Unit III: Cell Proliferation: Cancer

Biology, Clinical Manifestations, and Treatment of Cancer

Chapter 9

Cancer Epidemiology

Chapter 10

Cancer

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

Benign vs. Malignant Tumors

Benign	Malignant
Grow slowly	Grow rapidly
Well-defined capsule	Not encapsulated
Not invasive	Invasive
Well differentiated	Poorly differentiated
Low mitotic index	High mitotic index
Do not metastasize	Can spread distantly (metastasis)

Mitotic index = rate of growth

Classification and Nomenclature

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

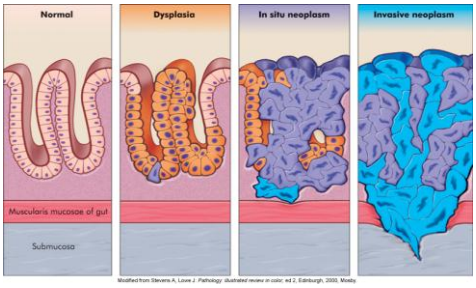
Classification and Nomenclature

- 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)

Classification and Nomenclature

- 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

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

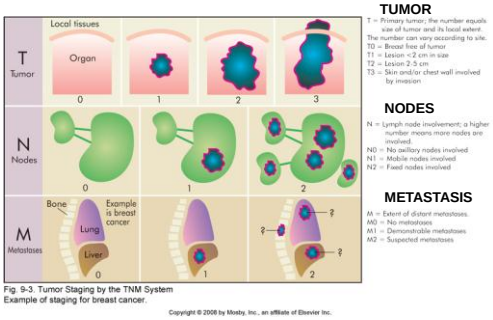
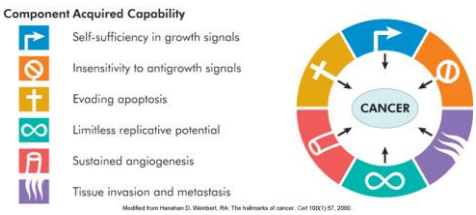


Fig. 9-3. Tumor Staging by the TNM System
Example of staging for breast cancer.

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 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

Chapter 10

Environmental Risk Factors

Increased
- Tobacco
- Radiation
  - Ionizing
  - UV
- Alcohol
- Sexual Behavior
- Diet
- Obesity
- Occupational Hazards
- Electromagnetic Fields ?

Decreased
* Exercise
* Proper Diet

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

Environmental Risk Factors

- 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

Environmental Risk Factors

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

Environmental Risk Factors

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

Environmental Risk Factors

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

Environmental Risk Factors

- 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

Cachexia

Clinical Manifestations of Cancer

- 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

Clinical Manifestations of Cancer

- 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

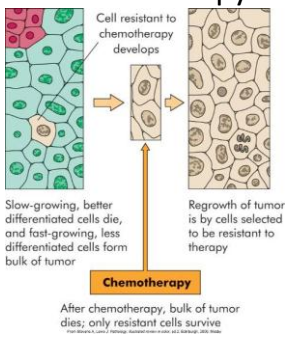
Cancer Treatment

- 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

Cancer Treatment

- Chemotherapy
  - Compartments
    1: cells undergoing mitosis and cytokinesis
    2: cells capable of entering the cell cycle in G_1 phase
    3: cells not dividing or have irreversibly left cell cycle
      - Cells in compartment 3 will die a natural death

Chemotherapy



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

Cancer Treatment

- 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)

Cancer Treatment

- 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. Pychologic 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