Neoplasia 2018
Lecture 1

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Dear All

- Welcome to this part of your course (introduction to pathology) where we will study neoplasia in detail.

- Please note that each lecture builds upon what's in the previous one, so **make sure you don't miss any lecture if you want to understand the subject fully.** This is especially important when we start talking about the genetic bases of cancer.

- My aim of these lectures is that you understand the main concepts and ***ENJOY*** the lectures

Lectures' design

- In the coming 11 lectures we will discuss neoplasia.
- For each lecture I'll send a power point containing ALL the material you need to know for exam purposes. These might seem long, but this is because they summarize the book and contain extra information as well as practice questions.
- At the beginning of each PowerPoint I'll describe the main intended learning outcomes ILOs of the lecture and the reference pages in the book (Robbins basic pathology 10th edition). I encourage you to read the book.
- At the end of each PowerPoint I'll summarize the main points of the lecture and include practice questions.
- I'm not going to use these PowerPoint presentations within the lectures but will cover everything in them. Don't worry just relax and enjoy!

Important note

- In some lectures, especially the one about epidemiology many numbers will be mentioned; DO NOT memorise these! My aim is that you understand concepts, not memorise percentages that do change from time to time.

- Histologic pics in these lectures are meant to make you familiar with certain concepts. You don't need to worry about them. I will not ask you about these in the exam.

Lectures' distribution

Lecture	Topic	Pages/ Robbins 10th
1	Epidemiology and nomenclature	189-192 and 196-200
2	Benign vs malignant tumours	192-196
3	Genetic lesions in cancer	201-204
4	Hallmarks of cancer: growth signals	205-208
5	Hallmarks: growth inhibition 1	208-211
6	Hallmarks: growth inhibition 2	211-214
7	Hallmarks: altered metabolism and evading death	214-218
8	Hallmarks: immortality, angiogenesis and mets	219-223
9	Evading immune system and genome instability	223-228
10	Etiology of cancer	229-235
11	Clinical manifestations of cancer	235-241

ILOS of lecture 1

- 1. To understand the burden of cancer, worldwide and in Jordan.
- 2.To be aware that cancer can be prevented.
- 3. To realise that prevention and early detection are the most important factors in decreasing cancer burden.
- 4. To know the basic concepts about epidemiology of cancer.
- 5. to understand the basic nomenclature of neoplasia.

Extent of the problem

- Cancer is the **second** leading cause of death worldwide, after cardiovascular disease.

- **<u>Cancer burden includes</u>** :

-morbidity (disease state) ,

-mortality (death),

-suffering due to pain or loss of body functions

-economic costs

-emotional problems.

WHO facts about cancer

- Cancer is the second leading cause of death globally, and was responsible for 8.8 million deaths in 2015. **Globally, nearly 1 in 6 deaths is due to cancer.**

- Approximately 70% of deaths from cancer occur in low- and middle-income countries.

- Around one third of deaths from cancer are due to the 5 leading behavioral and dietary risks: **high body mass index, low fruit and vegetable intake, lack of physical activity, tobacco use, and alcohol use.**

- *Tobacco use is the most important risk factor for cancer and is responsible for approximately 22% of cancer deaths.*

reference: http://www.who.int/news-room/fact-sheets/detail/cancer

WHO website quote

“Cancer prevention”
Between 30-50% of all cancer cases are preventable.
Prevention offers the most cost-effective long-term strategy for the control of cancer.
National policies and programmes should be implemented to raise awareness, to reduce exposure to cancer risk factors and to ensure that people are provided with the information and support they need to adopt healthy lifestyles.”

Note

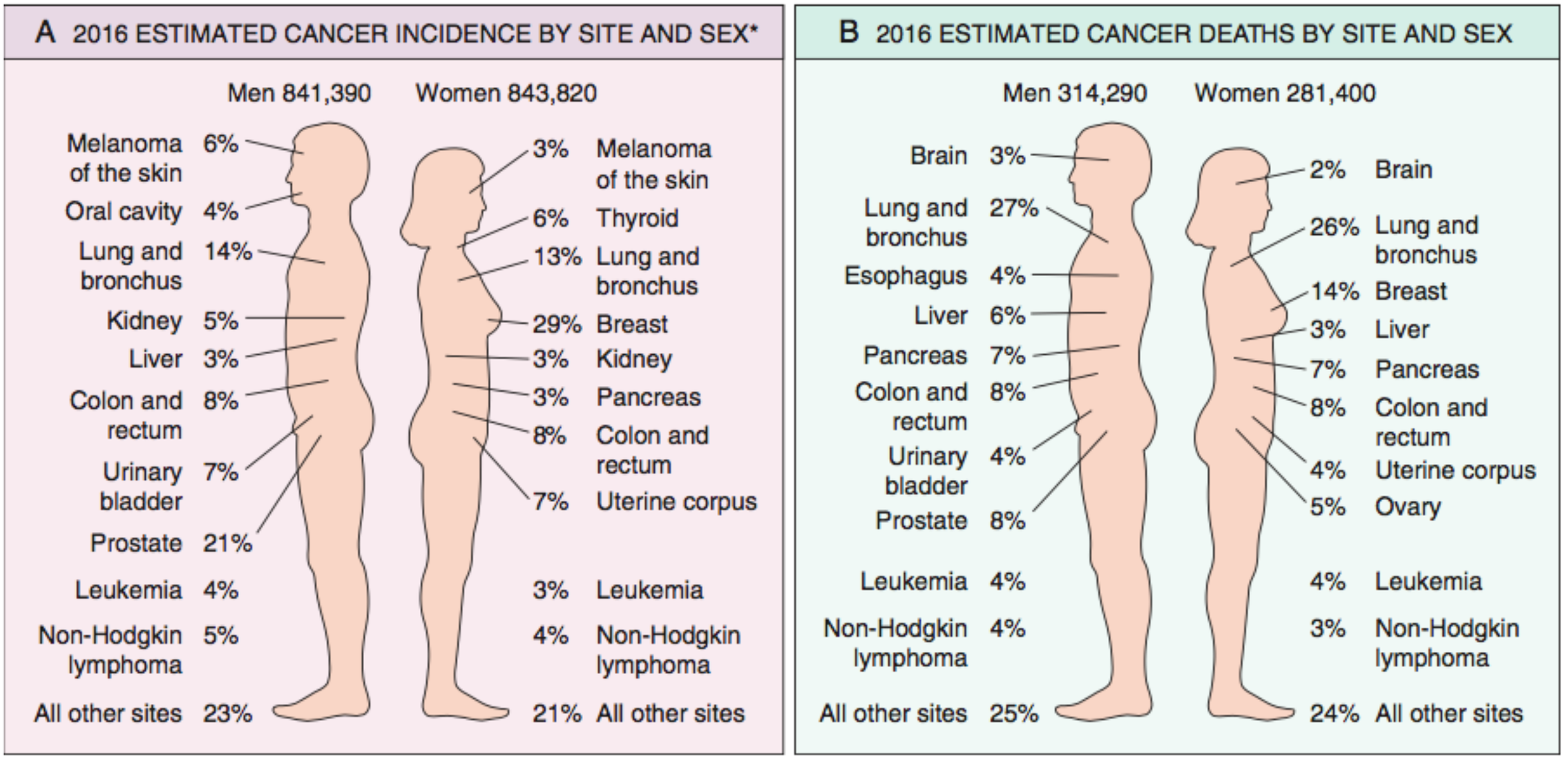
- Please note that treating cancer is ,in general, difficult, lengthy, costly and has many side effects, some of which can be lethal.

- So: prevention and early detection are our hope in defeating cancer.

- Prevention: via educating the public about the risk factors.

- Early detection: via screening and educating the public about the early symptoms of certain cancers.

Cancer epidemiology
USA



Comments on the previous slide

Note that:

- In the USA , the leading cause of cancer death in both sexes is lung cancer
- But the most common cancer in women is breast cancer and in men is prostate cancer.

Jordan

- National cancer registry collects data about cancer from ALL hospitals in the country.
- According to 2013 statistics the most common cancer among Jordanian males is colorectal cancer followed by lung cancer
- According to 2013 statistics, the most common cancer among Jordanian females is breast followed by colorectal cancer.

Jordanian cancer Registry

Published yearly, on the ministry of health website:
www.moh.gov.jo


The Hashemite Kingdom of Jordan

Ministry of Health

Non-Communicable Diseases Directorate

Jordan Cancer Registry

Cancer Incidence in Jordan - 2012

- From the previous slides, you note that there are differences in cancer epidemiology among different countries.

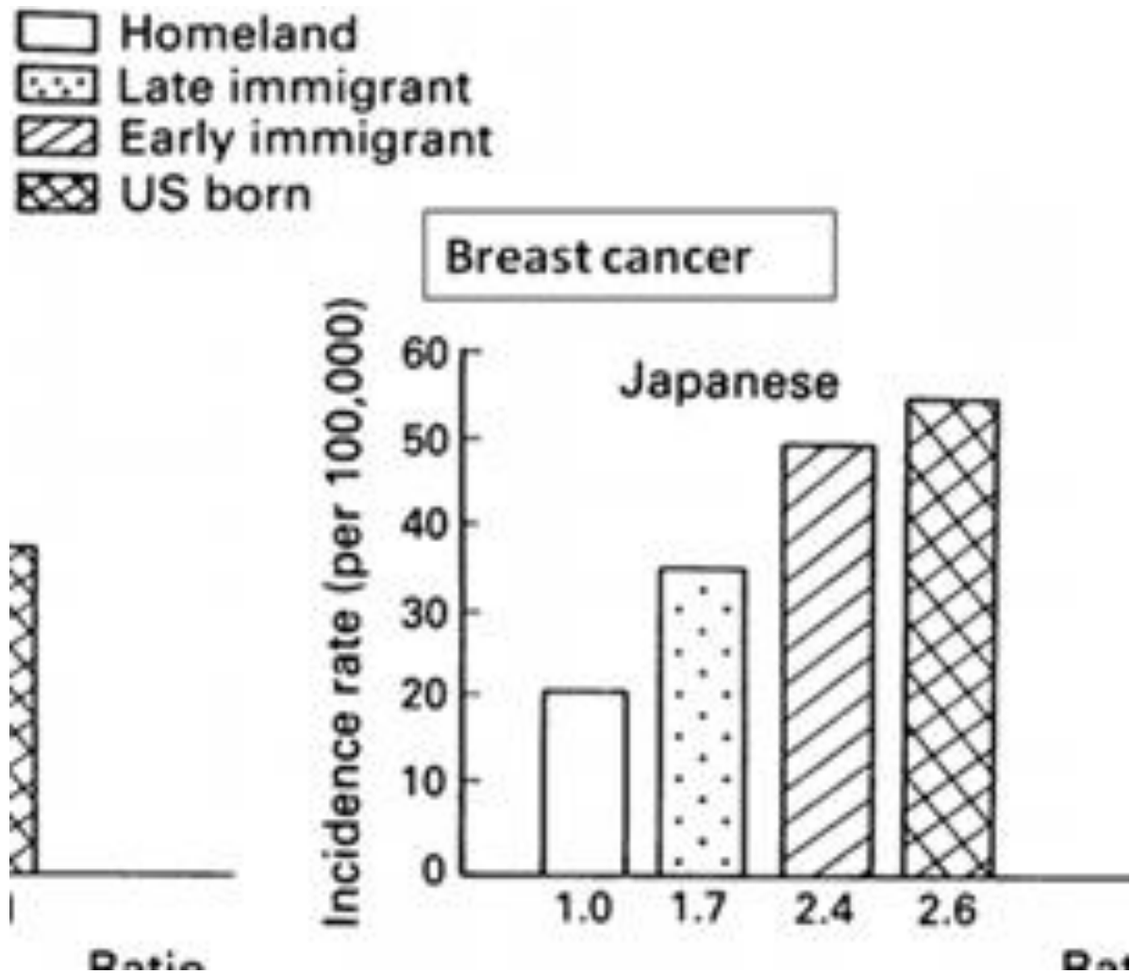
- The reasons are related to both genetic and environmental factors.

Geographic and environmental factors

- Environmental factors are the predominant cause of cancer
- Geographic variations in cancer incidence are due to different life styles and to environmental factors
- When people move from one geographic area to another, **subsequent generations** acquire the same risk of cancer development as original population.
- Why subsequent generations: because it takes time for migrants to fully adapt the new country's life style!
- Example: Stomach cancer is common in Japan. Japanese who migrate to USA have lower incidence of gastric cancer than Japanese in Japan.

effect of environmental factors

- Note how Japanese migrating to USA started having increased rate of breast cancer.
- This rate increased with generations (late immigrants in the pic) till it reached a similar incidence of cancer of native USA residents.



heredity

- Some cancers have inherited predisposition, but still the majority of these need environmental factors to develop cancer
- Only 5-10% of cancers are inherited.
- This inheritance is usually indirect and its effect is subtle

Changing trends

- Cancer incidence and mortality can change according to treatments or to changes in environmental factors.

- Example 1: Colorectal cancer incidence has decreased in USA during the last decade due to awareness of risk factors and to screening programmes.However in Jordan, Colorectal carcinoma is increasing.

- Example 2: Cervical cancer has decreased in the West due to screening (cervical smear tests).

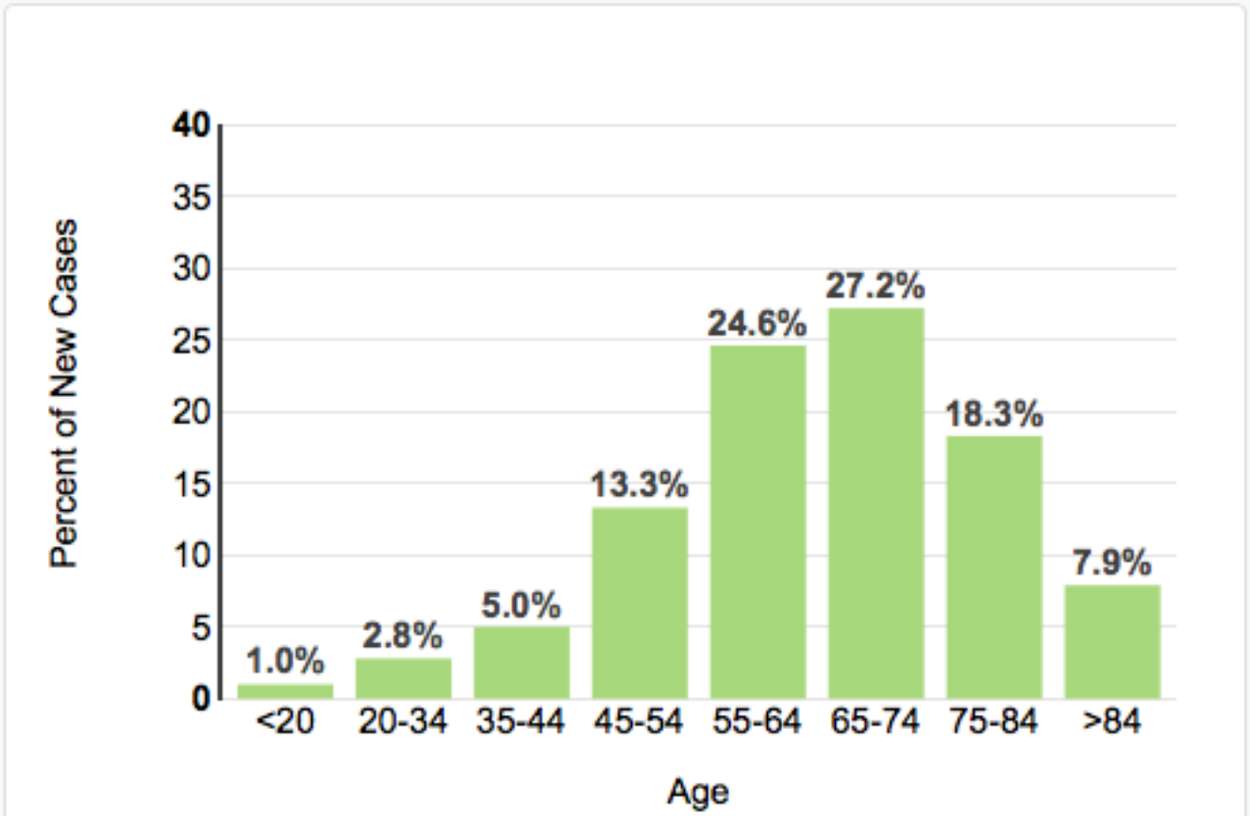
- Example 3: Lung cancer was uncommon among women worldwide. But when more women started to smoke, lung cancer increased among them.

Cancer and age

- In general , frequency of cancer increases with age.
- Why: accumulation of mutations takes time! And immunity declines with ageing.
- However, cancer occurs in children. It is responsible for 10% of all deaths in children younger than 15 years.
- Most common childhood tumors: leukemias, lymphomas, CNS tumors and soft tissue and bone sarcomas.

Cancer and age.. USA data

Percent of New Cases by Age Group: Cancer of Any Site



Cancer of any site is most frequently diagnosed among people aged 65-74.

Median Age At Diagnosis
66

SEER 18 2011-2015, All Races, Both Sexes

The language

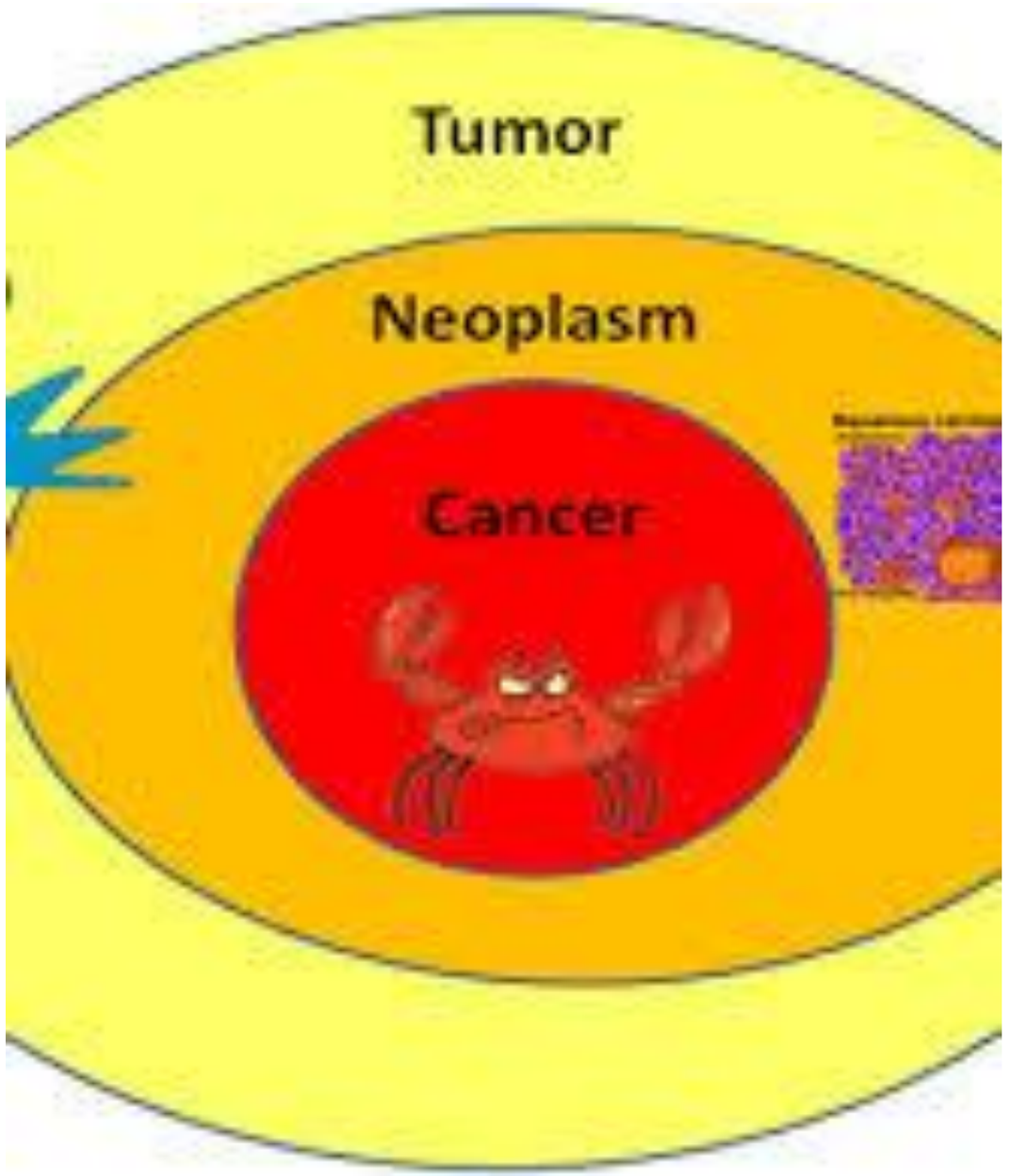
- Neoplasm (ورم)means a new growth.
- neoplasm is defined as “An abnormal mass of tissue that results when cells divide more than they should or do not die when they should”
- Neoplasms can be benign (حميد) or malignant (خَبيث)
- Cancer is a malignant neoplasm.
- Tumour: usually used to mean a neoplasm, although strictly speaking tumour means a mass.
- Mass is a swelling, an increase in size, which can be neoplastic or non-neoplastic (swelling due to inflammation for example)

- Tumour is a term meaning a swelling due to any cause. it includes neoplastic and non-neoplastic conditions.

- Choristomas (described later) are masses (tumours) that are non-neoplastic.

- The difference between a neoplastic and non-neoplastic process is the presence of specific mutations in neoplasms.

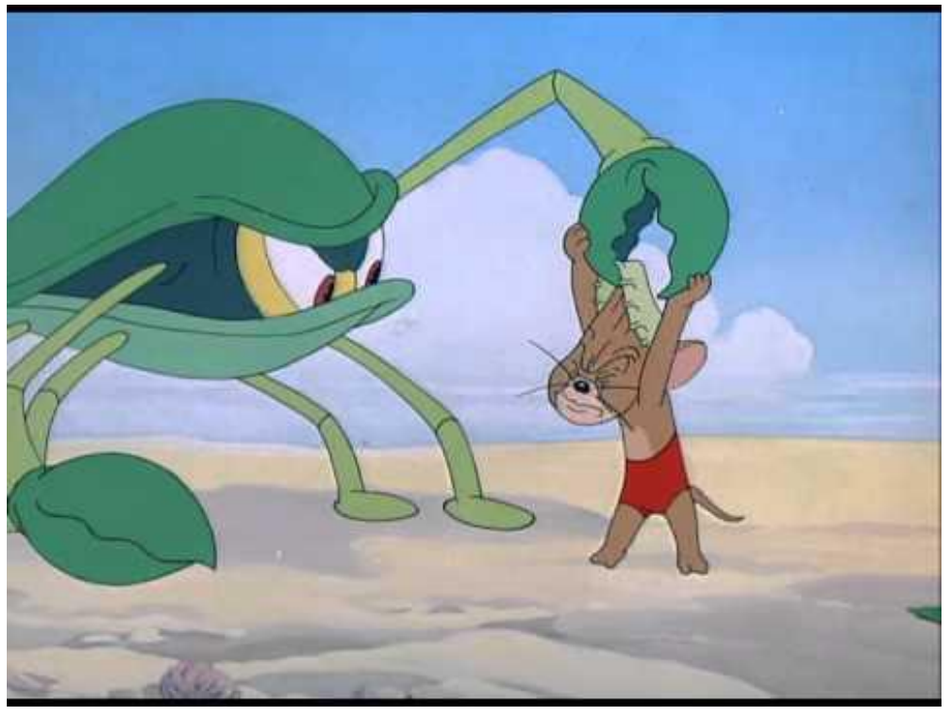
- HOWEVER, in clinical practice most people use the term “tumour” for neoplasms.



Fun fact!

- Hippocrates was the first to name masses of cancerous cells *karkinos* — Greek for crab.

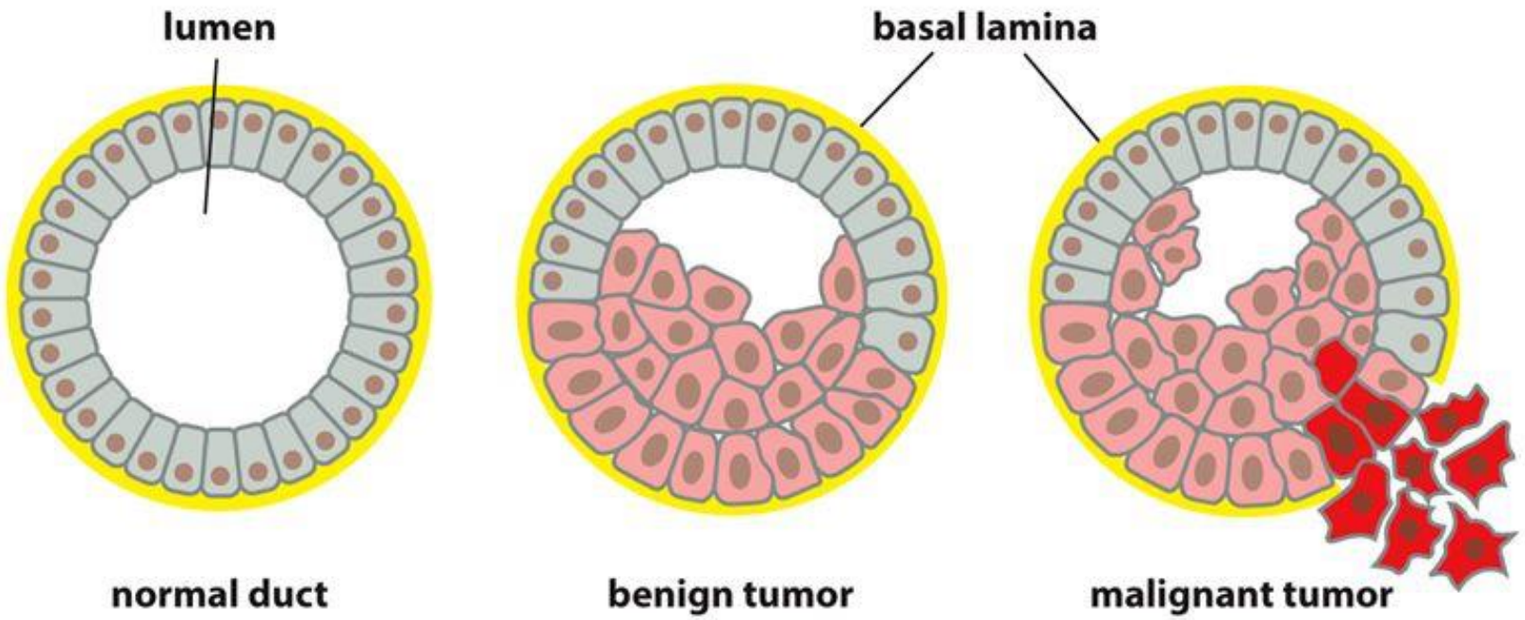
- Howard Markel, a medical historian, mentioned several hypotheses on why Hippocrates named the disease after a crab: 1. Cancerous tumors are hard, like the shell of the crab
2. they cause pain like when the crab pinches someone!
3. they are difficult to remove surgically, like when the crab pinches and doesn't let go!



Benign versus malignant neoplasms

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

Benign Versus Malignant Tumors



- Benign: Excessive proliferation; single mass
- Malignant: Cancer; invade surrounding tissue

Every rule has exceptions!

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

The language: tumour autonomy=استقلالية

- 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!

The language, again: tumour clonality ؛ استنساخ

- 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, we will come to this later!

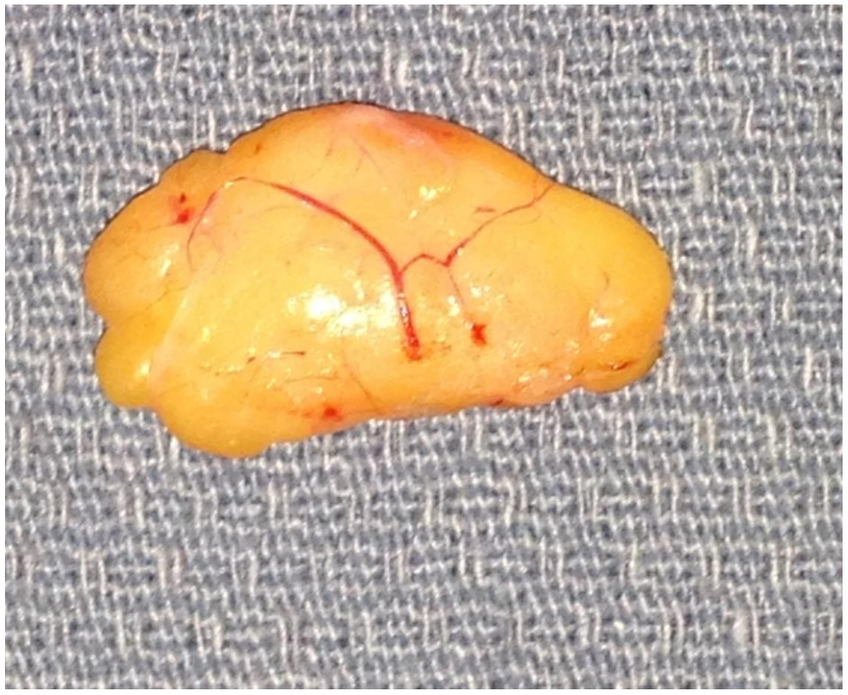
Nomenclature of tumours

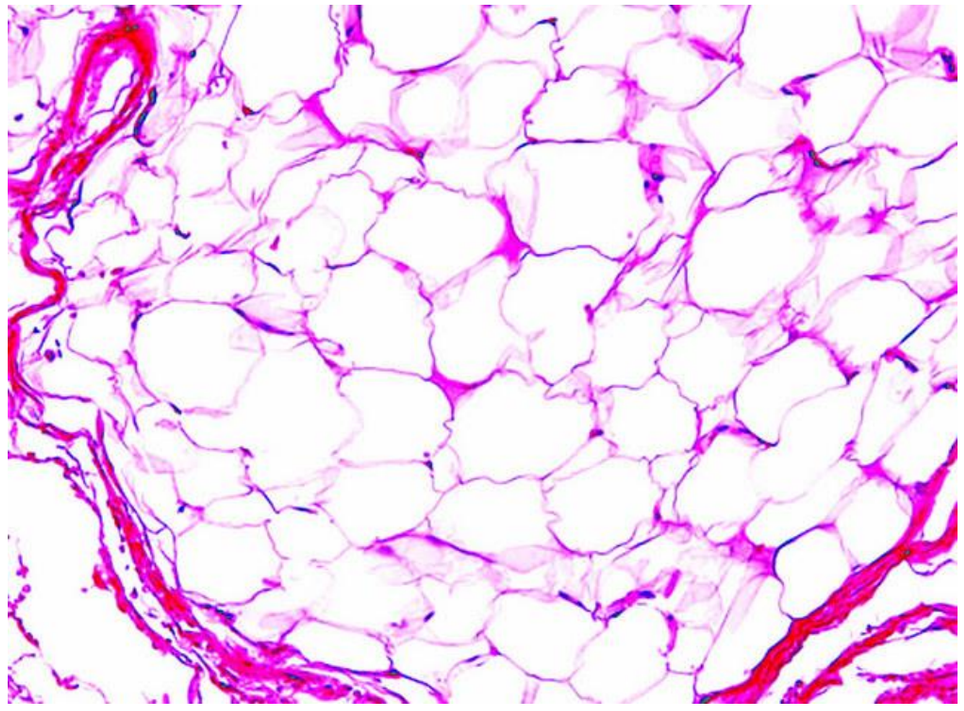
- Tumours are named according to the tissue they arise from.
- Benign tumours arising from epithelial or stromal tissue are named by adding “oma” at the end.
- A benign tumour arising from fatty tissue is called: lipoma, from fibrous tissue: fibroma and so on.
- Malignant tumours arising from epithelial tissues are called carcinomas (adenocarcinoma, squamous cell carcinoma), whereas malignant tumours arising from stromal tissues are called sarcomas (osteosarcoma, fibrosarcoma)

Nomenclature of benign tumors

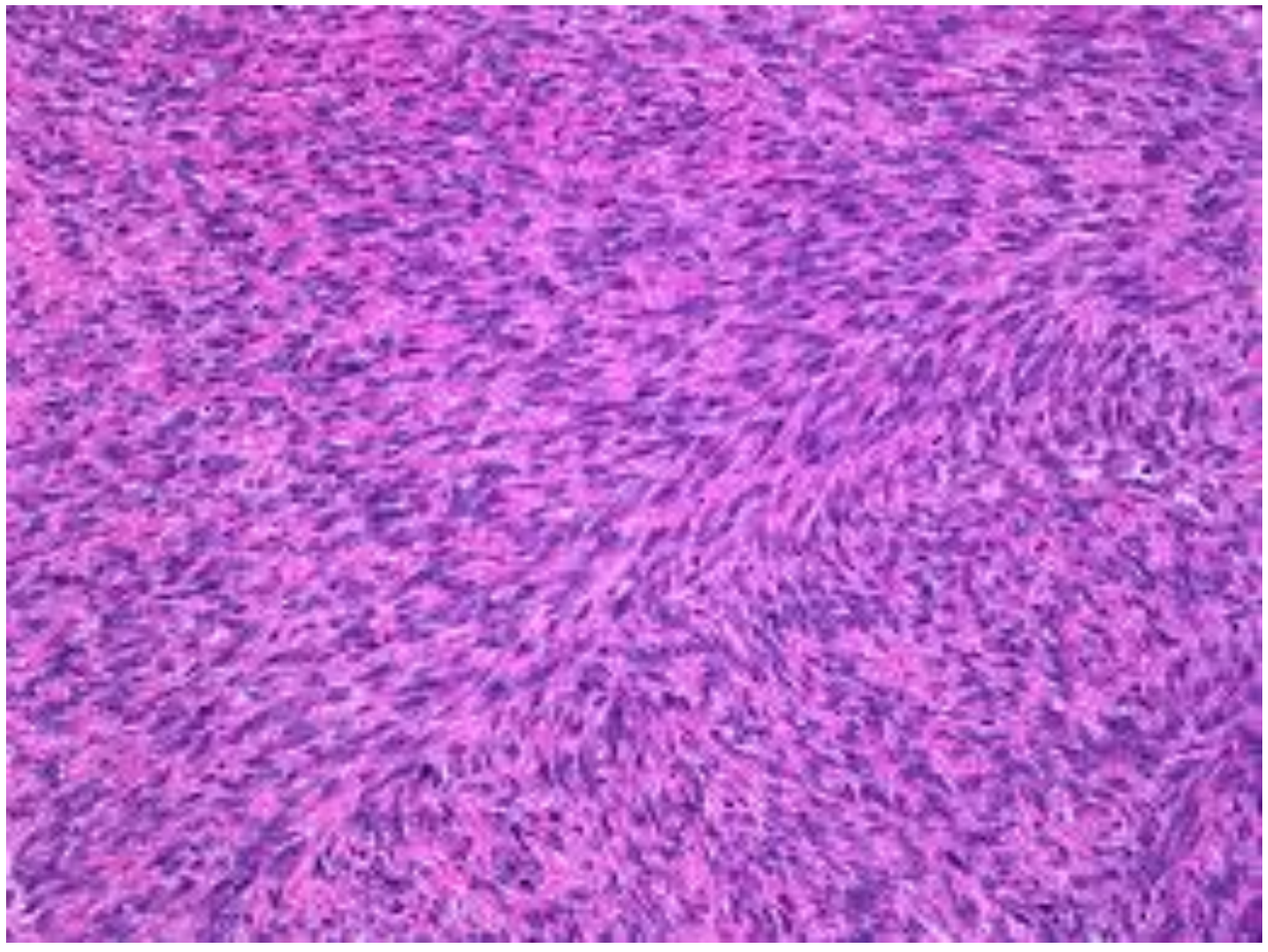
- Usually named by adding the suffix oma (Fibroma, chondroma, osteoma)

lipoma: benign tumour arising from fat tissue“lipid”





leiomyoma: benign, arising from smooth muscle.



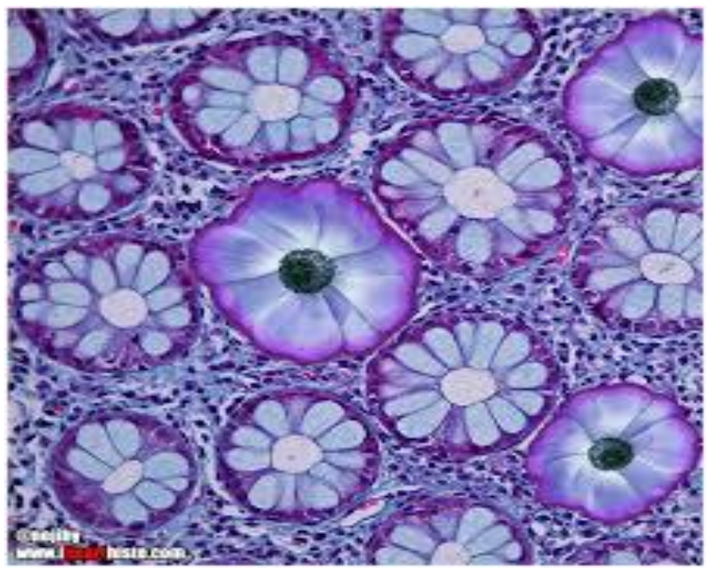
- What about benign tumours arising from **glandular tissue?** (see next slide for the definition of glandular epithelium)

- These are called adenomas

- Adenoma= benign epithelial neoplasm <u>forming</u> glands **or** neoplasm <u>derived from</u> glands even if it doesn't produce glands

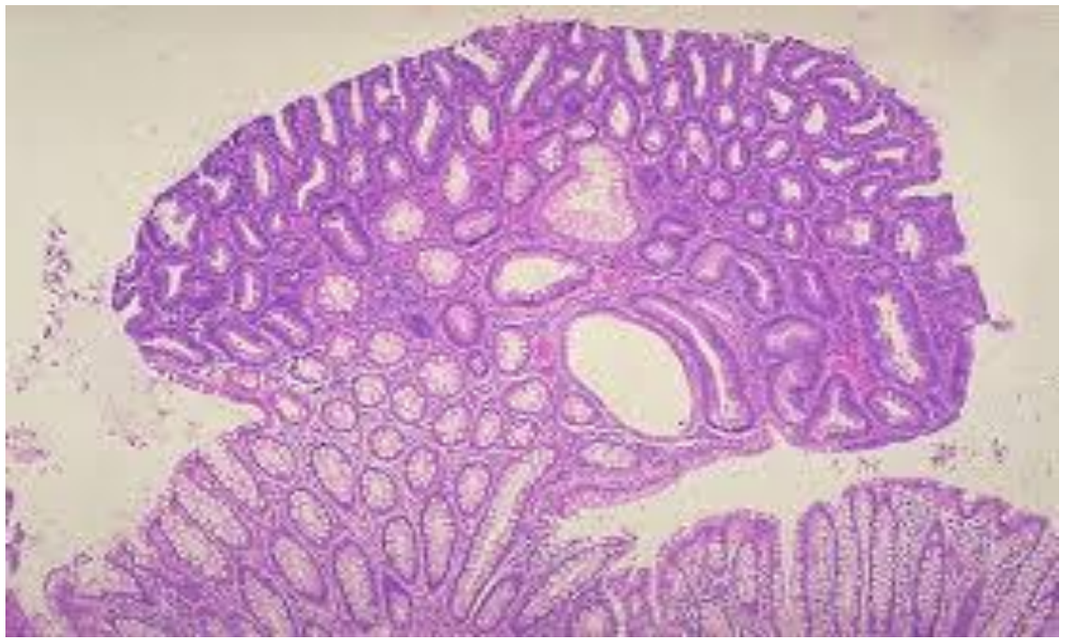
Glandular epithelium

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



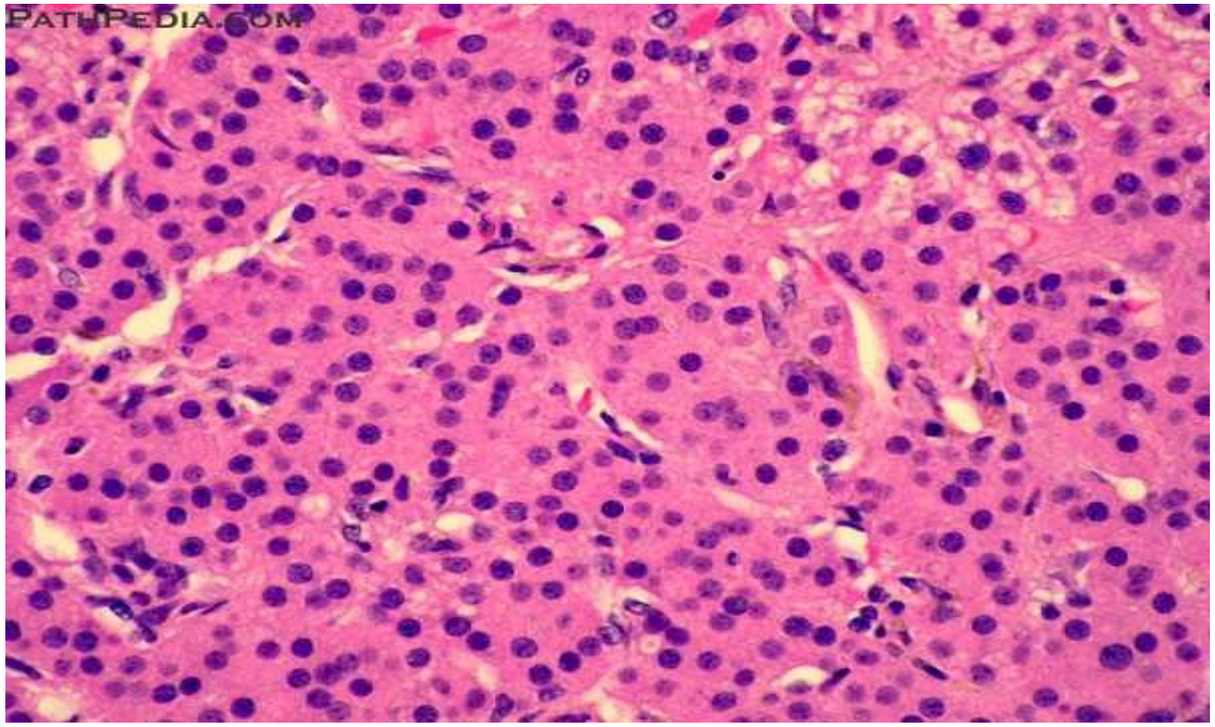
Adenoma/ colon, here the tumour is forming glands, and derived from glandular epithelium.

- Note : this is also called a polyp=الزوائد اللحمية (used more for macroscopic (gross) appearance, it means a mass projecting above the mucosa)

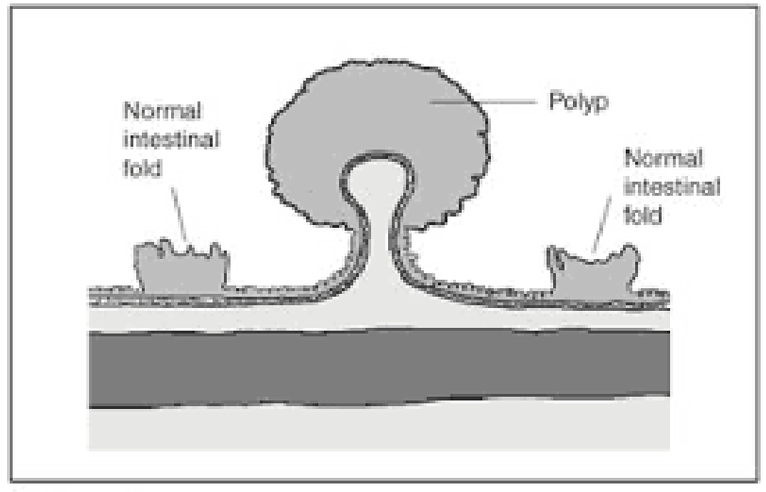


Adenoma/ adrenal gland

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



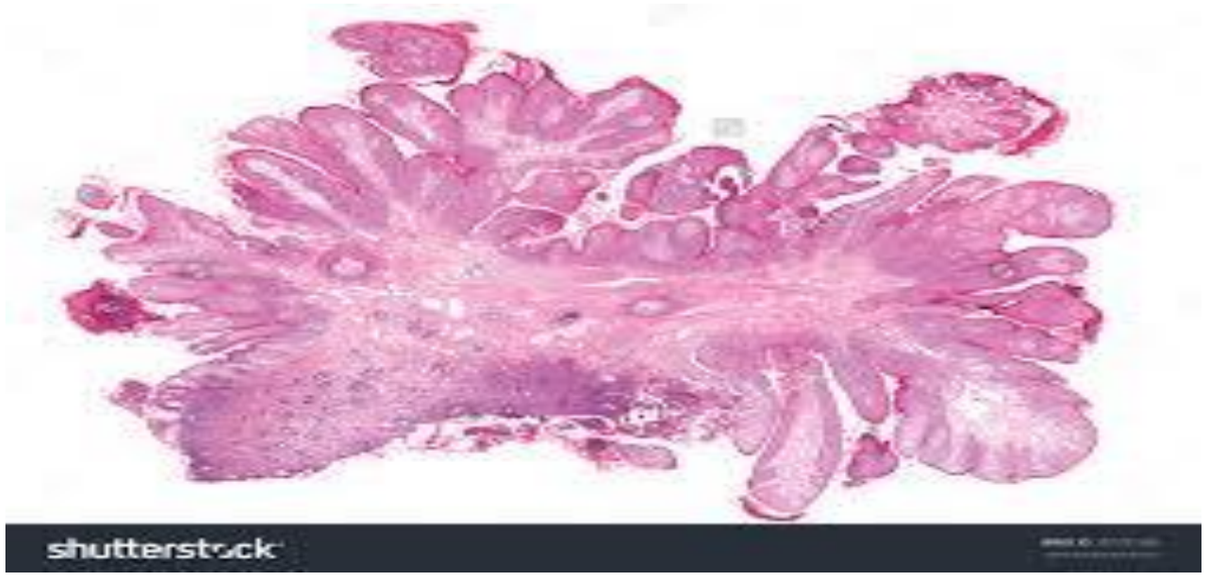
polyp



- Polyp: mass projecting above mucosal surface.
- this is a nonspecific term, usually used for the macroscopic appearance (what you see with your eyes without the microscope)
- 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)

Papilloma

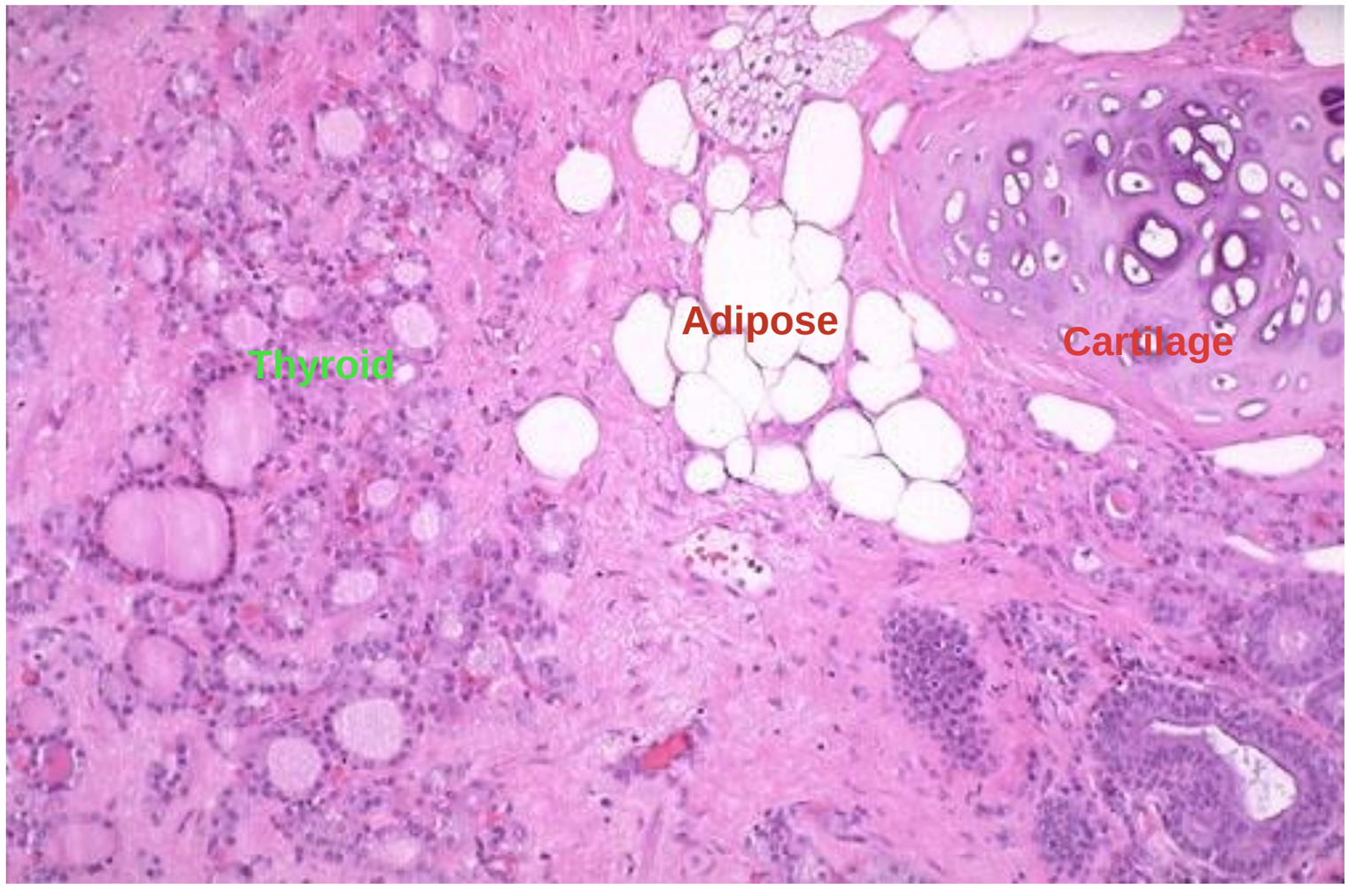
- Papilloma= benign epithelial neoplasm producing macroscopic or microscopic finger like projections



Teratoma: a strange tumour!

- is a 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

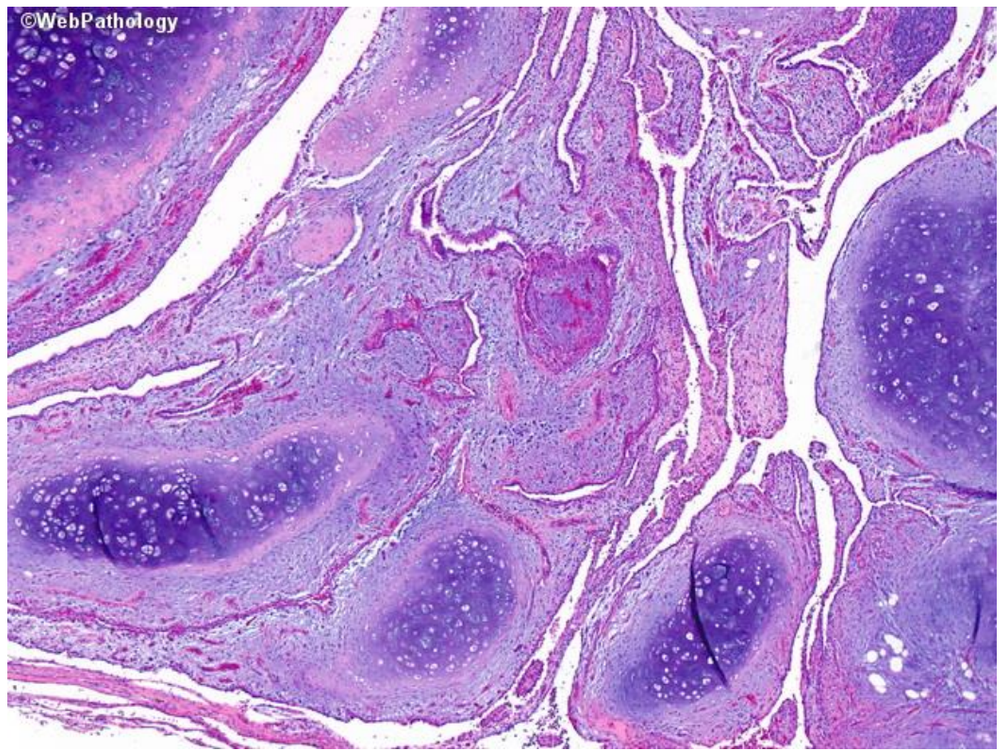
Teratoma: you can see any types of tissues mixed together



Teratoma: note the teeth!

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=ورم اغترابي

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

choristoma= heterotopia

Here we see pancreatic tissue in the wall of the gall bladder

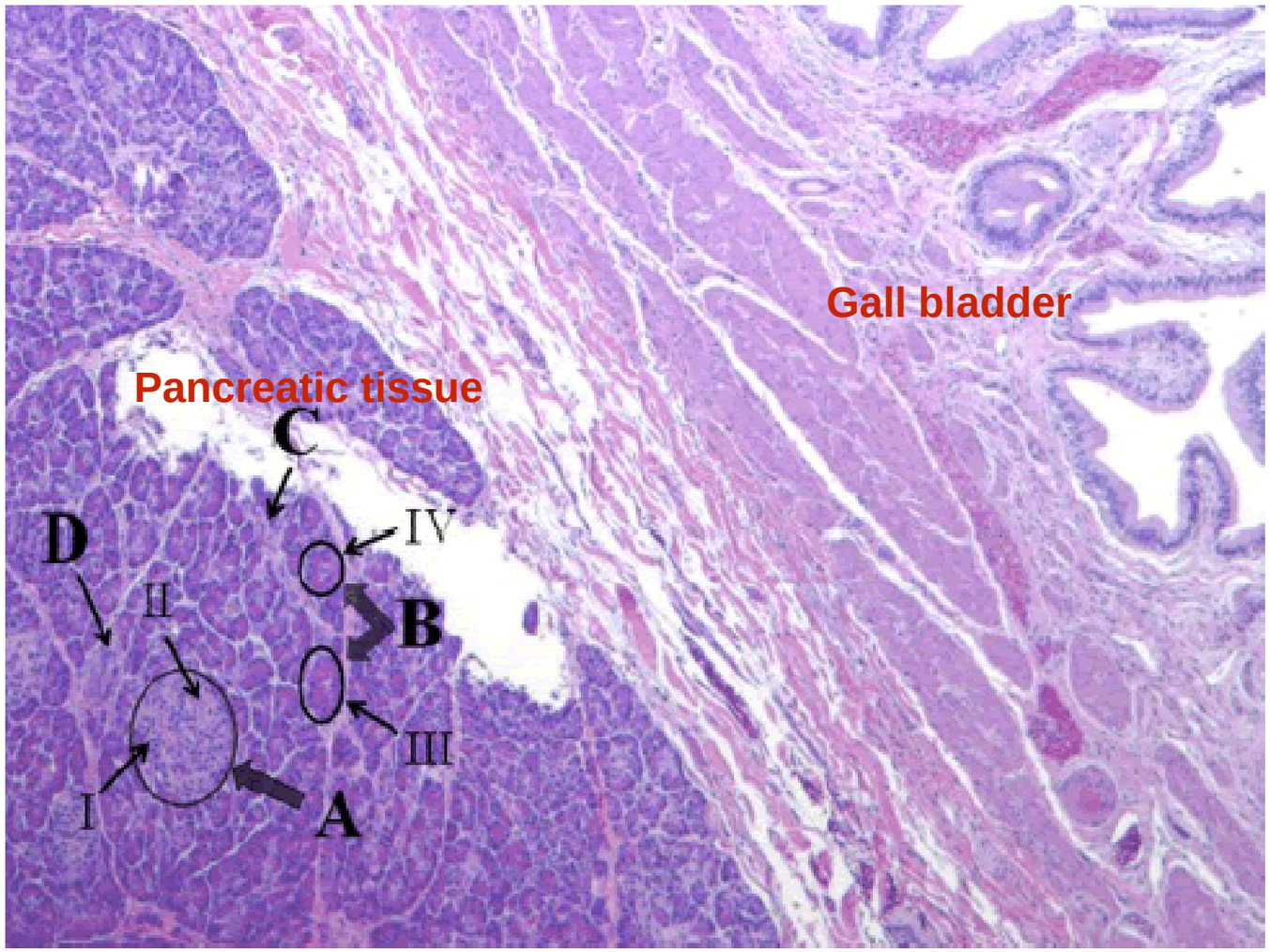


Figure 2. Hematoxylin and eosin stain of mass on gallbladder wall. A. Islet of Langerhans: I: alpha cells; II: beta cells. B. Exocrine acini: III: serous cells; IV: centroacinar cells. C. Intercalated duct. D. Interlobular duct.

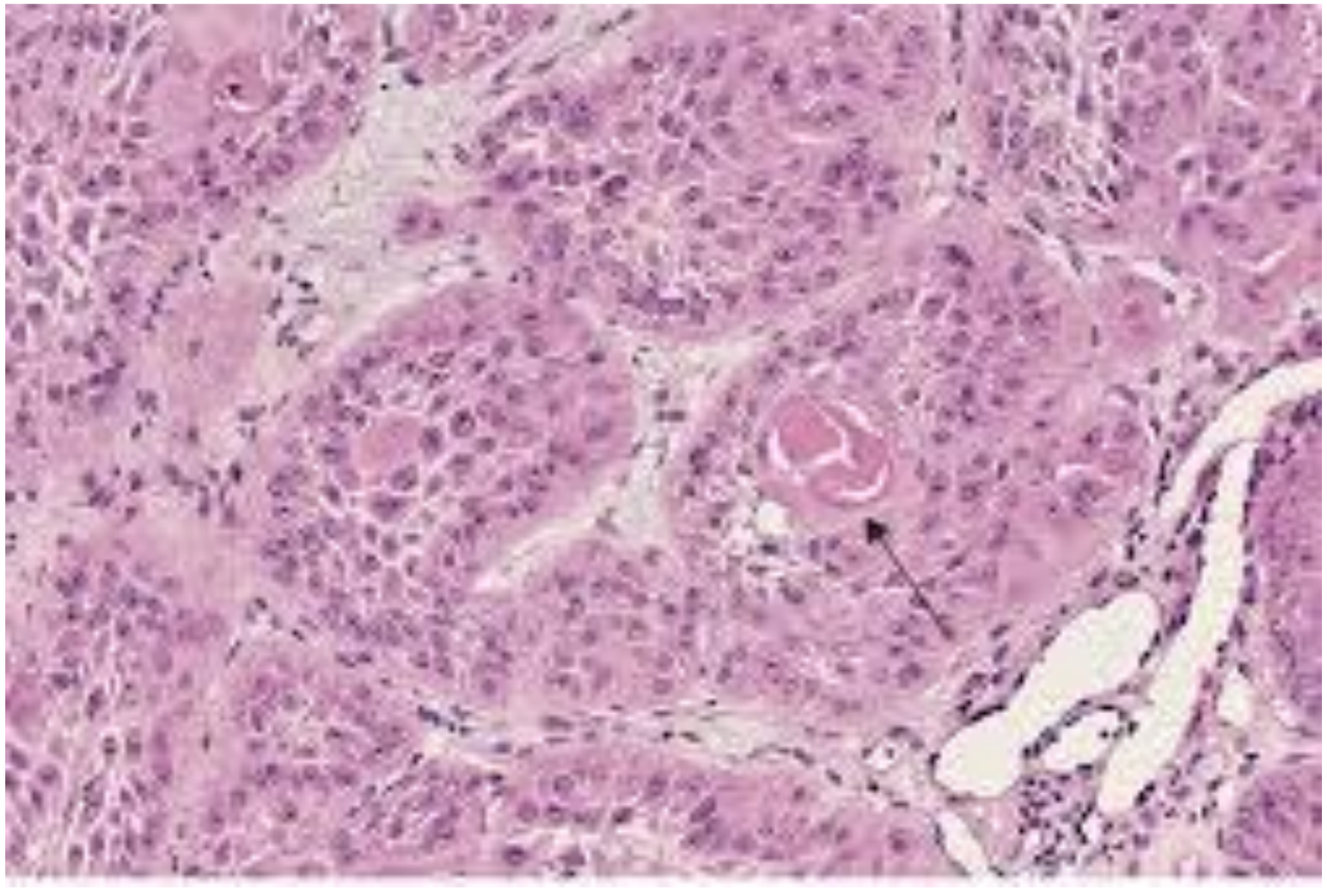
- **<u>Nomenclature of malignant tumors</u>**
- -malignant tumors arising in solid mesenchymal tissue: **sarcoma** .
- -sarcomas subdivided according to cell of origin: fibrosarcma, chondrosarcoma, leiomyosarcoma..

Blood neoplasms:

- 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



The exceptions!!

- Melanoma
- Seminoma
- Lymphoma
- Mesothelioma
- Multiple myeloma

- These are malignant OMAs

Summary 1/2

- Cancer is the second cause of death worldwide.
- One third of deaths from cancer are caused by obesity, physical inactivity, smoking, alcohol and low veg diet.
- Smoking is responsible for 20% of cancer deaths.
- Up to 50% of cancers are preventable.
- In USA the most common cancer is breast in women, and prostate in women.
- In Jordan the most common cancer is breast in women and colorectal in men.
- Environmental and genetic factors play a role in cancer development.
- Geographic variations in cancer incidence are related to environmental risk factors and variations in life style.
- Hereditary plays a role in cancer, mainly through inheriting a predisposition to cancer which needs environmental factors to develop.
- Rarely: there are inherited cancer syndromes.. we will mention these in details later.
- Risk of cancer increases with age.
- Cancer can occur in children with the commonest being: leukemias, lymphomas, CNS tumours, Sarcomas and bone tumours.

Summary 2/2

- Neoplasms are new growths with certain genetic changes. They can be benign or malignant.
- Benign tumors are named after the tissue they arise from with adding the suffix: oma.
- Malignant tumours arising from epithelial tissues are carcinomas whereas malignant ones arising from stromal tissue are sarcomas.
- Adenomas are benign neoplasms arising from glandular tissue OR forming glands.
- Hamartoma is a benign neoplasm characterised by haphazardly arranged tissue components endogenous to the tissue or organ they are arising from
- Choristomas are non-neoplastic, congenital proliferations of normal tissue in an abnormal location (ectopic tissue)
- Teratomas are tumours arising in the ovary or testis and show tissue components from the three germ cell lines in different combinations. Teratomas can be benign or malignant.
- Polyp is a macroscopic, not microscopic term, that refers to a projection above a mucosal surface. The majority are benign neoplasms but they could be non-neoplastic (inflammatory polyps) or malignant tumours with a polypod appearance (mainly in the GIT)

Test yourself: Match the lesions in column A with their best description in column B

A	B
Amass in the upper oesophagus composed of normal-looking gastric mucosa	Adenoma
a testicular tumour composed of a cyst lined by respiratory mucosa. The cyst wall contains neural tissue	Choristoma
A brain tumour composed ofdisorganized neural and glial cells	Sarcoma
A colonic mass forming rounded structures lined by mucin secreting cells	Teratoma
An invasive tumour composed of malignant smooth muscle cels.	Hamartoma

Answers

A	B	Explanation
Amass in the upper oesophagus composed of normal-looking gastric mucosa	**Choristoma**	this is normal tissue in an abnormal location.
a testicular tumour composed of a cyst lined by respiratory mucosa. The cyst wall contains neural tissue	**Teratoma**	these can contain any type of tissue from any germ cell line
A brain tumour composed of disorganized neural and glial cells	**Hamartoma**	Haphazard arrangement of endogenous elements
A colonic mass forming rounded structures lined by mucin secreting cells	**Adenoma**	rounded structure, secretory: this is glandular.
An invasive tumour composed of malignant smooth muscle cels.	**sarcoma**	Malignant stromal tumors are sarcomas

Thank you

Don’t get lost in the detail

Look at the bigger picture