Cancer

- Derived from Greek word for crab, karkinoma
- Malignant tumor
- Tumor
  - Also referred to as a neoplasm—new growth

**Benign vs. Malignant Tumors**

<table>
<thead>
<tr>
<th>Benign</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grow slowly</td>
<td>Grow rapidly</td>
</tr>
<tr>
<td>Well-defined capsule</td>
<td>Not encapsulated</td>
</tr>
<tr>
<td>Not invasive</td>
<td>Invasive</td>
</tr>
<tr>
<td>Well differentiated</td>
<td>Poorly differentiated</td>
</tr>
<tr>
<td>Low mitotic index</td>
<td>High mitotic index</td>
</tr>
<tr>
<td>Do not metastasize</td>
<td>Can spread distantly (metastasis)</td>
</tr>
</tbody>
</table>

Mitotic index = rate of growth

Act. Benign vs Malignant

**Classification and Nomenclature**

- Benign tumors
  - Named according to the tissues from which they arise, and include the suffix “-oma”
    - Lipoma
    - Glioma
    - Leiomyoma
    - Chondroma

- Malignant tumors
  - Named according to the tissues from which they arise
    - Malignant epithelial tumors are referred to as carcinomas
      - Adenocarcinoma (from glandular epithelium)
    - Malignant CT tumors are referred to as sarcomas
      - Rhabdomyosarcomas (from skeletal muscle)

- Cancers of lymphatic tissue are lymphomas
- Cancers of blood-forming cells are leukemias
- Carcinoma in situ (CIS)
  - Epithelial malignant tumors that have not broken through BM or invaded the surrounding stroma

Act. Origin of Cancers
Classification and Nomenclature

Stages of Cancer Spread

- Stage 1: Confined to organ of origin
- Stage 2: Locally invasive
- Stage 3: Spread to lymph nodes
- Stage 4: Spread to distant sites
- CIS special case

Tumor Staging by TNM System

Tumor Markers

- Tumor cell markers (biologic markers) are substances produced by cancer cells or that are found on plasma cell membranes, in the blood, CSF, or urine
  - Hormones (Epi – in blood, adrenal medullary tumor)
  - Enzymes
  - Genes
  - Antigens (PSA – in blood, prostate cancer)
  - Antibodies

Hallmarks of Cancer

Viruses and Cancer

- Implicated
  - Hepatitis B and C viruses
  - Epstein-Barr virus (EBV)
  - Kaposi's sarcoma herpesvirus (KSHV)
  - Human papillomavirus (HPV)
  - Human T cell leukemia–lymphoma virus (HTLV)
**Bacterial Cause of Cancer**

- *Helicobacter pylori*
  - Chronic infections are associated with:
    - Peptic ulcer disease
    - Stomach carcinoma
    - Mucosa-associated lymphoid tissue lymphomas

**Inflammation and Cancer**

- Chronic inflammation is an important factor in development of cancer
  - Cytokine release from inflammatory cells
  - Free radicals
  - Mutation promotion
  - Decreased response to DNA damage

**Tumor Spread**

- Direct invasion of contiguous organs
  - Known as local spread
- Metastases to distant organs
  - Lymphatics and blood
- Metastases by way of implantation

**Local Spread**

- Invasion
  - Cellular multiplication
    - Mitotic rate vs. cellular death rate
  - Mechanical pressure
  - Release of lytic enzymes
  - Decreased cell-to-cell adhesion
  - Increased motility
    - Intravasation
    - Extravasation

**Three-Step Theory of Invasion**

- Tumor cell attachment
  - Fibronectin and laminin
- Degradation or dissolution of the matrix
  - Enzymes
- Locomotion into the matrix
  - Invadopodia (pseudopodia)

**HeLa cell**

- a cell type in an **immortal cell line** used in research
- one of the oldest, most commonly used human cell lines
- derived from cervical cancer cells taken from Henrietta Lacks
- patient eventually died of her cancer on October 4, 1951
- cell line was found to be remarkably durable
- cells propagated by George Otto Gey
- first human cell line to prove successful in vitro, which was a scientific achievement for the benefit of science
- neither Lacks nor her family gave Gey permission
  - (at that time, permission was neither required nor sought)
- HeLa cells were used by Jonas Salk to test the first polio vaccine in the 1950's
Concept Check

• 1. Neoplasia  a. abnormal proliferating cells w/ higher degree of autonomy

• 2. Anaplasia  b. lack of differentiation, primitive cells

• 3. Autonomy  c. cancer cells' independence from normal cell controls

• 4. Tumor markers  d. substances produced by cancer cells

• 5. Which characterizes cancer cells?
   – A. Poorly differentiated
   – B. Metastasis
   – C. Infiltrative growth
   – D. Poor cell cohesiveness
   – E. All of the above

• 6. Which is/are not malignant?
   – A. Glioma
   – B. Adenocarcinoma
   – C. Rhabdomyoma
   – D. Leukemia
   – E. A and C

7. Metastasis is:
   – A. Alteration in normal cell growth
   – B. Growth of benign or malignant cells
   – C. Mutational
   – D. Ability to establish a secondary neoplasm at a new site

8. CIS is:
   – A. Preinvasive
   – B. Glandular or epithelial lesion
   – C. Teratoma
   – D. Carcinoma that has broken through BM
   – E. Both a and b are correct

Cancer Epidemiology, Manifestations, and Treatment
Chapter 10

Environmental Risk Factors

<table>
<thead>
<tr>
<th>Increased</th>
<th>Decreased</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco</td>
<td>Exercise</td>
</tr>
<tr>
<td>Radiation</td>
<td>Proper Diet</td>
</tr>
<tr>
<td>Alcohol</td>
<td></td>
</tr>
<tr>
<td>Sexual Behavior</td>
<td></td>
</tr>
<tr>
<td>Diet</td>
<td></td>
</tr>
<tr>
<td>Obesity</td>
<td></td>
</tr>
<tr>
<td>Occupational Hazards</td>
<td></td>
</tr>
<tr>
<td>Electromagnetic Fields</td>
<td></td>
</tr>
</tbody>
</table>

Environmental Risk Factors

• Tobacco
   – Multipotent carcinogenic mixture
   – Linked to cancers of the lung, lower urinary tract, aerodigestive tract, liver, kidney, pancreas, cervix
   – Linked to myeloid leukemia
**Environmental Risk Factors**

- **Ionizing radiation**
  - Emission from x-rays, radioisotopes, and other radioactive sources
  - Exposure causes cell death, gene mutations, and chromosome aberrations
  - Bystander effects
  - Poor gene repair
  - Changes in gap junction intercellular communication

- **Ultraviolet radiation**
  - Causes basal cell carcinoma, squamous cell carcinoma, and melanoma
  - Principal source is sunlight
  - Ultraviolet A (UVA) and ultraviolet B (UVB)
  - Promotes skin inflammation and release of free radicals

- **Alcohol consumption**
  - Risk factor for oral cavity, pharynx, hypopharynx, larynx, esophagus, and liver cancers
  - Cigarette/alcohol combination increases a person’s risk

- **Sexual reproductive behavior**
  - Carcinogenic types of human papilloma virus
  - High-risk HPV

- **Physical activity**
  - Reduces cancer risk
  - Decreases insulin and insulin-like growth factors
  - Decreases obesity
  - Decreases inflammatory mediators and free radicals
  - Increased gut motility

- **Occupational hazards**
  - Substantial number of occupational carcinogenic agents
    - Asbestos
    - Dyes, rubber, paint, explosives, rubber cement, heavy metals, air pollution, etc.
    - Radon
Environmental Risk Factors

• Electromagnetic fields
  – Carcinogenic?
  • Are they, or aren’t they?

Environmental Risk Factors

• Diet
  – Xenobiotics
    • Toxic, mutagenic, and carcinogenic chemicals in food
    • Activated by phase I activation enzymes
    • Defense mechanisms
      – Phase II detoxification enzymes
    • Examples
      – Compounds produced in the cooking of fat, meat, or proteins
      – Alkaloids or mold by-products

Environmental Risk Factors

• Obesity
  – Correlates with the body mass index (BMI)
  – Adipose tissue is active endocrine and metabolic tissue

Environmental Risk Factors

• Obesity
  – In response to endocrine and metabolic signaling, adipose tissue releases free fatty acids
  • Increased free fatty acids gives rise to insulin resistance and causes chronic hyperinsulinemia
  • Correlates with colon, breast, pancreatic, and endometrial cancers

Clinical Manifestations of Cancer

• Pain
  – Little or no pain is associated with early stages of malignancy
  – Influenced by fear, anxiety, sleep loss, fatigue, and overall physical deterioration
  – Mechanisms
    • Pressure, obstruction, invasion of sensitive structures, stretching of visceral surfaces, tissue destruction, and inflammation

Clinical Manifestations of Cancer

• Fatigue
  – Subjective clinical manifestation
  – Tiredness, weakness, lack of energy, exhaustion, lethargy, inability to concentrate, depression, sleepiness, boredom, and lack of motivation
  – Suggested causes
    • Sleep disturbance, biochemical changes (cytokines), secondary to disease and treatment, psychosocial factors, level of activity, nutritional status, and environmental factors
Clinical Manifestations of Cancer

- Syndrome of cachexia (Gr. “bad condition”)  
  - Most severe form of malnutrition  
  - Present in 80% of cancer patients at death  
  - Includes:  
    - Anorexia, early satiety, weight loss, anemia, asthenia, taste alterations, and altered protein, lipid, and CHO metabolism

Anemia

- A decrease of hemoglobin in the blood  
- Mechanisms  
  - Chronic bleeding resulting in iron deficiency, severe malnutrition, medical therapies, or malignancy in blood-forming organs

Leukopenia and thrombocytopenia

- Direct tumor invasion to the bone marrow causes leukopenia and thrombocytopenia  
- Chemotherapy drugs are toxic to the bone marrow

Infection

- Risk increases when the absolute neutrophil and lymphocyte counts fall

Cancer Treatment

- Chemotherapy  
  - Use of nonselective cytotoxic drugs that target vital cellular machinery or metabolic pathways critical to both malignant and normal cell growth and replication  
  - Goal  
    - Eliminate enough tumor cells so body’s defense can eradicate any remaining cells

Chemotherapy

- Compartments  
  1: cells undergoing mitosis and cytokinesis  
  2: cells capable of entering the cell cycle in G1 phase  
  3: cells not dividing or have irreversibly left cell cycle  
    - Cells in compartment 3 will die a natural death
Cancer Treatment

- Ionizing radiation
  - Eradicate cancer without excessive toxicity
    - Avoid damage to normal structures
  - Ionizing radiation damages the cancer cell’s DNA
- Surgery
  - Biopsy and lymph node sampling
    - Sentinel nodes
  - Debulking surgery – remove most of tumor
  - Palliative surgery – relief of symptoms
- Hormone therapy
  - Receptor activation or blockage
  - Interferes with cellular growth and signaling

Immunotherapy

- Theoretically, antitumor responses can selectively eliminate cancer cells while sparing normal cells
- Immune memory is long lived
- Numerous immunologic mechanisms are capable of rejecting different types of cancer
- Biologic response modifiers (BRMs)

Other forms of immunotherapy

- Interferon administration
- Antigens
- Effector cell lymphokines
- Monoclonal antibodies

Side Effects of Cancer Treatment

- Gastrointestinal tract
- Bone marrow
- Hair and skin
- Reproductive tract

Concept Check

1. Likely cause for fatigue in cancer patients:
   - A. Biochemical changes due to treatment
   - B. Muscle loss
   - C. Psychologic factors
   - D. All of the above

2. The pain experience with cancer:
   - A. Affects the patient only in the early stages
   - B. Occurs in bone metastasis
   - C. Due to tissue necrosis
   - D. Both b and c are correct