

---

# PATHPHYSIOLOGY CANCER

Dr. Debra Laskin  
Room 002 William Levine Hall  
EOHSI Room 414

[laskin@eohsi.rutgers.edu](mailto:laskin@eohsi.rutgers.edu)

Textbook: Chapter 9

# Cancer (Neoplastic Disease)

---

- Second leading cause of death in the US (500,000/year)
- Incidence is increasing, mortality is decreasing; early detection
- Most common type: **skin cancer**  
75% all other malignancies occur in 10 anatomical sites: colon, rectum, breast, lung and bronchus, prostate, uterus, lymph organs, bladder, stomach, blood and pancreas.
- **Cancer deaths:**  
Males: lung (31%); prostate (10%); colon & rectum (10%)  
Female: lung (25%); breast (15%); colon & rectum (11%); ovaries (5%)
- Major cause of cancer: **cigarette smoking:**  
15% of all cancer deaths

# Cancer

---

**Cancer:** derived from Greek word for crab;  
Hippocrates- appendage like projections from crab  
Many different diseases

**common feature:** abnormal cell growth

- shift in control mechanisms for growth and differentiation; infiltration into organs; Interference with normal function

**Tumor:** “swelling” (classical defn; Greek)  
Today- readily defined mass of abnormally growing tissue

**Neoplasm:** new growth; autonomous

**Benign tumor**

**Malignant  
Cancer**

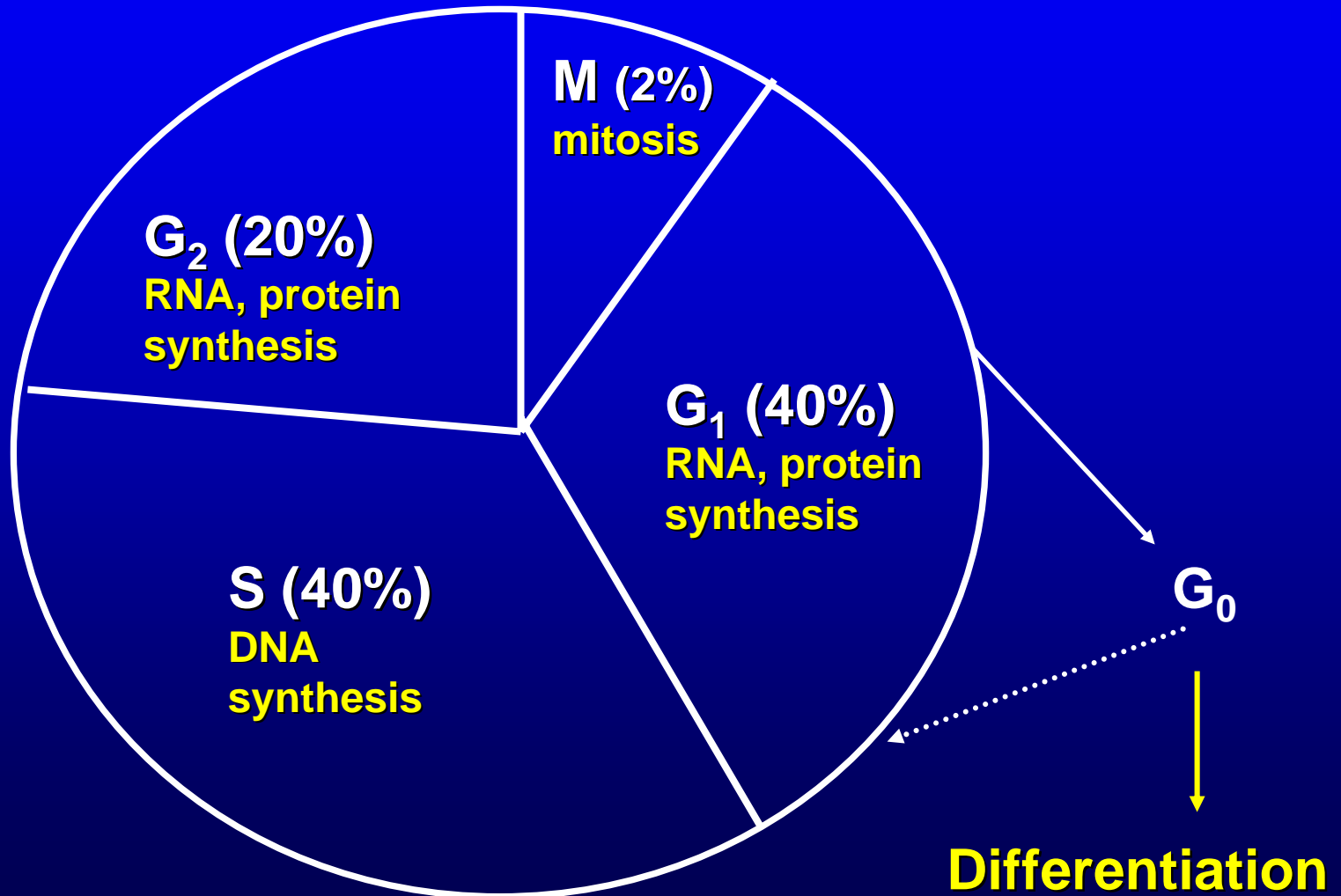
# Abnormalities Associated with Tumors

---

- ◆ **Hypertrophy:** increase in cell size
- ◆ **Hyperplasia:** increase in cell number
- ◆ **Dysplasia:** abnormal appearance of a cell; (earliest form of preneoplastic lesion); epithelial layer; change in cell size, shape, organization; graded: low → high
- ◆ **Metaplasia:** reversible *replacement* of one mature cell by another  
ex., epithelial metaplasia: columnar epithelial cells of respiratory tract → squamous epithelium  
redirection of differentiation

# Cell Cycle

---



# Cell Cycle Phase

---

Tumors consist of heterogeneous populations of cells, some growing, some dormant; in different phases of cell cycle

## Phases of Cell Cycle

- ◆ M: (mitosis, 2%); prophase, metaphase, anaphase, telephase
- ◆  $G_1$  (Gap 1, 40%): determines length of cell cycle, varies:  
 $G_0$ : dormant cells (not cycling); resting or differentiating
- ◆ S: (40%) DNA synthesis
- ◆  $G_2$  (Gap 2, 20%): RNA and protein synthesis

**Doubling time:** time for total number of cells in a tumor to double; to go through cell cycle once

# Genetics of Cancer

---

Cancer- disease of aging

**Mutation Theory:** cancer caused by mutations; with time, number of mutations (hits) increases; when sufficient number occurs clonal proliferation of → mutated cell

## Types of mutations:

- Mutations in normal genes (proto-oncogenes) controlling proliferation (growth factors, receptors-EGFr, intracellular signaling-ras); become **oncogenes**
- Suppression of anti-cancer genes or **tumor suppressor genes** (retinoblastoma gene)
- Resistance to apoptosis (p53 mutations)

# Characteristics of Cancer Cells

---

## Altered Growth

uncontrolled proliferation; loss of contact inhibition, loss of cell-cell communication, become autonomous; **immortal**

## Altered Morphology

Pleomorphic- many different shapes

## Anaplasia

dedifferentiation- loss or lack of differentiation; change in size, shape, DNA content

# Characteristics of Cancer Cells

---

## Karyotypic Changes

**Polyploidy:** cell division produces more than two sets of chromosomes

**Aneuploidy:** daughter cells receive uneven number of chromosomes

# Classification of Tumors

---

## Behavioristic:

### Benign

encapsulated  
differentiated  
rare mitosis  
slow growth  
little anaplasia  
\*non-invasive  
\*no metastasis

### Malignant (cancer)

nonencapsulated  
nondifferentiated  
common mitosis  
rapid growth  
anaplasia  
\*invasive  
\*metastatic

# Classification of Tumors

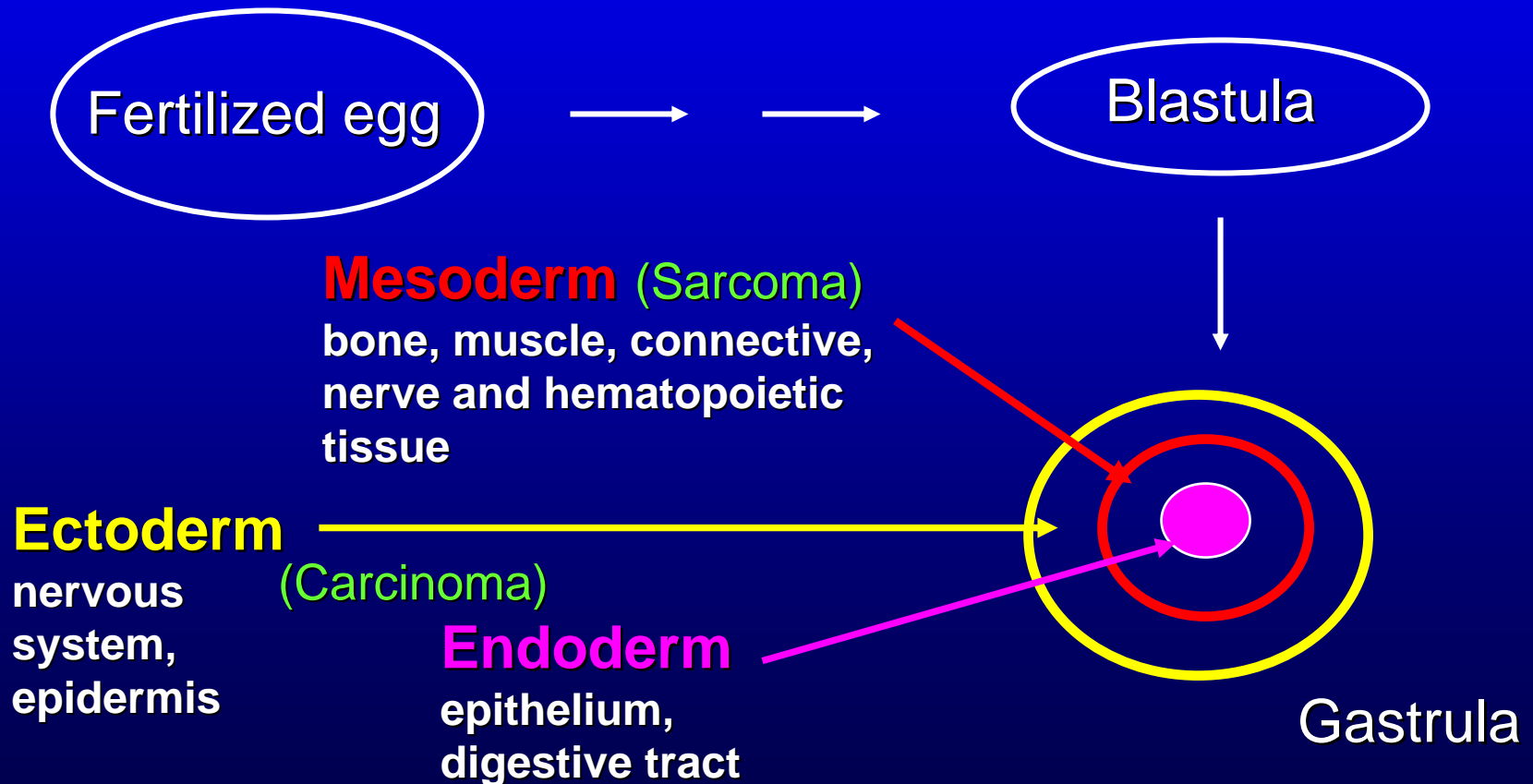
---

**Histiogenetic:** based on tissue origin

- ◆ **Epithelial:** squamous cells; basal cells; glandular or ductal cells
- ◆ **Connective tissue:** bone, cartilage, fibrous tissue
- ◆ **Hematopoietic:** leukocytes, lymphatic tissue, plasma cells
- ◆ **Nervous system tumors:** nerve tumors

# Classification of Tumors

## Embryonic Classification



# Embryonic Classification

---

**Sarcomas:** arise from mesenchymal (mesoderm) or connective tissue;  
ex., osteogenic sarcoma (from bone);  
rhabdomyosarcomas (from skeletal muscle);  
lymphosarcoma (from lymph tissue)

**Carcinomas:** arise from endothelial and epithelial tissues (ectoderm and endoderm);  
ex., hepatocellular carcinoma;  
*adenocarcinomas*- arise from ductal or glandular tissue

**Teratomas**- neoplasm of multiple tissue origin;  
derived from all 3 germ lines

# Types of Tumors

---

**Solid Tumors:** can occur in any organ or tissue

**Carcinomas:** originate from endothelial and epithelial cells (ectoderm and endoderm); ex., squamous cell (basal cells skin); glandular epithelium (breast)

**Sarcomas:** originate in mesenchymal cells (mesoderm); ex., osteogenic sarcoma (osteoblasts, chondroblasts, fibroblasts)

# Types of Tumors

---

**Hematologic Malignancies:** cancers arising from blood forming organs and cells

- ◆ **Leukemias:** WBC – proliferation of immature, committed bone marrow cells; types: ALL, AML, CLL, CML multiple myeloma
- ◆ **Lymphomas:** tumor of lymph system
  - Hodgkin's Disease (lymph nodes)
  - Non Hodgkin's lymphoma

# Staging Cancer

---

- ◆ **Stage 1:** confined to the organ of origin
- ◆ **Stage 2:** locally invasive
- ◆ **Stage 3:** spread to regional structures (ex., lymph nodes)
- ◆ **Stage 4:** spread to distant sites

# Etiology of Cancer

---

## **Environmental factors (80-90%)**

chemicals, diet, industrial pollution, medical treatment

## **Immunological defects**

## **Radiation**

## **Oncogenic viruses**

## ***Contributing factors:***

age, sex, race, genetic predisposition, environmental exposure levels, behavioral habits, occupation

# Environmental Agents

---

## Chemicals

- ◆ **Carcinogens:** chemicals that cause cancer; ex., polycyclic aromatic hydrocarbons, benzo(a)pyrene, 3-methylcholanthrene
- ◆ **Co-carcinogens:** work with carcinogens
- ◆ **Tumor promoters:** promote the action of carcinogens

initiation → promotion → tumor formation

# Environmental Agents

---

## Drugs

### ◆ **Immunosuppressive agents**

Immune surveillance: macrophages and T cells

- AIDS: Kaposi's sarcoma
- Renal transplants: reticulo cell sarcoma (150x); others (2x)

### ◆ **Common drugs** (<1% of all cancers)

DES, chlorpromazine, reserpine, estrogens, oral contraceptives, anticancer drugs

# Environmental Agents

---

**Radiation:** most systemically studied

- ◆ **Ionizing Radiation:** high energy chronic exposure to x-rays and radioactive chemicals → skin cancer, leukemia; *medical, diagnostic, occupational exposure* nuclear fallout Japan

<sup>131</sup>I for treatment of goiter

- ◆ **Mechanism:**

Specific mutations → DNA strand breaks; often requires multiple hits

Ex., Incidence of leukemia in radiologists 1900-1950 (3-4x); Hiroshima survivors (2x)

# Environmental Agents

---

## Radiation

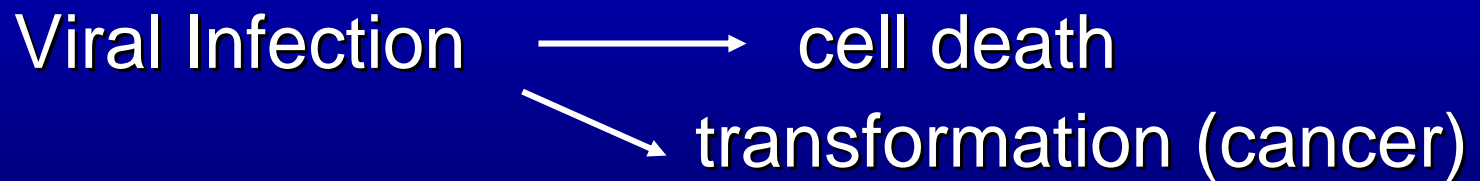
- ◆ **Ultraviolet Radiation** (2900-3400 Å)
  - Sunlight – greatest source of exposure: results in skin tumors; malignant melanoma
  - Correlate incidence skin cancer to exposure to sun; latitude, clothing, farmers

# Environmental Agents

---

## Oncogenic Viruses

- ◆ **RNA viruses** (acutely transforming retroviruses)
- ◆ **DNA viruses** (HSV, EBV)



Viral oncogenes (RNA or retroviruses)- get inserted into genome; disregulate proliferation

# Contributing Factors

---

**Occupation:** determines exposure levels

1780: P. Potts

1900's: radium dial painters

1950's: shoe store x-ray machines

1990's: Industrial chemical workers

BCME, CMME

metals

vinyl chloride

benzene

PCB's

asbestos

# Contributing Factors

---

## Age:

- ◆ Cancer is a disease of aging
- ◆ **Latency:** time for for genetic or epigenetic changes to be expresses
- ◆ Mutations

# Contributing Factors

---

## Hormones:

- ◆ Beatson (1800): identified causal relationship between breast cancer and ovaries
- ◆ Hormones: maintain internal milieu; abnormal production → derangement of homeostasis → neoplasia  
ex. DES (Herbst, 1971)  
1<sup>st</sup> trimester exposure → vaginal adenosis; clear cell and squamous cell carcinoma in female offspring; infertility

# Hereditary Factors

---

**Heredity Factors:** Most involve environmental interaction with DNA; Polygenic or multifactorial inheritance

- ◆ **Autosomal dominant:** no apparent environmental cause; pheochromocytoma, retinoblastoma
- ◆ **Autosomal recessive:** usually DNA repair defects; involve environmental agents; xeroderma pigmentosa (UV); ataxia telangiectasia (ionizing radiation)
- ◆ **Genetic Predisposition:** cancer genes; breast cancer (3x); lung cancer; colon cancer

# Geography

---

**Diet:** ingestion of carcinogens (aflatoxin; nitrates, nitrites)  
Cancers of digestive tract (ex., stomach cancer)  
Incidence: Japan vs. U.S.

## Environmental Pollution:

- **Air** large cities increase levels hydrocarbons  
urban cigarette smokers increased incidence  
lung cancer; greater than heavy rural  
smokers; carcinogen interactions
- **Water**

# Geography

---

**Occupation**

**Behavioral Habits**

**Sun**

If change geography, offspring acquire  
incidence of new environment