Neoplasia
Mechanisms of Human Disease
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[Modified from original lecturer, Theresa Kristopaitis, MD]

In 1713, Bernardino Ramazzini observed a virtual absence of cervical cancer and relatively high incidence of breast cancer in nuns—possibly due to celibacy?

In 1775, Percival Pott described occupational cancer in chimney sweeper, cancer of the scrotum, which was caused by soot collecting in the skin folds of the scrotum.

Thomas Venner of London was one of the first to warn about the dangers of tobacco in his Life Fish, published in London in 1620. He wrote that "immoderate use of tobacco hurts the brain and the eye and induces swelling of the limbs and the heart."
Concepts

- Basic Definitions
- Nomenclature
- Features of benign vs malignant neoplasms
- Cancer epidemiology
- Carcinogenesis/Molecular Basis of Cancer
- Clinical aspects of neoplasia
- Diagnosis

- Neoplasia - “new growth”
  - Disorder of cell growth
  - Triggered by series of acquired mutations of single cell and its clones
  - monoclonal, autonomous, irreversible

- Tumor - abnormal growth of tissue

- Oncology - Onkos, tumor; logos, study of

- Benign tumors - remain localized, do not metastasize

- Malignant tumors - invade, destroy, metastasize

- Cancer - generic term for malignant neoplasm
Two Basic Components

ALL TUMORS (benign and malignant) have two basic components

- **Parenchyma**
  - Neoplastic cells
    - Largely determines biologic behavior
    - Source for the name of the neoplasm
    - Neuroectodermal, epithelial, or mesenchymal in origin

- **Stroma**
  - Connective tissue, blood vessels, immune system cells
  - "Support" growth and spread of neoplasm

Tumor Classification

- Tumors are classified according to their cell of origin

- Most tumors originate from one cell (monoclonal) and of one parenchymal cell type

- Some rare tumors contain cells from more than one germ layer (teratomas)
## Tumors: One parenchymal cell type

<table>
<thead>
<tr>
<th>Tissue of Origin</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesenchyme</td>
<td>Fibroma</td>
<td>Fibrosarcoma</td>
</tr>
<tr>
<td>Fibrous Tissue</td>
<td>Chondroma</td>
<td>Chondrosarcoma</td>
</tr>
<tr>
<td>Osteoid Ossicles</td>
<td>Osteoma</td>
<td>Osteosarcoma</td>
</tr>
<tr>
<td>Blood vessels</td>
<td>Hemangiosarcoma</td>
<td></td>
</tr>
<tr>
<td>Smooth muscle</td>
<td>Leiomyosarcoma</td>
<td></td>
</tr>
<tr>
<td>Skeletal muscle</td>
<td>Rhabdomyosarcoma</td>
<td></td>
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## “Mixed Tumors” derived from 1 germ cell layer

- Single neoplastic clone capable of divergent differentiation
  - Derived from 1 germ cell layer
  - More than 1 neoplastic cell type

- Example — Salivary Gland
  - Clone capable of epithelial and myoepithelial differentiation
  - Pleomorphic adenoma
    - Neoplastic epithelial cells scattered in neoplastic myxoid stroma

## “Mixed Tumors”:
More than one neoplastic cell type

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<tr>
<td>Derived from 1 germ cell layer</td>
<td>Pleomorphic Adenoma</td>
<td>Malignant mixed tumor of salivary gland</td>
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</table>
Mixed tumors composed of cells belonging to > 1 germ cell layer

- Totipotential germ cells differentiate into any cell types found in human body
  - Neoplasms originate in gonads, abnormal midline embryonic rests

Examples

LIPOMA – tumor of fat (mesenchymal) - BENIGN

- Adipocytes nuclei pushed to periphery
- Capsule
Liposarcoma (Mesenchymal)- Malignant

ADENOMA of the colon (Epithelial)- Benign

Adenocarcinoma of colon (Epithelial) Malignant
Characteristics of Benign vs Malignant Neoplasms

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<td>Cell Morphology</td>
<td>Well-differentiated (resemble normal tissue counterpart) to dysplastic</td>
<td>Well-differentiated to very de-differentiated (aplastic) Pleomorphic (variation in nuclear size and shape) Abnormal nuclear morphology High N:C ratio Hyperchromatic Prominent nucleoli Mitoses</td>
</tr>
<tr>
<td>Rate of Growth</td>
<td>Most grow slowly</td>
<td>Highly variable and unpredictable Usually varies with degree of differentiation</td>
</tr>
<tr>
<td>Spread of Tumor</td>
<td>Most encapsulated stay localized</td>
<td>Infiltrate and destroy locally Ability to Metastasize</td>
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Differentiation

Normal skin - Epidermis

Well-differentiated squamous cell carcinoma of the skin. Tumor cells strikingly similar to normal squamous epithelial cells, with intercellular bridges and nests of keratin (arrow).
Anaplastic tumor cells
Cellular and nuclear variation in size and shape.

Abnormal tripolar spindle (mitosis)

Spread of Tumor

Fibroadenoma of Breast
Encapsulated small tumor (T) is sharply demarcated from the whiter breast tissue (B)
Breast Carcinoma

*Lesion is retracted, infiltrating surrounding breast substance. Lesion may feel very firm. Desmoplasia.

Normal Breast

Ductules

Duct

Fibroadenoma

Benign glands (G)
Benign fibrous stroma (S)

Breast Carcinoma

Invasion of stroma by nests and cords of malignant cells.
DYSPLASIA

- "Disordered growth"
- Principally found in epithelium
- Mutations leading to cytological and architectural changes of epithelial cells
  - Pleomorphism
  - Hyperchromatic nuclei
  - High N/C ratio
  - Mitotic figures above basal layer
  - Disorderly maturation and/or disorderly architecture
- DOES NOT PENETRATE BASEMENT MEMBRANE

Normal squamous epithelium

Squamous dysplasia
failure of normal differentiation, marked nuclear and cellular pleomorphism, numerous mitotic figures extending toward the surface

Dysplasia
- MAY BE precursor to malignant transformation
  - Mild to moderate dysplasias may regress (ie reversible)
    - particularly if inciting causes are removed
Normal squamous epithelium

Squamous Carcinoma In-Situ

Entire thickness of the epithelium is replaced by atypical dysplastic cells. There is no orderly differentiation of squamous cells. The basement membrane is intact, and there is no tumor in the subepithelial stroma.

Squamous Cell Carcinoma

Invasion of malignant cells into stroma

Dysplasia

- Dysplasia often occurs in metaplastic epithelium
  - Self check – Define metaplasia

- Examples
  - Squamous cell carcinoma of the uterine cervix
  - Squamous cell carcinoma of the lung
Metastasis

Pathways of spread

- Direct seeding of body cavities and surfaces
- Lymphatic spread
- Hematogenous spread

Liver Studded with Metastatic Cancer
Peritoneal carcinomatosis. The mesentery attached to a loop of small bowel is studded with small nodules of metastatic ovarian carcinoma.