Pulse.

Easy

PATHOLOGY

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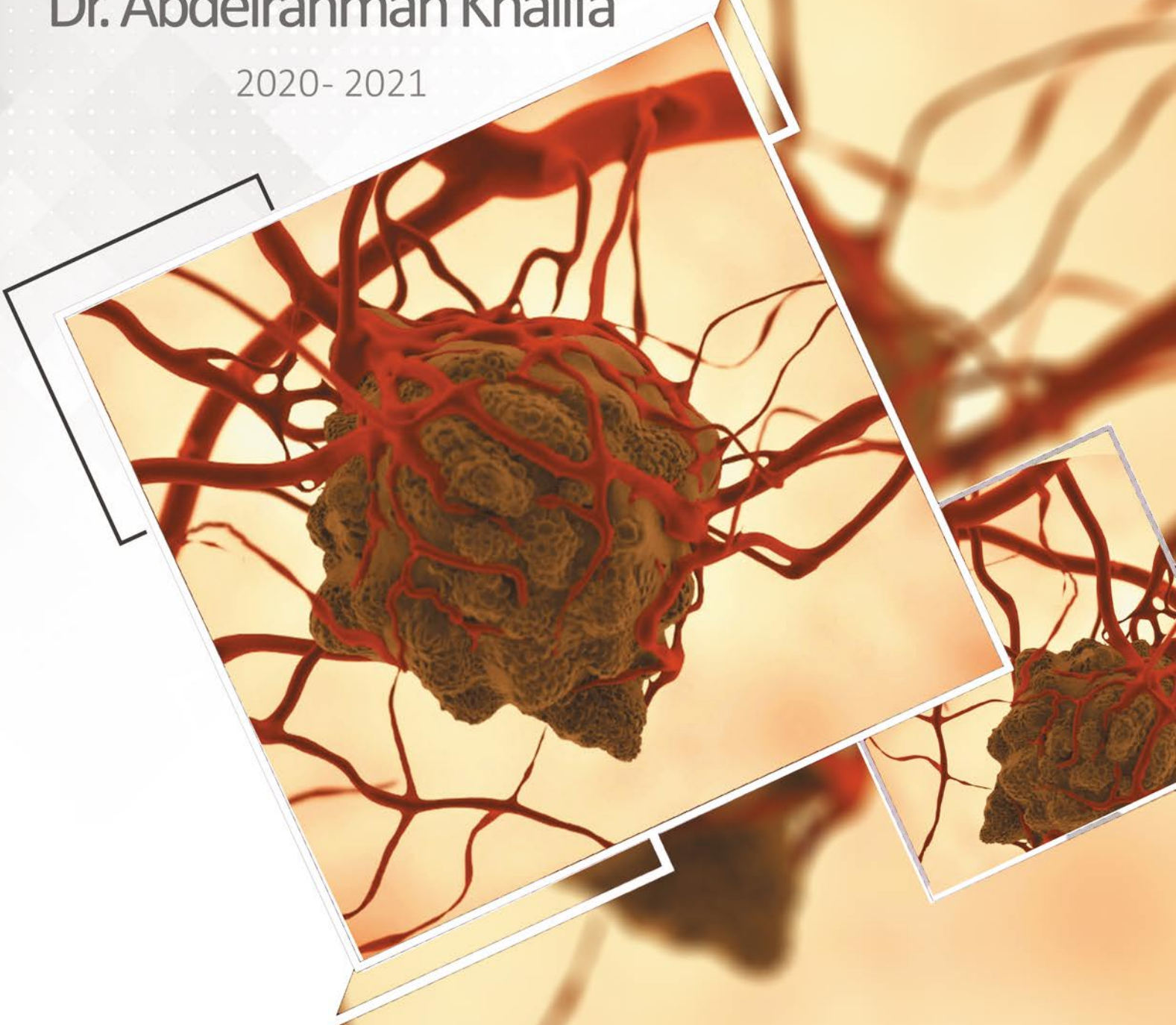
2020- 2021



Neoplasia

Part 1

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Easy Pathology

Neoplasia

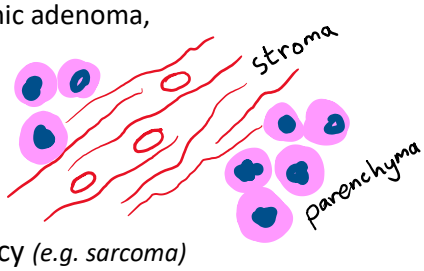
Mass of cells, with uncontrolled, irreversible & and unlimited proliferation

Classifications:

According to Behavior:	According to Origin:
-Benign (no invasion, no spread)	**-Epithelial**
-Malignant (invasive, with distant spread)	**-Mesenchymal**
-Locally malignant (invasive, with no spread)	**-Others** (Leukemia, melanoma, Embryonic tumors)

Microscopic features:

- **Structure:**
  - **Parenchyma**
    - Epithelial tumors: acini , papillae , sheets , or cords
    - mesenchymal tumors: Bundles , whorls **with matrix** (e.g. cartilage)
    - some tumors show mixed pattern (e.g. pleomorphic adenoma, fibroadenoma, carcinosarcoma)

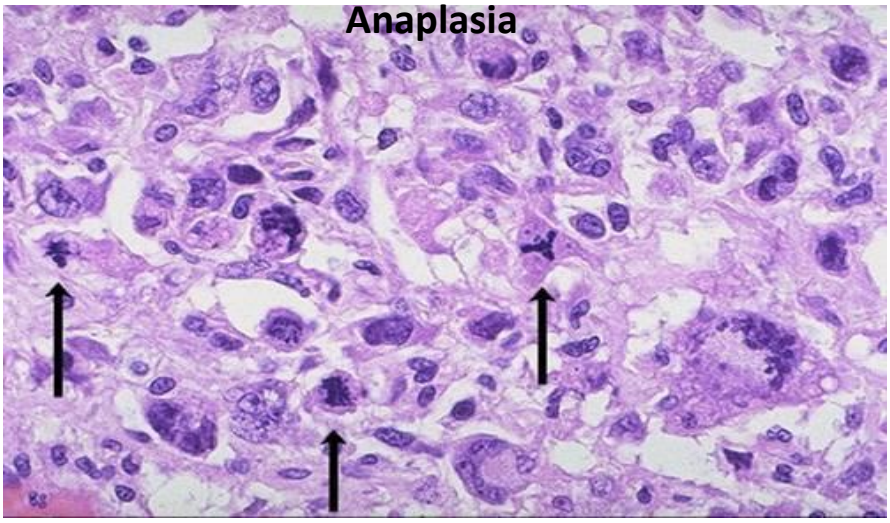


  - **Stroma** formed of:
    - Collagenous fibrous tissue
      - Stimulated by b-FGF
      - Scant stroma → gives fleshy consistency *(e.g. sarcoma)*
      - Excess (desmoplasia)→ firm gritty (e.g. scirrhus carcinoma)
    - Blood vessels (newly formed by Angiogenesis from preexisting ones)

- **Differentiation** **similarity to origin**. Variable according to type benign or malignant
  differentiation is defined as the extent of morphological and functional resemblance of parenchymal tumor cells to normal cells
-

- **Anaplasia** loss of differentiation, with morphological abnormality
  - **Pleomorphism** *variable shape & size of tumor cells*
  - **Hyperchromatism** *dark stained (increased nucleoprotein)*
  - **Increased N/C ratio** *> 1:4*
  - **Frequent mitoses & Abnormal mitotic figures** *(tripolar, multipolar)*
  - **Abnormal nuclei (Anisonucleosis)** *vesicular, pleomorphic*
  - **Prominent & multiple nucleoli**
  - **Tumor giant cells (**large cells , with multiple bizarre nuclei**)**
  - **Loss of polarity** disturbed orientation and arrangement
  - **Functional Changes** (better differentiated tumors secrete hormone, bile or keratin)
  - **Chromsomal changes** (mutated genes & increased number of chromosomes→ large nucleus)
    e.g. Philadelphia chromosome in Chronic myloid Leukemia

- **Inflammatory reaction** caused by **2ry infection** of ulcer - or **immune reaction** against tumor (e.g. Inflammatory cells in Seminoma)
  inflammatory reaction : chronic inflammation or granuloma



Dysplasia

Disordered proliferation arrangement and morphology of cells but not neoplastic

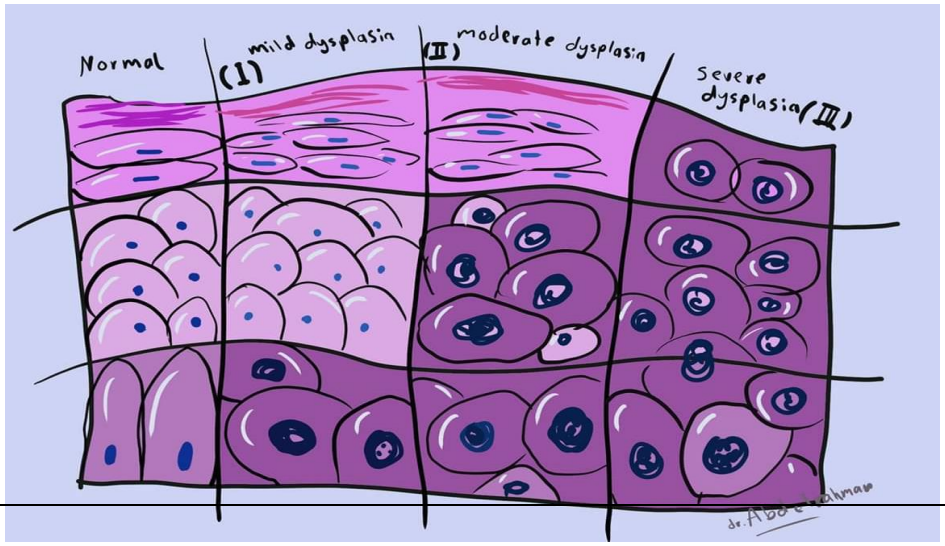
Site surface **epithelium** and glands . caused by chronic irritation (e.g. prolonged inflammation)

Microscopic changes : disorder of arrangement + Anaplasia (enumerate)

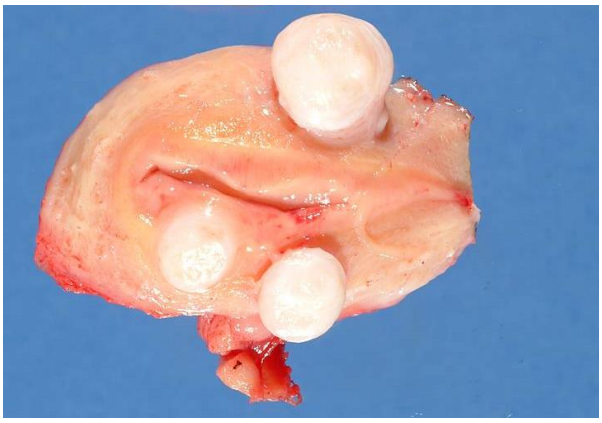
Grades of dysplasia in Stratified Squamous epithelium:

- **Grade I (mild)** : dysplasia of the lower third (reversible)
- **Grade II (moderate)**: dysplasia of the lower 2/3 (reversible)
- **Grade III (severe)**: dysplasia of the full thickness → may change to Carcinoma in situ (CIS) not invading basement membrane

Fate: Dysplasia is precancerous but reversible



		Benign tumors	Malignant tumors
Behaviour	Rate of growth	**Slow** (could be rapid in Leiomyoma, which is hormonal-dependant) some tumors may shrink suddenly due to ischemia e.g. pituitary adenoma	**Fast** Lead to central ischemic necrosis -but Some tumors may shrink & disappear due to host immunity (e.g. melanoma, choriocarcinoma)
	Mode of growth	Expansion	Invasion and destruction
	Effect	Compression – obstruction – hormonal secretion	Same…….. + effects of metastasis
	Spread & metastasis	Absent	present
	Recurrence	Not recurrent	Recurrent *(why?)*
	Prognosis	Good prognosis	Bad prognosis
Gross	Shape & boundaries	**In solid organs:** Rounded – oval **surface epith.:** papillae - polyp	**In solid organs:** irregular ill-defined **surface epith.:** fungating – ulcer-diffuse thickening
	Capsule	**Capsulated** Except leiomyoma, well-demarkated by compressed tissue (false capsule)	**Not capsulated** Some are partially capsulated (e.g. follicular carcinoma of thyroid)
	Surrounding tissue	**compressed**	**infiltrated**
Micro	Differentiation	Well differentiated	Variable well, moderate, poor, or undifferentiated
	Anaplasia	Absent	Present
	Chromosomal changes	Infrequent	Present

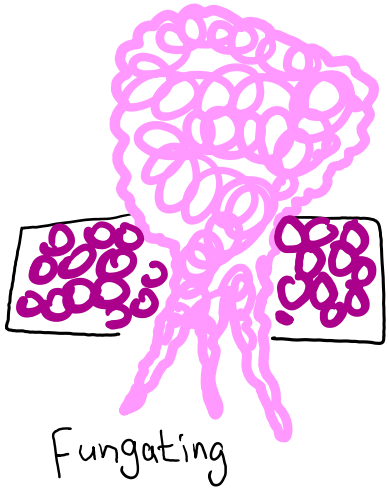


The most important feature of malignancy is Invasion & metastasis

		Carcinoma	Sarcoma
origin		**epithelial**	**mesenchymal**
Behaviour	Rate of growth	Lass Rapid	Rapid
	Mode of growth	infiltration	Infiltration and Expansion
	Spread	Early lymphatic → late blood	Early blood spread
	Prognosis	Relatively better	worse
	incidence	More common	Less common
	Age	Old age	Young age
Gross	Size	Relatively Smaller	Large bulky mass
	Shape	**In solid organs:** irregular ill-defined **surface epith.:** fungating – ulcer- diffuse thickening	irregular ill-defined
	C/S	Grayish white (better stroma) Less necrosis and hemorrhage.	Homogenous with extensive necrosis and hge.
	Consistency	**Firm**	**Soft fleshy**
Micro	Differentiation	More	Less
	Cohesion	**More cohesive** Arranged in sheets, glands, cords Separated by stroma, or papillae	**Less cohesive** Highly cellular Individual cells
	Anaplasia	present	more
	Stroma	Less vascular Well formed fibrous stroma	highly vascular scant fibrous stroma

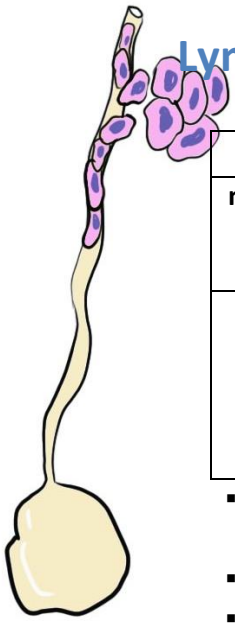
N.B. Malignant ulcer :

Raised everted edge – Necrotic hemorrhagic floor – Fixed indurated base

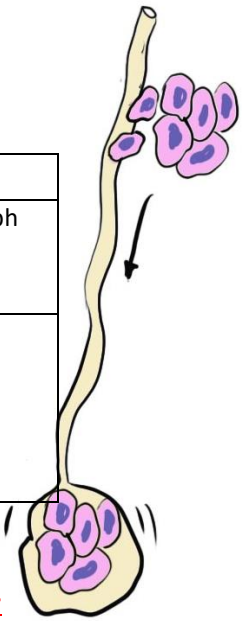


Methods of spread of Malignant tumors

- Benign tumor, Locally malignant tumors , & malignant brain tumors → No spread
- The more Anaplasia & tumor size → more likely is the spread
- 30% of malignant tumors → evident metastasis & 20% → occult metastasis



Lympatic spread *(more common in **carcinomas**)*



	Lymphatic permeation	Lymphatic Embolism
mechanism	Proliferation of tumor cells inside lymph vessel as a cord	movement of tumor emboli by lymph vessels into lymph nodes → found subcapsular → then destroy L.N.
Effects	**-Lymphatic edema** **- Retrograde lymphatic spread** (GIT & prostatic carcinoma → reach supra clav L.N. **Virchow's L.N**.)	**-Regional LN:** large, firm, fixed **-Spread to other LNs** **-Late blood spread** (?)

- **L.N. enlargement** in tumor is due to metastasis or Reactive Lymphadenitis and histocytosis caused by cancer products.
- GIT and some breast carcinomas → reach both ovaries by lymphatics **Krukenberg tumor**
- **Sentinel L.N.** is the 1st L.N. receiving metastasis in regional L.N.

Hematogenous spread *(early in sarcomas)*

Mechanism:

- ***Direct invasion*** *of blood vessels (mostly veins) →tumor embuls covered by platelets as a thrombus → reach distant site → early blood spread (common in **sarcoma**) .*
  Invasion of arteries is rare because of thick wall and elastic lamina
- ***Lymphatic spread*** *→ late blood spread (**carcinoma**)*
- *Some **carcinomas** invade blood vessels: .Thyroid, HCC, RCC, prostatic*
  Renal cell carcinoma often invades renal vein to inferior vena cava

Common Sites of metastasis:

- ***Lung*** Receive metastasis from tumors drained by systemic veins
  e.g. RCC invades renal vein → inferior vena cava → right side of the heart
- ***Liver*** Receive metastasis from organs drained by portal vein (GIT)
- ***Bone & Brain***

Organ Tropism

- Arrest of tumor emboli in vessels of specific organs by binding between adhesion molecules of tumor cells and specific receptors on target endothelium
- **Thyroid, Lung, breast, renal, & prostatic carcinomas → bone metastasis**
- **Sarcomas → bone, Liver and Lung metastasis**
- **Bronchial carcinoma → Brain, liver and adrenal metastasis**
- **Seminoma & RCC → Lung metastasis**

spleen ,**heart** & **skeletal muscles** do **not allow** tumor metastasis to grow

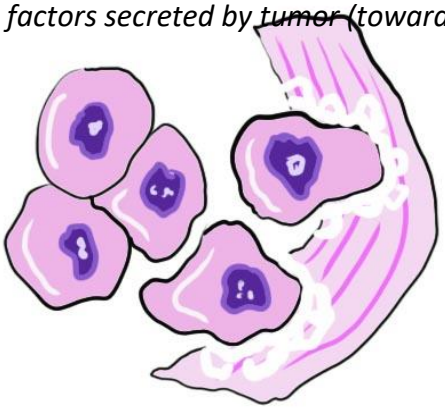
Spread through body cavities

- **Serous sac (Transceolomic):**
  e.g. ovarian tumors→ peritoneal , mesothlioma→ pleural ,
  GIT tumors → ovarian implantation (**Krukenberg tumor**)
- **CSF** : e.g. medulloblastoma → implanted in meninges

Perineural

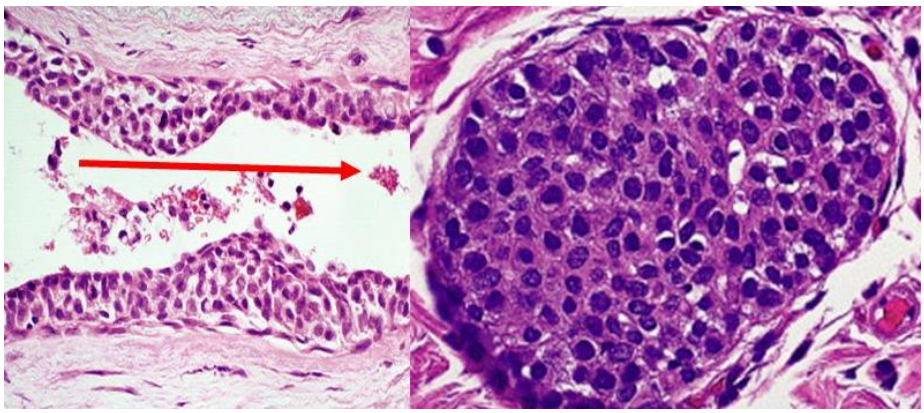
*Prostatic, Pancreatic, and Parotid adenoid cystic carcinoma → secrete **MMPs** → invade nerve → Pain. Poor prognosis*

Direction of growth is controlled by Growth factors secreted by tumor (towards the weakest point)



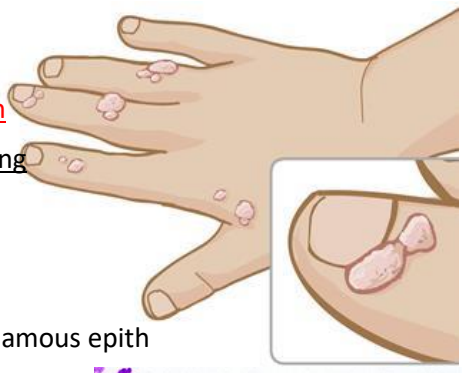
Intraepithelial (canalicular)

- Duct carcinoma may reach lobules through ducts
- Endometrial carcinoma reach ovaries through Fallopian tube
- Renal Cell Carcinoma reach urinary tract through ureter



Epithelial Tumors

Papilloma

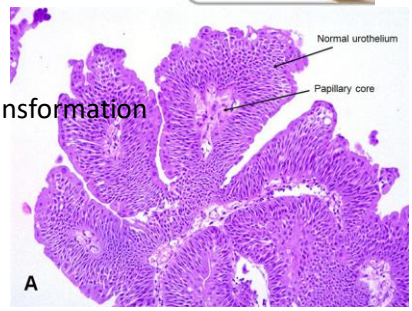


Benign tumor of surface epithelium

Gross: papillae *(pedunculated – sessile)* - Single or multiple branching

Micro:

- **Core:** vascular fibrous tissue
- **Covered**: by proliferated epithelium
  - Squamous Cell Papilloma → covered by str. Squamous epith
  - Transitional Cell Papilloma→ transitional
  - Columnar Cell Papilloma → columnar



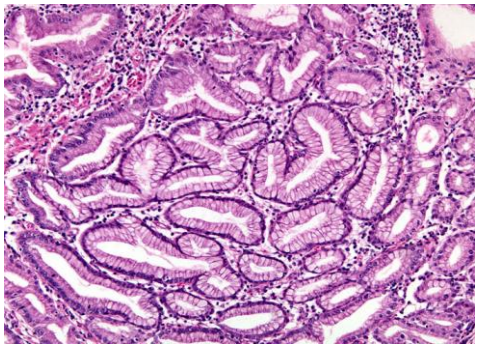
Complications ulceration → bleeding & 2ry infection . Malignant transformation

Adenoma

Benign tumor of glandular epithelium

Sites

- Glands *(endocrine – exocrine)* : breast, thyroid, ovary, salivary…etc.
- GIT : Gastric ,intestinal, colonic & bronchi



Gross

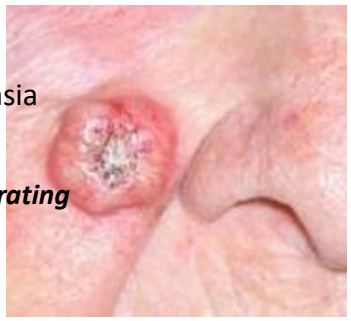
- Capsulated well defined in solid organs
- Polyp in GIT
- Cystic containing secretion, or papillary cystic

Micro: glandular tissue & stroma

Complications

- Secretion of hormones *(e.g. thyroid adenoma)*
- Malignant transformation *(GIT adenomas are precancerous)*

Squamous cell carcinoma SCC



Malignant tumor of stratified Squamous epithelium

Sites: str. Sq. epithelium *(enumerate?)* - On top of squamous metaplasia

Gross:

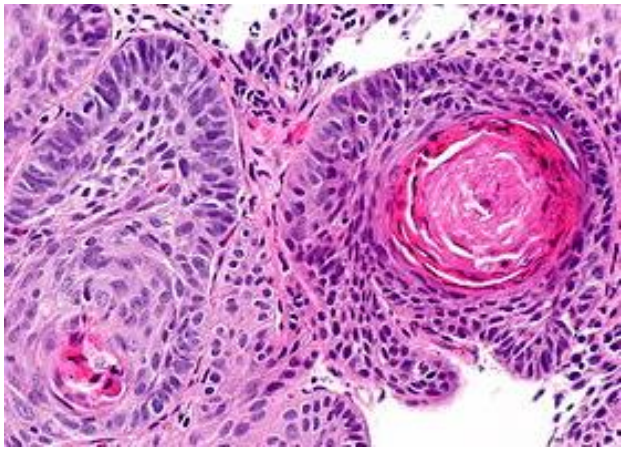
Fungating, ***Ulcer***: inverted edge , necrotic floor ,hard base, ***infiltrating***

Micro:

- masses of malignant str. Sq. epith.
- variable in shape and size
- may show keratinized nests
- separated by stroma

Broder's grading:

- **Grade I** : 50% - 100% of masses → cell nest
- **Grade II:** 25% - 50% of masses → cell nest
- **Grade III:** less than 25% of masses → cell nest
- **Grade IV:** no cell nest



Carcinoma in situ (CIS)

Malignant epithelial changes, before invasion of basement membrane

Sites: glandular & surface epithelium: e.g. **B**reast, **B**ladder, **B**ronchi, **C**ervix, **S**kin… etc.

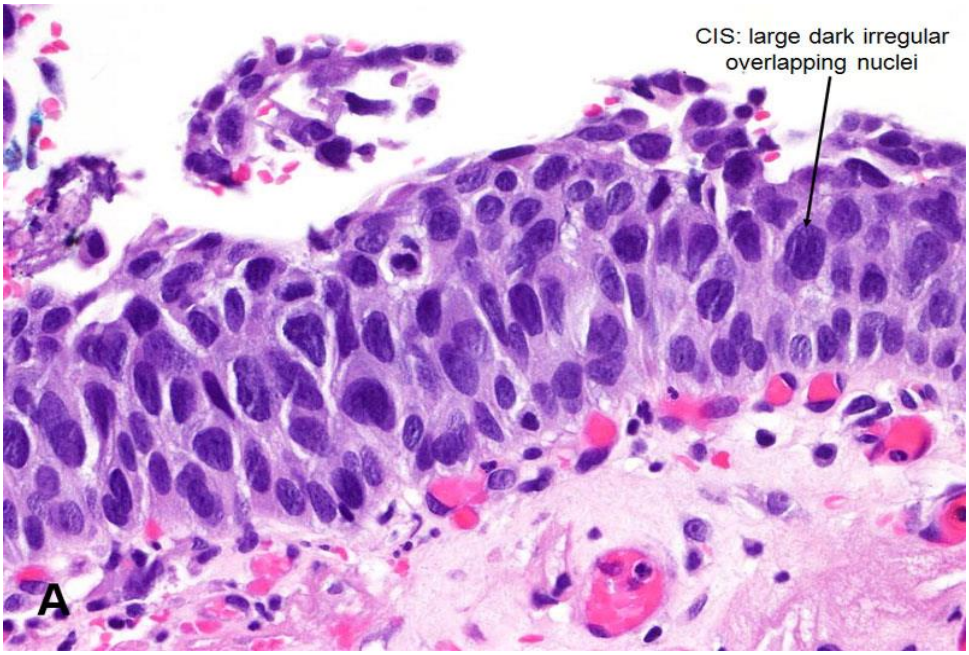
Micro:

Anaplasia *(enumerate..?)*

Loss of polarity (i.e. irregular arrangement of cells)

Basement membrane is intact

Fate: Invasive Carcinoma ***after few years***



Basal cell carcinoma

Locally malignant 'Rodent ulcer' (the most common malignant of skin)

Sites: Skin (upper part of the face, around the eye), neck, back, shoulder, hands
the commonest site: above a line drawn from angle of mouth to ear lobule. (sun exposed)

P.F. U.V. rays, Arsenic , radiation , Fair white people , more in males

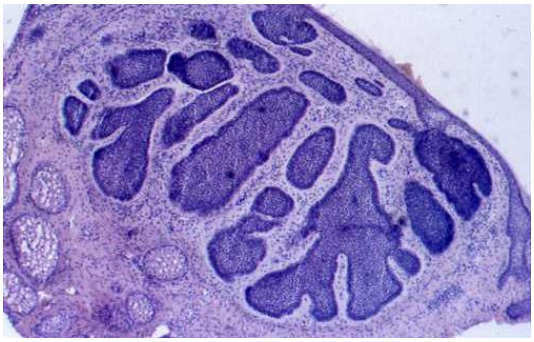
Gross:

- Red nodule (sometimes brown)
- Ulcer: inverted rolled in edge – necrotic floor – fixed base

Micro:

Malignant Cells with scant cytoplasm:

- Forming basaloid masses
- Peripheral pallisading
- Surrounded by stroma
- Melanin pigment

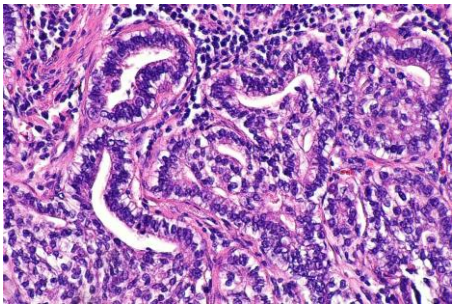


Complications

Local invasion
2ry infection of deep ulcers → lymphadenitis

Glandular-carcinoma

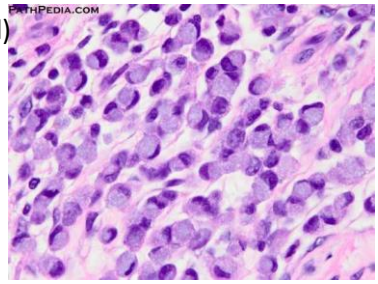
Adenocarcinoma 'Malignant tumor of glands'



- Well deffrentiated : malignant **acini** & stroma
- Poorly differentiated : malignant cells , less **acini**

Mucoid : extracellular mucin lakes & malignant glands (e.g. colorectal carcinoma)

Signet ring: adeocarcinoma , with intracellular mucin (signet ring cell)
e.g. Gastric carcinoma & Krukenberg
local spread is more aggressive



C.T. Tumors

Benign: e.g. Lipoma, fibroma

Gross: Capsulated well defined . **micro:** similar to origin

Malignant: Sarcomas

Haemangioma

The most common benign tumor

Sites: Subcutaneous – organs *(e.g.liver)*

Gross:

shape: irregular patch or swelling **color:** red, brown, blue

Micro:

- Vascular spaces lined with endothelium, containing RBCs
  - Small spaces in **Capillary hemangioma** (usually in skin)
  - Larger spaces in **Cavernous hemangioma** (skin < organs as liver and tongue)
- Fibrous stroma between vessels

Lymphangioma

tumor forming vascular spaces containing lymph

Sites: Head , neck (Cystic hygroma of newborn) , Submucous (lip, and tongue) – organs *(e.g.liver, spleen)*

Gross:

shape: patch or swelling **capsule:** absent **color:** pale

Macro-glossia: enlarged tongue , macro-chelia: enlarged lips

Micro:

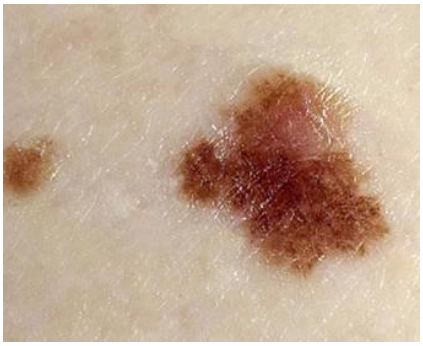
- Vascular spaces lined with flat endothelium, containing Lymph & lymphocytes
  - Small spaces in **Capillary lymphangioma**
  - Larger spaces in **Cavernous lymphangioma**
- Fibrous stroma between spaces

Nevus

Benign tumor of melanocytes

Gross: well defined Flat or elevated papule, brown or black

Microscopic Types: junctional – compound - intradermal



Melanoma

malignant tumor of melanocytes

Gross: nodule or malignant ulcer

Microscopic: malignant melanocytes, invading dermis

prognosis depends on **depth of invasion**

Teratoma

Composite tumor, forming ectodermal, mesodermal, and endodermal tissues, not related to site of origin

Origin: Totipotent stem cell

- Embryonic rests *: present in midline & congenital*
- Germ cell → *gonadal & acquired*

Types:

- **Mature (benign)** well deferentiated mixed tissue
- **Immature (malignant)** immature fetal tissue
- **Mature with malignant transformation** (e.g. mature with squmaous cell carcinoma or adenocarcinoma)
- **Mono-dermal** single type of mature tissue not related to site of origin
  e.g. Struma-ovarii (normal thyroid tissue in ovary)

Embryonic tumors

Malignant tumor of embryonic tissue in children less than 5 years

Origin: Embryonic cells (partially differentiated cells)

Micro: Blastemal cells : small rounded or oval– dark neuclei

Types:

- Medulloblastoma (Cerebellum)
- Retinoblastoma (eye)
- Hepatoblastoma (liver)
- Neuroblastoma (adrenal medulla) the most comon
- Nephroblastoma or Wilm's tumor (renal)

Hamartoma

Tumor-like mass of disorganized mature tissue

- Lung hamartoma: bronchi, vessels, and cartilage
- Liver hamartoma: Liver cells , bile ducts, & vessels

Choristoma (heterotopia): congenital ectopic tissue , e.g. pancreatic tissue in stomach

Locally malignant tumors

- Slower rate of growth
- Local invasion
- Rare distant spread
- Morphologically similar to malignant
- Better prognosis
- Includes:
  - **A**damentenoma
  - Astrocytoma grade II
  - **B**asal cell carcinoma
  - **C**arcinoid
  - **D**esmoid tumor
  - Giant cell tumor (Osteoclastoma)

Grading of malignant tumor:

is microscopic evaluaton of differentiation (similarity to origin) ,depends on similarity to origin and mitosis

I: well differentiated

II: moderately differentiated **III**: poorly diff. **IV**: undefferentiated

Staging of malignant tumor: is evaluation of extension and spread , *which is much more important than grading, and requires clinical and radiological investigations. requires Radiology (CT, MRI, Pet) + Clinical + pathological examination*

TNM system

T: tumor size & extent, **N:** number of affected LNs , **M:** distant blood metastasis

Tis: CIS T1: <2cm T2: 2-5 cm T3: 5-10cm T4: >10 cm

N0: no LN mets. N1:regional LN N2:extensive regional LN mets. N3: distant LN mets.

M0: no distant spread M1: distant blood spread

1-Pigmented malignant ulcer in the face could be one of the following (Except)

a-Melanoma b-Basal cell carcinoma

c- Hemangioma d-none

2- Staging of malignant tumors evaluates :

a-differentiation b-necrosis

c- a&b d- tumor extension

3- Signet ring carcinoma is a type of:

a-Squamous cell carcinoma b-Adenocarcinoma

c- Anaplastic carcinoma d- none of the above

4-Hamartoma is:

a-Mixed germ cell tumor b-Malignant

c-Tumor like developmental abnormality d-Locally malignant

5-Krukenberg tumor is:

A-Peritoneal sarcoma b-Benign ovarian tumor

c- Gastric carcinoma d- all of the above

6-All are embryonic tumors (except):

a-Nephroblastoma b-Hepatoblastoma

c- Embryonal rhabdomyosarcoma d- Teratoma

7-Virchow's lymph node , all of the following are true (except):

a-induced by lymphatic embolism b-Left supraclavicular

c- Gastric carcinoma is the origin d- Enlarged and fixed

8-Sarcoma is :

a-Malignant of epithelium b-common to form malignant ulcer

c- Highly vascular d- Common below 6 years

9-The following feature is characteristic for Basal cell carcinoma :

a-Keratinized nests b-Blood metastasis is common

c- Pallisading d- Skin is not the only site of origin

10-All The following tumors send metastasis (Except):

a-Gastric carcinoma b-Adamantinoma

c- Broncheogenic carcinoma d- Squamous cell carcinoma

11-The following are complications of benign tumors (except):

a-hormonal imbalance b-Obstruction of tubes

c- Hepatic metastasis d- Compression of vital organs

12-Struma ovarii is an ovarian tumor showing:

A-Metastatic thyroid tissue b-normal thyroid tissue

c- Immature teratoma d- Hamartoma

13-Broder's grading of Squamous cell carcinoma depends on:

A-Invasion b-Keratinized cell nests

c- Metastasis d- Inflammation

14- The most reliable prognostic factor of melanoma:

A-Vertical thickness b-Radial diameter

c- Darkness of color d- Anaplasia

15- Which of the following lesions is locally malignant:

A-Giant cell tumor b-Endometrial hyperplasia

c- Congenital nevus d- Hemangioma

True/ False:

1- Stage T2 N2 M0 has better prognosis than stage T3 N0 M0
2- Spindle cell sarcoma is a well differentiated sarcoma
3- Teratoma is epithelial in origin
4- Carcinoma in situ has local invasion without distant metastasis
5- The commonest site of cystadenoma is the breast
6- Adenocarcinoma has better prognosis than mucoid carcinoma
7- Papilloma is a benign capsulated tumor
8- Desmoplasia is an extensive fibrous reaction inside tumor
9- Mucoid carcinoma has better prognosis than adenocarcinoma
10- Prostatic carcinoma is painful due to perineural invasion
11- Virchow's L.N. is a result of retrograde lymphatic permeation
12- Some malignant tumors may reach the brain without lung metstasis
13- Krukenberg tumor is a bilateral ovarian metastasis of gastric carcinoma
14- Sarcomas are commonly sending metastasis to L.N.s
15- Malignant ulcer has undermind edges & smooth floor

Q1: A female patient has a small benign pigmented lesion on the face:
What is the diagnosis?
What are the histologic type of this lesion?
What are the clinical sign, which indicate malignant transformation in this lesion?

Q2: A child has a malignant tumor of the eye globe, inoculation was done, histologic examination of the tumor shows infiltration by malignant small round cells:
What is the diagnosis?
What is the most important risk factor for this lesion?
What is the cell of origin of this lesion?
Enumerate other four sites of this lesion originating from the same cell of origin?

MCQ

Q1: Choristoma is:
a) Benign tumor
b) Locally malignant
c) Tumor like
d) Highly malignant
e) Carcinoma in situ

Q2: The commonest site of signet ring carcinoma is:
a) Stomach
b) Breast
c) Liver
d) Lung
e) Urinary bladder

Q3: A benign tumor in the uterine myometrium is:
a) Rhabdomyoma
b) Chondroma
c) Fibroma
d) Leiomyoma
e) lipoma

Q4: A biopsy from the cervix (cervical biopsy) showing dysplastic squamous epithelial cell occupying the entire thickness of epithelium with no evidence epithelial maturation and intact basement membrane is called as:
a) Atypical hyperplasia
b) Mild to moderate dysplasia
c) Moderate to severe dysplasia
d) Carcinoma in situ

Q5: A 50-year-old female present with a breast lump. Excisional biopsy was done and revealed malignant cells arranged in masses, clusters, cords with occasional glandular differentiation. These malignant cells were surrounded by dense collagenous stroma. Which of the following terms best describes the surrounding stroma?

a) Anaplasia

b) Desmoplasia

c) Well differentiation

d) Dedifferentiation

Q6: The term desmoplasia refers to:

a) An irregular accumulation of blood vessels

b) Maturation of spatial arrangement of cells

c) Metastatic involvement of surrounding tissue

d) Normal tissue misplaced within another organ

e) Proliferation of non-neoplastic fibrous tissue

Q7: which of the following describes the histologic features choristoma?

a) Benign neoplasm of glandular epithelium

b) Ectopic island of normal tissue

c) Benign neoplasm formed of benign tissue of all 3 germ like

d) Disorganised normal tissue that form a localized mass

e) Aggregate of epitheloid cells and chronic inflammatory cells

Q8: A 20-year-old female has an ovarian mass removed. The mass is 10 cm in diameter and cystic on cut section. The cavity was filled with hair and sebaceous like material. Histologic examination revealed a cyst wall lined by stratified squamous epithelium and show cartilage, fat, respiratory epithelium and salivary gland tissue. What is the diagnosis of such tumor?

a) Teratoma

b) Chondroma

c) Hamartoma

d) Choristoma

e) Blastoma

Q9: Locally aggressive tumours are:

a) Malignant tumours that invade locally & very rarely can metastasize

b) Malignant tumours that are small in size & spread only to very near lymph nodes

c) Benign tumours showing some cytological criteria of malignancy but not all of them

d) Mixed tumours with both epithelial & mesenchymal cell of origin

Q10: benign tumours that can turn malignant:

a) Melanoma & hepatoma
b) Haemangioma & leiomyoma
c) Colonic adenoma & neurofibroma
d) Liver haemangioma & liver cell adenoma
e) Seminoma & lymphoma

Q11: A 67-year-old female was diagnosed as having papillary serous cystadenocarcinoma of the ovary. She was dead and autopsy revealed multiple scattered tiny masses on the peritoneal surface with prescence of marked ascites. Which of the following routes of metastases accounts for the autopsy findings?

a) Direct extension of the tumour
b) Haematogenous spread
c) Lymphatic spread
d) Transcoelomic spread

Q12: An 80-year-old male had been diagnosed as having prostatic adenocarcinoma. Histologic grading of the patient's carcinoma is based primarily on which of the following criteria?

a) Lung metastases
b) Invasion of prostatic capsule
c) Extent of lymph nodes involvement by malignant glands
d) Resemblance to normal prostatic tissue
e) Volume of prostatic gland involvement by the tumour

Q13: A 60-year-old man with hilar lung mass that was diagnosed as having squamous cell carcinoma of the main bronchus by biopsy and pathologic examination. If staging of this tumour following resection and further investigation was denoted as T1 N1 M1, which of the following findings is mostly likely present in this man?

a) Brain metastases
b) Infiltration of chest wall
c) Elevation of corticotropin
d) Poorly differentiated tumour cells
e) Extensive lymph node infiltration