MED444
KING SAUD UNIVERSITY

PATHOLOGY TEAMWORK

MED444

Properties of benign & malignant tumors

highly recommend you to watch this for neoplasms + record DR.saleh aldeligan from 443 PAL

OBJECTIVES

- Compare between benign & malignant tumors in terms of differentiation, rate of growth, local invasion & metastases.
- Identify the morphological features that differentiate between benign & malignant tumors.
- Define the terms: differentiation & anaplasia.
- List the pathways by which malignant tumors spread.
- Define the terms: dysplasia & carcinoma in situ.

COLOR INDEX:

MAIN TEXT (BLACK)

FEMALE SLIDES (PINK)

MALE SLIDES (BLUE)

IMPORTANT (RED)

DR'S NOTE (GREEN)

EXTRA INFO (GREY)

Features to distinguish between benign & malignant tumors:

1. A-Differentiation & anaplasia
2. B- Local invasion
3. C- Rate of growth
4. D- Metastasis

Are characteristics seen only in the parenchymal cells that constitute the transformed elements of neoplasms.

Features to distinguish between benign & malignant tumors:

01

Differentiation & anaplasia

the extent to which the parenchymal cells of the tumor resemble their normal counterparts morphologically and functionally.

Differentiation & Anaplasia

• Differentiation:

GIRL'S SLIDES

- Well differentiated → closely resemble their normal counterparts
  Usually benign, the rest is malignant.
- Moderately differentiated
- Poorly differentiated
- Undifferentiated (Anaplasia) → Total loss of differentiation.

Differentiation

Malignant neoplasms

are characterized by a wide range of parenchymal cell differentiation, from well differentiated to completely undifferentiated.

The stroma carrying the blood supply is crucial to the growth of tumors but does not aid in the separation of benign from malignant ones.

Anaplastic: when they are composed of undifferentiated cells.

Benign neoplasms

Well-differentiated: The more differentiated, the similar they are to their normal counterparts in shape & function.
E.g. Benign produces the same hormones as normal cells.

Lipoma

Lipoma close to lipid=fat

mature fat cells laden with cytoplasmic lipid vacuoles.

Chondroma

mature cartilage cells that synthesize their usual cartilaginous matrix (evidence of morphologic and functional differentiation)

Cont..

Differentiation & Anaplasia

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The stroma carrying the blood supply is crucial to the growth of tumors but does not aid in the separation of benign from malignant ones.

Anaplastic: when they are composed of undifferentiated cells.

Anaplastic: loss of structural and functional differentiation.

Hallmark of malignancy.

The amount of stromal connective tissue determines the consistency (texture) of neoplasm.

Eg: Desmoplasia: Dense, abundant fibrous stroma produced by certain cancers. it makes them hard. so called (scirrhous tumors.)

Benign neoplasms

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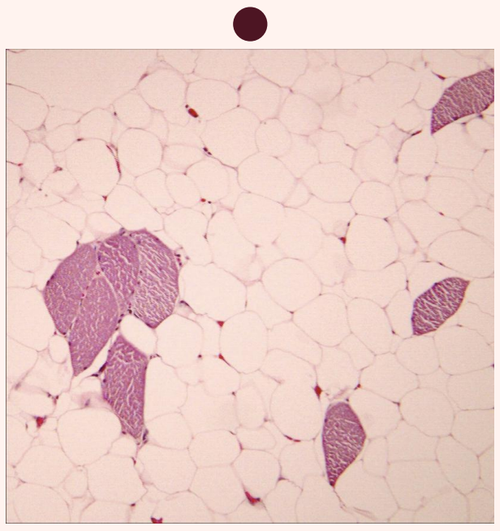
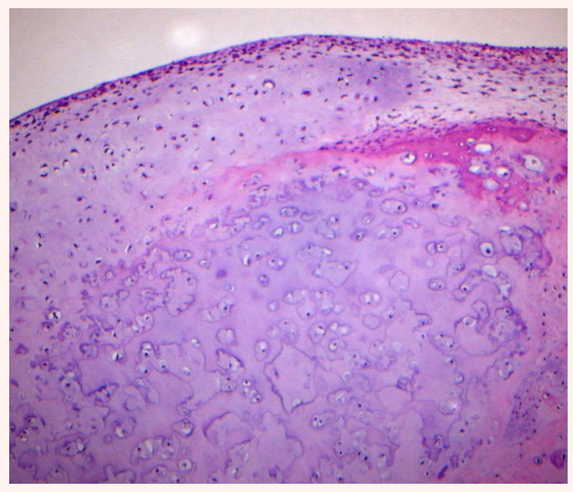
mature fat cells laden with cytoplasmic lipid vacuoles.



Chondroma

mature cartilage cells that synthesize their usual cartilaginous matrix (evidence of morphologic and functional differentiation)



- In well-differentiated benign tumors, mitosis are usually rare and are of normal configuration.

The more differentiated the tumor cell, the more completely it retains the functional capabilities of its normal counterparts.

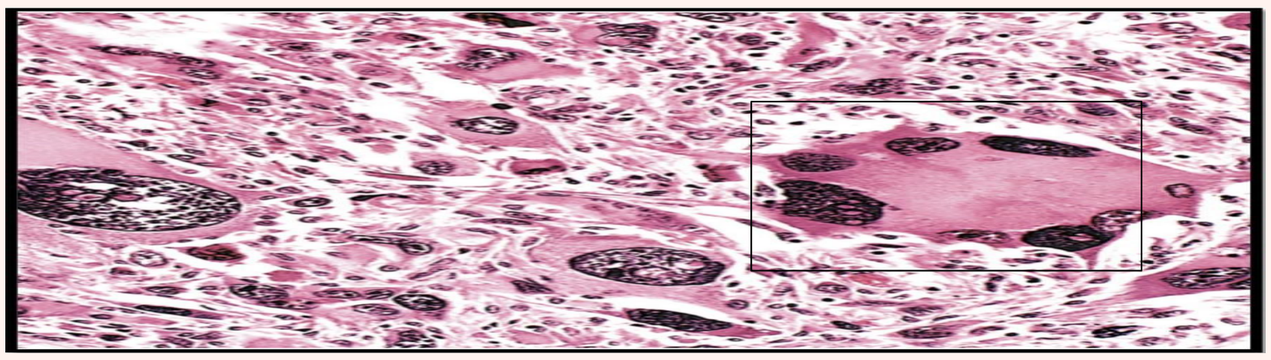
- e.g. benign neoplasms and even well-differentiated cancers of endocrine glands frequently elaborate the hormones characteristic of their origin.

Features to distinguish between benign & malignant tumors (Anaplastic cells):

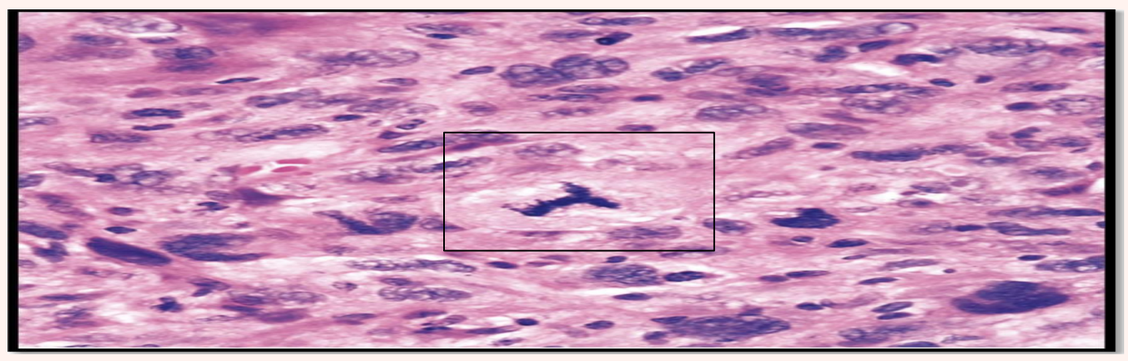
It’s important important to recognize the following histopathological features in any neoplasm:

- ➢ Pleomorphism: variation in size and shape
- ➢ Hyperchromasia (dark nuclei) due to coarse & clumped chromatin
- ➢ Prominent nucleoli
- ➢ Enlarged nuclei resulting in an increase of nuclear to cytoplasm ratio (that may approach 1:1 instead of the normal 1:4 or 1:6)
- ➢ Mitoses often are numerous (atypical or typical), tripolar or quadripolar mitotic figures.
- ➢ Giant cells: larger than their neighbors & possess either one enormous nucleus or several nuclei.
- ➢ Anaplastic nuclei are variable and bizarre in size and shape.
- ➢ They lose normal polarity: fail to develop recognizable patterns of orientation to one another.

➢ Tumor Giant Cells



➢ Atypical Mitosis



- Some cancers may elaborate fetal proteins not produced by comparable cells in the adult. Cancers of nonendocrine origin may produce so-called **ectopic hormones.**
- The more rapidly growing and the more anaplastic a tumor, the less likely it is to have specialized functional activity.

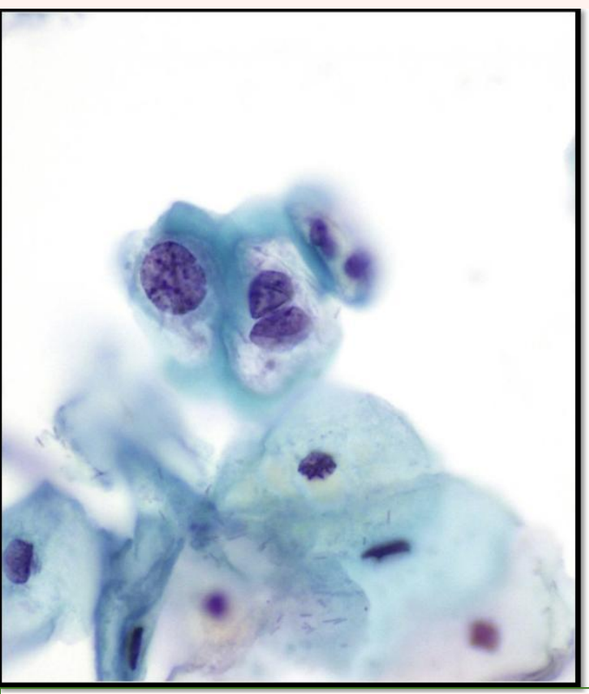
Dysplasia and carcinoma in-situ

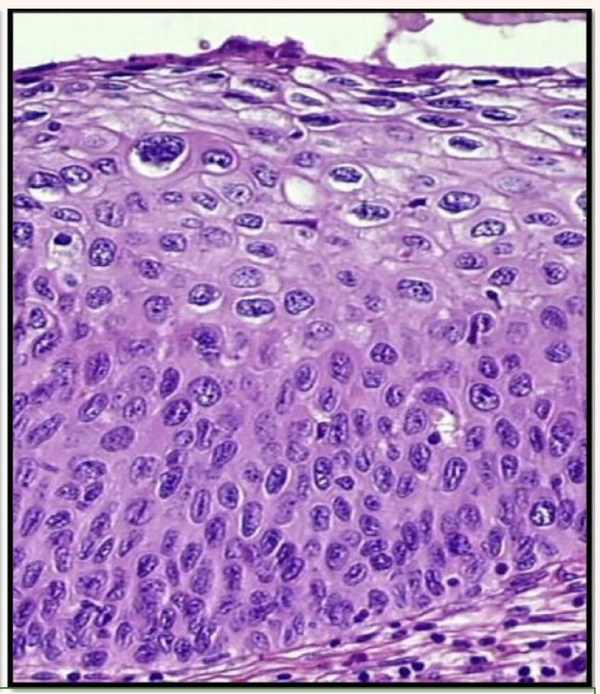
Metaplasia: change in mature to other mature cells,reversible, not directly links to neoplasm.

	Dysplasia	Carcinoma in situ(in location)
Definition	A loss in the uniformity of the individual cells and a loss in their architectural orientation (loss of maturation) It is a non-neoplastic process but a premalignant condition (pre-cancer)	an intraepithelial (inside the mucosa) malignancy (has all features) in which malignant cells involve the entire thickness of the epithelium without penetration of the basement membrane. If dysplastic changes involve the entire thickness of the epithelium it is called carcinoma-in-situ. **a pre invasive stage of cancer.**
Location	occurs mainly in the epithelia.(epithelium)	It is applicable only to epithelial neoplasms
Reversible or irreversible	Dysplasia may be reversible	Irreversible
Cancerous or not	➢ Does not mean cancer ➢ Does not necessarily progress to cancer	➢ It displays the cytological features of malignancy without invading the basement membrane
How it differs from cancer	➢ Lack of invasiveness ➢ Reversibility	➢ It is a true neoplasm with all of the features of malignant neoplasm **except** invasiveness.
Histological Features Of Dysplasia	Dysplastic cells show a degree of: pleomorphism, ↑N:C ratio, hyperchromasia, irregular nuclei, increased mitosis, loss of polarity & a disordered mutation Or total failure of maturation. Dysplastic cells show some features but no to the point of cancer.(note 443)	
The risk of invasive cancer in dysplasia varies with	➢ grade of dysplasia (mild, moderate, severe) ➢ - duration of dysplasia ➢ site of dysplasia	

Dysplasia and carcinoma in-situ (cont.)

Dysplasia

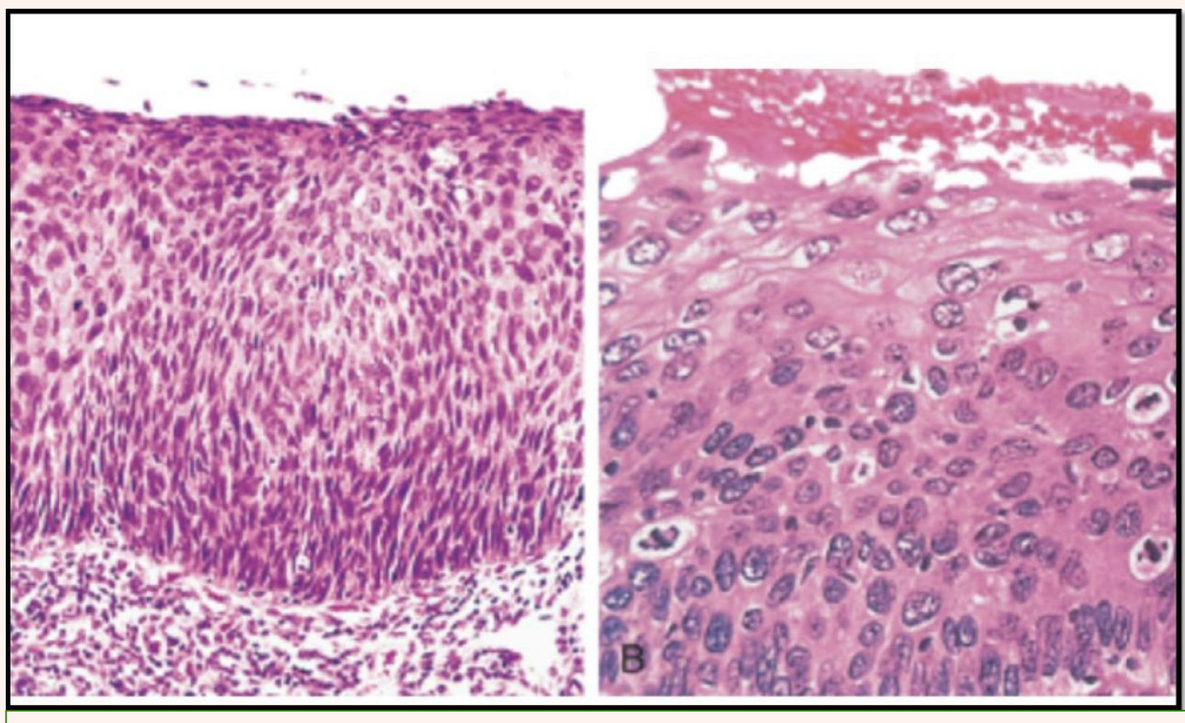




Cytology:
Hyperchromasia
enlarged but not severe.

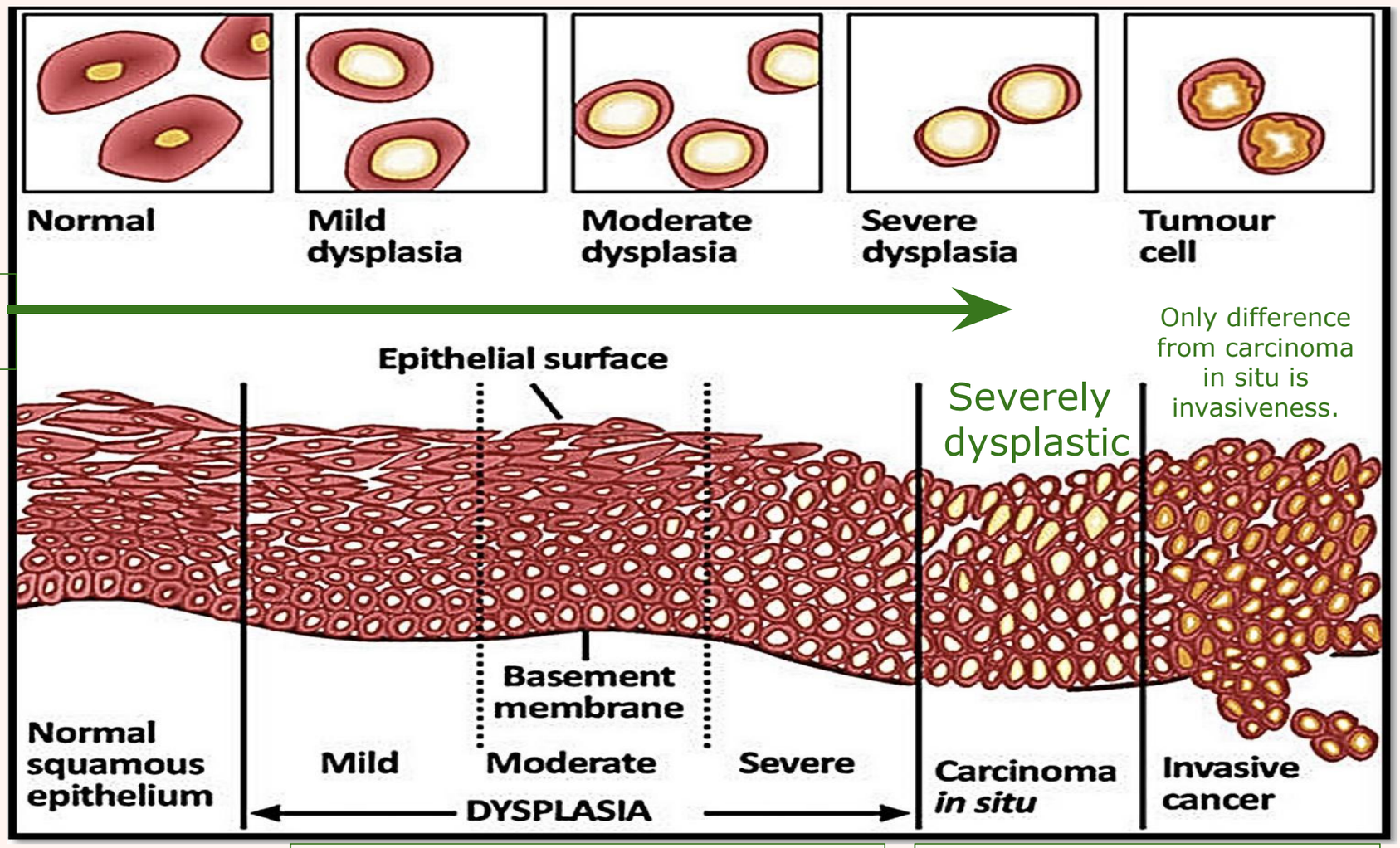
Histology:
Few atypical cells/loss of maturation in layers.
Note443

Carcinoma in-situ



Situ= location, no invasiveness
Loss of maturation, basement membrane is not invaded

Risk increases



Reversible/no invasion
Some features but mild

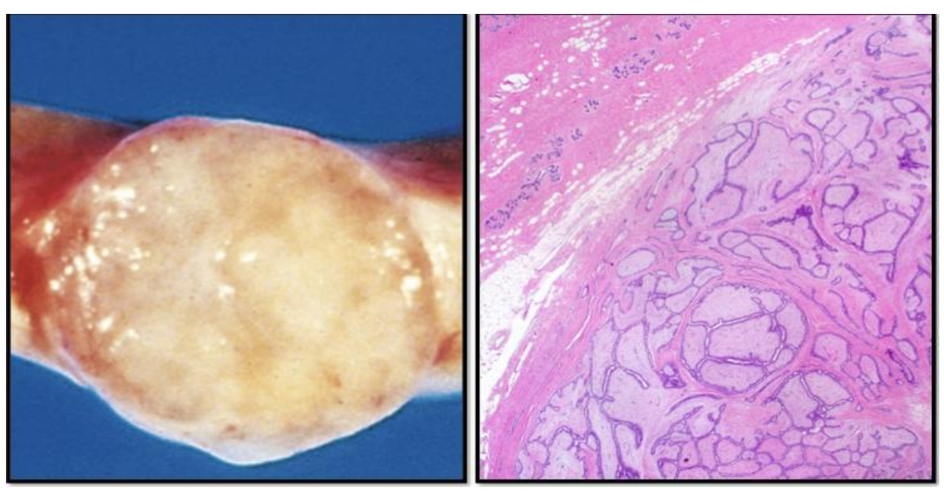
Irreversible

Features to distinguish between benign & malignant tumors:

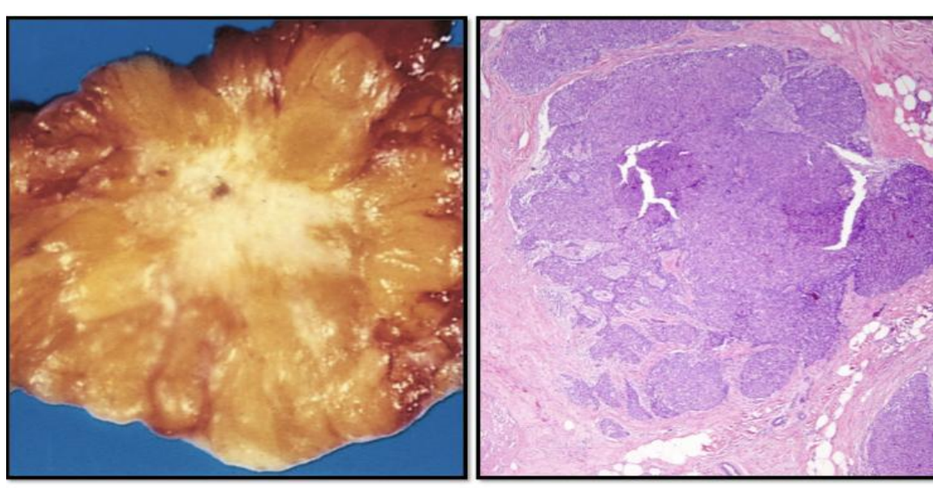
02

Rate of growth and local invasion

	Benign of tumors	Malignant tumors (cancers)
Rate of Growth	➢ **Grow slowly,** ➢ **their growth is affected by:** ➢ adequate blood supply ➢ Location ➢ hormones e.g.leiomyoma of the uterus. ➢ Many exceptions to this generalization, however, and some benign tumors grow more rapidly than some cancers.	➢ grow fast, (metastasizing: spreading locally and to distant sites & causing death) ➢ usually correlates inversely with their level of differentiation.
Local invasion	➢ remain localized. ➢ cannot invade. ➢ usually encapsulated (not all) ➢ (surrounded by a fibrous capsule). ➢ For example, as adenomas slowly expand, most develop an enclosing fibrous capsule that separates them from the host tissue. ➢ Although encapsulation is the rule in benign tumors, the lack of a capsule does not mean that a tumor is malignant.	➢ invade the underlying basement membrane or stroma. ➢ Progressive invasion ➢ Destructive. ➢ They are usually not capsulated. ➢ The infiltrative mode of growth makes it necessary to remove a wide margin of surrounding normal tissue when surgical excision of a malignant tumor is attempted. ➢ Surgical pathologists carefully examine the margins of resected tumors to ensure that they are devoid of cancer cells (clean margins). ➢ Next to the development of metastases, local invasiveness is the most reliable feature that distinguishes malignant from benign tumors.



Local invasion



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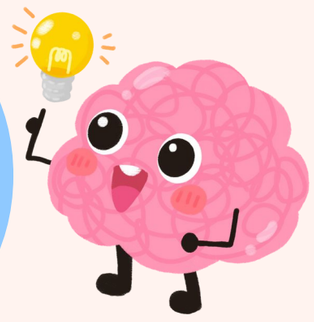

Rate of growth factor continue...

• there is wide variation in the rate of growth. Some grow slowly for years and then enter a phase of rapid growth, signifying the emergence of an aggressive subclone of transformed cells. Others grow relatively slowly and steadily.

• Rapidly growing malignant tumors often contain central areas of ischemic necrosis, because the tumor blood supply, derived from the host, fails to keep pace with the oxygen needs of the expanding mass of cells.

Cancer Stem Cells and Lineages:

• The continued growth and maintenance of many tissues that contain short-lived cells, such as the formed elements of the blood and the epithelial cells of the gastrointestinal tract and skin, require a resident population of tissue stem cells that are long-lived and capable of self-renewal.

• Cancers are immortal and have limitless proliferative capacity, indicating that like normal tissues, they also must contain cells with "stem-like" properties.

• The cancer stem cell hypothesis posits that, in analogy with normal tissues, only a special subset of cells within tumors has the capacity for self-renewal.
The concept of cancer stem cells has several important implications. Most notably, if cancer stem cells are essential for tumor persistence, it follows that these cells must be eliminated to cure the affected patient.

• Thus, the limited success of current therapies could be explained by their failure to kill the malignant stem cells that lie at the root of cancer.

Features to distinguish between benign & malignant tumors continue...

3 Metastasis

DEFINITION

It is the development of secondary implants of a tumor that are discontinuous with the primary tumor & located in remote tissues (far from origin).

DR'S NOTE

- Discontinuous indicates metastasis.
- Continuous indicates local invasion.

- More than any other attribute, the property of metastasis always identifies a neoplasm as malignant. It is the most important sign of malignancies.
- Cancer have different ability to metastasize.
- Approximately 30% of patients present with clinically evident metastases, excluding skin cancers other than melanomas.
- Generally, the more anaplastic and the larger the primary tumor, the more likely it metastasizes. but as with most rules, there are exceptions. Like extremely small cancers have been known to metastasize; conversely, some large and ominous-looking lesions may not.

Pathways of Malignant Neoplasm Dissemination (metastasis pathways)

Seeding within body cavities	Lymphatic spread	Hematogenous spread
Occurs when neoplasms invade a natural body cavity. Seedings are deposits of tumors in cavities.	More typical of carcinomas.	Favored by sarcomas but can occur in carcinomas.
Particularly characteristic of cancers of the ovary, which often cover the peritoneal surfaces widely.	Breast carcinoma → axillary lymph node Lung carcinomas → bronchial lymph node	Veins are more commonly invaded, because they have a thin wall. The liver and lungs are the most frequently involved secondary sites.

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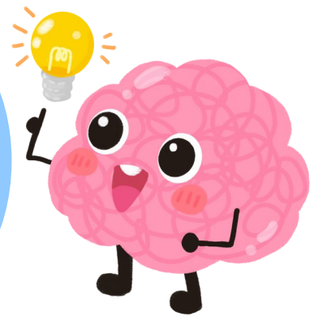


Rate of growth factor continue...

→ **Lymphatic spread:**

• A "sentinel lymph node" is the first regional lymph node that receives lymph flow from a primary tumor. It can be identified by injection of blue dyes or radiolabeled tracers near the primary tumor.

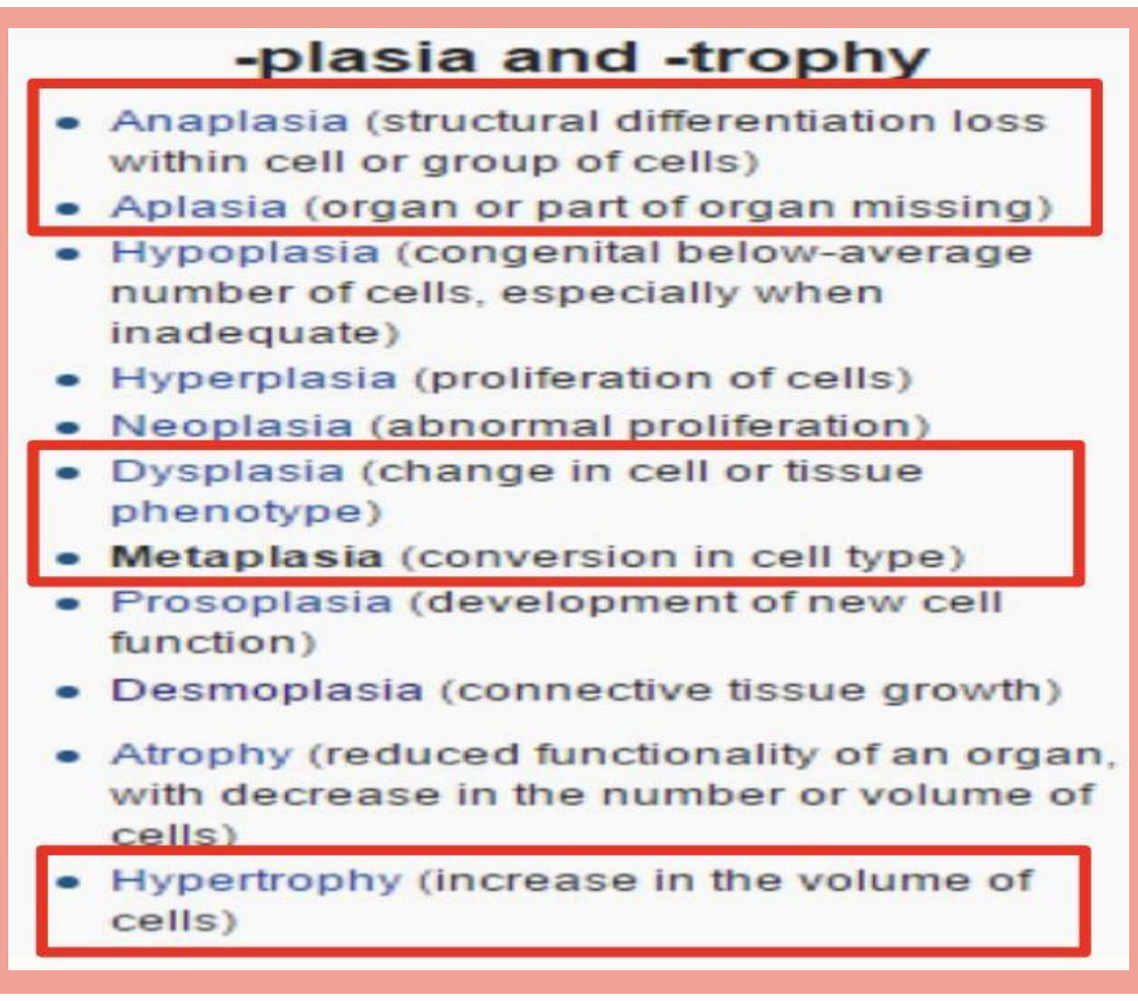
• Biopsy of sentinel lymph nodes allows determination of the extent of spread of tumor and can be used to plan treatment.

• Although enlargement of nodes near a primary neoplasm should arouse concern for metastatic spread, it does not always imply cancerous involvement. Thus, histopathologic verification of tumor within an enlarged lymph node is required.

→ **Hematogenous spread:**

• With venous invasion, the blood-borne cells follow the venous flow draining the site of the neoplasm, with tumor cells often stopping in the first capillary bed they encounter.

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



Thanks Team 443

Summary

Characteristics of Benign and Malignant Tumors:

- Benign and malignant tumors can be distinguished from one another based on the degree of differentiation, rate of growth, local invasiveness, and distant spread.
- Benign tumors resemble the tissue of origin and are well differentiated; malignant tumors are poorly or completely undifferentiated (anaplastic).
- Benign tumors are slow-growing, whereas malignant tumors generally grow faster.
- Benign tumors are well circumscribed and have a capsule; malignant tumors are poorly circumscribed and invade the surrounding normal tissues.
- Benign tumors remain localized to the site of origin, whereas malignant tumors are locally invasive and metastasize to distant sites.

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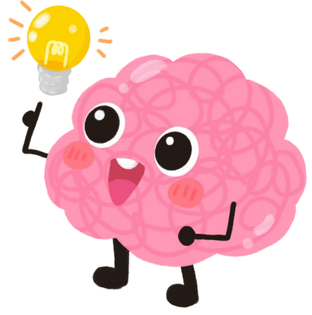

KEYWORDS

Metastasis	It is the development of secondary implants of a tumor that are discontinuous.
Lymphatic spread	More typical of carcinomas.
Hematogenous spread	Favored by sarcomas.
Benign neoplasm	Well-differentiated
Benign of tumors	Grow slowly
Malignant of tumors	Grow fast
Carcinoma in situ	Pre invasive stage of cancer

MCQ

1- Which term is used to describe a malignant neoplasm that involves the entire thickness of the epithelium without penetration of the basement membrane?			
A) Dysplasia	B) Carcinoma in situ	C) Anaplasia	D) Metaplasia
2- Which of the following describes Carcinoma in-situ?			
A) Pre-cancer	B) Metastasis tumor	C) pre invasive stage of malignancy	D) Well-differentiated tumor
3- Characterized by a wide range of parenchymal cell differentiation, from well differentiated to completely undifferentiated?			
A) Benign neoplasm	B) Dysplasia	C) Carcinoma in situ	D) Malignant neoplasm
4- The most important sign of malignancies is?			
A) Metastasis	B) Rate of growth	C) Anaplasia	D) Local invasion
5- What is the common characteristic of carcinoma?			
A)Hematogenous spread	B) Lymphatic spread	C) Metastasis in skeletal muscles	D) Seeding within body cavities

MCQ

6- What term is used to describe the loss of structural and functional differentiation in tumor cells?			
A) Differentiation	B) Anaplasia	C) Dysplasia	D) Carcinoma in situ
7- Differentiation refers to:			
A)The ability of tumor cells to invade nearby tissues	B) The rate of growth of a tumor	C)The resemblance of tumor cells to their normal counterparts	D)The ability of tumor cells to spread to distant sites
8- Which term is used to describe the increase in the volume of cells?			
A) Hypertrophy	B) Atrophy	C) Aplasia	D) Metaplasia
9- Which one of the following is a malignant neoplasm?			
A) melanoma	B) mesothelioma	C) seminoma	D)A&B&C

Answers (Don't look):

1/B — 2/C — 3/D — 4/A — 5/B — 6/B — 7/C — 8/A — 9/D

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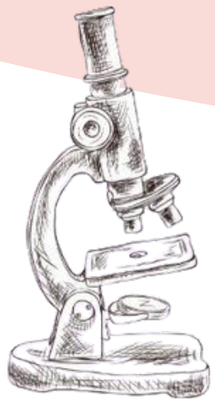

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