CANCER
Nomenclature - Histopathology

Why it is important to give the right name to a CANCER disease

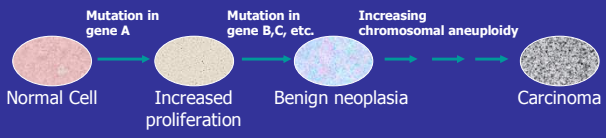
understanding the pathology and/or histology of cancer helps you:

- to make a correct diagnosis (fundamental step for a correct therapy)
- to formulate a better research question (fundamental for studying the etiology, the molecular pathogenesis, and the progression of the disease)
- to design novel targeted therapeutic strategies

Neoplasia

- Benign tumours :
  - Will remain localized
  - **Cannot (by definition= DOES NOT) spread to distant sites**
  - Generally can be locally excised
  - Patient generally survives
- Malignant tumours:
  - Can invade and destroy adjacent structure
  - **Can (and OFTEN DOES) spread to distant sites**
  - Cause death (if not treated)

Cancer is not a single static state but a progression and mixture of phenotypic and genetic/epigenetic changes that proceed toward greater aggressive biological behavior



Cancer Hystopathology Diagnosis

- Biopsy
- Fine-Needle aspiration (FNA)
- Exfoliative cytology (pap smear)
- Biochemical markers (PSA, CEA, Alpha-fetoprotein)

Neoplasia

- two basic components:
  - **Parechyma:** made up of neoplastic cells
  - **Stroma:** made up of non-neoplastic, host-derived connective tissue and blood vessels

The parenchyma:
Determines the biological behavior of the tumor
From which the tumour derives its name

The stroma:
Carries the blood supply
Provides support for the growth of the parenchyma

NOMENCLATURE

The most basic classification of human cancer is the **organ or body location** in which the cancer arises

1. Principle of nomenclature

(1) Benign tumors

Attaching the suffix "-oma" to the type of cell (glandular, muscular, stromal, etc) plus the organ: e.g., adenoma of thyroid.

More detail:

The name of organ and derived tissue/ cell + morphologic character + oma

e. g. skin papilloma, ovarian cyst adenoma

(2) Malignant tumors (cancers)

① Carcinoma: Malignant tumors of epithelial cell origin

The name of organ and derived tissue/ cell + carcinoma.

e. g. adenocarcinoma of thyroid.

More details:

The name of organ and derived tissue/ cell + morphologic futures + carcinoma

e. g. papillary carcinoma of skin, ovarian cystadenocarcinoma, oat (small) cell carcinoma of lung, signet ring cell (cell with a large vacuole) carcinoma of stomach

② **Sarcoma:** malignant tumors arising in mesenchymal tissue or its derivatives

The name of organ

and derived tissue/ cell + sarcoma

e. g. leiomyosarcoma of uterus

(3) Special nomenclature

① Blastoma: tumours rigging in immature tissue or nervous tissue, most of them are malignant

e.g. medulloblastoma retinoblastoma, nephroblastoma

② Some tumors attaching the suffix-oma. But malignant

e. g. seminoma, lymphoma, melanoma, dysgerminoma, endodermal sinus tumor

③ Some malignant tumors, but called disease.

e. g. leukemias, paget's disease

④ Some malignant tumors nominated by scientists' name

e. g. Hodgkin's disease, Ewing's tumor

⑤ Mixed tumors: tumors which derived from one germ layer may undergo divergent defferentiation creating

e. g. mixed tumor of salivery gland

⑥ Teratomas: tumors containing mature or immature cells or tissues representative of more than one germ layer and sometimes all the three layers.

⑦ Hamartoma: tumor-like malformation composed of a haphazard arrangement of tissues indigenous to the particular site, which is totally benign.

Neoplasia nomenclature
- historic eponyms – "first described by…"

Hodgkin's disease	Malignant lymphoma (HL) of B Ly cell origin
Burkitt tumor	NHL – B Ly cell in children (jaw and GIT)
Ewing tumor	Bone tumor (PNET)
Grawitz tumor	Kidney tumor - clear cell adenocarcinoma
Kaposi sarcoma	Malignant tumor derived from vascular epithelium (AIDS)
Brenner tumor	Ovarian tumor derived from Brenner cells
Askin tumor	Malignant chest wall tumor of PNET
Merkel tumor	Skin tumor derived from Merkel cell

Mesenchymal – connective tissue & endothelial related

Benign	Malignant
• Fibroma	• Fibrosarcoma
• Lipoma	• Liposarcoma
• Chondroma	• Chondrosarcoma
• Osteoma	• Osteogenic sarcoma
• Hemangioma	• Angiosarcoma
• Meningioma	• Invasive meningioma
	• Synovial sarcoma
	• Mesothelioma

Epithelial origin

Benign	Malignant
• Adenoma	• **Squamous cell carcinoma**
• Renal tubular adenoma	• Basal cell carcinoma
• Liver cell adenoma	• Adenocarcinoma
• Hydatidiform mole	• Renal cell carcinoma
	• Hepatocellular carcinoma
	• Choriocarcinoma
	• Seminoma
	• **Embryonal carcinoma**

Macroscopic Criteria for Classification of:

Benign	Malignant
• Structure typical of tissue of origin	• Atypical structure
• Encapsulated	• Locally invasive, infiltrating
• Slow growth	• Rapid & erratic growth
• No metastasis	• Metastasis

Microscopic Criteria for Classification of:

Benign	Malignant
• Well differentiated	• Generally less well differentiated to undifferentiated (anaplastic)
• Uniform	• Pleomorphic
• N:C = 1:4 or 1:6	• N:C = 1:1
• Rare *normal* mitotic figures	• Hyperchromatic
• Normal orientation	• More mitoses, abnormal & bizarre
• Abundant stroma	• Loss of polarity
	• Tumor giant cells

The first step toward epithelial neoplasia is cellular transformation

Traditionally, two forms of cellular transformation have been recognized that are potentially reversible, but may be steps toward a neoplasm. These are:

- **Metaplasia**: the exchange of *normal epithelium* for another type of epithelium. Metaplasia is reversible when the stimulus for it is taken away.
- **Dysplasia**: a *disordered growth and maturation of an epithelium*, which is still reversible if the factors driving it are eliminated.

However, **Hyperplasia**: *an increase in the number of phenotypically normal cells*, may also reflect an early stage of transformation.

Dysplasia

- *"disordered growth"*
- Loss in uniformity of the individual cells
- Loss of architectural orientation
- Pleomorphism
- Hyperchromatic
- Increased mitoses (normal)

Carcinoma in situ

- Dysplastic changes involve entire thickness of epithelium
- If left untreated, will progress to invasive cancer

Neoplasia

- Dysplasia :
  - Definiton: a loss in the uniformity of the individual cells and a loss in their architectural orientation.
  - Non-neoplastic
  - Occurs mainly in the epithelia
  - Dysplastic cells shows a degree of : pleomorphism, hyperchrmasia,increased mitosis and loss of polarity.

Dysplasia

- Clinical significance:
  - It is a premalignant condition.
  - The risk of invasive cancer varies with:
- ✓ grade of dysplasia (mild, moderate, sever)
- ✓ duration of dysplasia
- ✓ site of dysplasia

Neoplasia

- Dysplasia does not mean cancer
- Dyplasia does not necessarily progress to cancer
- Dysplasia may be reversible
- If dysplastic changes involve the entire thickness of the epithelium it is called :

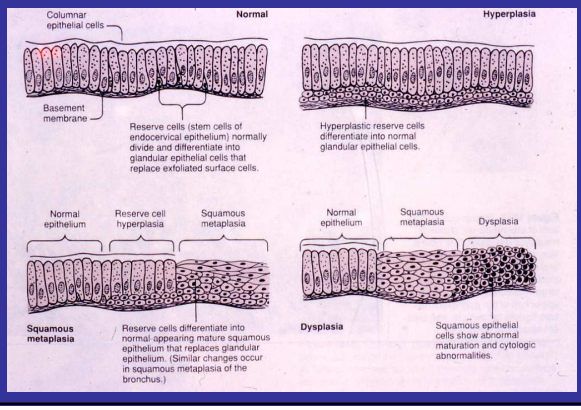
  CARCINOMA IN-SITU

Dysplasia Features:

- Increased rate of multiplication.
- Disordered maturation.

- **Nuclear abnormality**
  - Increased N/C ratio
  - Irregular nuclear membrane
  - Increased chromatin content
- **Cytoplasmic abnormalities** due to failure of normal

CHANGES IN UTERINE CERVIX



Neoplasia

- Carcinoma in-situ
  - Definition: an intraepithelial malignancy in which malignant cells involve the entire thickness of the epithelium without penetration of the basement membrane.
  - Applicable only to epithelial neoplasms.

Metastases

- A primary neoplasm is more likely to appear within an organ as a solitary mass.
- The presence of metastases are the best indication that a neoplasm is malignant. The original clone of cells that developed into a neoplasm may not have had the ability to metastasize, but continued proliferation of the neoplastic cells and acquisition of more genetic mutations within the neoplastic cells can give them the ability to metastasize.

Spread of Tumors

- Direct invasion – infiltration & destruction of surrounding tissue
- Metastasis – noncontiguous spread to other organ/body locations
  - Lymphatics – carcinomas, lymphatic drainage
  - Veins & arteries – sarcomas, *renal cell carcinoma, hepatocellular carcinoma*
  - Implantation – "open field", ovarian carcinomas, appendix = *pseudomyxoma peritonei*

Nomenclature of tumors

Tissue of Origin	Benign	Malignant
Composed of One parenchymal cell Type		
Mesenchymal tumors		
Connective tissue and derivatives	Fibroma Lipoma Chondroma Osteoma	Fibrosarcoma Liposarcoma Chondrosarcoma Osteogenic sarcoma
Endothelial and related tissues		
Blood vessels	Hemangioma	Angiosarcoma
Lymph vessels	Lymphangioma	Lymphangiosarcoma
Synovium		Synovial sarcoma
Mesothelium		Mesothelioma
Brain coverings	Meningioma	Invasive meningioma

Nomenclature of tumors

Tissue of Origin	Benign	Malignant
Blood cells and related cells		
Hematopoietic cells		
Lymphoid tissue		
Muscle		
Smooth	Leiomyoma	Leiomyosarcoma
Striated	Rhabdomyoma	Rhabdomyosarcoma
Epihelial tumors		
Stratified squamous	Squamous cell papilloma	
Basal cells of skin or adnexa		
Epithelial lining		
Glands or ducts	Adenoma Papilloma Cystadenoma	

Nomenclature of tumors

Tissue of Origin	Benign	Malignant
Epihelial tumors Stratified squamous Basal cells of skin or adnexa Epithelial lining Glands or ducts	Squamous cell papilloma Adenoma Papilloma Cystadenoma	Squamous cell or epidermoid carcinoma Basal cell carcinoma Adenocarcinoma Papillary carcinoma Cystadenocarcinoma

Nomenclature of tumors

Tissue of Origin	Benign	Malignant
Respiratory passages Neuroectoderm Renal epithelium Liver cells Urinary tract epithelium (transitional) Placental epithelium (trophoblast) Testicular epithelium (germ cells)	Nevus Renal tubular adenoma Liver cell adenoma Transitional cell papilloma Hydatidiform mole	Bronchogenic carcinoma Bronchial adenoma (carcinoid) Malignant melanoma Renal cell carcinoma Hepatocellular carcinoma Transitional cell carcinoma Choriocarcinoma Seminoma Embryonal carcinoma

Nomenclature of tumors

Tissue of Origin	Benign	Malignant
More Than One Neoplastic Cell Type- Mixed Tumors, Usually Derived From One Germ Layer Salivary glands	Pleomorphic adenoma (mixed tumor of salivary origin)	Malignant mixed tumor of salivary gland origin
Breast Renal anlage	Fibroadenoma	Malignant cystosarcoma phyllodes Wilms tumor

Nomenclature of tumors

Tissue of Origin	Benign	Malignant
More Than One Neoplastic Cell Type Derived From More Than One Germ Layer- Tera- fogenous		
Totipotential cells in gonads or in embryonic rests	Mature teratoma, dermoid cyst	Immature teratoma, teratocarcinoma

Neoplasia

- **Adenoma** : benign epithelial neoplasms producing gland pattern….OR … derived from glands but not necessarily exhibiting gland pattern
- **Papilloma** : benign epithelial neoplasms growing on any surface that produce microscopic or macroscopic finger-like pattern

TERATOMA

- Teratoma:
  - **Teratoma contains recognizable mature or immature cells or tissues representative of more than one germ-cell layer and some times all three.**
  - **Teratomas originate from totipotential cells such as those normally present in the ovary and testis.**

If all the components parts are well differentiated, it is a benign (mature) teratoma.
If less well differentiated, it is an immature (malignant) teratoma.

TERATOMA

- **Such cells have the capacity to differentiate into any of the cell types found in the adult body. So they may give rise to neoplasms that mimic bone, epithelium, muscle, fat, nerve and other tissues.**
- **Most common sites are: ovary & testis**

TERATOMA

- **If all the components parts are well differentiated, it is a benign (mature) teratoma.**
- **If less well differentiated, it is an immature (malignant) teratoma.**

WHAT ARE HAMARTOMAS AND CHORISTOMA?

Hamartoma: a mass composed of cells native to the organ

e.g. pulmonary hamartoma.

Choristoma: a mass composed of normal cells in a wrong location

e.g. pancreatic choristoma in liver or stomach.

- Malformation and not neoplasm.

Hamartoma and Choristoma

- **They are distinguished from neoplasms by the fact that they do not exhibit continued growth. they are group of tumor-like tissue masses which may be confused with neoplasms**

Staging and Grading

Staging and Grading

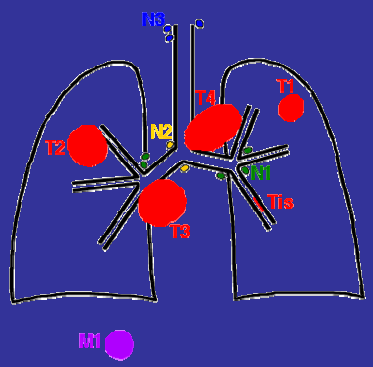
- Devised for malignant neoplasms
- The stage and/or grade generally determine the treatment and the prognosis
- In general, the higher the stage, the larger a neoplasm is and the farther it has likely spread.
- In general, the higher the grade, the more likely it is that the tumor is rapidly growing and will invade and metastasize.

Staging Tumors: **Extent of Spread**

- Generally correlates better with prognosis than histopathologic grading
- Used in therapy selection
- Union Internationale Centre Cancer (UICC)
  - TNM system
- American Joint Committee (AJC) on Cancer Staging
  - Stages 0 – IV

Staging of Malignant Neoplasms

Stage	Definition
Tis/T0	In situ, non-invasive (confined to epithelium)
T1	Small, minimally invasive within primary organ site
T2	Larger, more invasive within the primary organ site
T3	Larger and/or invasive beyond margins of primary organ site
T4	Very large and/or very invasive, spread to adjacent organs
N0	No lymph node involvement
N1	Regional lymph node involvement
N2	Extensive regional lymph node involvement
N3	More distant lymph node involvement
M0	No distant metastases
M1	Distant metastases present



In the diagram above utilizing a lung carcinoma as an example, the principles of staging are illustrated:

Grading = degree of differentiation

- Grading schema are based upon the microscopic appearance of a neoplasm with H&E staining.
- In general, a higher grade means that there is a lesser degree of differentiation and the worse the biologic behavior of a malignant neoplasm will be.
- A well-differentiated neoplasm is composed of cells that closely resemble the cell of origin
- A poorly differentiated neoplasms have cells that are difficult to recognize as to their cell of origin.
- Grading schema have been devised for many types of neoplasms, mainly carcinomas.
- Most grading systems have three or four grades (designated with numbers or roman numerals).

Grading of Malignant Neoplasms

Grade	Definition
I	Well differentiated
II	Moderately differentiated
III	Poorly differentiated
IV	Nearly anaplastic