Neoplasia
Lecture 1

NEOPLASIA

- **Cancer is the second leading cause of death in the United States**

Characteristics of (3) cancers: Using it to differentiate cancer from other growth of cells in the body

1. Cancer is a genetic disorder caused by DNA mutations.

- **Most pathogenic mutations are either induced by (1) exposure to mutagens or occur (2) spontaneously as part of aging**

- Cancers frequently show epigenetic changes, such as focal increases in DNA methylation and alterations in histone modifications which may themselves stem from acquired mutations in genes that regulate such modifications.
- These genetic and epigenetic changes alter the expression or function of key genes that regulate fundamental cellular processes such as growth, survival, and senescence.

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Explanation

Cancers often have abnormal epigenetic changes, meaning changes that affect gene activity without altering the DNA sequence itself. Two common changes are:

1. **DNA Methylation:** Normally, adding methyl groups to DNA can silence genes. In cancer, some regions of DNA become overly methylated, turning off important tumor-suppressor genes that prevent cancer growth.
2. **Histone Modifications:** Histones are proteins around which DNA is wrapped. Chemical changes to histones can loosen or tighten this wrapping, affecting gene expression. In cancer, these modifications can activate oncogenes (cancer-promoting genes) or silence tumor-suppressor genes.

These epigenetic changes can be triggered by mutations in genes that control DNA methylation or histone modification processes, contributing to cancer development.

"Heritable" means that something can be passed from one generation to the next. In the case of cancer cells, it means that genetic changes (mutations) in a cancer cell's DNA are copied and passed on when the cell divides. So, the new cells that come from the original cancer cell will also have the same mutations.

2. Genetic alterations in cancer cells are heritable

Cells bearing mutations that provide a growth or survival advantage outcompete their neighbors and thus come to dominate the population.

Explanation

Genetic alterations in cancer cells are heritable, meaning they can be passed down to new cells when the cancer cell divides. If a mutation gives the cancer cell an advantage, like faster growth or resistance to death, it allows that cell to survive better and multiply more than normal cells. Over time, these "stronger" cancer cells outcompete normal cells, becoming the dominant population in the tissue.

groups of cancer cells that come from the original cancer cell but have developed additional genetic mutations over time

Emergence of genetically distinct subclones with more aggressive characteristics is an important concept referred to as tumor progression

process by which cancer becomes more aggressive and dangerous over time

3. Mutations and epigenetic alterations impart to cancer cells a set of properties that are referred to collectively as *cancer hallmarks.*

These properties produce the cellular phenotypes that dictate the natural history of cancers as well as their response to various therapies.

NOMENCLATURE

* Tumor cells aren't present in the body unless some cells acquire gene mutations leading to cell transformation

- ***Neoplasia*** **literally means "new growth."**

- Neoplastic cells are said to be transformed because they continue to replicate,apparently oblivious to the regulatory influences that control normal cells.

- Neoplasms enjoy a degree of autonomy and tend to increase in size regardless of their local environment. ⟶ They don't depend on reviving signals for growth. Continuous increasing in size without negative control presented in normal cells

- All neoplasms depend on the host for their nutrition and blood supply.
- Neoplasms derived from hormone responsive tissues often also require endocrine support.

Extra explanation for better understanding

Neoplasms from hormone-responsive tissues (like breast, prostate, or endometrium) often need hormones to grow because these tissues normally rely on hormones for their function. For example, breast cancer can depend on estrogen, and prostate cancer on testosterone. Blocking these hormones with treatments like hormone therapy can slow or stop the tumor's growth.

- **In common medical usage a neoplasm often is referred to as a *tumor.***
- **The study of tumors is called *oncology* (from *oncos,* "tumor," and *logos,* "study of")**
- **Neoplasms are divided into benign and malignant depending on a tumor's potential clinical behavior.**

* Differentiating between benign and malignant tumors is important to determine what's the outcome of the neoplastic process

Benign tumors

According to biological behavior

- A tumor is said to be *benign* when its microscopic and gross characteristics are considered to be relatively innocent implying that it will remain localized and is amenable to local surgical removal.

Very important characteristic that they can be removed surgically because they are localized to the site of tumor

Malignant tumors

refers to any abnormal tissue or damage in the body

Lesion can invade and destroy adjacent structures and spread to distant sites (metastasize) to cause death.

- Malignant tumors are collectively referred to as *cancers*, derived from the Latin word for “crab”

Difficult to be excised (removed) because they tend to invade and destroy adjacent tissues

All tumors, benign and malignant, have two basic components:

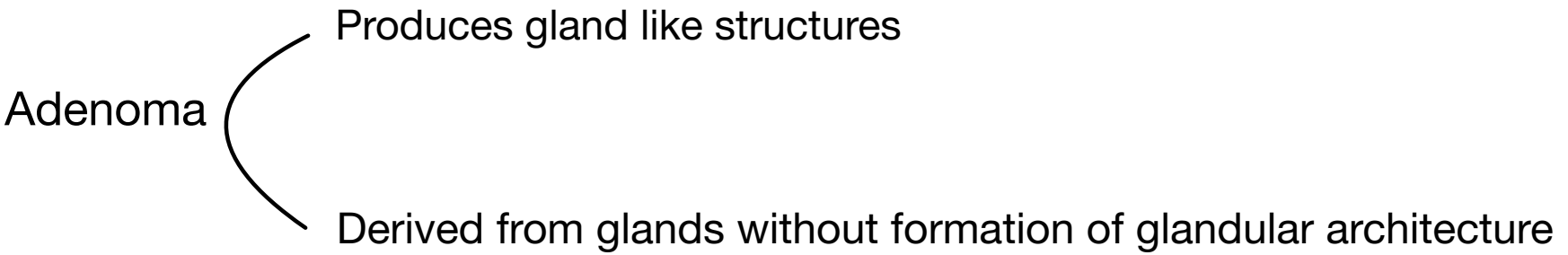
(1) The *parenchyma* made up of transformed or neoplastic cells (abnormal cells)

(2) The supporting *stroma* which host-derived, made up of connective tissue, blood vessels, and host-derived inflammatory cells

Benign Tumors

In order to designate tumor , we depend on the cell type which consists of the tumor's parenchyma

- **Benign tumors are designated by attaching the suffix -*oma* to the cell type from which the tumor arises.**
- **A benign tumor arising in fibrous tissue is a *fibroma***
- **A benign cartilaginous tumor is a *chondroma***



- ***Adenoma*** is generally applied not only to benign epithelial neoplasms that produce gland-like structures but also to benign epithelial neoplasms that are derived from glands but lack a glandular growth pattern.
- Examples

Colonic adenoma — Arise from colonic mucosa usually forms glandular structures

Thyroid adenoma — Arise from thyroid tissue , they don't produce glands , they are composed of cells that function as thyroid follicular cells

Thyroid adenoma

Arise from thyroid tissue , they don’t produce glands , they are composed of cells that function as thyroid follicular cells

Extra explanation for better understanding

The thyroid gland has different types of cells, and **follicular cells** are the ones responsible for making thyroid hormones, like **T3** and **T4**. These hormones help control your metabolism and many other body functions.

Now, in a **thyroid adenoma**, the tumor is made up of cells that are very similar to these **follicular cells**. In fact, the tumor cells **act like** thyroid follicular cells — meaning they might still be able to produce thyroid hormones, just like normal cells.

However, the key difference is that **the tumor cells grow in an abnormal way**, forming a lump. The tumor doesn't form actual new thyroid glands; it just consists of these follicular-like cells that are overgrowing and forming a mass.

To summarize:

- The tumor cells are similar to normal thyroid cells (called follicular cells).
- They might produce thyroid hormones, but they are disorganized and grow in a lump (adenoma).
- This means the tumor is made of cells that "work like" thyroid cells, but it isn't forming new thyroid tissue or glands.

- **Papillomas** are benign epithelial neoplasms growing on any surface, that produce microscopic or macroscopic fingerlike fronds.
- A **polyp** is a mass that projects above a mucosal surface, as in the gut, to form a macroscopically visible structure
- Polyps can be:

1. Benign
2. Malignant
3. Non-neoplastic as inflammatory polyps

Term that is used to describe Mass projection over mucosal surface

Polyp is a descriptive term so it can be benign or malignant (gross description)

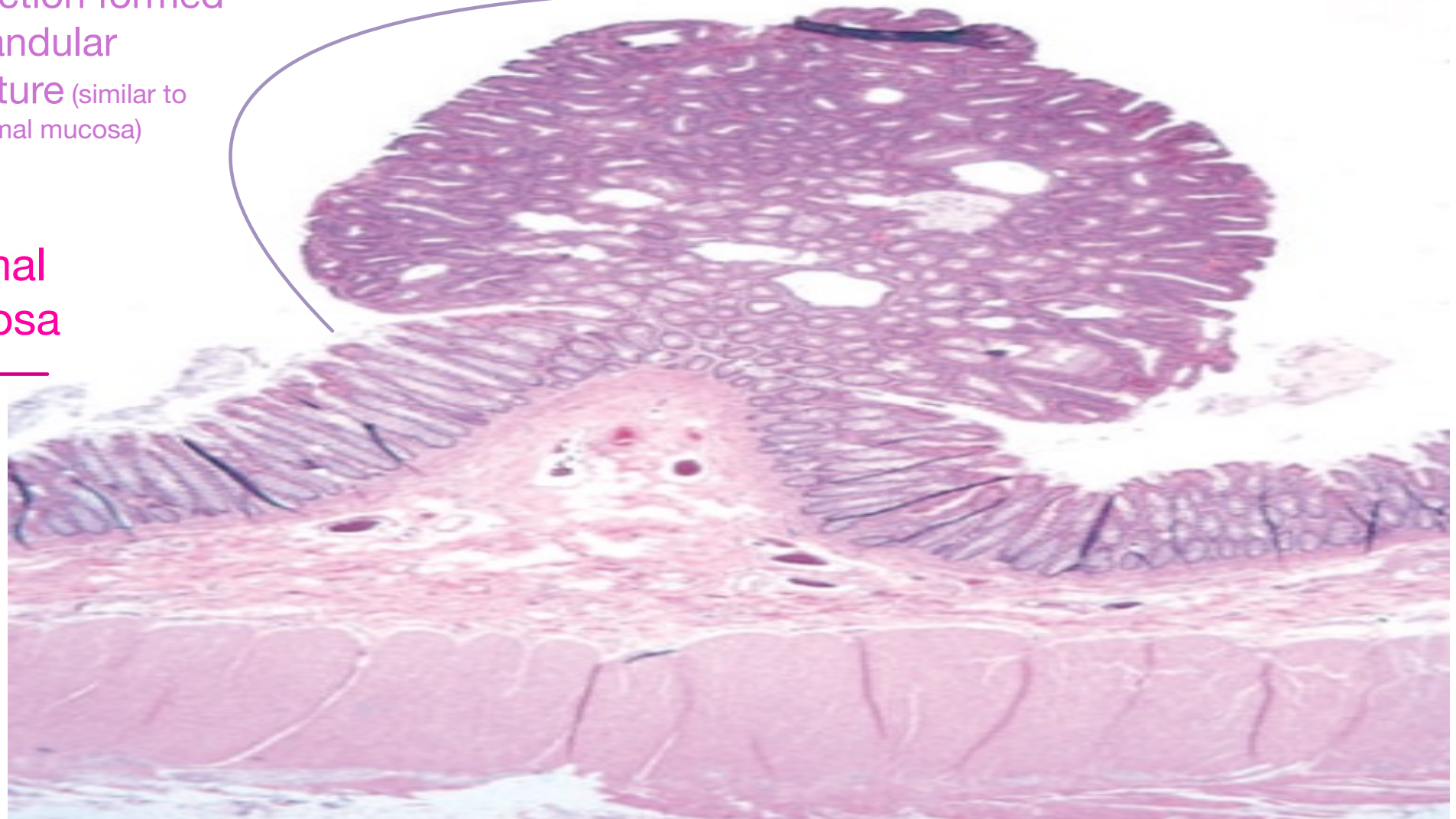
To differentiate between them we examine it under the microscope

Colonic polyp

*polyp usually used in clinical practice to describe lesions in mucosal sites

Projection formed of glandular structure (similar to the normal mucosa)

Normal mucosa



If polyp produces cystic masses as part of architecture it's called cystadenomas

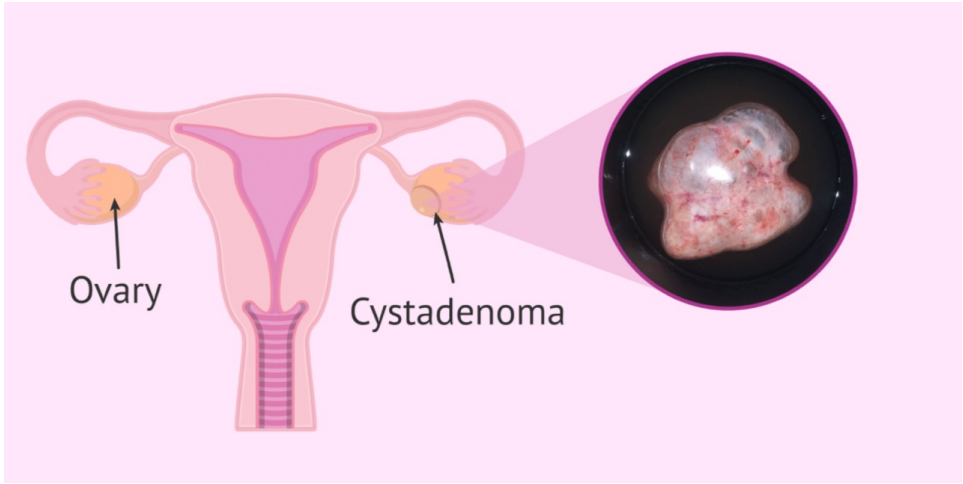
- **Cystadenomas** are hollow cystic masses that typically arise in the ovary

Some of glandular structures forms cystic masses because they are dilated

In cystadenomas, glandular structures are abnormal growths of glandular tissue. When it is said that "some of the glandular structures form cystic masses because they are dilated," it means that certain areas of the glandular tissue have enlarged or expanded to form fluid-filled sacs, or cysts. This dilation occurs due to the accumulation of secretions or fluids within the glandular spaces, which may happen when normal drainage is obstructed or altered.

Cystadenomas are benign (non-cancerous) tumors that typically form in organs with glandular tissue, such as the ovaries or pancreas. The cystic masses are not solid but rather contain fluid, leading to the cystic appearance when viewed under a microscope or during imaging studies.

Cystadenoma



Malignant Tumors

Cancerous (sarcoma)

- **Malignant neoplasms arising in "solid" mesenchymal tissues or its derivatives are called *sarcomas***
- **Malignant neoplasms arising from the mesenchymal cells of the blood are called leukemias or lymphomas**

Blood

Lymph nodes

- **Sarcomas are designated based on their cell-type composition presumably reflects their cell of origin.**

- **Examples**

Liposarcoma Malignant tumor in adipose tissue

Chondrosarcoma Malignant tumor in cartilaginous tissue

Fibrosarcoma Malignant tumor in fibrous tissue

- **Malignant neoplasms of epithelial cells are called carcinomas regardless of the tissue of origin.**
- **Examples**
- **Carcinomas that grow in a glandular pattern are called adenocarcinomas**
- **Carcinoma that produce squamous cells are called squamous cell carcinomas**
- **Carcinomas arising from renal tubules Renal cell adenocarcinoma**

There are many sites in the cell which can form such a tumor so we need to be specific

We add the site of tissues as :

Mixed tumors

It is important to recognise that tumors arise from one cell type

- **Mixed tumors are still of monoclonal origin but the progenitor cell in such tumors has the capacity to differentiate down more than one lineage.**
- **Examples**

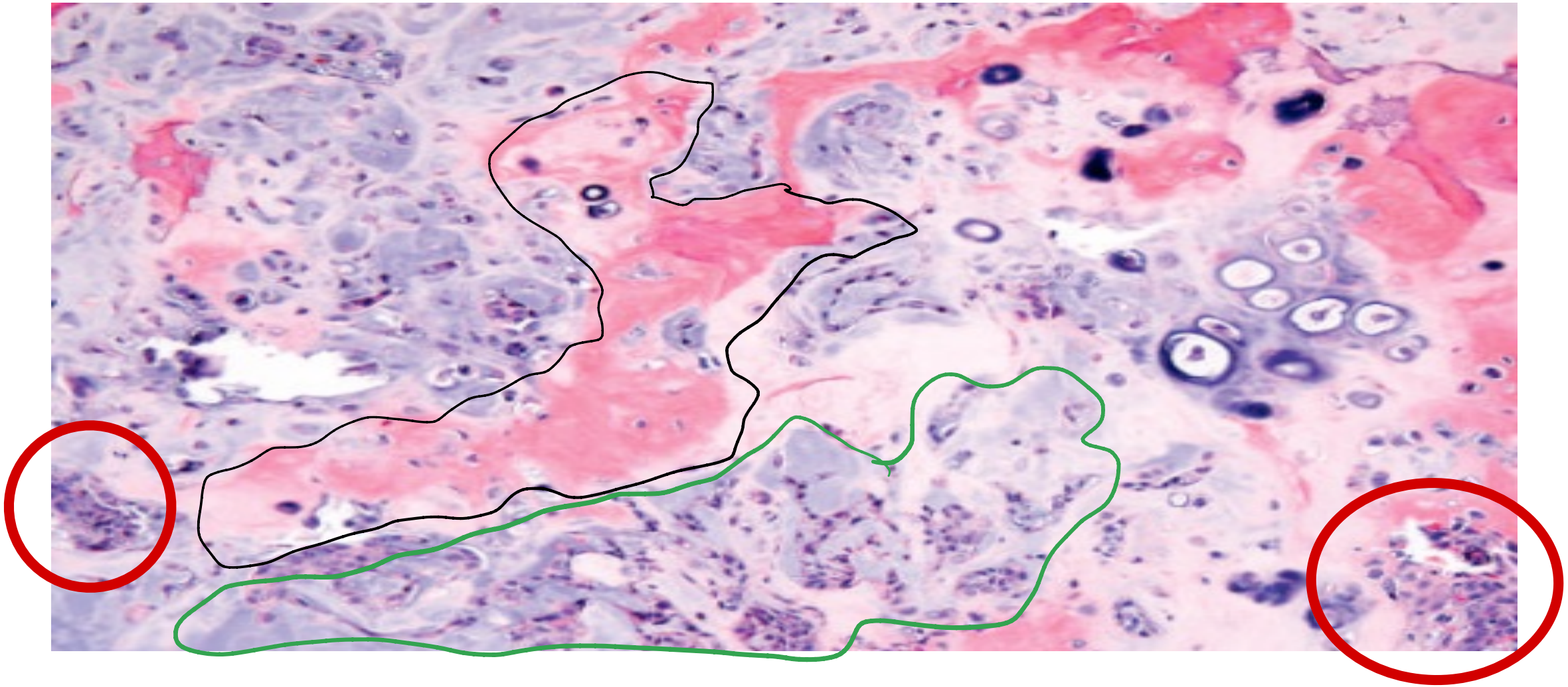
They produce more than one cell type or tissue in the same tumors due to their differentiating abilities

1. mixed tumor of salivary gland (pleomorphic adenoma).

These tumors have obvious epithelial components dispersed throughout a fibromyxoid stroma with islands of cartilage or bone

Pleomorphic adenoma of salivary gland

Bone tissue 🦴 Cartilaginous tissue Epithelial islands



2. Fibroadenoma of the female breast

Benign mixed tumor

It consists of a mixture of proliferating ductal Epithelial cells **elements and fibrous tissue**

Only the fibrous component is neoplastic

We make the diagnosis depending on the appearance of fibrous tissue in this tumor

Teratoma

- **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 and sometimes all three**
- **Teratomas originate from totipotential germ cells**
- **Ovaries, testis, mid line embryonic rests are common sites** → common.

Differentiate into different type of tissues leading to different type of tissue with tumors

(Involves all tissue in the body)

- **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 and sometimes all three

Further exploration for better understanding

A **teratoma** is a type of tumor that can have different types of body tissues mixed together. This happens because it comes from very early cells that have the ability to turn into any kind of tissue in the body (from skin to muscle to brain tissue).

For example:

- If you look at a teratoma under a microscope, you might see hair, fat, and even parts that look like teeth—all in the same tumor!
- This happens because the tumor forms from special cells that normally create a whole person during development, but in this case, they grow abnormally into a lump.

There are two types:

- **Mature teratoma:** The tissues look like normal, developed body tissues.
- **Immature teratoma:** The tissues are less developed and look like early, embryonic tissue.

- **Teratomas originate from totipotential germ cells**

Totipotential germ cells are special cells that have the ability to develop into **any type of cell** in the body, including extraembryonic tissues like the placenta. This makes them the most flexible or "powerful" type of stem cells.

- **<u>One Parenchymal Cell Type</u>**
- **Connective tissue and derivatives**
- Fibroma - Fibrosarcoma
- Lipoma - Liposarcoma
- Chondroma -Chondrosarcoma
- Osteoma - Osteogenic sarcoma

- **Endothelium and related cell types**
- Blood vessels : Hemangioma- Angiosarcoma
- Lymph vessels :Lymphangioma - Lymphangiosarcoma
- Mesothelium : X - Mesothelioma
- Brain coverings : Meningioma - Invasive meningioma

Simple Rule:

- **Meningioma** = Benign
- **Invasive Meningioma** = Malignant

Mesothelioma is almost always **malignant** (cancerous). It is a rare and aggressive cancer that typically arises from the **mesothelium**, the protective lining around organs like the lungs, heart, or abdomen.

- **Blood cells and related cell types**
- **No benign tumors**
- Hematopoietic cells : Leukemias — Abnormal cells in the blood
- Lymphoid tissue : Lymphomas
  - Different types of lymphoma depending on the cell type and maturation of tumor cells

- **Muscle**
- Smooth : Leiomyoma - Leiomyosarcoma
- Striated : Rhabdomyoma - Rhabdomyosarcoma

- **Skin**
- **Stratified squamous : Squamous cell papilloma - Squamous cell or epidermoid carcinoma**
- **Basal cells of skin or adnexa : Basal cell carcinoma**
- **Tumors of melanocytes : Nevus - Malignant melanoma**

Benign Malignant

- **Epithelial lining of glands or ducts**
- **Adenoma - Adenocarcinoma**
- **Papilloma - Papillary carcinomas** → Depend on gross characteristics because they usually produce large masses/projection over the surfaces
- **Cystadenoma - Cystadenocarcinoma**

If they contain dilated glands

- **Lung :** Bronchial adenoma - Bronchogenic carcinoma
- **Kidney :** Renal tubular adenoma - Renal cell carcinoma
- **Liver :** Liver cell adenoma - Hepatocellular carcinoma
- **Bladder :** Urothelial papilloma - Urothelial carcinoma
- **Placenta :**Hydatidiform mole - Choriocarcinoma
- **Testicle :** No benign - Seminoma , Embryonal carcinoma

Mixed tumors

- **Salivary glands : Pleomorphic adenoma (benign)**
- **Renal anlage : Wilms tumor (malignant)**

Totipotential cells in gonads or in embryonic rests

- **Mature teratoma, Immature teratoma, teratocarcinoma**

↳ Immature.

From the recorded lecture

Agents or groups of Agents	Human cancer, Site and type for which Reasonable evidence is available
Arsenic and arsenic compounds	Lung, Skin, Hemagiosarcoma
Asbestos	Lung, mesothelima; gastrointestinal tract (esophagus, stomach, large intestine)
Benzene	Leukemia, Hodgkin lymphoma
Beryllium and beryllium compounds	Lung
Cadmium and cadmium compounds	Prostate
Chromium compounds	Lung
Ethylene Oxide	Leukemia
Nickel compounds	Nose, Lung
Radon and its decay products	Lung

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واللهم صلّ وسلّم وبارك على سيدنا محمد
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Sara Jaradat