Chapter 20

Neoplasms and Cancer

Terminology:

Tumor – a swelling (not necessarily a growth).

Neoplasm – a new growth.

Benign Neoplasm – will not kill host
except if in a compromised location like the brain.

Malignant Neoplasm - aka "Cancer".
- will kill host.
- uncontrolled growth.
- locally invasive or
- spreads (metastasis).

Nomenclature

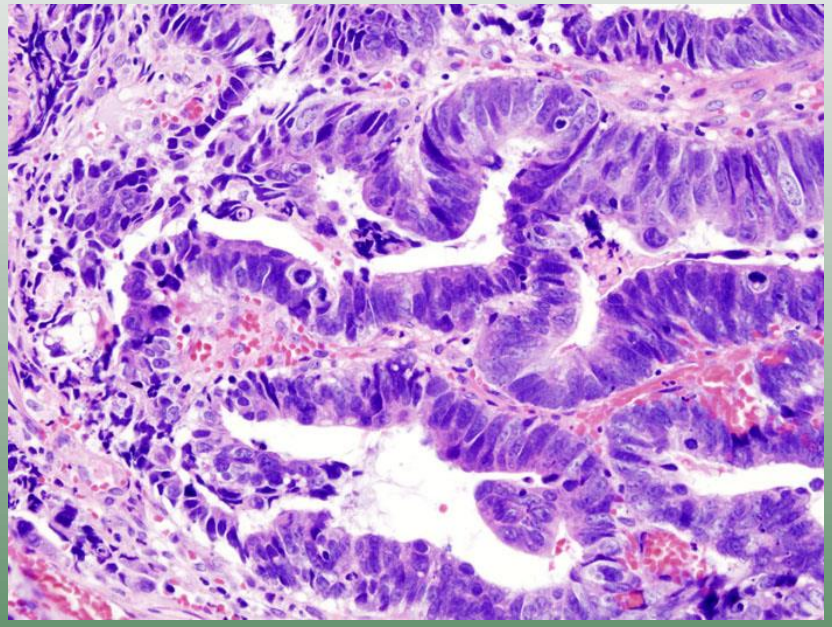
	Benign	**Malignant**
Suffix	-oma	-carcinoma - sarcoma
Gland Tumor	Adenoma	Adenocarcinoma
Fat Cell Tumor	Lipoma	Liposarcoma

Some malignant tumors have unique names:

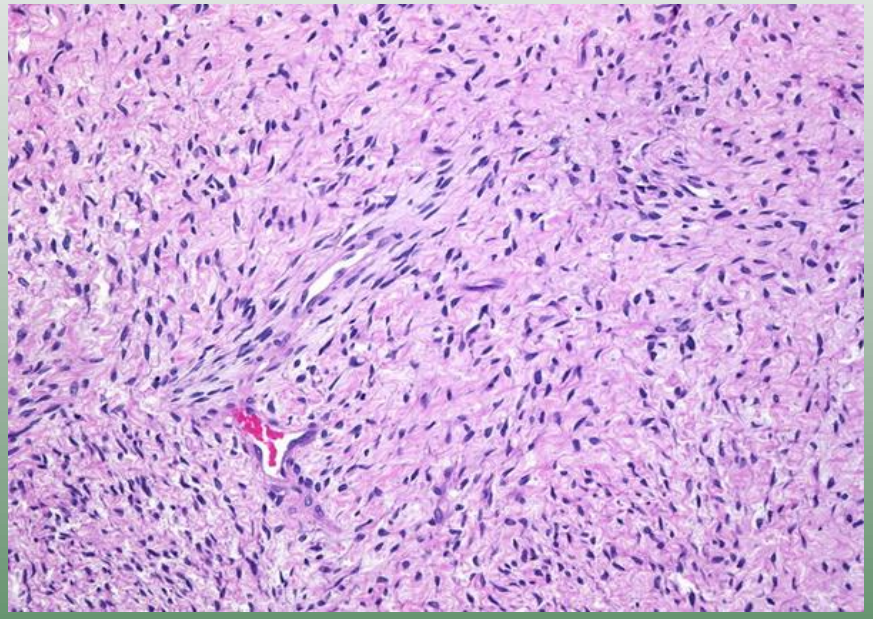
- Hodgkin's disease: a type of lymphoma.
- Wilms' tumor: a type of malignant kidney tumor in Children.
- Leukemia: a general term for malignancies of white blood cells.

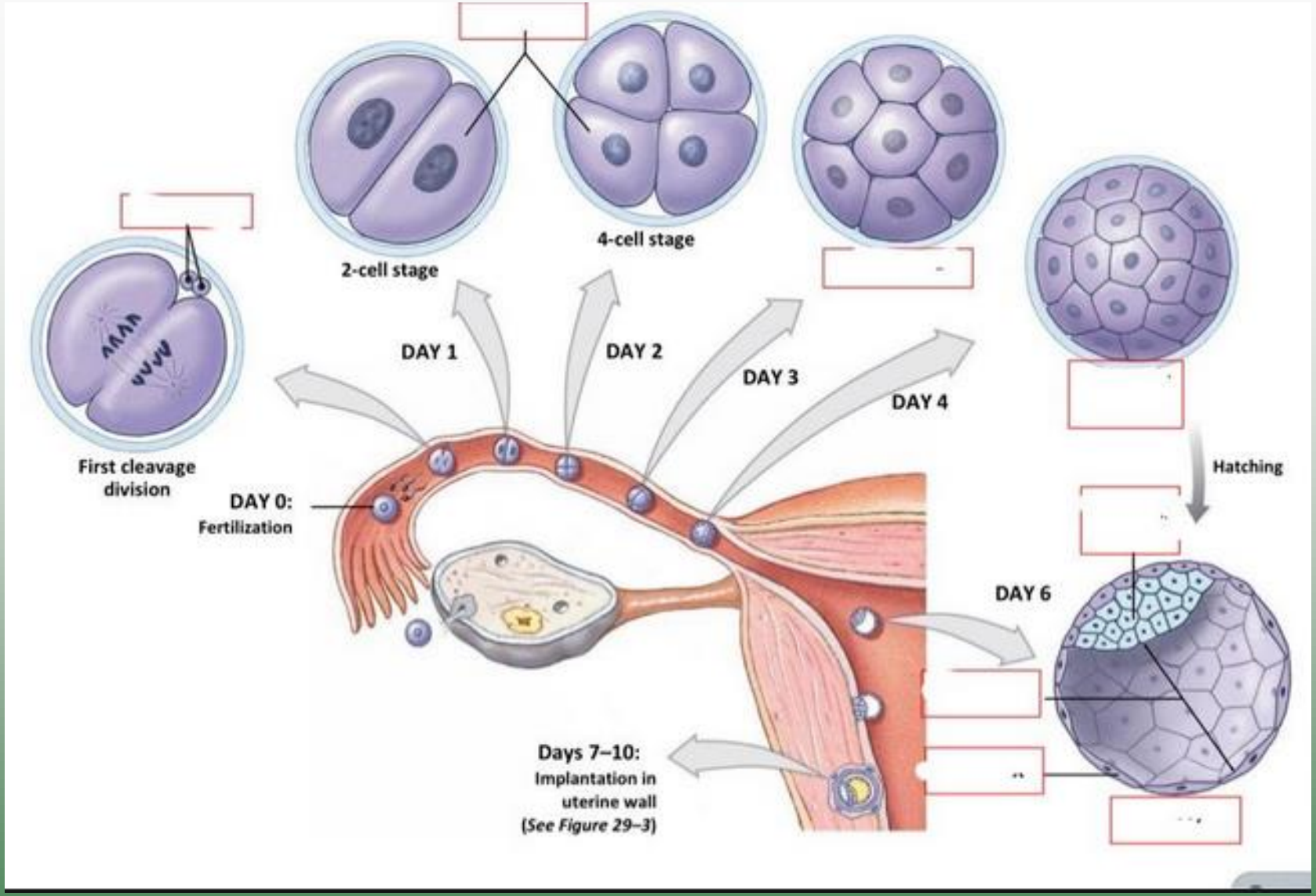
Two Main Categories of Cancer

Carcinoma



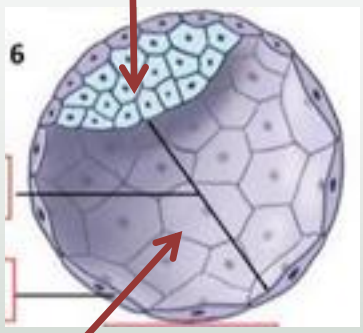
Sarcoma



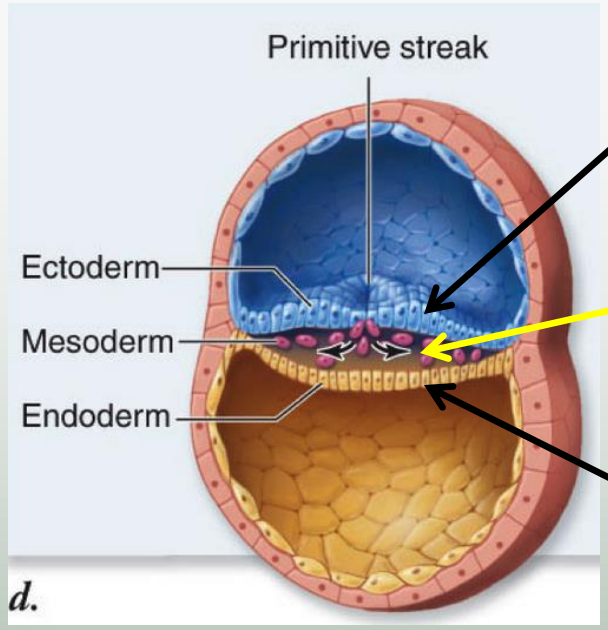


Development Post Fertilization

inner cell mass



Single cavity



Carcinoma

Sarcoma

Carcinoma

Ectoderm, Endoderm ---> Epithelial Tissues, Glands, and Organs

Mesoderm ---> Soft Tissues (muscle, nerve, fat, blood vessels).

Ectoderm, Endoderm ---> Epithelial Tissues, Glands, and Organs

Sqaumous lining cells in mouth ---> Squamous Carcinoma

Duct cells in breast ---> Ductal Carcinoma

Prostate glands ---> Prostate Carcinoma

Mesoderm ---> Soft Tissues (muscle, nerve, fat, blood).

Muscle cells ---> Myosarcoma

Fat Cells ---> Liposarcoma

White blood cells ---> Leukemia and Lymphoma

Neoplasms

- Cellular growth that no longer responds to normal genetic controls
- Cell continues to reproduce, without need for them to reproduce
- Deprives other cells of nutrition
- Neoplasms may consist of atypical or immature cells.
- Characteristics of each tumor depend on:
  - Type of cell from which the tumor arises
  - Unique structure and growth pattern

Benign and Malignant Neoplasms

- Benign neoplasms.
  - Usually differentiated cells that reproduce at a higher rate than normal
  - Encapsulated
  - Tissue damage
    - This is a result of compression of adjacent structures.
    - It can be life-threatening in the brain.
- Malignant neoplasms.
  - Undifferentiated, nonfunctional cells
  - Rapid reproduction—abnormal mitotic figures
  - Infiltrate or spread into surrounding tissue
  - Spread to distant sites

Characteristics of Benign and Malignant Tumors

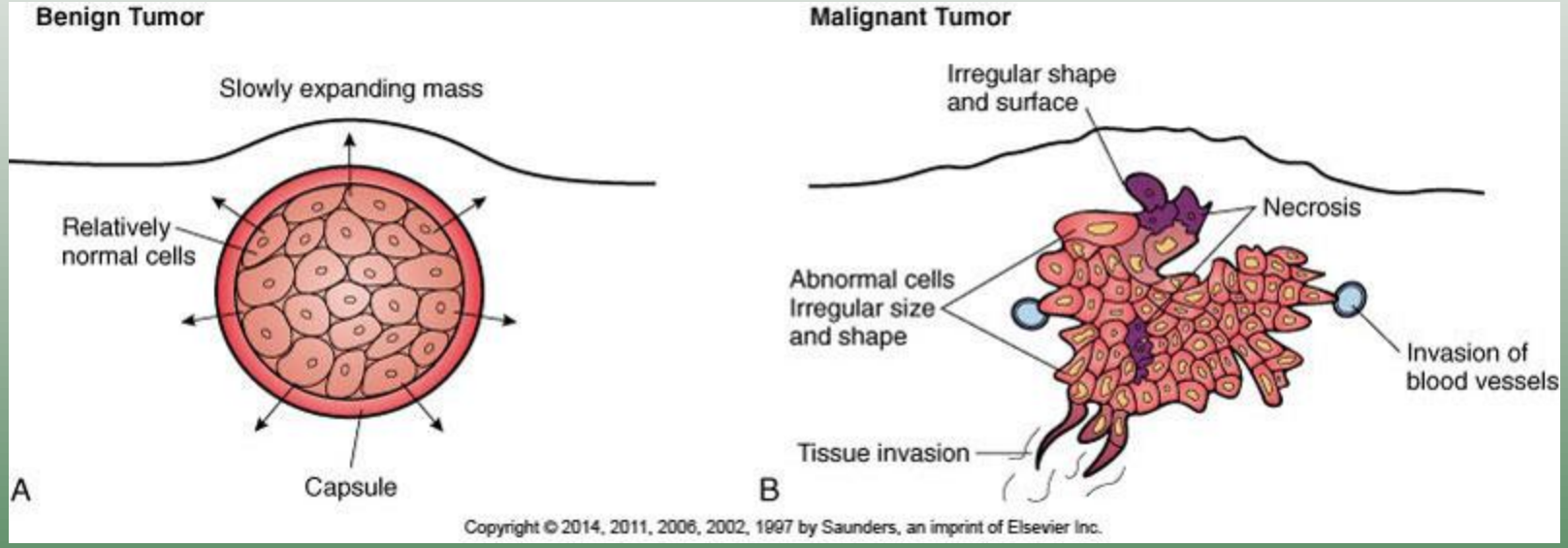


TABLE 20-2 Characteristics of Benign and Malignant Tumors

	Benign Tumors	Malignant Tumors
Cells	Similar to normal cells	Varied in size and shape with large nuclei
	Differentiated	Many undifferentiated
	Mitosis fairly normal	Mitosis increased and atypical
Growth	Relatively slow	Rapid growth
	Expanding mass	Cells not adhesive, infiltrate tissue
	Frequently encapsulated	No capsule
Spread	Remains localized	Invades nearby tissues or metastasizes to distant sites through blood and lymph vessels
Systemic effects	Rare	Often present
Life-threatening	Only in certain locations (e.g., brain)	Yes, by tissue destruction and spread of tumors

Paraneoplastic Syndrome – malignancy secretes a hormone that has a systemic effect (example hypercalcemia).

Malignant Neoplasms: Cancer

- Mass compresses blood vessels.
  - Leads to necrosis and inflammation around tumor
- Tumor cells may secrete enzymes or hormones.
  - Break down of proteins and cells
  - Systemic effects, such as altered calcium levels
- Inflammation and loss of normal cells
  - Lead to progressive reduction in organ integrity and function
  - [Glucocorticoid steroids help reduce inflammation]
- Angiogenesis
  - Some tumor cells secrete growth factors.
    - Stimulate the development of new capillaries in the tumor

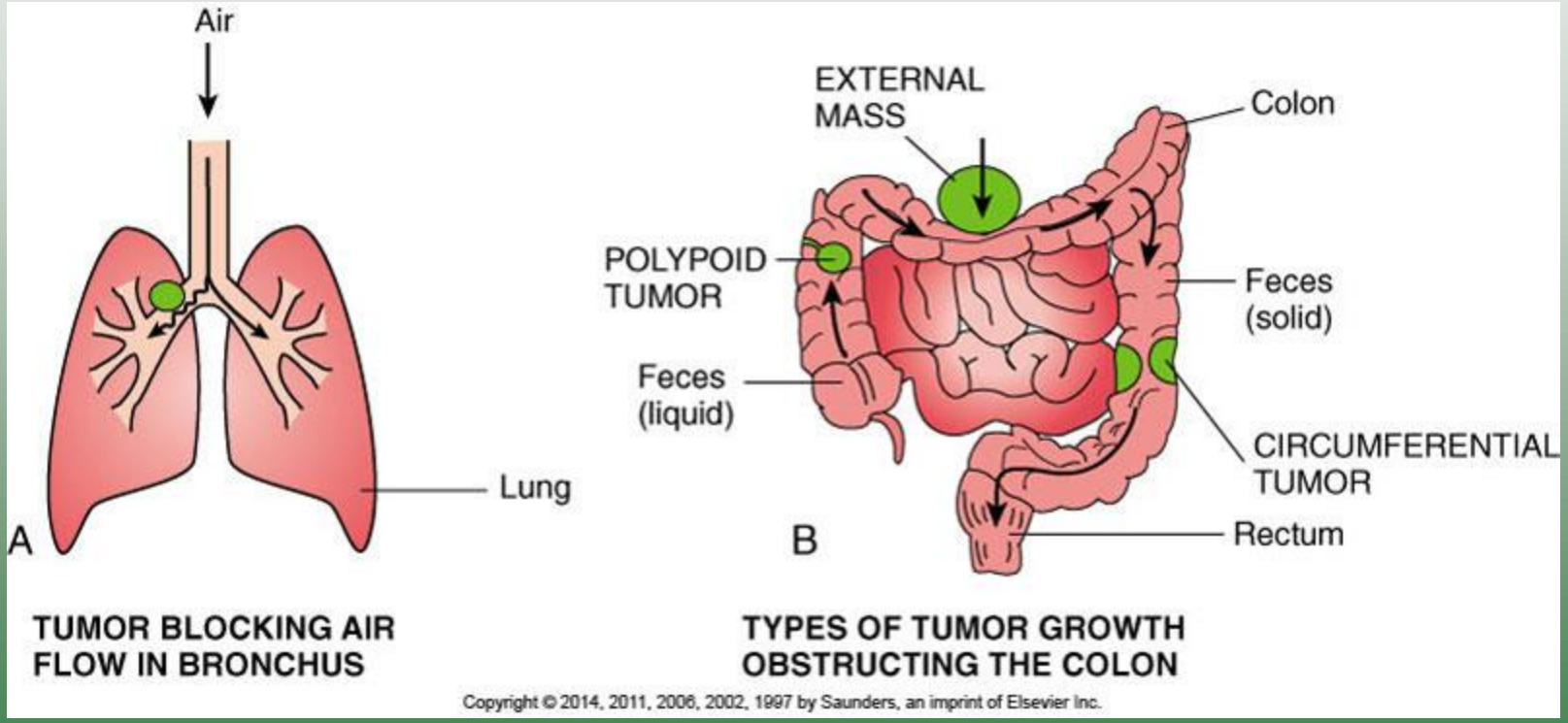
Warning Signs of Cancer

1. Unusual bleeding or discharge anywhere in the body.
2. Change in bowel or bladder habits (prolonged diarrhea or discomfort).
3. Change in a wart or mole (color, size, shape).
4. A sore that does not heal.
5. Unexplained weight loss.
6. Anemia and ersisten fatigue.
7. Persistent cough or horseness without reason.
8. A solid lump (tumor) in the breast, testis, anywhere.

Local Effects of Neoplasms

- Pain
  - May be absent until very late stages
  - Occurs when tumor is well advanced
  - Severity depends on the type of tumor
- Obstruction
  - Occurs when tumor compresses a duct or passageway or blood or lymphatic vessel.
  - Digestive tract (*bloating, vomiting, severe pain*).
  - Airflow in bronchi (*problem breathing, cough blood*).
- Tissue necrosis and ulceration
  - May lead to bleeding or infection around the tumor

Obstruction by Tumors



Systemic Effects of Malignant Tumors

- Weight loss and cachexia
  - Anorexia, fatigue, pain, stress
  - Increased demands on the body from tumor cells
- Anemia
  - Caused by blood loss at tumor site
  - Nutritional deficits may reduce hemoglobin synthesis.
- Severe fatigue
  - Caused by inflammatory changes, cachexia, anemia
  - Stress of treatment schedule
  - Psychological factors

Systemic Effects of Malignant Tumors

- Effusions
  - Inflammation causes fluid buildup in body cavities.
- Infections
  - Occur frequently as resistance declines
- Bleeding
  - Tumor cells may erode the blood vessels.
- Paraneoplastic syndrome
  - Associated with certain tumor types
  - Tumor cells release hormones.

Diagnostic Tests

- Routine screening
  - Essential for early detection
  - Following treatment to detect any further tumors
- Self-examination
  - Early detection if done consistently
    - Breast, testicular, and skin examinations are important.
- Blood tests
  - Measure blood cell levels during treatment
  - May detect tumor markers (e.g., PSA test)

Cancer Incidence

Men	Women
➢ Prostate cancer	Breast cancer
➢ Lung cancer	Lung cancer
➢ Colorectal cancer	Colorectal cancer

Lung Cancer: screen with CT scan.

<for smokers, may not help>

Colon Cancer: screen with colonoscopy.

<polyps precede cancer>

Breast Cancer: self exam and mamograms.

<survival related to size at diagnosis>

<women find before doctors>

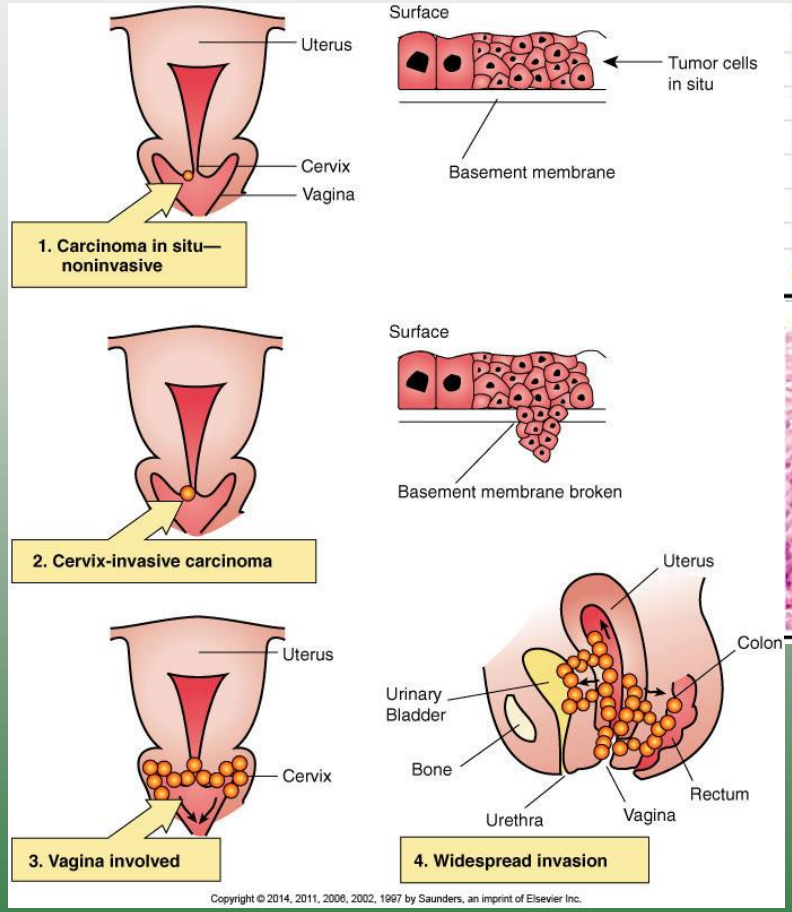
Cervical Cancer: PAP smears.

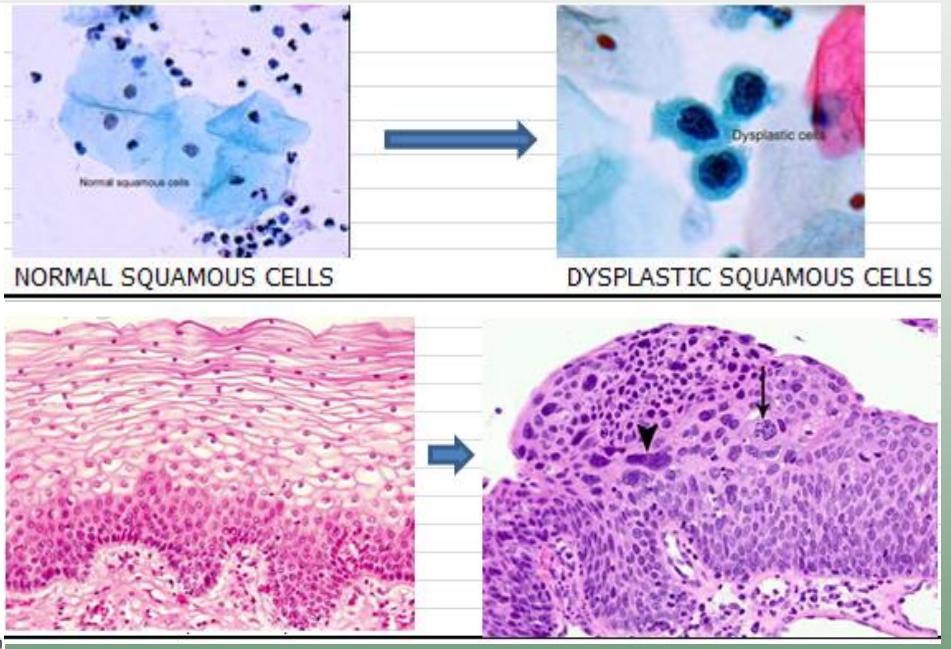
<detects precancerous stage>

Diagnostic Tests

- Radiographic, ultrasound, MRI, CT
- Methods of visualizing changes in tissues or organs
- Cytological tests - biopsy or cell sample
  - Histological and cytological examinations to determine degree of differentiation and tumor type
  - May be tested for growth promoter sensitivities, (e.g., estrogen-dependent tumors)
  - Most dependable confirmation of malignancy

Invasive Carcinoma of the Cervix

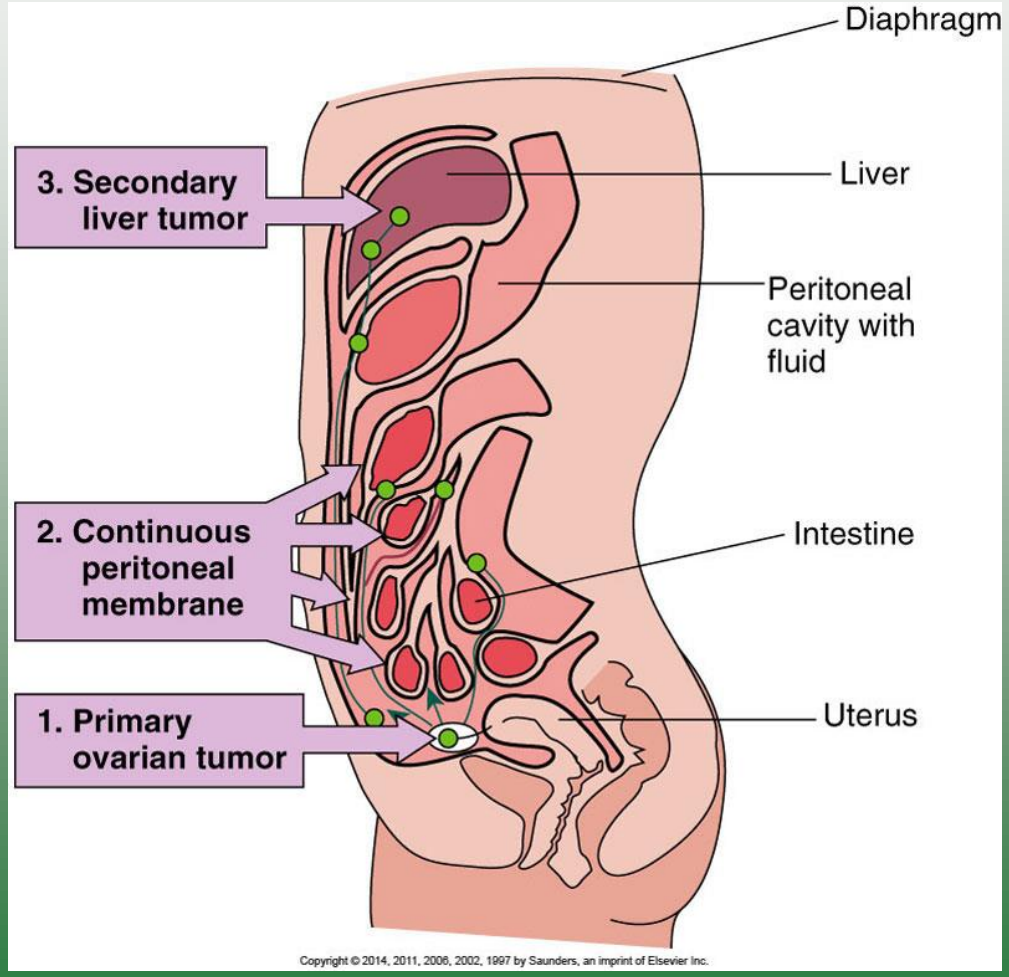




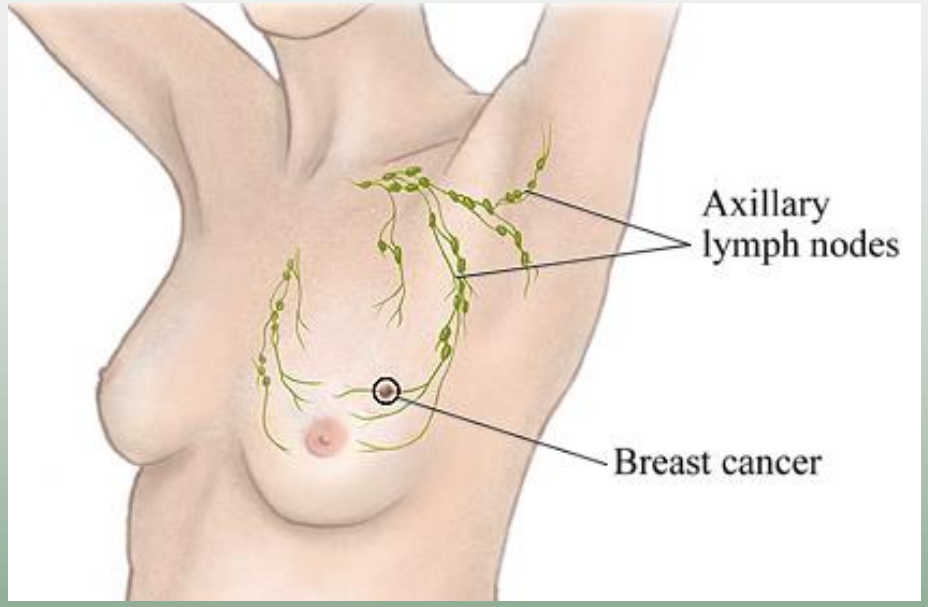
Spread of Malignant Tumors

- Invasion
  - Local spread
  - Tumor cells grow into adjacent tissues
- Metastasis
  - Spread to distant sites
  - Via blood or lymph or other body fluids
  - Example: Carcinoma of the colon spreads to the liver.

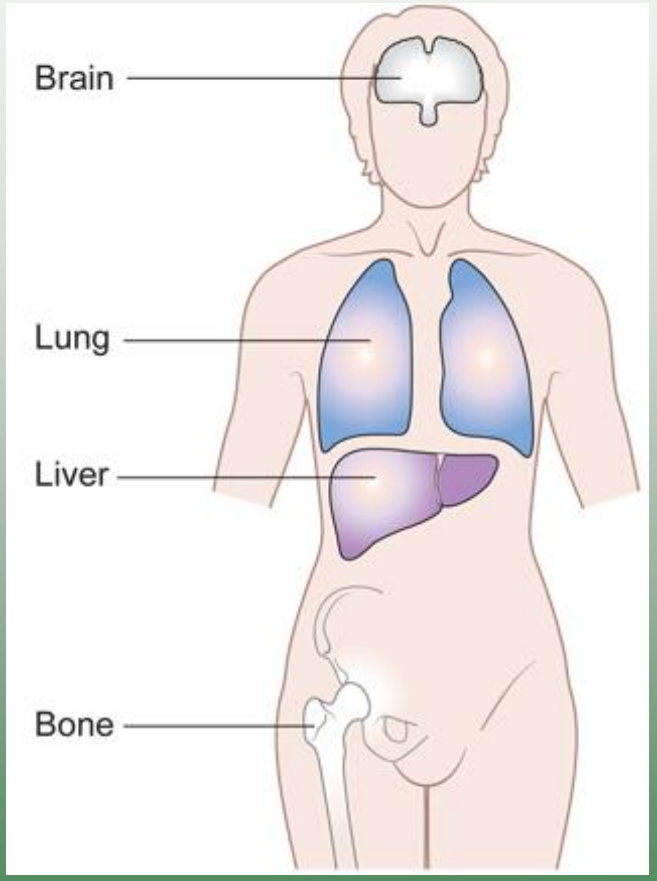
Ovarian Cancer Spread Through Pelvic and Peritoneal Cavity Fluids



Metastatic Breast Cancer



Lymphatic Spread



Hematogenous Spread

Staging Cancer

- Essential to standardize comparative studies of treatments and outcomes
- Used to estimate prognosis
- Most common system used is the TMN system:
  - Size of primary tumor (T)
  - Involvement of regional lymph nodes (N)
  - Spread (metastasis) of tumor (M)

Grading Cancer

Histologic appearance in the microscope.

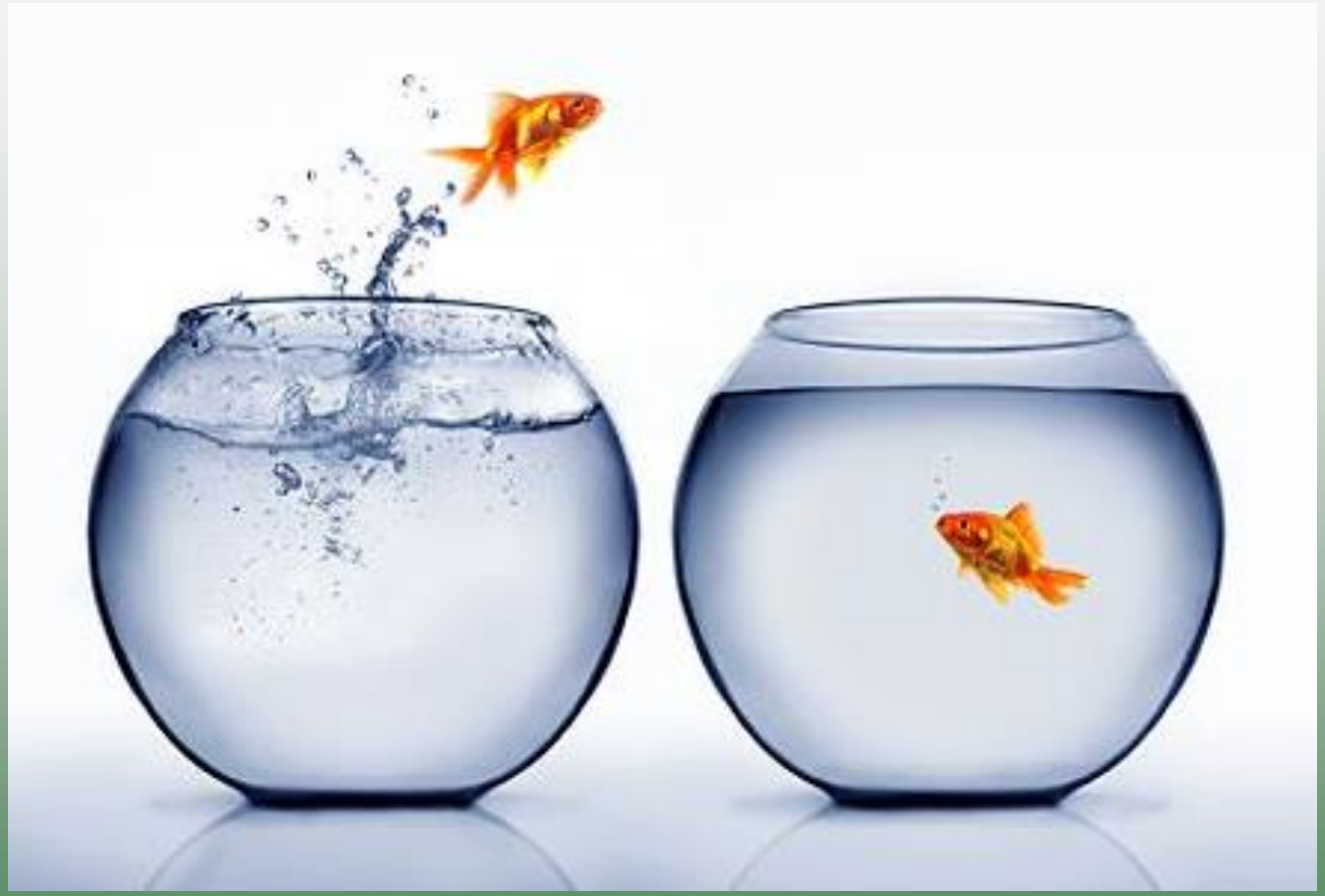
Low Grade is well differentiated:
(looks like tissue of origin)

High Grade is anaplastic or poorly differentiated to the point that there it is not obvious from what tissue the cancer came.

Hints to remember difference between Stage and Grade.

SS – Stage is Spread (how far)

GH – Grade is Hisologic Appearance.



Carcinogenesis

- Process whereby normal cells are transformed into cancer cells

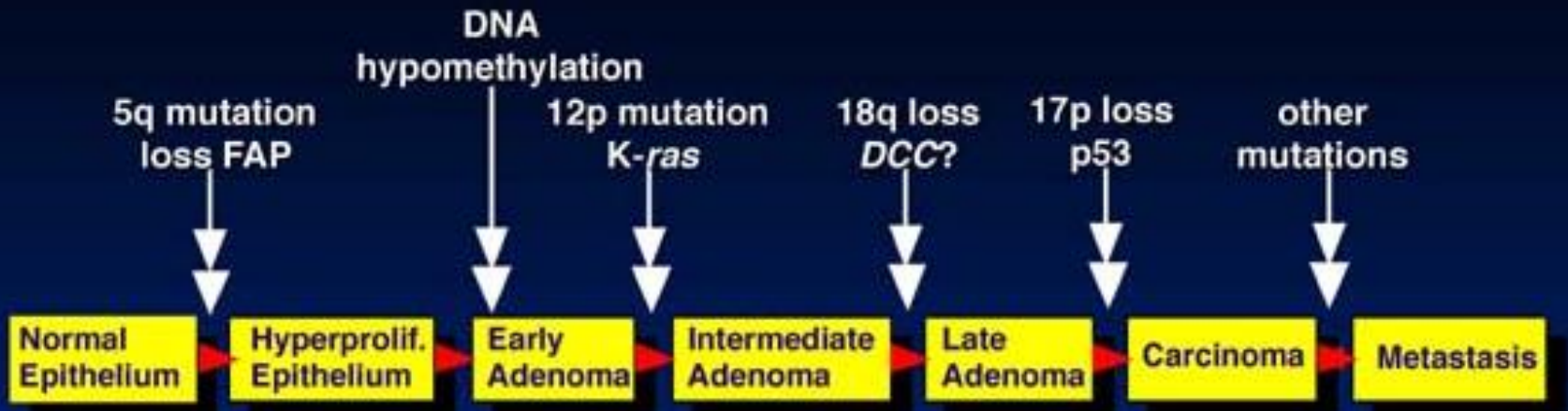
- Multifactorial means that there are multiple causes for cancer:
- - Genetic
- - Chemicals (carcinogens).
- - Radiation (medical, industrial, sun)
- - Virus

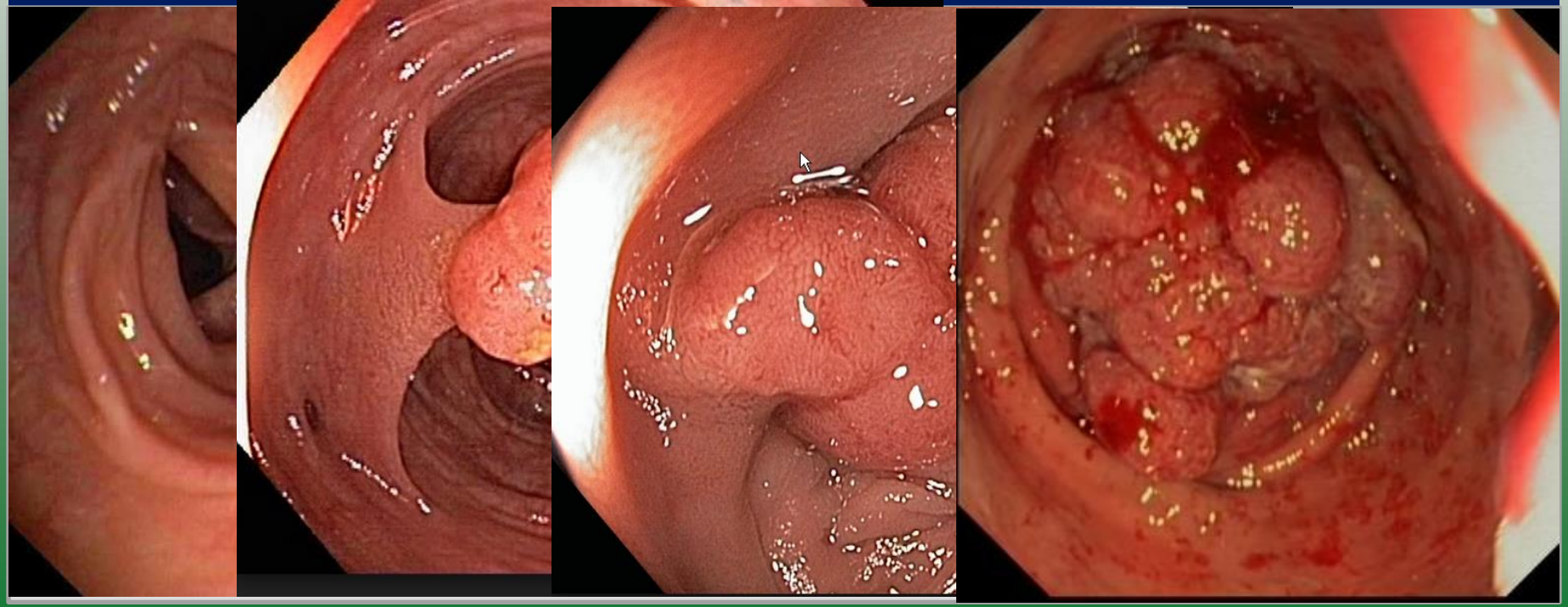
2 Stage Model of Carcinogenesis

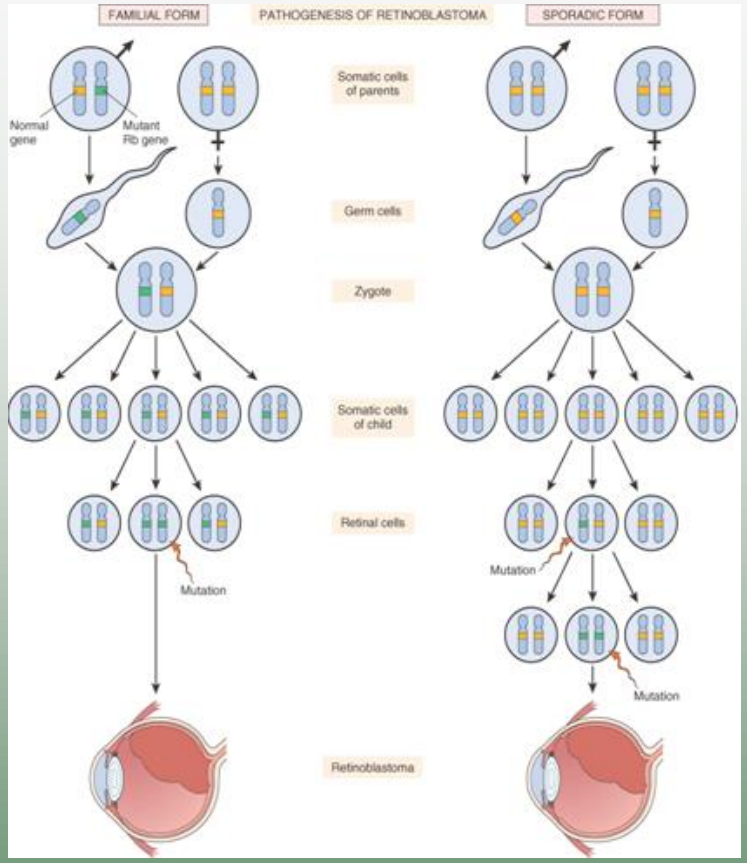
1. **Initiation:** in this stage, there is irreversible damage to the DNA (from one of the multifactorial casues).

2. **Promotion:** these agents, by themselves, can not cause cancer, but “promoters” act on initiated cells and facilitate their transformation to cancer.

Multi-Stage Carcinogenesis







Two Hit Hypothesis Retinoblastoma

What happens in this model when the p53 tumor supressor gene is muated?

- tumor supressor gene, operative, in the eye.

- recessive trait, have to loose both alleles to get cancer. (it is not localized to one place like the retinoblastoma gene)

- familial (inherited) vs sporadic.

Sporadic Model:
- One tissue/organ involved.

Familial Model:
- Cancer in multiple sites/organs.
"Li-Fraumeni Syndrome"

Risk Factors

- Genetic factors
  - Oncogenes that regulate all growth
- Viruses
  - Oncoviruses alter host cell's DNA.
- Radiation
  - Ultraviolet rays
  - X-rays and gamma rays
  - Radioactive isotopes
  - Risk is increased with higher cumulative dosage.

Risk Factors (Cont'd)

- Chemicals (check health and safety information)
  - Organic solvents
  - Asbestos
  - Heavy metals
  - Formaldehyde
  - Chemotherapy agents
- Biological factors
  - Chronic irritation and inflammation
  - Age
  - Diet
  - Hormones

Risk Reduction

- Limit UV exposure from sun or tanning booths.
- Regular medical and dental examinations
- Self-examination
- Diet
  - Increased fiber content
  - Reduced fats
  - Five to ten servings of fresh fruits and vegetable daily. These foods contain antioxidants, which reduce changes in DNA.

Immunity and Cancer Risk

- Cell-mediated immunity recognizes some tumor cells and destroys them.
- Immunization for cervical cancer and hepatitis is recommended to reduce cancer risk from infection.

Treatment

- Depends on specific cancer
  - Surgery, chemotherapy, immunotherapy, radiation
  - Combination of the above

Surgery

- Minimally invasive and tissue sparing vs radical surgery:
  - Use of laproscope, heals quick vs large abdominal incision.
  - Lumpectomy and sentinel node vs radical mastectomy.
  - Limb salvage vs amputation.
- Radiofrequency ablation (RFA)
  - Alternative to surgery: small needle inserted and radiofrequencies generate heat that kills cancer.

Radiation Therapy

- May be used alone or combined with other therapies
- Causes mutations or alterations in target DNA
- Most effective in rapidly dividing cells
- Some types of cancers are radioresistant.
- May be used as an adjuvant therapy prior to surgery to shrink tumor

Radiation Therapy (Cont'd)

- Methods of administration
  - External sources—cobalt machine
    - Radiation for a short time to specific site in the body
    - Requires multiple treatments
  - Internal Insertion of radioactive material at the tumor site
    - Treat specific cancers (e.g., cervical or oral tumors).
  - Instill radioisotope in a solution into a body cavity.
    - Monitor to ensure that there is no leakage
    - Radioisotopes may be given by injection for specific tumors.

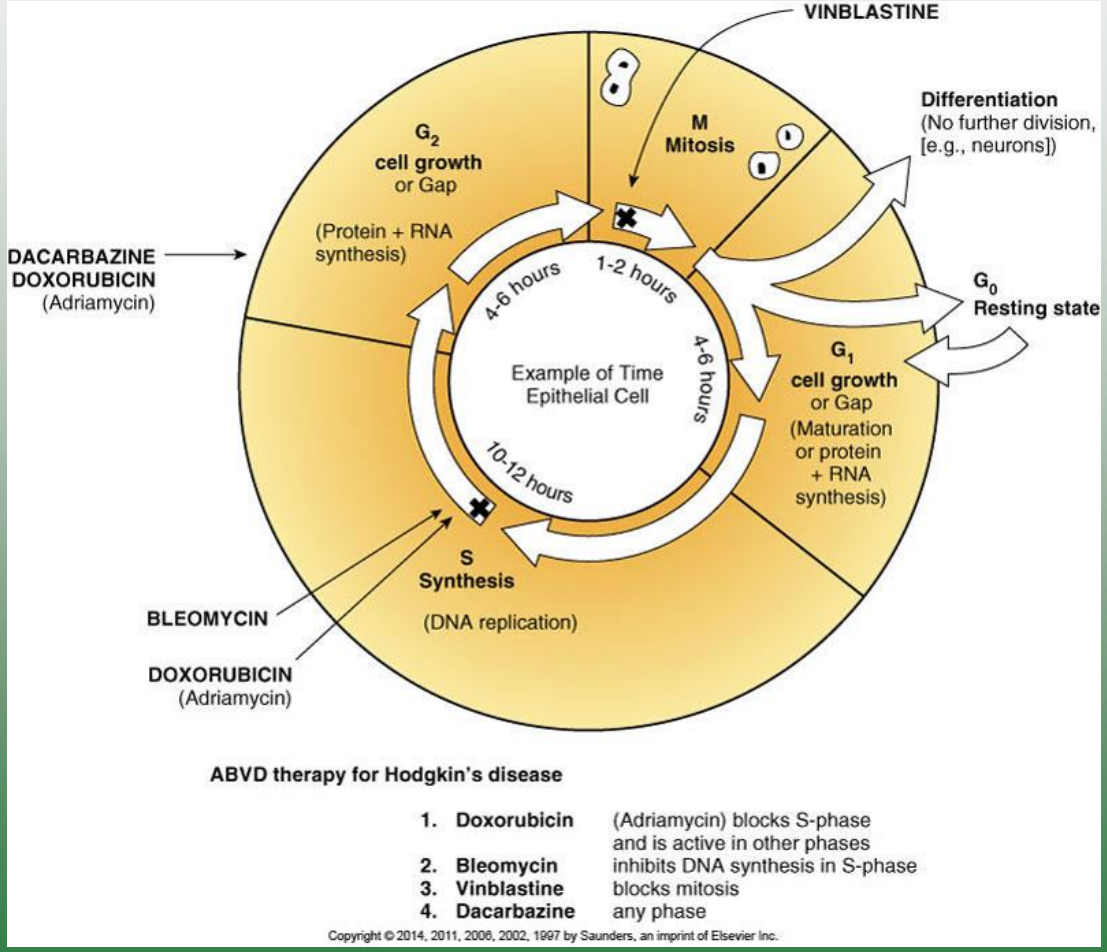
Adverse Effects of Radiation

- **Bone marrow depression**
  - Decreased leukocytes—increase risk of infection
  - Decreased erythrocytes—fatigue, tissue breakdown
  - Decreased platelets—excessive bleeding
- Epithelial cell damage
  - Damage to blood vessels and skin, hair loss
- Infertility
  - Caused by abdominal radiation
- Nonspecific fatigue and lethargy
  - Can lead to mental depression

Chemotherapy

- Antineoplastic drugs
- Can be used alone or in combination with surgery or radiation
- Usually combination of two to four drugs
  - Given at periodic intervals
  - Classifications include:
    - Antimitotics
    - Antimetabolites
    - Alkylating agents
    - Antibiotics
  - Drugs interfere with protein synthesis and/or DNA replication.

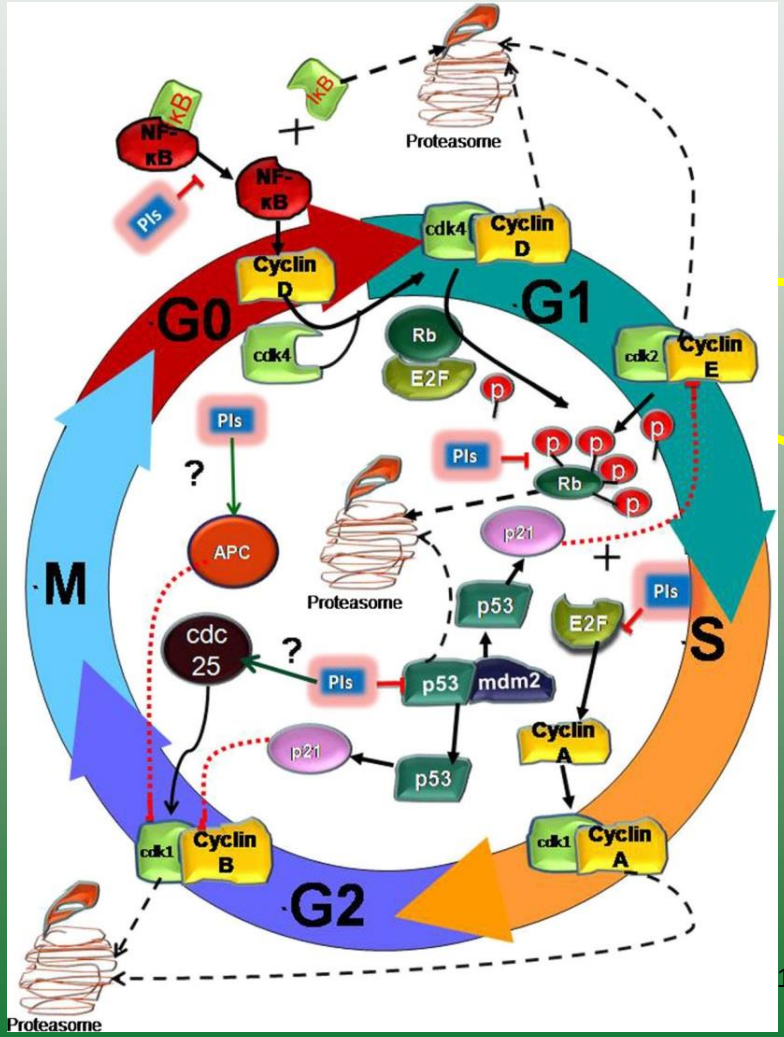
Cell Cycle and Chemotherapy



ABVD therapy for Hodgkin's disease

1.	**Doxorubicin**	(Adriamycin) blocks S-phase and is active in other phases
2.	**Bleomycin**	inhibits DNA synthesis in S-phase
3.	**Vinblastine**	blocks mitosis
4.	**Dacarbazine**	any phase

Cell Cycle and p53



P53 Pathway
Stop Cycle
Check for DNA damage

No

Yes

Repair

Apoptosis

programed cell death

Adults: more defective p53, so less chemo enhanced p53 killing of defective cells.

Pediatric: p53 available to kill
p53 available to be enhanced by chemo

Elephants do not get cancer

23 pairs of p53 Gene !!!

Adverse Effects of Chemotherapy

- **Bone marrow depression**
  - Limiting factor with chemotherapy
  - Blood test taken before each treatment
  - Nadir is point of lowest cell count—different points in cycle
- Nausea
  - May occur prior to, during, or shortly after treatment
  - Antiemetic drugs helpful for decreasing nausea
  - Vomiting due to gastrointestinal irritation and also from stimulation of the vomiting centers in the brain.

Adverse Effects of Chemotherapy (cont'd.)

- Epithelial cell damage
  - Occurs easily
  - Hair loss
  - Breakdown of skin and mucosa
- Damage to specific areas
  - With some antineoplastic drugs
  - Fibrosis in the lungs
  - Damage to myocardial cells
  - Kidney damage

Other Drugs

- Blocking agents
  - Act to block receptors for growth promoters on cancer cells
- Biological response modifiers (BRMs)
  - Augment the natural immune response
- Angiogenesis inhibitors
  - Inhibit the stimulus for growth of blood vessels
- Analgesics
  - Prescribed to alleviate pain
  - May be used in high dosages

Nutrition

- Patients with advanced cancer are often malnourished.
- Contributing factors
  - Change in taste sensation
  - Anorexia
  - Vomiting and/or diarrhea from treatments
  - Sore mouth or loss of teeth
  - Pain and fatigue
  - Malabsorption caused by inflammation in the digestive tract

Complementary Therapies

- May include
  - Massage
  - Meditation
  - Counseling
  - Exercise
  - Therapeutic touch
  - Research-based evidence has not been published for:
    - Raw food macrobiotic diet
    - Use of insulin and glucose with chemotherapy
- Health care workers need to be aware of these different types of therapies to advise patients.

Prognosis

- Cancer-free state generally defined as 5-year survival without recurrence
- Some cancers such as childhood leukemias can be considered cured after a 10-year, cancer-free period.
- Remission—no clinical signs of cancer
  - Client may experience several remissions
- Life expectancy and death rates for specific cancers vary.

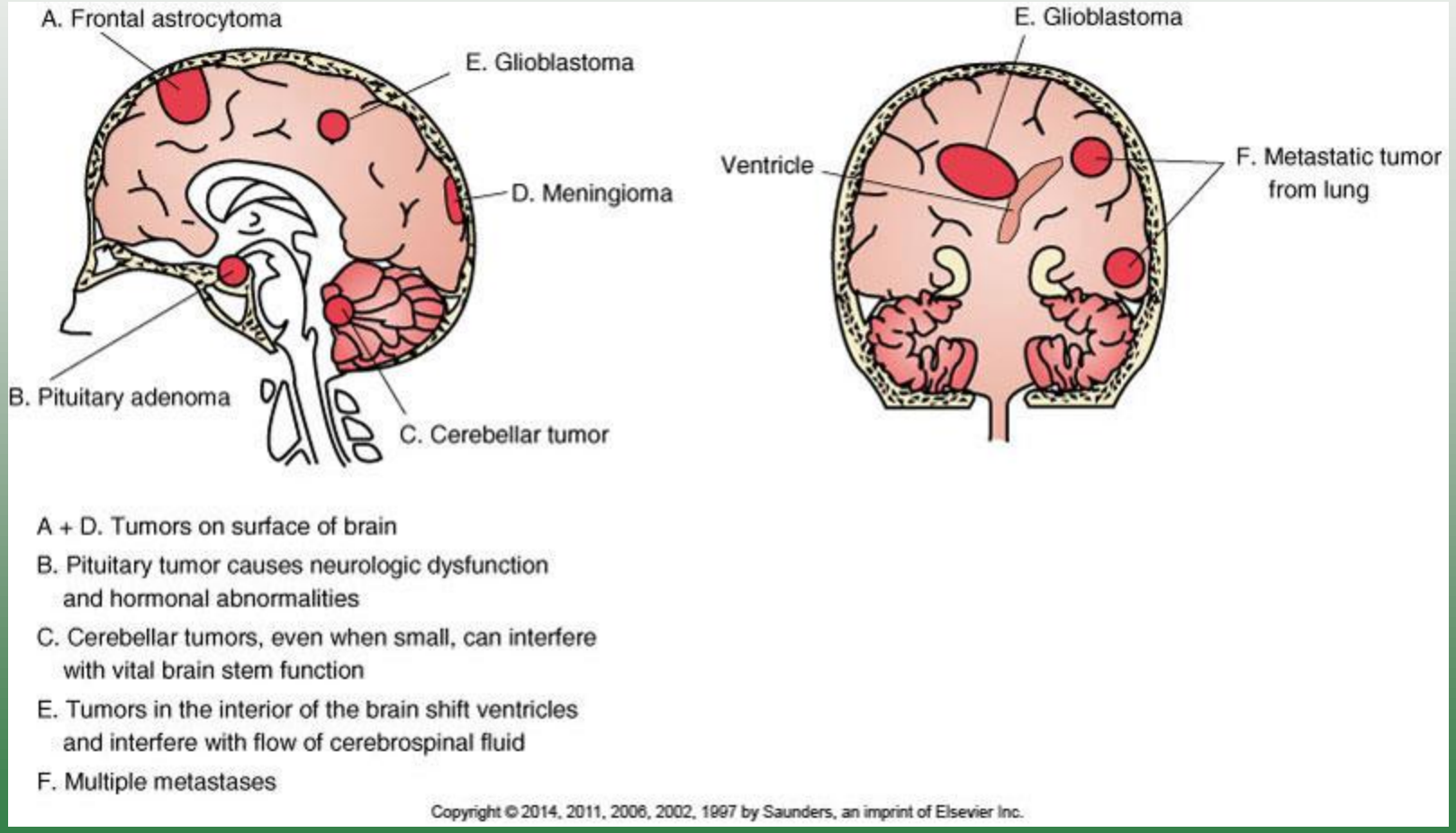
Info on Specific Malignant Neoplasms

- Skin cancer
  - Visible, easily diagnosed and treated
  - Excellent prognosis, with exception of malignant melanoma
- Ovarian cancer
  - Poor prognosis because of hidden nature of cancer
  - High mortality rates
- Brain tumors
  - Both benign or malignant tumors are life-threatening because of compression of brain tissue.
  - Primary tumor usually fatal; thus, no metastasis

Basal Cell Carcinoma

From Lookingbill D, Marks J: Principles of Dermatology, ed 3, Philadelphia, 2000, Saunders.

Brain Tumors in Various Locations



A + D. Tumors on surface of brain

B. Pituitary tumor causes neurologic dysfunction and hormonal abnormalities

C. Cerebellar tumors, even when small, can interfere with vital brain stem function

E. Tumors in the interior of the brain shift ventricles and interfere with flow of cerebrospinal fluid

F. Multiple metastases