Cancer

Difficult to Define

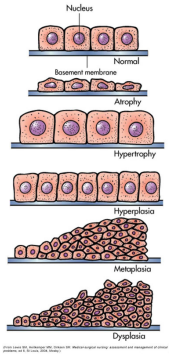
- Classic definition: tissue overgrowth which is independent of the laws governing the remainder of the body. Serves no purpose to the body.
- Tumor
  - Original definition: mass greater than 2cm
  - Neoplasm
    - Not all are cancer
    - Malignant vs. benign

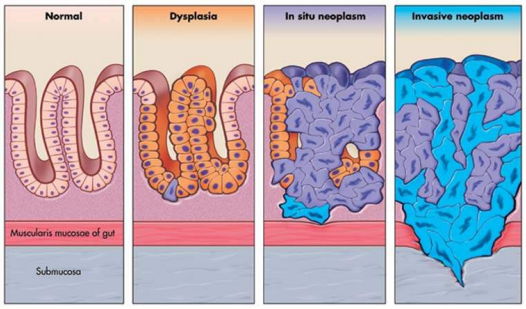
Tumors

- Benign
  - Grow slowly
  - Well-defined capsule
  - Are not invasive
  - Well differentiated
  - Low mitotic index
  - Do not metastatize
- Malignant
  - Grow rapidly
  - Not encapsulated
  - Invade local tissue
  - Anaplasia: poorly differentiated
  - High mitotic index
  - Metastasis (secondary tumor)

Cellular Adaptation

- Atrophy
- Hypertrophy
- Hyperplasia
- Metaplasia
- Non adaptive changes
  - Dysplasia
  - Neoplasia





(Modified from Stevens A, Lowe J: *Pathology*, ed 2, London, 2000, Mosby.)

Naming Cancers

- Carcinoma: epithelial cells
- Adenocarcinoma: glandular tissue
- Sarcoma: connective tissue
- Lymphoma: lymph tissue
- Leukemia: blood forming tissue (marrow)
- Fibroma
- Osteoma
- Chondroma

Tumor Markers

- Chemicals produced by cancer cells
  - May be present in blood, CSF, or tumor cell membranes
  - Usually similar or same as tissues that gave rise to tumor or fetal proteins from that tissue
    - Pheochromocytoma: epinephrine
    - Prostate cancer: prostate specific antigen (PSA)
    - Liver cancer: alpha fetoprotein (AFP)
    - CEA: GI tract cancers
    - CA-124: ovarian cancers
  - Can be used to screen for cancer or measure success of treatment

Hallmarks of Cancer

- Self-sufficiency in growth signals
- Insensitivity to antigrowth signals
- Evading apoptosis
- Limitless replicative potential
- Sustained angiogenesis
- Tissue invasion and metastasis

Carcinogenesis

- Genetic
  - Protooncogenes
  - Tumor suppressor genes
  - Apoptosis genes
  - DNA repair genes
- Stages
  - Initiation: mutation
  - Promotion: increased cell growth
  - Progression: invasiveness, angiogenesis

Protooncogenes

- Vulnerable genes
  - Mutation causes oncogenes
  - New or inherited
- Mutations
  - Point
  - Gene amplification
  - Chromosomal Rearrangement
  - Viral Insertion – HPV, HCV, EBV

Telomeres

- End cap of chromosomes
- Aging causes loss of telomere
- Telomerase in germ cells (embryonic)

Factors in Cancer Development

- Inflammation
- Family history: 2 possibilities
- Viruses
- Bacteria: H. pylori
- Environmental factors

Environmental Factors

- Tobacco use
- Ionizing radiation
- UV radiation
- ETOH consumption
- Sexual and reproductive behavior
- Physical activity
- Occupational
- Air pollution
- EMFs
- Stress
- Diet

Cancer Mets and Staging

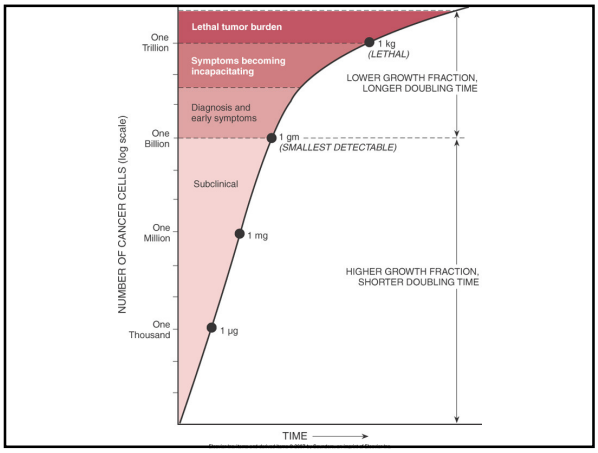
- Common mets sites: BBLL
  - Brain
  - Bones
  - Liver
  - Lungs
- Staging systems (various): carcinoma
  - Stage 1: confined to organ
  - Stage 2: locally invasive
  - Stage 3: lymph node invasion
  - Stage 4: spread to distant sites

Neoplasm-Host Interaction

- Cosmetic
- Tissue Compression or destruction
  - Ischemia
  - Altered or impaired function
- Increased Metabolic Demand – Cachexia
- Blood Supply
- Growth factors
- Immune Response

Clinical Manifestations

- Pain: usually in late stage
  - Fear, anxiety, sleep, fatigue, culture
  - Likely caused by cytokine action on C/PNS
- Fatigue
- Cachexia (TNF-α)
  - Increased metabolic load
  - Alterations in taste
  - Protein degradation
  - ↓Low albumin, ↓clotting, ↓immune, anemia

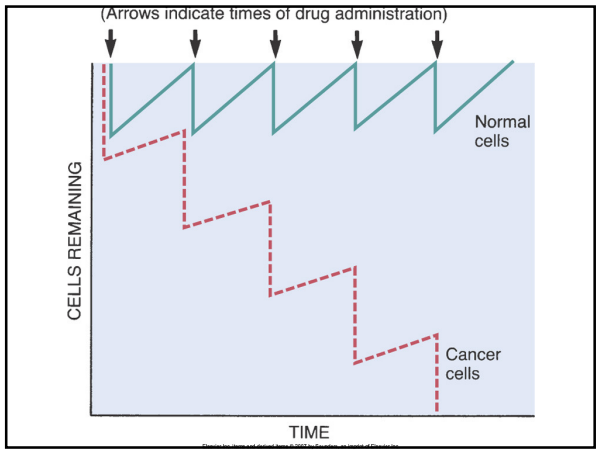


Clinical Manifestations

- Anemia
  - Fatigue, pallor, dyspnea on exertion
- Thrombocytopenia (Platelets < 150,000)
  - Bleeding
- Leukopenia (WBC < 5,000)
  - Infection

Cancer Treatment

- Chemotherapy
  - Usually targets high growth cells
  - Single agent
  - Combination
  - Dose intensity: kill the cancer before we kill pt
  - Compartments: only kills mitotic cells
    - Cell undergoing mitosis
    - Cells in gap phase
    - Cells that do not divide



Cancer Treatment

- Radiation
- Surgery
  - Local surgery
  - Sentinel nodes (skip metastasis)
  - Debulking
- Hormonal Therapy
- Immunotherapy

Cancer Immunotherapy

- Immunomodulating Agents
- Interferons
- Antigens (Tumor painting)
- Effector Cells and lymphokines
  - LAK
- Monoclonal Antibodies
- Dendritic Cell activation

Side Effects of Cancer Treatment

- Cells are same as body cells
- Treatment usually causes collateral damage
- GI tract:
  - Nausea
  - Stomatitis
  - Thrush/Diarrhea
  - Anorexia
  - Malabsorption

Side Effects

- Bone marrow suppression
  - Anemia
  - Leukopenia
  - Thrombocytopenia
- Hair and Skin
- Reproductive tract
  - Gamete banking
- Secondary tumors
- Remission
- “Cancer survivor”

Major Drug Classes

- Cytotoxic drugs: kills quickly growing cells
  - Many Cytotoxic cells are so toxic, they must be handled with gloves and administered in central lines
  - Star: Methotrexate: mimics folic acid
    - Cancer cells can't replicate DNA
- Glucocorticoids:
  - Directly kill cancer cells of lymph tissue
  - Decrease nausea when combined with anti-emetics
  - Promote appetite and sense of well-being

Major Drug Classes

- Hormone Modifiers: usually antagononize sex hormones in prostate and breast cancer
- Immunostimulants
- Targeted drugs: target specific cancer antigens or pathways.

Diagnosis: Warning Signs

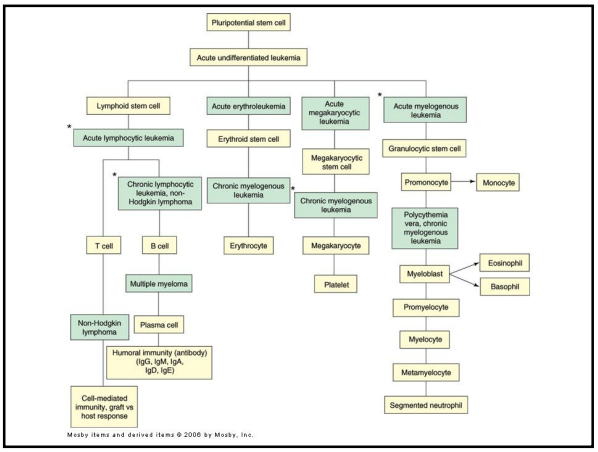
- Lump or swelling
- A sore that doesn't heal
- Recent change in a wart/mole
- Unusual bleeding or discharge
- Changes in bladder or bowel habits
- Nagging cough or hoarseness
- Difficulty in swallowing or dyspepsia

Diagnosis: Clinical Aspects

- Persistence of symptoms
- Cancer markers
- Identification of Mass – usually radiology
  - X-ray, CT, MRI, nuclear scans, PET scan
  - Visual (-scope)
- **Morphologic confirmation!!!!!!!!!!**
  - Biopsy and cytology

Leukemia

- Cancer of blood producing cells
- Types
  - AML: Acute Myelogenous Leukemia
  - ALL: Acute Lymphocytic Leukemia
  - CML: Chronic Myelogenous Leukemia
  - CLL: Chronic Lymphocytic Leukemia
- Acute: undifferentiated,rapid onset
- Chronic: mature cells, slow onset



ALL

- Most common child leukemia (80%)
- Mortality in adults is much higher
- ALL is caused by loss of differentiation
  - Stuck dividing, don't leave marrow
  - Accumulate, crowd out other cells
- Numerous subtypes based on genetic factors
  - Cure rate 60% to 90%

AML

- Accumulation of blast cells
  - Replace normal RBC, granulocytes and platelets
- More common as get older; peaks in 60's

Acute Leukemia Manifestations

- Fatigue
- Bleeding
- Infection
- Anorexia
- Spleen, liver, node enlargement
- CNS: H/A, vomiting, palsy, sensory impairment

Eval & Treatment

- CBC with peripheral smears
- Bone marrow biopsy
  - Sedation/Anesthetic/Analgesia
  - Pressure to prevent bleeding
- Chemotherapy
- Stem cell transplant
- Supportive therapy
  - Transfusions, abx, allopurinol

CLL

- Monoclonal expansion of B cells
- Deficit in mature B cells
- Accumulation of cells in marrow does not interfere with normal blood production
- Most common manifestations are infections and secondary cancers
- Rare under age 45

CML

- Begins in a stem cell, but favors myeloid differentiation
- Myeloid function is relatively normal
- Manifestations similar to AML, but take longer to appear

Eval & Treatment

- CBC
- Bone marrow biopsy
- CLL: treatment relieves symptoms but no significant increase in lifespan

Myeloma

- Cancer of Plasma Cells
  - Increase in ?
- Manifestations
  - Skeletal pain
  - Renal failure
  - Infections
  - Bone destruction: hypercalemia
- Eval: bone scan, CT, MRI
- TX: chemotherapy and Stem cell transplant