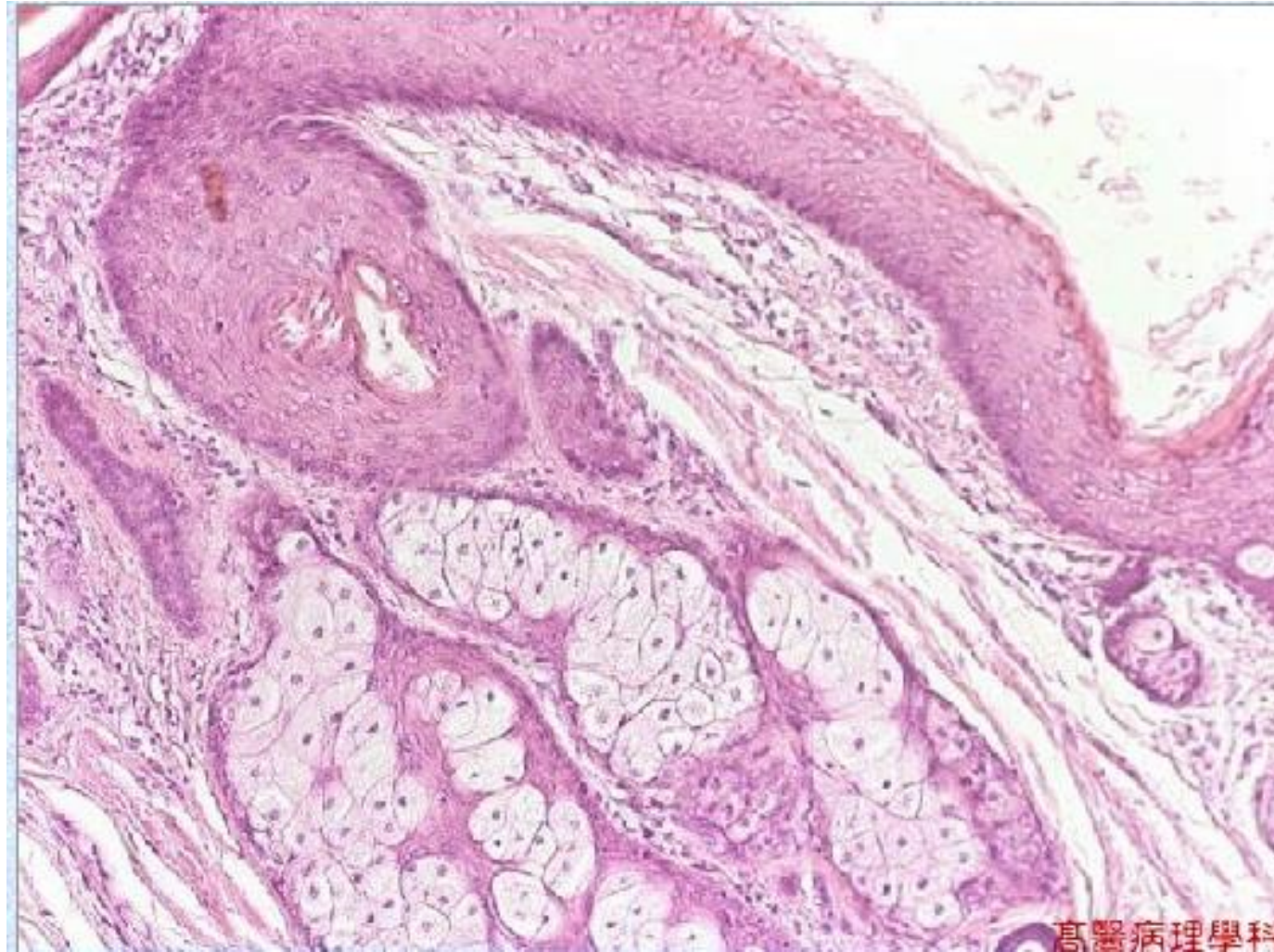
- The great majority of neoplasms, even mixed tumors, are composed of cells from a single germ layer.
- **An exception is a tumor called a teratoma**, which contains recognizable mature or immature cells or tissues belonging to more than one germ cell layer (and sometimes all three).
- Teratoma originates from germ cells that are normally present in the ovary and testis and sometimes also found in abnormal midline embryonic rests
- Such cells can differentiate into any of the cell types found in the adult body and so, may give rise to neoplasms that contain, in a **helter-skelter fashion**, bone, epithelium, muscle, fat, nerve, and other tissues.
- Common pattern is seen in the ovarian cystic teratoma (dermoid cyst), which create a cystic tumor lined by skin replete with hair, sebaceous glands, and tooth structures.



# va Teratoma



# va Teratoma



Mature skin with sebaceous glands and hair follicles.



# ❖ Misnomers



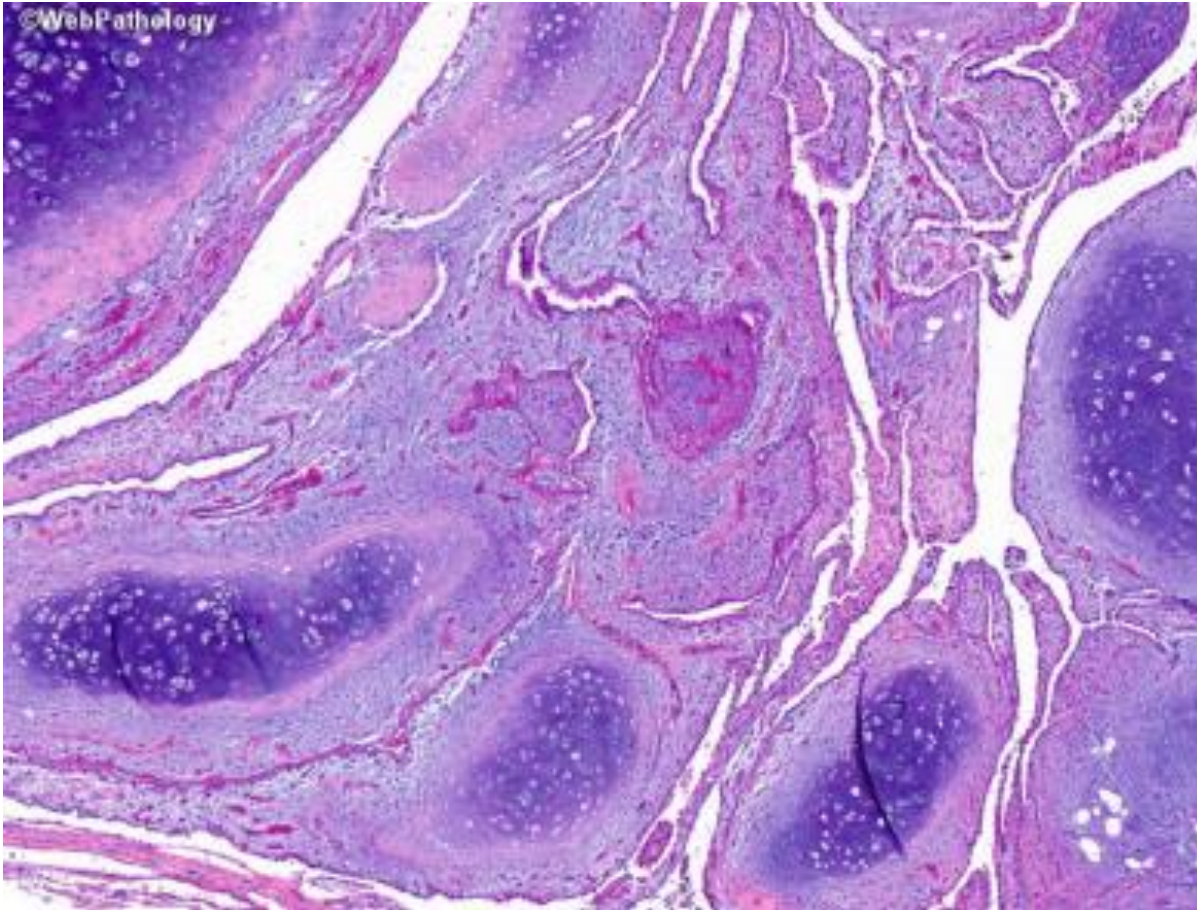
- There are some inappropriate usages. For instance, benign-sounding designations such as lymphoma, melanoma, mesothelioma, and seminoma are used for certain malignant neoplasms
- **Hamartoma** is a mass of disorganized tissue resembling the involved site, such as the lung or the liver.
- ✓ Although historically thought of as developmental malformations, hamartomas have clonal chromosomal aberrations that are acquired through somatic mutations and are best considered unusual benign neoplasms.
- **Choristoma** is a congenital anomaly consisting of a heterotopic nest of cells. For example, a small nodule of pancreatic tissue may be found in the submucosa of the stomach, duodenum, or small intestine → The designation -oma, connoting a neoplasm, gives these lesions an undeserved gravity, as they are usually trivial.

# VA Misnomers

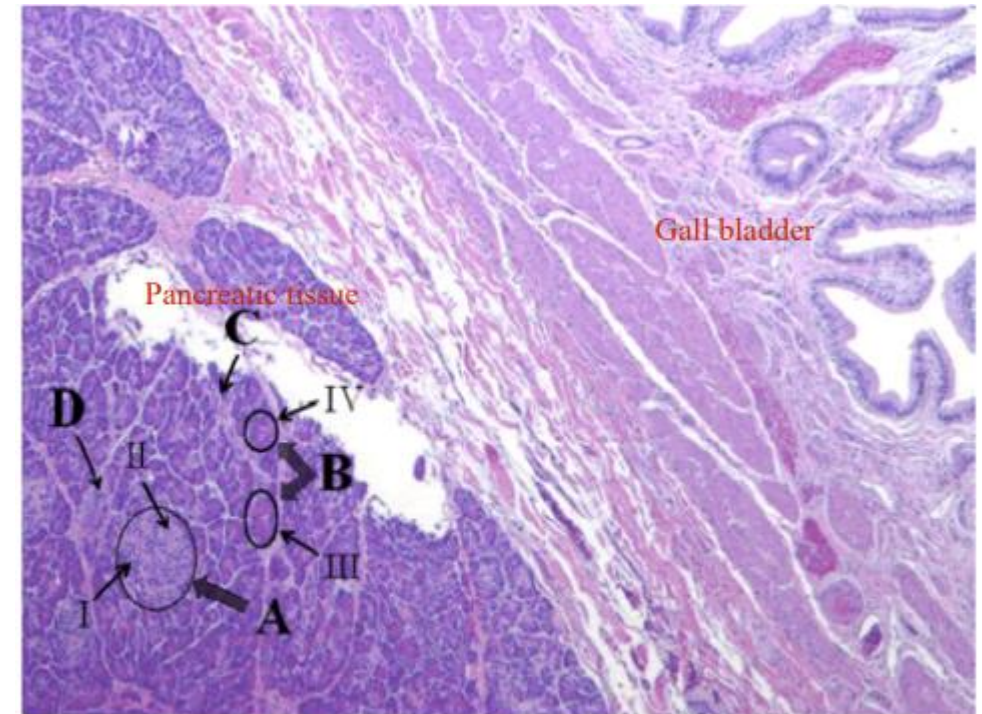


- **Hamartomas:** are disorganized but benign masses composed of cells indigenous to the involved site.
- Once thought to be a developmental malformation unworthy of the -oma designation, many in fact have clonal chromosomal aberrations that are acquired through somatic mutations and on this basis are now considered neoplasm.
- **Choristoma:** is a heterotopic rest of cells. For example, a small nodule of well-developed and normally organized pancreatic tissue may be found in the submucosa of the stomach, duodenum, or small intestine.

# VA Misnomers



Pulmonary hamartoma, there are tissues normally found in the lung (alveoli, cartilage..) but are not in the normal organization



**Figure 2.** Hematoxylin and eosin stain of mass on gallbladder wall. A. Islet of Langerhans: I: alpha cells; II: beta cells. B. Exocrine acini: III: serous cells; IV: centroacinar cells. C. Intercalated duct. D. Interlobular duct.



Tissue of Origin	Benign	Malignant
<b>Tumors Composed Predominantly of a Single Cell Type</b>		
<b>Connective tissue and derivatives</b>	Fibroma	Fibrosarcoma
	Lipoma	Liposarcoma
	Chondroma	Chondrosarcoma
	Osteoma	Osteosarcoma
<b>Endothelium and related cell types</b>		
Blood vessels	Hemangioma	Angiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma
Mesothelium		Mesothelioma
Brain coverings	Meningioma	Invasive meningioma
<b>Blood cells and related cell types</b>		
Hematopoietic cells		Leukemias
Lymphoid tissue		Lymphomas
<b>Muscle</b>		
Smooth	Leiomyoma	Leiomyosarcoma
Striated	Rhabdomyoma	Rhabdomyosarcoma





<b>Skin</b>		
Stratified squamous	Squamous cell papilloma	Squamous cell or epidermoid carcinoma
Basal cells of skin or adnexa		Basal cell carcinoma
Tumors of melanocytes	Nevus	Melanoma
<b>Epithelial lining of glands or ducts</b>	Adenoma	Adenocarcinoma
	Papilloma	Papillary carcinomas
	Cystadenoma	Cystadenocarcinoma
<b>Lung</b>	Bronchial adenoma	Bronchogenic carcinoma
<b>Kidney</b>	Renal tubular adenoma	Renal cell carcinoma
<b>Liver</b>	Hepatic adenoma	Hepatocellular carcinoma
<b>Bladder</b>	Urothelial papilloma	Urothelial carcinoma
<b>Placenta</b>	Hydatidiform mole	Choriocarcinoma
<b>Testicle</b>		Seminoma Embryonal carcinoma
<b>Ovary</b>	Serous cystadenoma, mucinous cystadenoma	Serous cystadenocarcinoma, mucinous cystadenocarcinoma

**Tumors Composed of Multiple Cell Types Normally Derived From the Same Germ Cell Layer**

Salivary glands	Pleomorphic adenoma (mixed tumor of salivary gland)	Malignant mixed tumor of salivary gland
Renal anlage		Wilms tumor

**Tumors Composed of Multiple Cell Types Normally Derived From More Than One Germ Cell Layer**

Totipotential cells in gonads or in embryonic rests	Mature teratoma, dermoid cyst	Immature teratoma, teratocarcinoma
---	-------------------------------	------------------------------------



«Wherever the art of medicine is loved,  
there is also a love of humanity.»

- Hippocrates-

