Disorders of Growth and Tumors

Introduction:

Tumor – Swelling / new growth / mass

Two types of growth disorders:
- Non-Neoplastic: Secondary / adaptation due to other cause.
- Neoplastic: Primary growth abnormality.

Non-Neoplastic Proliferation: Controlled & Reversible

- Hypertrophy – increase in size
- Hyperplasia – increase in number
- Metaplasia – Change
- Dysplasia – Disordered

Neoplastic Proliferation: Uncontrolled & Irreversible

- Benign tumors are localized and non-invasive.
- Malignant (Cancer) are spreading and invasive.

Nomenclature: Cell of origin + Suffix. (Oma, Carcinoma & Sarcoma)

- Fibroma - Fibrosarcoma
- Osteoma - Osteosarcoma
- Adenoma - Adenocarcinoma
- Papilloma - Squamous cell carcinoma
- Chondroma – Chondrosarcoma

Diagnosis:

- History of Clinical examination
- Radiographic analysis – X-Ray, US, CT, MRI
- Laboratory analysis – Tumor markers
- Cytology – Pap smear, Fine Needle Aspiration Biopsy (FNAB)
- Biopsy - Histopathology, markers.
- Autopsy – Research, learning & teaching

Biology of Tumor

- Grading – Differentiation
- Staging – Progression
TNM: Staging of tumor:

- **T1N1M0** – Means primary tumor is within the organ but cancer cells have spread to local lymphnodes, there is no metastasis.
- **T3N0Mo** - Means tumor has spread beyond primary organ but has not spread to lymphnodes or other sites.

Neoplasia

Cancer Incidence

- 1.4 million new cases of cancer last year
- 565,000 deaths from cancer last year
- Cancer is 2nd leading cause of death (after heart disease)
- Most common cancers
  - Men: Prostate
  - Women: Breast
- Decrease in death rates for:
  - Cervical cancer (pap smears)
  - Colon cancer (earlier detection)
  - Breast cancer (earlier detection)
  - Lung cancer in men (less smokers)
  - Some types of leukemia (new treatment)
- Increase in death rates for:
  - Lung cancer in women (more smokers)
Environmental carcinogens

- Sunlight: skin cancer
- Smoking: lung cancer
- Alcohol: liver, breast cancers
- HPV: cervical carcinoma

Occupational carcinogens

- Asbestos (roofing, tiles): mesothelioma
- Benzene (light oil, solvents): leukemia
- Beryllium (missile fuel): lung cancer
- Cadmium (batteries): prostate cancer
- Radon (uranium decay, mines): lung cancer
- Vinyl chloride (refrigerants): angiosarcoma and liver cancer
- Nickel (welding, ceramics): nose and liver cancers

Age

Cancer is most frequent at the two extremes of age.

- Elderly
  - Frequency of cancer increases with age
  - Most cancer deaths occur between 55-75
- Children
  - 10% of all childhood deaths
  - Leukemia/lymphoma, CNS tumors, sarcoma

Heredity

- Inherited cancer syndromes
  - Dominantly inherited
  - Retinoblastoma
  - Familial polyposis coli
- Familial cancers
  - Most common sporadic cancers have familial forms too.
  - Breast, colon, ovary, brain are most common
  - Occur often earlier
- Syndromes of defective DNA repair
  - Recessively inherited
  - Xeroderma pigmentosum
Acquired Preneoplastic Syndromes

- Persistent regenerative cell replication
  - Chronic skin fistula → squamous cell carcinoma
  - Cirrhosis → liver cancer
- Hyperplastic and dysplastic proliferations
  - Atypical endometrial hyperplasia → endometrial cancer
  - Dysplastic bronchial mucosa → lung cancer
- Chronic atrophic gastritis → stomach cancer
- Chronic ulcerative colitis → colon cancer
- Leukoplakia → squamous cell carcinoma

Definitions of Neoplasm

Neoplasm = mass of tissue that grows excessively, and keeps growing even if you remove the stimulus that started it off.

Benign vs. Malignant

Benign tumors

- Small
- Slow-growing
- Non-invasive
- Well-differentiated
- Stay localized

Malignant tumors

- Large
- Fast-growing
- Invasive
- Poorly-differentiated
- Metastasize

Benign Tumors: Usually designated by adding “-oma” to cell type

- adenoma – benign tumor arising from glandular cells
- leiomyoma – benign tumor arising from smooth muscle cells
- chondroma – benign tumor arising from chondrocytes
**Other benign tumor names**

- papilloma – has finger-like projections
- polyp – projects upward, forming a lump
- cystadenoma – has hollow spaces (cysts) inside

**Malignant Tumors**

Carcinomas – arise in epithelial tissue

- adenocarcinoma – malignant tumor of glandular cells
- squamous cell carcinoma – malignant tumor of squamous cells

Sarcomas – arise in mesenchymal tissue

- chondrosarcoma – malignant tumor of chondrocytes
- angiosarcoma – malignant tumor of blood vessels
- rhabdomyosarcoma – malignant tumor of skeletal muscle cells

**Mixed Tumors:** “Mixed” tumors show divergent differentiation. Not to be confused with teratomas.

Examples

- pleomorphic adenoma – glands + fibromyxoid stroma
- fibroadenoma – glands + fibrous tissue

**Confusing Terms**

- Malignant tumors that sound benign
  - melanoma
  - seminoma
  - lymphoma
  - mesothelioma

- Non-tumors that sound like tumors
  - hamartoma – mass of disorganized indigenous tissue
  - choristoma – heterotopic rest of cells

- Names that seem to come out of nowhere
  - leukemia
  - nevus
  - hydatidiform mole
Tumor nomenclature

<table>
<thead>
<tr>
<th>Tissue of origin</th>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrous tissue</td>
<td>Fibroma</td>
<td>Fibrosarcoma</td>
</tr>
<tr>
<td>Fat</td>
<td>Lipoma</td>
<td>Liposarcoma</td>
</tr>
<tr>
<td>Cartilage</td>
<td>Chondroma</td>
<td>Chondrosarcoma</td>
</tr>
<tr>
<td>Bone</td>
<td>Osteoma</td>
<td>Osteogenic sarcoma</td>
</tr>
<tr>
<td>Blood vessels</td>
<td>Hemangioma</td>
<td>Angiosarcoma</td>
</tr>
<tr>
<td>Mesothelium</td>
<td></td>
<td>Mesothelioma</td>
</tr>
<tr>
<td>Hematopoietic cells</td>
<td></td>
<td>Leukemia</td>
</tr>
<tr>
<td>Lymphoid cells</td>
<td></td>
<td>Lymphoma</td>
</tr>
<tr>
<td>Squamous epithelium</td>
<td>Squamous cell papilloma</td>
<td>Squamous cell carcinoma</td>
</tr>
<tr>
<td>Glandular epithelium</td>
<td>Adenoma</td>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td></td>
<td>Papilloma</td>
<td>Papillary adenocarcinoma</td>
</tr>
<tr>
<td></td>
<td>Cystadenoma</td>
<td>Cystadenocarcinoma</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>
<tr>
<td>Melanocytes</td>
<td>Nevus</td>
<td>Melanoma</td>
</tr>
</tbody>
</table>
Differentiation and Anaplasia

**Differentiation** = how much the tumor cells resemble their cells of origin

- **well-differentiated** – closely resembles normal counterpart
- **moderately-differentiated** – sort of resembles normal counterpart
- **poorly-differentiated** – doesn’t resemble normal counterpart

- Benign tumors are usually well-differentiated
- Malignant tumors can show any level of differentiation

**Anaplasia:** “to form (-plasia) backwards (ana-)”

Just means cells are very poorly-differentiated. Almost always indicates malignancy.

**Anaplastic cells show:**

- Pleomorphism
- Hyperchromatic, large nuclei
- Bizarre nuclear shapes, distinct nucleoli
- Lots of mitoses, and atypical mitoses
- Architectural anarchy

**Dysplasia = disorderly (dys-) growth (-plasia)**

- “Dysplasia” is used to describe disorderly changes in non-neoplastic epithelial cells.
- Graded as mild, moderate or severe.
  - Mild-moderate: usually reversible
  - Severe: usually progresses to carcinoma in situ (CIS).
- Next step after CIS: invasive carcinoma.

**Rate of Growth**

1. Malignant tumors grow faster than benign ones.
2. Poorly-differentiated tumors grow faster than well-differentiated ones.
3. Growth is dependent on:
   - Hormonal factors
   - Blood supply
Age of tumor

- Early on (subclinical), GF (growth factors) high.
- Later (clinically detectable), GF low.

Type of tumor

- Leukemias, lymphomas, small-cell lung cancer: high GF
- Breast, colon cancer: low GF

Important for treatment

- High GF tumor: treat with chemotherapy/radiation
- Low GF tumor: treat by surgery.

Local Invasion

- Benign tumors
  - Stay where they are.
  - Can’t invade or metastasize.
  - Usually encapsulated.

- Malignant tumors
  - Infiltrate, invade, destroy surrounding tissue.
  - Then metastasize to other parts of body.
  - Not encapsulated.

Metastasis

Metastasis = development of secondary tumor implants in distant tissues

Half of all patients with malignancies have mets at the time of diagnosis!!

Metastasis depends on:

- Type of tumor
- Size of tumor
- Degree of differentiation of tumor
Metastasis can occur though three ways:

- Seeding
- Lymphatic spread
- Hematogenous spread

1. Seeding
   a. Tumor invades body cavity
   b. Bits break off and implant on peritoneal surfaces
   c. Ovarian cancer

2. Lymphatic spread
   a. Tumor spreads to local lymph nodes
   b. Sentinel lymph node first
   c. Moves through thoracic duct
   d. Empties into subclavian vein

3. Hematogenous spread
   a. Veins are easier to invade than arteries
   b. Liver and lungs are most common metastatic tumors
   c. Some tumors like other sites better:
      - prostate → bone
      - most lung cancers → adrenals, brain
   d. Sarcomas like to spread this way (but so do carcinomas)