

Cancer Epidemiology, Manifestations, and Treatment

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Environmental Risk Factors

- Tobacco
 - Multipotent carcinogenic mixture
 - Linked to cancers of the lung, lower urinary tract, aerodigestive tract, liver, kidney, pancreas, cervix uteri
 - Linked to myeloid leukemia
- 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 papillomavirus
 - 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
- Electromagnetic fields
 - Carcinogenic - Are they, or aren't they?

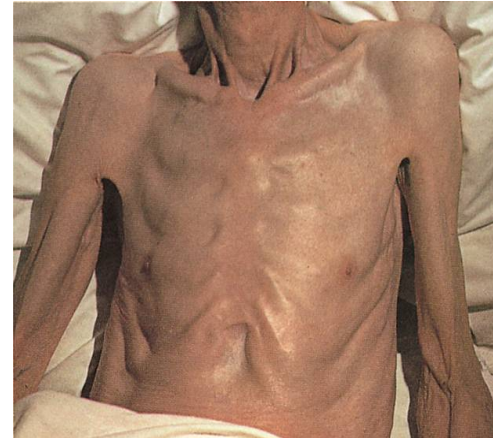
Environmental Risk Factors

- 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
- Obesity
 - Correlates with the body mass index (BMI)
 - Adipose tissue is active endocrine and metabolic tissue
 - 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
- 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 from circulating cytokines, secondary to disease and treatment, psychosocial factors, level of activity, nutritional status, and environmental factors

- Syndrome of cachexia
 - 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 carbohydrate metabolism



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
- 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
- Paraneoplastic syndromes
 - Symptom complexes that cannot be explained by the local or distant spread of the tumor or by the effects of hormones released by the tissue from which the tumor arose

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 the body's defense can eradicate any remaining cells
- Chemotherapy – Compartments (See picture page 58)
 - 1: cells undergoing mitosis and cytokinesis
 - 2: cells capable of entering the cell cycle in the G₁ phase
 - 3: cells not dividing or that have irreversibly left the cell cycle
 - Cells in compartment 3 will die a natural death
- Chemotherapy
 - Single-agent chemotherapy
 - Combination chemotherapy
 - Principle of dose intensity
 - Therapeutic index
 - Neoadjuvant chemotherapy

Cancer Treatment

- Ionizing radiation
 - Goals
 - 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
 - Palliative surgery
- 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

