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 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

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

Mutation in gene A
Mutation in gene B, C, etc.
Increasing chromosomal aneuploidy
Normal Cell
Increased proliferation
Benign neoplasia
Carcinoma

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

The stroma: Carries the blood supply Provides support for the growth of the parenchyma
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 differentiation creating
         e. g. mixed tumor of salivery gland
Teratomas: tumors containing mature or immature cells or tissues representative of more than one germ layer and sometimes all the three layers.

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

Mesenchymal – connective tissue & endothelial related

Benign
- Fibroma
- Lipoma
- Chondroma
- Osteoma
- Hemangioma
- Meningioma

Malignant
- Fibrosarcoma
- Liposarcoma
- Osteosarcoma
- Chondrosarcoma
- Angiosarcoma
- Kaposi sarcoma
- Synovial sarcoma
- Mesothelioma

Epithelial origin

Benign
- Adenoma
- Renal tubular adenoma
- Liver cell adenoma
- Hydatidiform mole

Malignant
- Squamous cell carcinoma
- Basal cell carcinoma
- Adenocarcinoma
- Renal cell carcinoma
- Hepatocellular carcinoma
- Choriocarcinoma
- Seminoma
- Embryonal carcinoma

Macroscopic Criteria for Classification of:

Benign
- Structure typical of tissue of origin
- Encapsulated
- Slow growth
- No metastasis

Malignant
- Atypical structure
- Locally invasive, infiltrating
- Rapid & erratic growth
- Metastasis

Microscopic Criteria for Classification of:

Benign
- Well differentiated
- Uniform
- N.C = 1:4 or 1:6
- Rare normal mitotic figures
- Normal orientation
- Abundant stroma

Malignant
- Generally less well differentiated to undifferentiated (anaplastic)
- Pleomorphic
- N.C = 1:1
- Hyperchromatic
- More mitoses, abnormal & bizarre
- Loss of polarity
- Tumor giant cells

Neoplasia nomenclature - historic eponyms – “first described by…”

<table>
<thead>
<tr>
<th>Benign Tumor</th>
<th>Malignant Tumor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hodgkin’s disease</td>
<td>Malignant lymphoma (HL) of B Ly cell origin</td>
</tr>
<tr>
<td>Burkitt tumor</td>
<td>NHL – B Ly cell in children (jaw and GIT)</td>
</tr>
<tr>
<td>Ewing tumor</td>
<td>Bone tumor (PNET)</td>
</tr>
<tr>
<td>Grawitz tumor</td>
<td>Kidney tumor - clear cell adenocarcinoma</td>
</tr>
<tr>
<td>Kaposi sarcoma</td>
<td>Malignant tumor derived from vascular epithelium (AIDS)</td>
</tr>
<tr>
<td>Brenner tumor</td>
<td>Ovarian tumor derived from Brenner cells</td>
</tr>
<tr>
<td>Askin tumor</td>
<td>Malignant chest wall tumor of PNET</td>
</tr>
<tr>
<td>Merkel tumor</td>
<td>Skin tumor derived from Merkel cell</td>
</tr>
</tbody>
</table>
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.

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**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

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**Neoplasia**

- Dysplasia:
  - Definition: 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, hyperchromasia, increased mitosis and loss of polarity.

**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

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**Neoplasia**

- Dysplasia does not mean cancer
- Dysplasia 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
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

<table>
<thead>
<tr>
<th>Tissue of Origin</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Composed of One parenchymal cell Type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mesenchymal tumors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connective tissue and derivatives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endothelial and related tissues</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood vessels</td>
<td>Hemangioma</td>
<td>Angiosarcoma</td>
</tr>
<tr>
<td>Lymph vessels</td>
<td>Lymphangiomma</td>
<td>Lymphangiosarcoma</td>
</tr>
<tr>
<td>Sinus</td>
<td></td>
<td>Syneovial sarcoma</td>
</tr>
<tr>
<td>Mesothelium</td>
<td>Meningioma</td>
<td>Mesiatheloma</td>
</tr>
<tr>
<td>Brain coverings</td>
<td></td>
<td>Invasive meningioma</td>
</tr>
</tbody>
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Nomenclature of tumors

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<tr>
<th>Tissue of Origin</th>
<th>Benign</th>
<th>Malignant</th>
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</thead>
<tbody>
<tr>
<td>Blood cells and related cells</td>
<td></td>
<td>Leiomysarcoma</td>
</tr>
<tr>
<td>Hematopoietic cells</td>
<td>Leiomyoma</td>
<td>Rhabdomyoma</td>
</tr>
<tr>
<td>Lymphoid tissue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muscle</td>
<td>Smooth</td>
<td>Leiomysarcoma</td>
</tr>
<tr>
<td>Striated</td>
<td></td>
<td>Rhabdomyosarcoma</td>
</tr>
<tr>
<td>Epithelial tumors</td>
<td></td>
<td></td>
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<tr>
<td>Stratified squamous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal cells of skin or adnexa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epithelial lining</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glands or ducts</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoma</td>
<td>Papilloma</td>
<td>Squamous cell papilloma</td>
</tr>
<tr>
<td>Papilloma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cystadenoma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tissue of Origin</td>
<td>Benign</td>
<td>Malignant</td>
</tr>
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</tr>
<tr>
<td>Stratified squamous Basal cells of skin or adnexa Epithelial lining Glands or ducts</td>
<td>Squamous cell papilloma</td>
<td>Squamous cell or epidermoid carcinoma Basal cell carcinoma</td>
</tr>
<tr>
<td>Respiratory passages Neuroectoderm Renal epithelium Liver cells Urinary tract epithelium (transitional) Placental epithelium (trophoblast) Testicular epithelium (germ cells)</td>
<td>Nevus Adenoma Papilloma Carcinoma Cystadenoma</td>
<td>Adenocarcinoma Papillary carcinoma Cystadenocarcinoma</td>
</tr>
<tr>
<td>Salivary glands Plasmacytoma Mixed tumor of salivary origin Malignant mixed tumor of salivary gland origin</td>
<td>Fibroadenoma Malignant mixed tumor of salivary gland origin</td>
<td>Malignant mixed tumor of salivary gland origin</td>
</tr>
<tr>
<td>Breast Renal anlage</td>
<td>Fibroadenoma</td>
<td>Malignant cystadenoma phylloides Wilms tumor</td>
</tr>
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</tr>
</tbody>
</table>

**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

- 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 Tumors: Extent of Spread

**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

**Stage**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
<td>No lymph node involvement</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node involvement</td>
</tr>
<tr>
<td>N2</td>
<td>Extensive regional lymph node involvement</td>
</tr>
<tr>
<td>N3</td>
<td>More distant lymph node involvement</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastases</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastases present</td>
</tr>
</tbody>
</table>

Grading

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 neoplasm has 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

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Well differentiated</td>
</tr>
<tr>
<td>II</td>
<td>Moderately differentiated</td>
</tr>
<tr>
<td>III</td>
<td>Poorly differentiated</td>
</tr>
<tr>
<td>IV</td>
<td>Nearly anaplastic</td>
</tr>
</tbody>
</table>