In 1713, Bernardino Ramazzini reported the virtual absence of cervical cancer and a relatively high incidence of breast cancer among nuns.

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

In 1726, Thomas Venner of London was one of the first to warn about tobacco dangers in his "Via Recta," published in London in 1620. He wrote that "immoderate use of tobacco hurts the brain and the eye and induces trembling 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></td>
<td>Chondroma</td>
<td>Chondrosarcoma</td>
</tr>
<tr>
<td></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>Leiomyoma</td>
<td>Leiomyosarcoma</td>
</tr>
<tr>
<td>Skeletal muscle</td>
<td>Rhabdomyoma</td>
<td>Rhabdomyosarcoma</td>
</tr>
</tbody>
</table>

“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

<table>
<thead>
<tr>
<th>Tissue of Origin</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Derived from 1 germ cell layer Salivary Glands [epithelium + myxoid stroma]</td>
<td>Pleomorphic Adenoma</td>
<td>Malignant mixed tumor of salivary gland</td>
</tr>
</tbody>
</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
Liposarcoma (Mesenchymal)- Malignant

ADENOMA of the colon (Epithelial)- Benign

Adenocarcinoma of colon (Epithelial) Malignant
Mesoderm: Cartilage

Endoderm: GI-type glands

Ectoderm: Epidermis and keratin

Characteristics of Benign vs Malignant Neoplasms

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

Cell morphology

Malignant cells from anaplastic carcinoma
High N:C Ratio
Prominent nucleoli
Pleomorphic
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)

Keratin Pearl
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

Benign glands (G)
Benign fibrous stoma (S)

Fibroadenoma

Breast Carcinoma
Invasion of stroma by nests and cords of malignant cells

Capsule

CM 1 2 3 4 5
**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

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**Dysplasia**

- MAY BE precursor to malignant transformation
  - Mild to moderate dyplasias 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.

End of Part I

Questions?
Kamran.mirza@lumc.edu