

# NEOPLASIA

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Abnormal cellular growth unresponsive to normal growth control mechanisms  
Cell constantly confronted with factors which stimulate inherent capacity for proliferation  
Every cell division (mitosis) presents potential for cancer  
Malignant cells contain usual cellular functions but lack ability to regulate them  
    Survival, proliferation, differentiation, expression  
    Lack of control proves lethal to the organism

## TERMINOLOGY

**Neoplasm** or **tumor** - group of neoplastic cells (may be benign or malignant)

**Benign neoplasm:** do not invade surrounding tissue

### **Malignant neoplasm**

Grow via invading surrounding tissue  
Can travel to an proliferate to distant sites - **metastasis**

**Cancer** - malignant entities (over 100) of uncontrolled cell growth and proliferation

### **Aberrant cellular growth**

- Alteration in normal cellular growth
- Cell escapes normal control cycle

**Anaplasia** - loss of cellular differentiation - cell less resembles parent cell

## Epidemiology

Second leading cause of death (cardiovascular is leading cause)  
Primarily a disease of aging - risk increases with advancing age  
    Strikes all ages - second only to accidents as cause of death in children  
    Bronchial/lung cancers are the deadliest form for both sexes  
    Breast cancer most common for women; prostate cancer most common for men  
80% cancers related to life-style and environmental **carcinogens**

## Risk Factors

Major risk factors:

**Tobacco, ETOH, diet, reproductive/sexual behavior, pollution, occupation, industrial products and medicines**

Other factors: **infectious agents, endogenous hormones, genetics**

## Classification of Neoplasms

Classed according to cell of origin and whether benign or malignant

Cell type is first part of name

Suffix "oma" forms last part of name

Example: leiomyoma (fibroid) - benign smooth muscle tumor (benign)

leiomyosarcoma - malignant smooth muscle tumor

Lipoma - benign fatty neoplasia (tumor)

Liposarcoma - malignant fatty tumor

### COMMON TERMINOLOGY

Squamous and basal epithelial	benign	papillomas
Glandular epithelia	benign	adenomas
Epithelial	malignant	carcinomas
Glandular origin	malignant	adenocarcinoma
Connective tissue/bone	malignant	sarcoma

Polyp: adenomas or papillomas growing at end of pedicle - may become malignant

## Benign Neoplasms

- Cells are **similar** in structure to **cells of origin**
- More cohesive than malignant neoplasms
- Growth occurs evenly from center of mass - **well defined border**
- Adjacent tissue pushed aside vs invasion with malignant growth
- Many tumors become encapsulated (connective tissue forms capsule)
- **Growth: slow** - limited to one area
- Blood supply: less profuse than malignant tumors
- Other defining characteristics
  - Seldom recurs after surgery
  - Seldom ulcerates or necroses
  - Rarely causes systemic problems (except hormone secreting tumors)
- Pathology arises from obstruction, pressure, secretion
- Enclosed space - benign neoplasms can be lethal
  - Skull - benign brain tumor can be fatal
  - Intestinal obstruction from benign tumor dangerous

## Malignant Neoplasms

**Atypical cellular structure** - **abnormal nuclear** divisions and **chromosomes**

Abnormal mitosis - abnormal cells; high percentage of cell death

Cells and nuclei vary in size and shape

**Loses differentiation** and resemblance to original cell

Differentiated cells: appear like parent cells (growth is slow)

Undifferentiated cells: do not resemble parent cells (growth is rapid)

Growth is noncohesive - pattern is irregular

Nonencapsulated - invade adjacent cells (vs pushing them aside with benign)

Develop **greater blood supplies** than normal tissue

Varying growth rates

**Metastases**: hallmark of malignancy - ability to spread to distant sites; establish new growth

Frequently recur; frequently cause systemic problems

**Carcinogens**: substances capable of inducing neoplastic growth

**Differentiation**: growth of malignant tumors correlates with level of differentiation

**Anaplasia**: refers to degree of undifferentiation

**Angiogenesis** - blood vessel growth - increased vascularity is critical for growth

**Anorexia-cachexia** syndrome

Tumor takes nutrients from host which alters normal body process

Produces tumor cachexia syndrome

### Tumor markers

Substances not normally present in blood

May indicate presence of particular type of cancer

Non-specificity limits use in establishing diagnosis or planning therapy

May be present in low levels normally or nonmalignant disease

Therapeutic usage

- Evaluate response to therapy

- Aid to detect residue disease or relapse

Markers in clinical practice

Oncofetal antigens (carcinoembryonic antigens) **alpha-fetoprotein**

Hormones: **human chorionic gonadotropin**; **antidiuretic hormone**

Tumor specific proteins: **immunoglobulins**; **prostate-specific antigen**

Normal enzymes: elevated

### Escape from immune surveillance

Failure of **host-versus-tumor reaction** - normally hosts rejects/destroys tumor cells

Tumor cells destroyed immune system cells

- **T-cell cytotoxic** response

- **Natural killer** (NK) cells

- **Macrophage**

- **B-cells** and complement activation

Immunocompromised patients at much greater risks for malignancy

How do tumor cells escape detection?

- Tumor cells may lack tumor-specific antigen
- Antigen may not be expressed at cell surface to be recognized as foreign
- Some tumors modulate or down-regulate expression of antigens
  - Occurs after exposure to immune system
  - Minimizes chances of detection

## Staging

- Attempt to describe/classify neoplasia
- Serves to determine treatment, estimate prognosis, facilitate info exchange
- **TNM** system generally accepted

<b>TNM STAGING SYSTEM</b>	
<b>T = Primary lesion and its extent</b>	
Tis - tumor in situ	
TX - extent of tumor cannot be adequately assessed	
T0 -T4 grades extent of tumor	
<b>N = Regional Lymph Node involvement</b>	
NX regional nodes cannot be assessed	
N0 no regional node metastases	
N1-N3 grades extent of nodal metastases	
<b>M = Distant metastasis</b>	
M0 - no evidence of metastasis	
M1 Distant metastases	
MX - Presence of metastases cannot be assessed	

## Malignant Metastasis

Ability of malignant neoplasm to spread to distant metastasis  
Clump of cells travels and becomes established at new site

### Invasion:

Rapid growth, mechanic pressure, decreased cell-to cell cohesiveness, increased in cell motility, destruction of host tissue by tumor cell-produced degradative enzymes (invading tumors must break through basement cell membrane)

**Cell Detachment** - easily shed; altered cell-to-cell adhesion

**Dissemination:** primarily through lymphatic system and blood vessels  
Millions are shed into circulation daily  
Majority of tumor cells entering circulation do not survive

**Lymphatic dissemination** - penetrates small lymphatic vessels  
Nodes enlarge when invaded; pattern of invasion varies  
Venous lymphatic communication transfers to blood

## Hematogenous dissemination

Tumor must penetrate capillary basement membrane  
Cell attaches then secretes degradative enzymes  
Most do not survive circulation; aggregation enhances survival

## Arrest, establishment and proliferation

Cells trapped in small vessels, break-through and grow  
Clump originally fed by diffusion; soon grows own vascular supply  
Tumor secretes angiogenesis factor - new blood vessels  
Tumor-host interaction determines outcome of subsequent growth

## Sites of Metastasis

Primary tumors have tendency to metastasize to specific organs  
Breast cancer tends to metastasize to lungs and brains  
Prostate and adrenals tend to metastasize to bone

Site of metastasis based on mechanical considerations  
Cellular size, pressure, vessel size, other physical features  
Vascularity at secondary site is essential

## Clinical Sequelae of Neoplasia

- Early stages are generally asymptomatic (cell mass too small to interfere with functions)
- Local alteration in function occurs as tumor grows
- With growth and metastases, the organism more significantly effected
  - Local disruption at distant sites
  - Biochemical and nutritional balance disruption
- Local manifestations
  - Function of location/size of tumor; distensibility of site
  - Tumor may compress surrounding tissue, organs and blood supply
  - Functional, compensatory and immune responses may ensue locally
- Systemic manifestations
  - May be first indication of malignancy - often accompany metastatic disease
  - Common symptoms: **anorexia, weight loss, malaise, anemia, infection**
  - **Paraneoplastic syndrome**: system-wide alternations in body process
    - Endocrine, nervous, hematologic, renal, GI symptoms

## COMMON NEOPLASTIC SYSTEMIC MANIFESTATIONS

### Endocrine Paraneoplastic Syndrome

- Hormones produced by neoplastic tissues
- Lung, thymus, pancreas tumors can produce adrenocorticotrophic hormones
- **Cushing's syndrome, hypercalcemia**

## Neurologic Paraneoplastic Syndromes

- Stimulation of antibody production by cancer
- Antibodies react with neuronal antigens - damage normal tissue; produce symptoms
- Cerebral: **ataxia, dysarthria, hypotonia, abnormal reflex, dementia, coma**
- Spinal: **muscle weakness, atrophy, spasticity, hyperreflexia, paralysis**
- Peripheral: **sensory loss, weakness, wasting, depressed reflex**

## Hematologic Paraneoplastic Syndrome

- Erythropoietin secreting tumor: **polycythemia**
- Tumor secretion: **disseminated intravascular coagulation**
- Tumor production of antiplatelet antibodies: **thrombocytopenia, aplastic anemia**

## Renal Paraneoplastic Syndromes

**Membranous glomerulonephritis** commonly associated with CA (lung, breast, GI)  
Tumor-associated antigens form immune complexes  
Immune complexes precipitate in glomeruli -> renal failure

## Gastrointestinal Paraneoplastic Syndrome

### **Malabsorption, liver dysfunction, anorexia-cachexia**

Lower **serum albumin** in over 90% of advanced disease

Protein loss through gut

Poor absorption of protein through intestine

**Liver** pathology: enlargement, decreased function

**Anorexia-cachexia syndrome** seen with most advanced malignancies

Anorexia, loss of body fat, protein loss

Depletion of essential nutrients, water and electrolyte imbalance

Major weight loss

Factors contributing to anorexia-cachexia syndrome

Loss of taste with malignancy or treatment

Competition of tumor for host nutrients

Classic illustration of malnutrition may present - **starvation, kwashiorkor**

## Generalized Effects - Paraneoplastic Phenomena

Metabolic alterations: lactic acidosis

Hyperlipidemia, amylase elevation, muscle and joint alterations

Fever (often unexplained) very common

May wax/wane with treatment and disease recurrence

Occurs with wide variety of neoplasms: