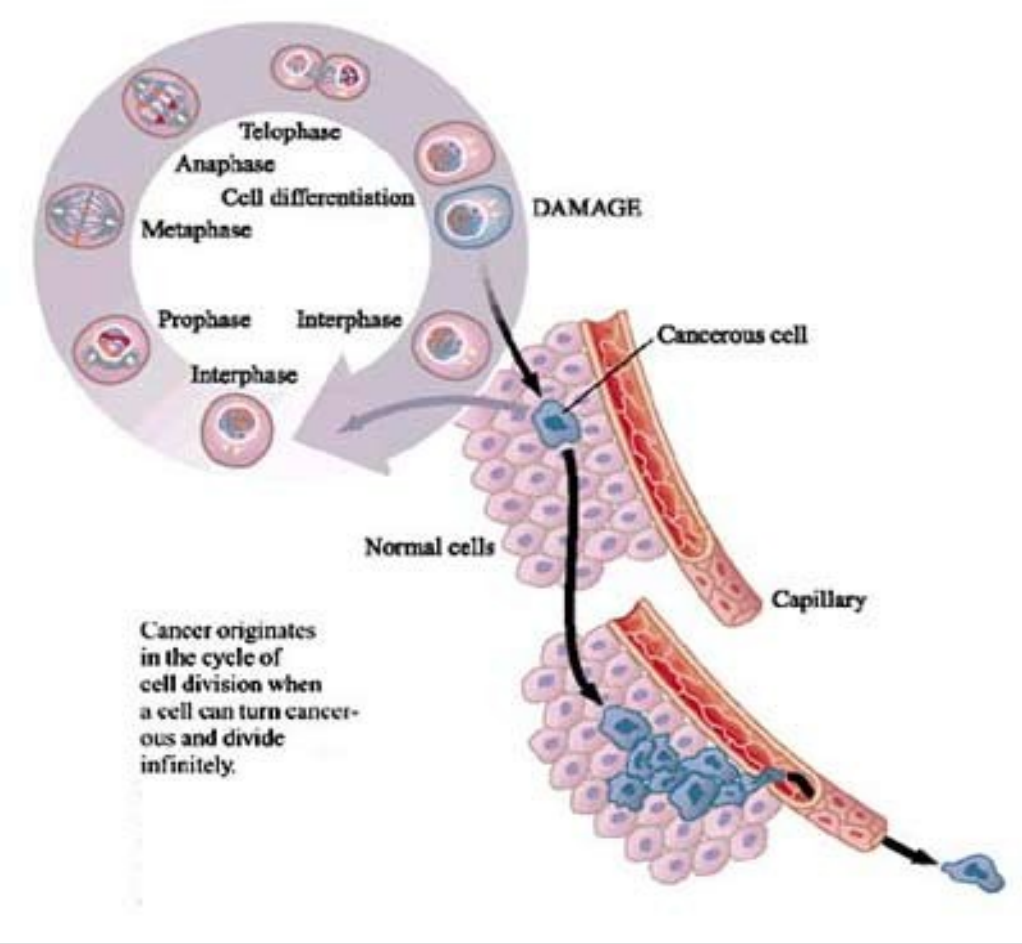
TUMOURS

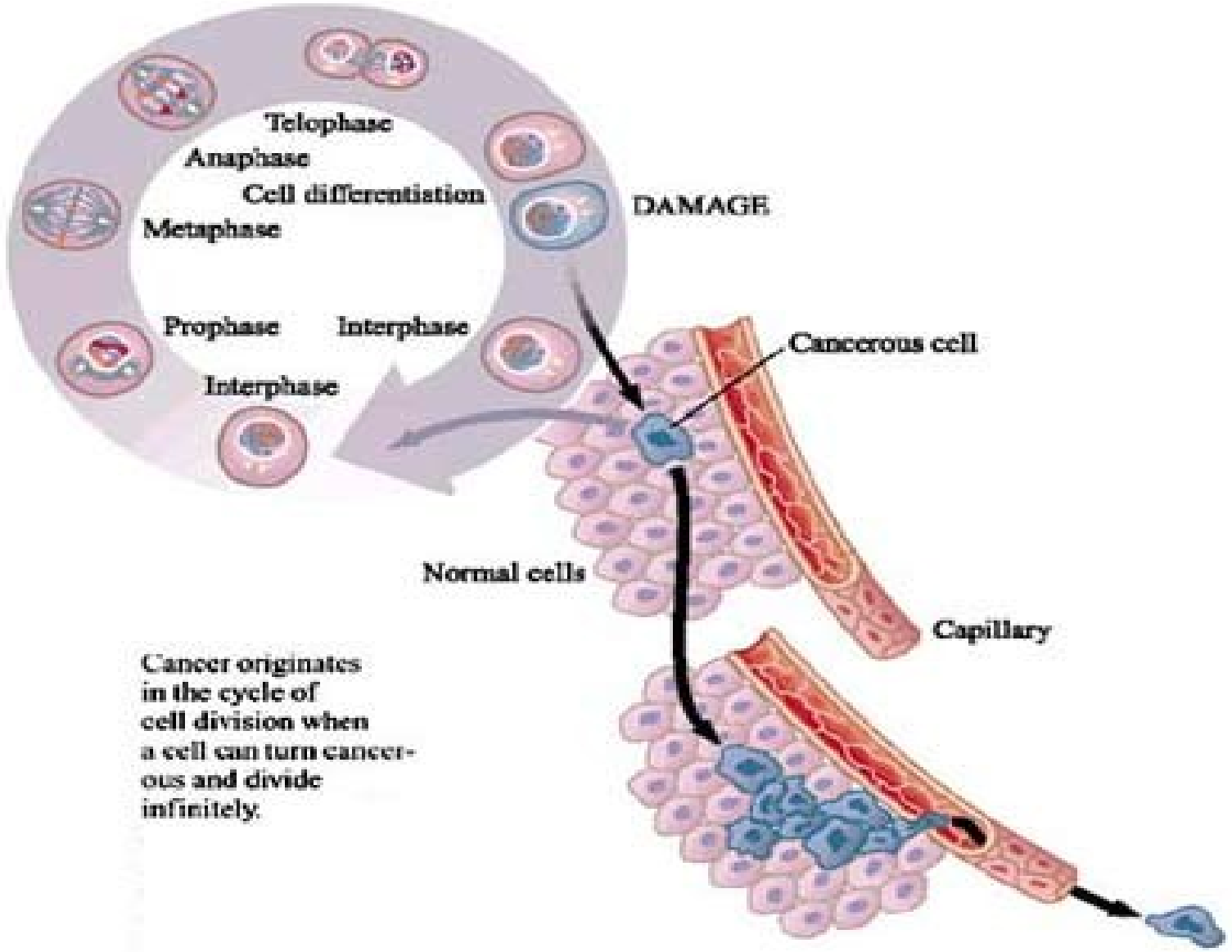

Telophase
Anaphase
Cell differentiation
Metaphase
Prophase
Interphase
Interphase
DAMAGE
Cancerous cell
Normal cells
Capillary
Cancer originates in the cycle of cell division when a cell can turn cancerous and divide infinitely.

DEFINITION:

- A neoplasm is defined as “ abnormal mass of tissue, the growth of which exceeds and is uncoordinated with that of the normal tissues and persists in the same excessive manner after the cessation of the stimuli which evoked the change.

DEFINITION cont…..

- The neoplasm is defined as “a mass of tissue formed as a result of abnormal, excessive, unco-ordinated and autonomous and purposeless proliferation of cells.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CELLULAR PROLIFERATION

- intracellular mechanism of control
- Growth fraction
- Cell cycle time
- Cell loss

- Neoplastic cell populations ignore this normal cell growth.

Cell membrane growth control mechanisms

- Appropriate cell recognition by membrane enzymes and surface sugars
- Cellular adhesion
- Desmosome
- Tight junction
- Gap junction
- Electrical charges

- Intercellular communication
- Growth stimulators
- Growth inhibitors

- Missing or abnormal glycolipids or glycoprotein's

- Decrease in number of Desmosome
- Tight junction
- Gap junction
- More negative electrical charges

- Lack of response to Growth stimulators and Growth inhibitors

CELLULAR DIFFERENTIATION

- **The normal cell look and act like the cell of origin (parent cell) and are called as <u>well differentiated cell</u>**

- **<u>Control of cellular differentiation</u>**
- **Procto-oncogenes**
- **Tumor suppressor genes**

- **Well differentiated (benign)**
- **Poorly differentiated**
- **Un-differentiated (anaplasia)**

- **Mutations of Procto-oncogenes and Tumor suppressor genes**

CATEGORIES OF TUMORS

1. **MIXED TUMORS**
   - Adenosquamous carcinoma
   - Collision tumor
2. **TERATOMAS**
   - benign or mature (ovarian Teratomas) or malignant or immature (testicular Teratomas).
3. **BLASTOMAS**
   - Nephroblastoma
   - Hepatoblastoma
4. **HAMARTOMA**

harmartoma of lung consists of mature cartilage, mature smooth muscle and epithelium.

5. **CHORISTOMA**

CHARACTERISTICS OF TUMOUR

- Rate of growth
- Clinical and gross features
- Microscopic features
- Local invasion (Direct spread)
- Metastasis (Distant spread)

I. RATE OF GROWTH

1. **Rate of division and destruction of tumour cells.**
2. **Degree of differentiation of the tumour.**

Regulation of tumour growth

i) Epidermal growth factor (EGF)
ii)Fibroblast growth factor (FRF)
iii) Platelet- derived growth factor (PDGF)
iv) Colony stimulating factor (CSF)
v) Transforming growth factors –B (TGF-B)
vi) Interleukins (IL)

II. CLINICAL AND GROSS FEATURES

CLINICAL FEATURES

benign tumors

- benign tumors are generally slow growing
- depending upon the location, may retain asymptomatic or may produce serious symptoms

malignant tumors

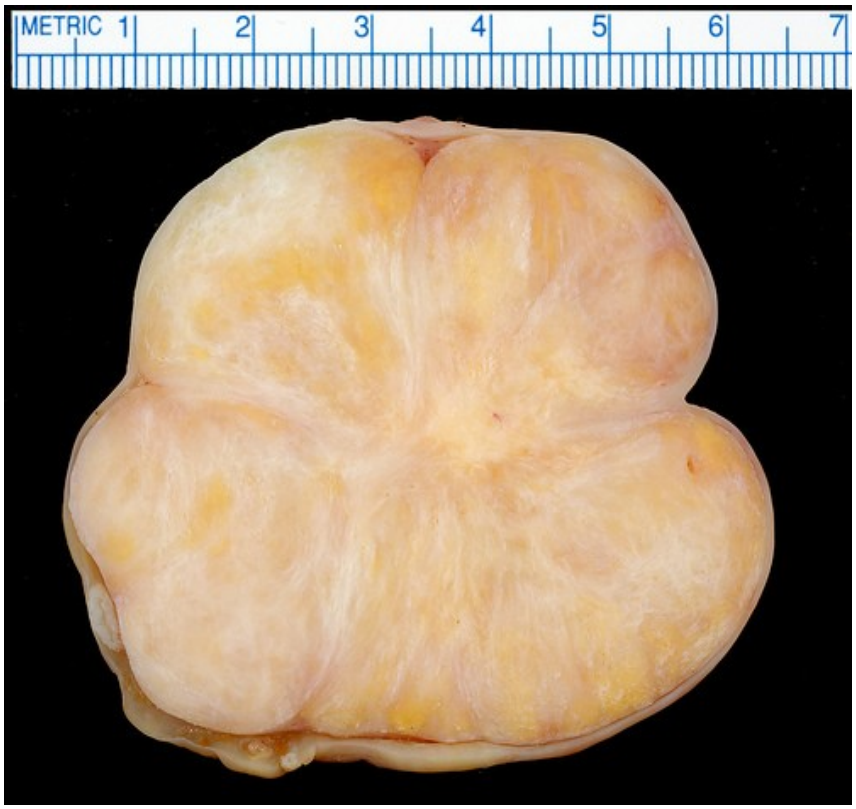
- grow rapidly
- may ulcerate on the surface
- invade locally into deeper tissues
- may spread to distant sites (metastasis)
- also produce systemic features as such as weight loss, anorexia and anemia.
- two of the cardinal clinical features of malignant tumors are: Invasiveness and metastasis.

The gross appearance

- **Benign tumors**
- **generally spherical or ovoid**
- **encapsulated or well-circumscribed**
- **freely movable**
- **more often firm and uniform, unless secondary changes like hemorrhage or infarction supervene.**

- **Malignant tumors**
- **usually irregular in shape**
- **poorly-circumscribed and extended in to the adjacent tissues. Secondary changes like hemorrhage, infraction and ulceration are seen more often.**

Benign tumors



III. MICROSCOPIC FEATURES

- 1. Microscopic pattern
- 2. Cytomorphology of neoplastic cells (differentiation and anaplasia);
- 3. tumour angiogenesis and stroma
- 4. Inflammatory reaction.

1. Microscopic pattern

- **The tumour cells may be arranged in a variety of patterns in different tumors**
- The epithelial tumours generally consist of acini, sheets, columns or cords of epithelial tumour cells that may be arranged in solid or papillary pattern.
- Haematopoietic tumours such as leukaemias and lymphomas often have none little stromal support.

2. Cyto morphology of neoplastic cells (differentiation and Anaplasia

- **Differentiation** is defined as the extent of morphological and functional resemblance of parenchymal tumour cells to corresponding normal cells .
- well- differentiated
- Poorly differentiated'.

- **Anaplasia** is lack of differentiation and is a characteristic feature of most malignant tumors.

Characteristics of anaplstic cells

- **Loss of polarity.**
- **Plemorphism.**
- **N: C ratio:**

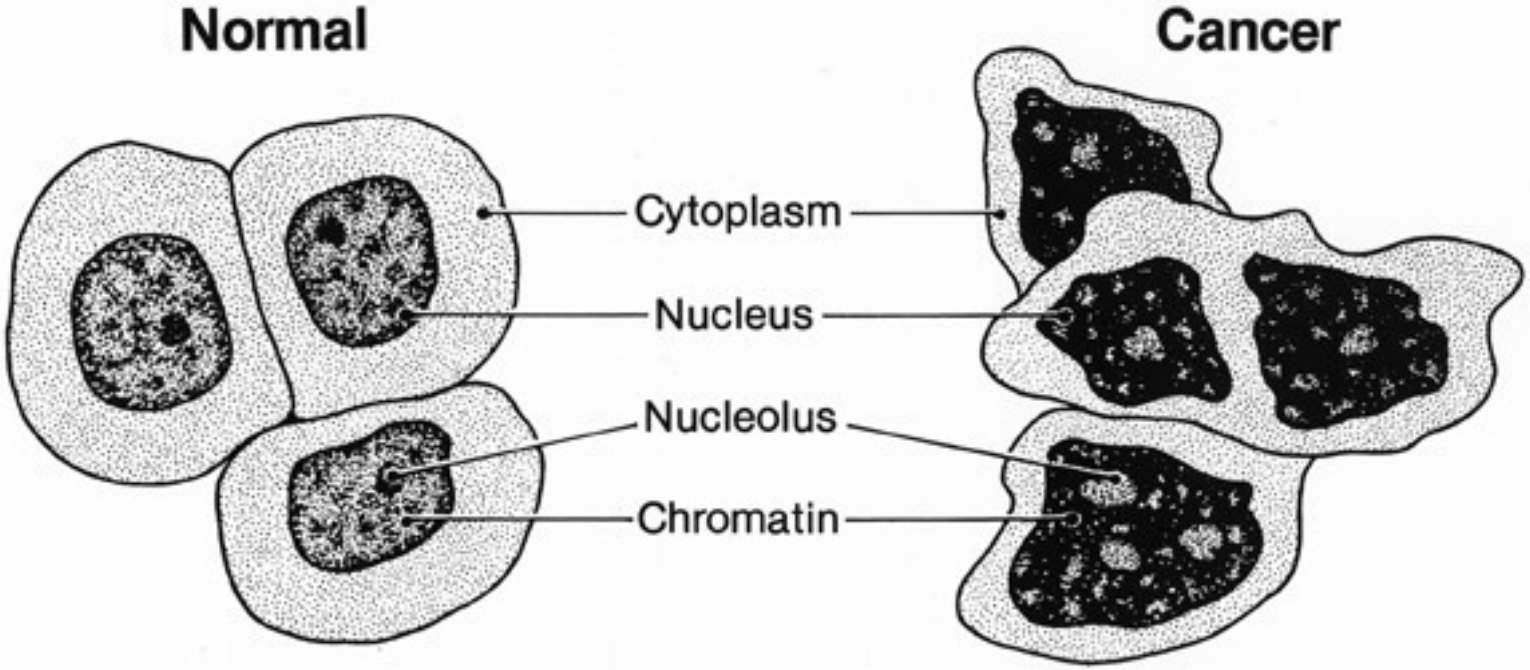
  increased from normal 1:5 to 1:1
- **Anisonucleosis.**
- **Hyperchromatism.**

- **Nucleolar change.**
- **Mitotic figure**
- Abnormal or atypical mitotic figures are more important in malignant tumors and are identified as tripolar, quadripolar and multipolar spindles in malignant tumour cells
- **Tumour giant cells**

  Multinucleate tumour giant cells or giant cells containing a single large and bizarre nucleus,
- **Functional (Cytoplasmic) changes**
- Structural anaplasia in tumors is accompanied with the functional anaplasia as appreciated from the cytoplasm constituents of the tumour cells.
- **Chromosomal abnormalities** deviations in both morphology and number of chromosomes.

Normal and Cancer Cells

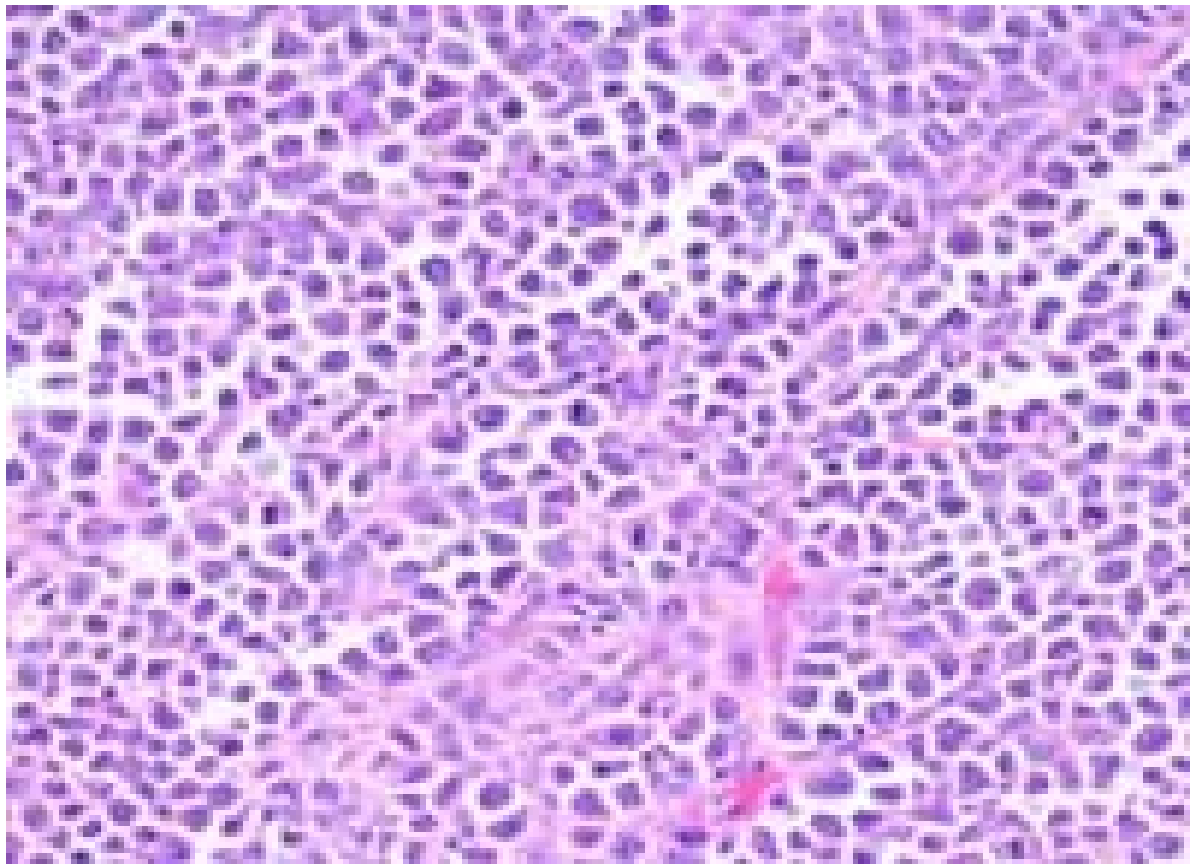
Structure



— Large cytoplasm
— Single nucleus
— Single nucleolus
— Fine chromatin

— Small cytoplasm
— Multiple nuclei
— Multiple and large nucleoli
— Coarse chromatin

ANAPLASIA



3. TUMOUR ANGIOGENESIS

Related morphologic features are as under:

- Micro vascular density
- as a marker to assess the rate of growth of tumors.
- Central necrosis
- core undergoes ischemic necrosis.

TUMOUR STROMA

- . The collagenous tissue in the stroma may be **scanty** or **excessive**. In the former case, the tumour is **soft and fleshly** (e.g. in sarcomas, lymphomas), while in the later case the tumour is **hard and gritty** (e.g. infiltrating duct carcinoma breast).
- Growth of fibrous tissue in tumour is stimulated by **basic fibroblast growth factor (bFGF)** elaborated by tumour cells.
- If the epithelial tumour is almost entirely composed of **parencymal cells,** it is called ***medullary*** *e.g.* medullary Carcinoma of the breast
- If there is **excessive connective tissue stroma** in the epithelial tumour, it is referred to as ***desmoplasia*** and the tumour is hard or *scirrhous e.g.* infiltrating duct carcinoma breast.

4. Inflammatory Reaction

- ulceration in the cancer
- cell-mediated immunologic response by the host in an attempt to destroy the tumour.
- example : seminoma testis, malignant melanoma of the skin, medullary carcinoma of the breast

iv. LOCAL INVASION (DIRECT SPREAD)

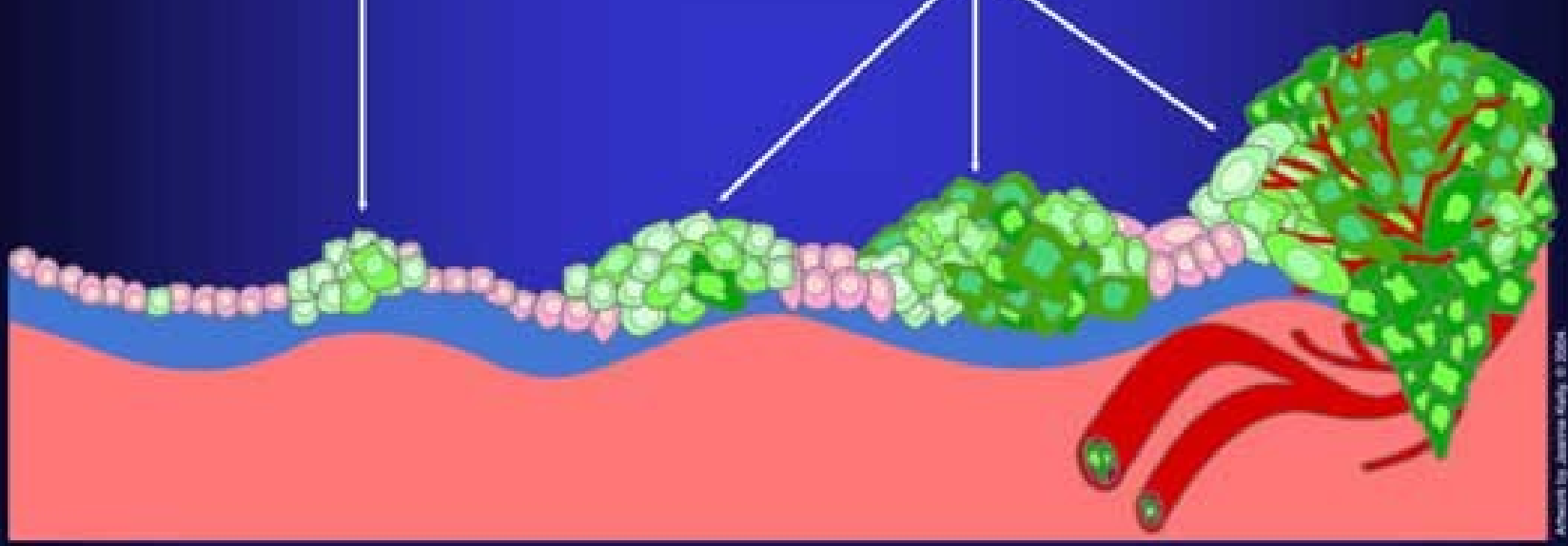
- **BENIGN TUMOURS**
- encapsulated or circumscribed masses
- *expand and push aside* the surrounding normal tissues without actually invading, infiltrating or metastasizing.

- **MALIGNANT TUMOURS**
- have the property of invasion, infiltration and destruction of the surrounding tissue, beside distant metastasis.
- Often, cancers extend through tissue spaces, permeate lymphatics, blood vessels, and may penetrate a bone b y growing through nutrient foramina.

Malignant versus Benign Tumors

Benign (not cancer) tumor cells grow only locally and cannot spread by invasion or metastasis

Malignant (cancer) cells invade neighboring tissues, enter blood vessels, and metastasize to different sites



Time

v. METASTASIS (DISTANT SPREAD)

- Metastasis (Meta= *transformation, stasis*= resident) is defined as spread of tumors by invasion in such a way that discontinues secondary tumour mass / masses are formed at the site of lodgment.

ROUTES OF METASTASIS

- Lymphatic spread
- Haematogenous spread
- Other route (Transcoelomic spread along epithelium-lined surfaces, spread via cerebrospinal fluid).

LYMPHATIC SPREAD

- The involvement of lymph nodes by malignant cells may be of two forms:
  - **Lymphatic permeation**.
  - **Lymphatic emboli**.
  - The results can be,
  - the whole lymph node may be replaced and enlarged by the metastatic tumour.
  - **regional nodal metastasis**
  - **regional lymphadenitis of sinus histiocytosis.**
  - **skip metastasis**
  - **retrograde metastases**
  - **Virchow's lymph node**

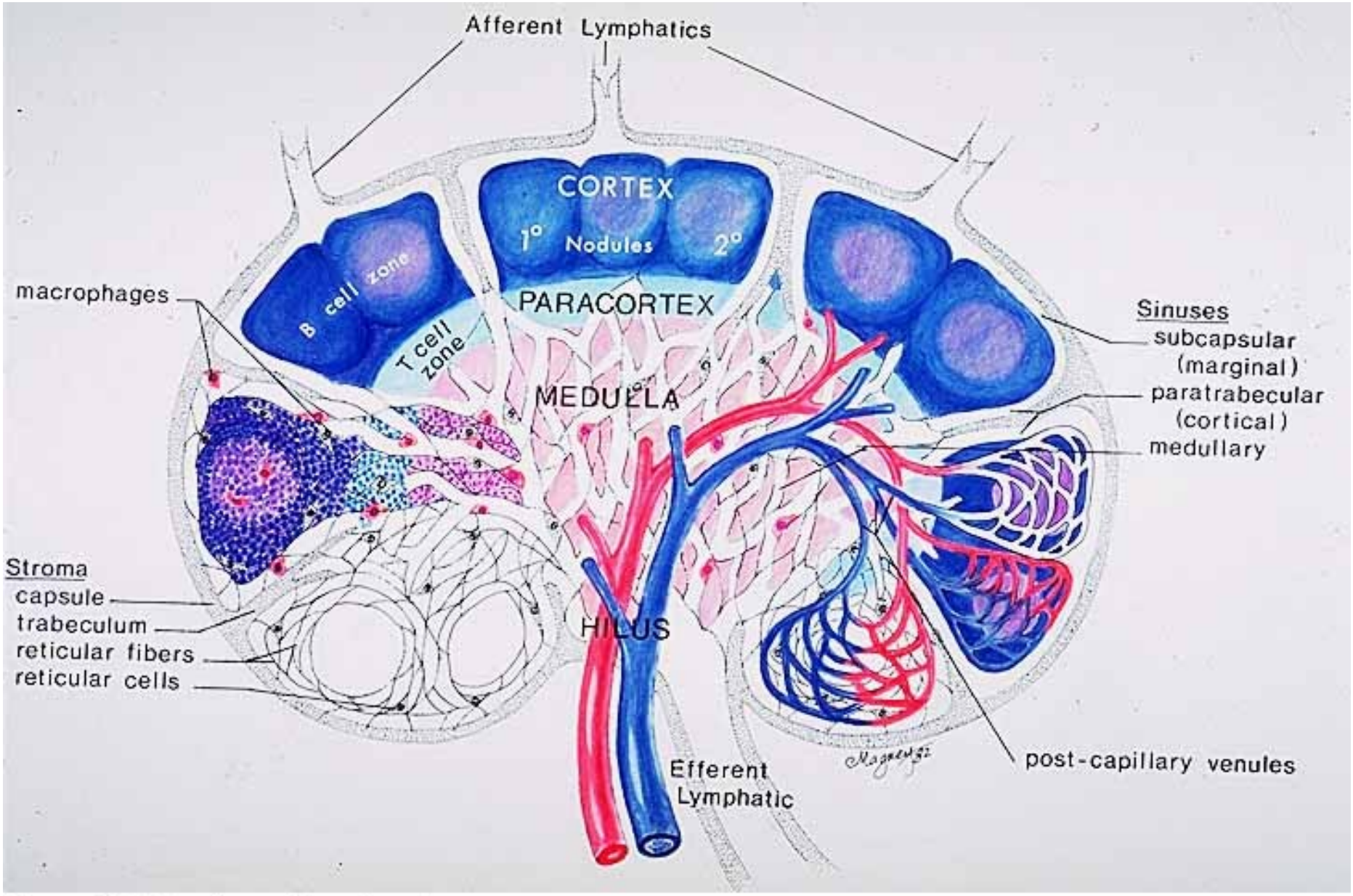
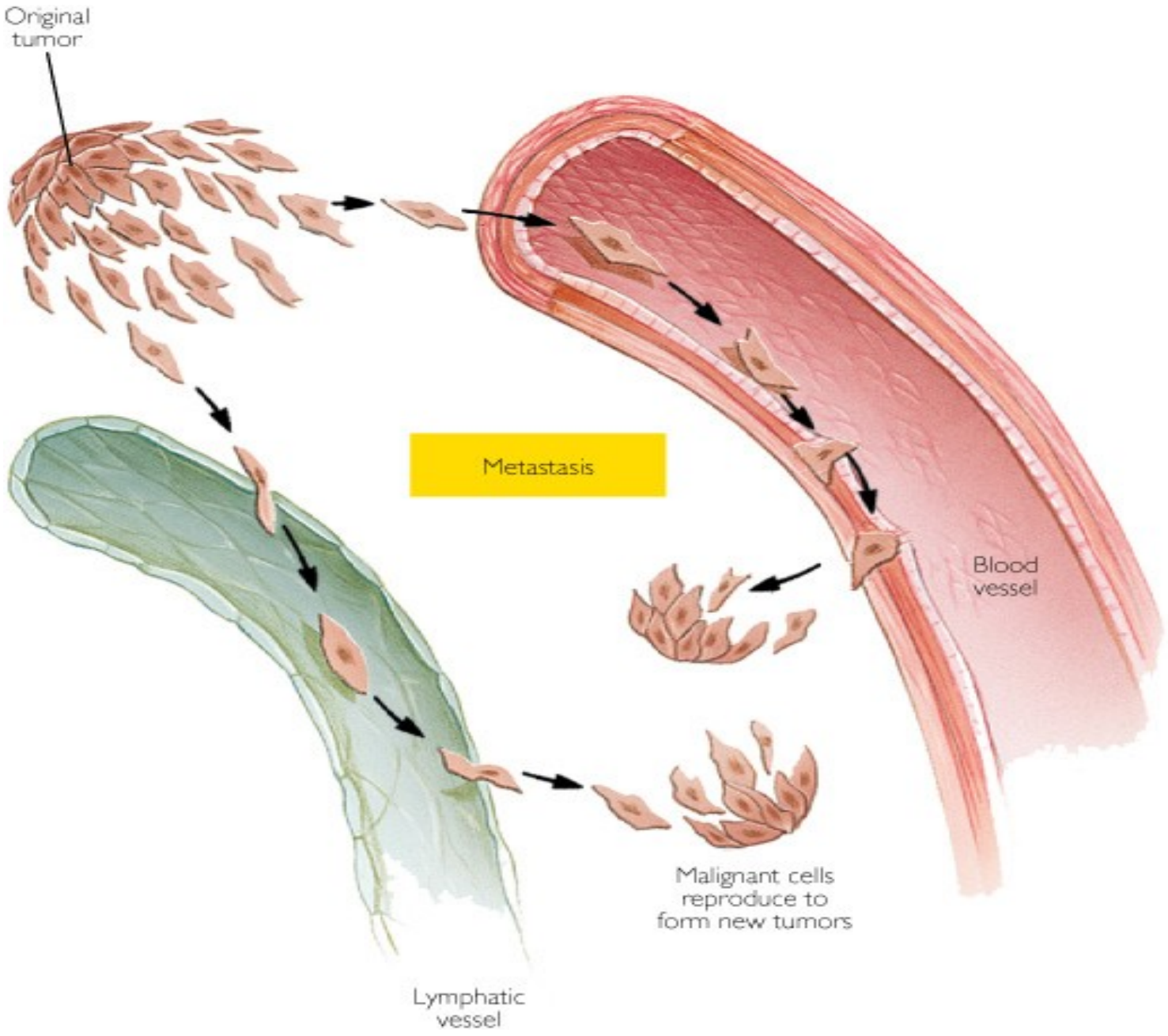


Figure 12. Structure of lymph node.

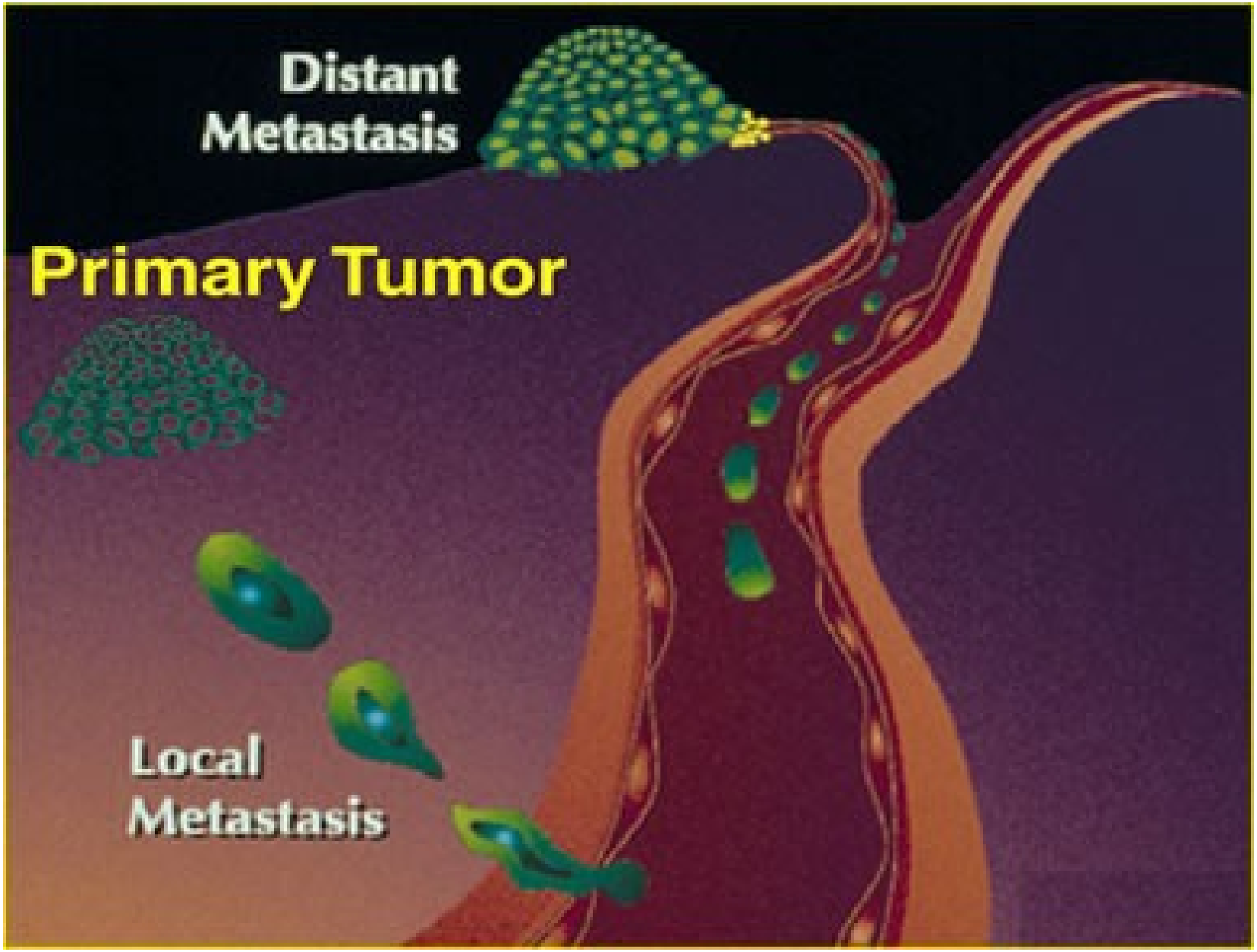

Original tumor
Metastasis
Blood vessel
Malignant cells reproduce to form new tumors
Lymphatic vessel

HAEMATOGENOUS SPREAD

- The common sites for blood- borne metastasis are: the liver, lungs, brain, bones, kidney and adrenals, all of which provide ‘good soil’ for the growth of ‘good seeds’ (seed-soil theory).
- **Systemic veins** :lungs
- **Portal *veins*** :liver.
- **Arterial spread** :by pulmonary capillary bed or pulmonary arterial route to kidneys, adrenals, bones, brains etc.
- **Retrograde spread** :unusual sites

  E.g. vertebral metastases in cancers of the thyroid and prostate.

- ***Macroscopically,*** blood –borne metastases in an organ appears as multiple, rounded nodules of varying size, scattered throughout the organ . Sometimes, the metastasis may grow bigger than the primary tumour. Metastatic deposits just like primary tumour may cause further dissemination via lymphatics and blood vessels
- ***Microscopically,*** the secondary deposits generally reproduce the structure of primary tumour. However, the same primary tumour on metastasis at different sites may show varying grades of differentiation, apparently due to the influence of local environment surrounding the tumour for its growth.


Distant
Metastasis
Primary Tumor
Local
Metastasis

3. SPREAD ALONG BODY CAVITIES AND NATURAL PASSAGES.

i) Transcoelomic spread.

cancers invade through the serosal wall of the coelomic cavity

↓

tumour fragments or clusters of tumour cells carried in the coelomic fluid

↓

implanted in Peritoneal cavity ,pleural and pericardial cavities.

ii) Spread along epithelial lined surfaces

iii) Spread via cerebrospinal fluid

iv) Implantation

FEATURES	BENIGIN	MALIGNANT
1 CLINICAL AND GROSS FEATURES		
1.Boundaries	Encapsulated or well-circumscribed.	Poorly circumscribed
2. Surrounding tissues	Often compressed	Usually invaded
3. Size	Usually small	Often larger
4. Secondary change	Occur less often	Occur more often

1	Pattern	Usually resembles the tissue of origin closely	Often poor resemblance to tissue of origin
2	Basal polarity	Retained	Often lost
3	Plemorphism	Usually not present	Often present
4	Nuclco-cytoplasmic ratio	Normal	Increased
5	Anisonucleosis	Absent	Generally present
6	Hyperchromatism	Absent	Often present
7	Mitosis	May be present but are always typical mitosis	Mitotic figures increased and are generally atypical and abnormal

8	Tumor giant cells	May be present but without nuclear atypia	Present with nuclear atypia
9	• Chromosomal abnormalities	Infrequent	Variably present
10	Function	Usually well maintained	May be retained, lost, or become abnormal

III	GROWTH RATE	Usually slow	Usually rapid
IV	LOCAL INVASION	Often compresses the surrounding tissues without invading or infiltrating them	Usually infiltrates and invades the adjacent tissues
V	Metastasis	Absent	Frequently present
VI	PROGNOSIS	Local complication	Death by local and metastasis complications

Tissue of origin	Benign	Malignant
Composed of one parencymal cell type	Fibrom,Lipoma,Chondroma,Osteoma	Fibrosarcoma, Liposarcoma Chondrosarcoma
Connective tissue and derivatives		Osteogenic sarcoma
Endothelial and related tissues		
Blood vessels	Hemangioma	Angio sarcoma
Lymph vessels	Lymphangioma	Lymphan giosarcoma
Synovium		Synovial sarcoma
Mesothelium		Mesothelioma
Brain Coverage's	Meningioma	Invasive meningioma
Blood cells and related cells		
Hemato poietic cells		Leukemia's
Lymphoid tissue		Lymphomas
Muscle Smooth	leiomyoma	leiomyo sarcoma

Tissue of origin	Benign	Malignant
Striated muscles	Rhabdomyoma	Rhabdomyosarcoma
Tumor of Epithelial origin		
Stratified squamous	Squamous cell	Squamous cell or epidermoid
Basal cells of skin or adenexa	Papilloma	
Basal cells of skin or adenexa		Basal cell carcinoma
Epithelial lining of gland or ducts	Adinoma, Papilloma Cystadenoma	Adenocarcinoma,Papillary Carcinoma Cystadenocarcinoma

CANCER

DEFINITION

- “Cancer is a group of more than 200 diseases characterized by uncontrolled and unregulated growth of cells.”
- Cancer encompasses a broad range of diseases of multiple causes that can arise in any cell of the body capable of evading regulatory controls over proliferation and differentiation.
- Cancer is a “malignant growth accompanied by abnormal cell division, invasion of surrounding tissues and metastasis to distant sites.”

Cancer incidence by site and gender:

Male	%	Female	%
Prostate	33	Breast	31
Lung	13	Lung	12
Colon/rectum	10	Colon/rectum	11
Urinary bladder	6	Uterus	6
Melanoma (skin)	5	Non – Hodgkin's lymphoma	4
Non – Hodgkin's lymphoma	4	Melanoma (skin)	4

Cancer death incidence by site and gender:

Type	%	Type	%
Lung and bronchus	31	Lung and bronchus	26
Prostate	10	Breast	15
Colon/rectum	9	Colon/rectum	10
Pancreas	6	Pancreas	6
Leukemia	4	Ovary	6
Liver	4	Leukemia	4
Esophagus	4	Non – Hodgkin's lymphoma	3
Non – Hodgkin's lymphoma	3	Uterus	3

ETIOLOGY

- **HOST SUSCEPTIBILITY**
- Genetic factors
- Hormonal factors
- Precancerous lesions
- Chronic irritation
- Immunological factors

- **ENVIRONMENTAL FACTORS**
- Ionizing radiation
- Chemicals
- **HEALTH PRACTICES**
- Tobacco use
- Alcohol use
- Diet
- Sexual practices
- Psychosocial factors
- **Others**
- Virus
- inflammatory conditions

VIRUS	ASSOCIATED CANCER
C type RNA	Leukemia
B type RNA	Breast cancer
Herpes II	Cancer of the cervix
Epstein Barr	Burkitt's lymphoma Nasopharyngeal cancers
Human Papilloma virus	Cancer of cervix , anogenital cancers

CLASSIFICATION OF TUMOR

Anatomic Site Classification

- the tumor is identified by the tissue of origin, the anatomic site, and the behavior of the tumor (i.e. benign or malignant).
- **Carcinomas** originate from embryonal ectoderm (skin and glands) and endoderm (mucous membrane linings of the respiratory tract, gastrointestinal tract, and genitourinary [GU] tract).
- **Sarcomas** originate from embryonal mesoderm (connective tissue, muscle, bone and fat). Lymphomas and leukemia's originate from the hematopoietic system.

Histological Classification

Here the appearance of cells and the degree of differentiation are evaluated pathologically.

- **Grade I**: Cells differ slightly from normal cells (mild dysplasia) and are well differentiated.
- **Grade II**: Cells are more abnormal (moderate dysplasia) and moderately differentiated.
- **Grade III**: Cells are very abnormal (severe dysplasia) and poorly differentiated.
- **Grade IV**: Cells are immature and primitive (anaplasia) and undifferentiated; cell of origin is difficult to determine.

Extent of Disease Classification

Clinical Staging

Determines the anatomic extent of the malignant disease process by stages:

- Stage 0: cancer in situ.
- Stage I: tumor limited to the tissue of origin; localized tumor growth.
- Stage II: limited local spread.
- Stage III: extensive local and regional spread.
- Stage IV: metastasis

(American Joint Committee on Cancer (AJCC) tumor site-specific rules.)

TNM Classification System

- This classification system is used to determine the anatomic extent of the disease involvement according to three parameters;
- tumor size and invasiveness (T)
- presence or absence of regional spread to the lymph nodes (N)
- metastasis to distant organ sites (M).

Primary Tumor (T)

- To No evidence of primary tumor
- Tis Carcinoma in situ
- T1-4 Ascending degrees of increase in tumor size and involvement
- Tx Tumor cannot be measured or found

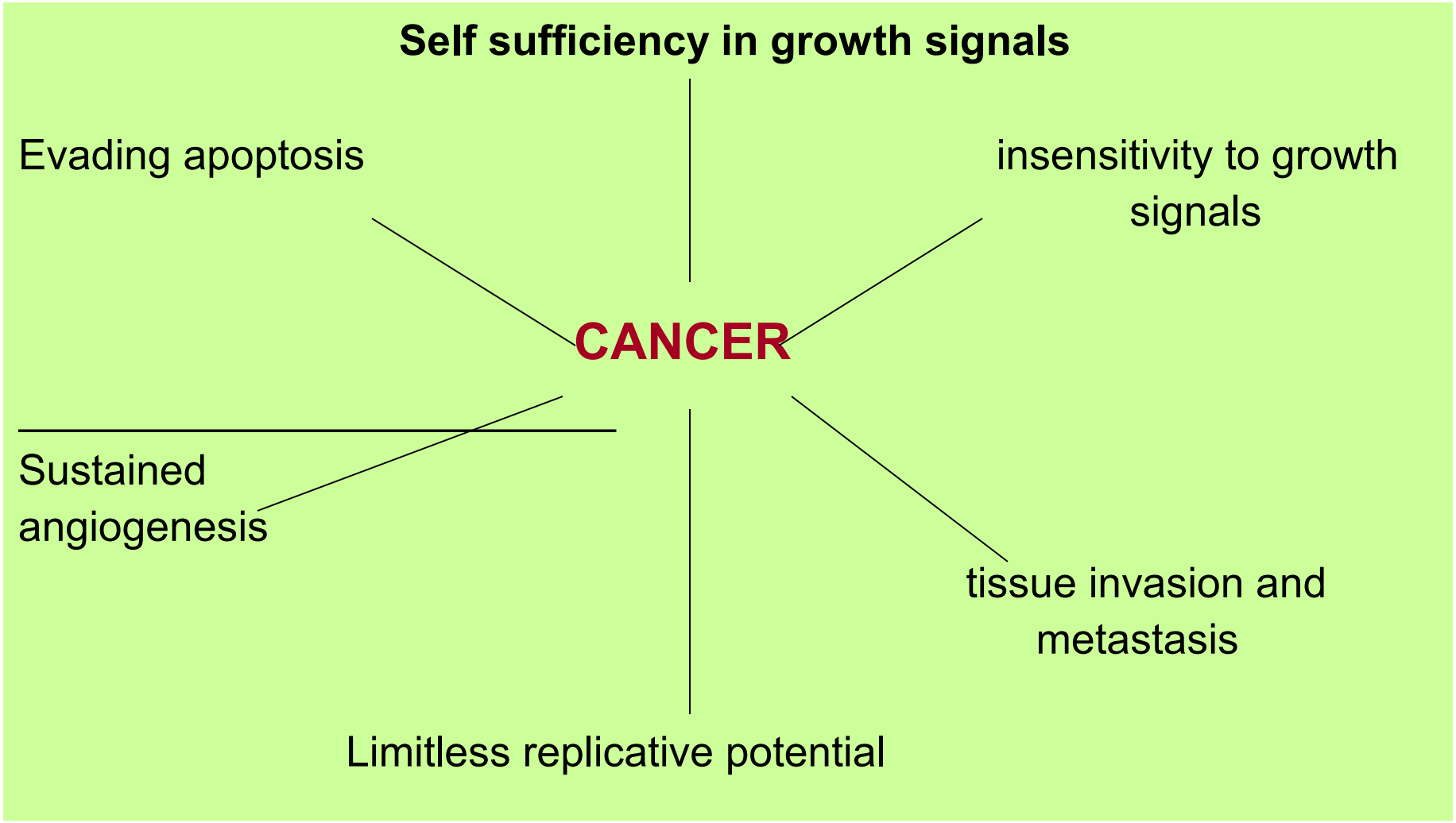
Regional Lymph Nodes (N)

- No No evidence of disease in lymph nodes
- N1-4 Ascending degrees of nodal involvement
- Nx Regional lymph nodes unable to be assessed clinically

Distant Metastases (M)

- Mo No evidence of distant metastases
- M1-4 Ascending degrees of metastatic involvement of the host, including distant nodes
- Mx cannot be determined

SIX HALL MARKS OF CANCER



CLINICAL ASPECTS OF NEOPLASIA

Two major aspects of clinical significance in assessing the course and management of neoplasia are:

- tumour-host inter-relationship (i.e. the effect of tumor on host and vice versa)
- laboratory diagnosis of cancer.

TUMOUR-HOST INTER-RELATIONSHIP

The natural history of a neoplasm depends upon 2 features:

- Effect of tumour on host
- Host response against tumour (Immunology of cancer)

EFFECT OF TUMOUR ON HOST

LOCAL EFFECTS. (due to their size or location.)

- **Compression**.
  e.g. a small benign tumour in ampulla of Vater may lead to biliary obstruction.

- **Mechanical obstruction**. Benign and malignant tumors in the gut may produce intestinal obstruction.

LOCAL EFFECTS.

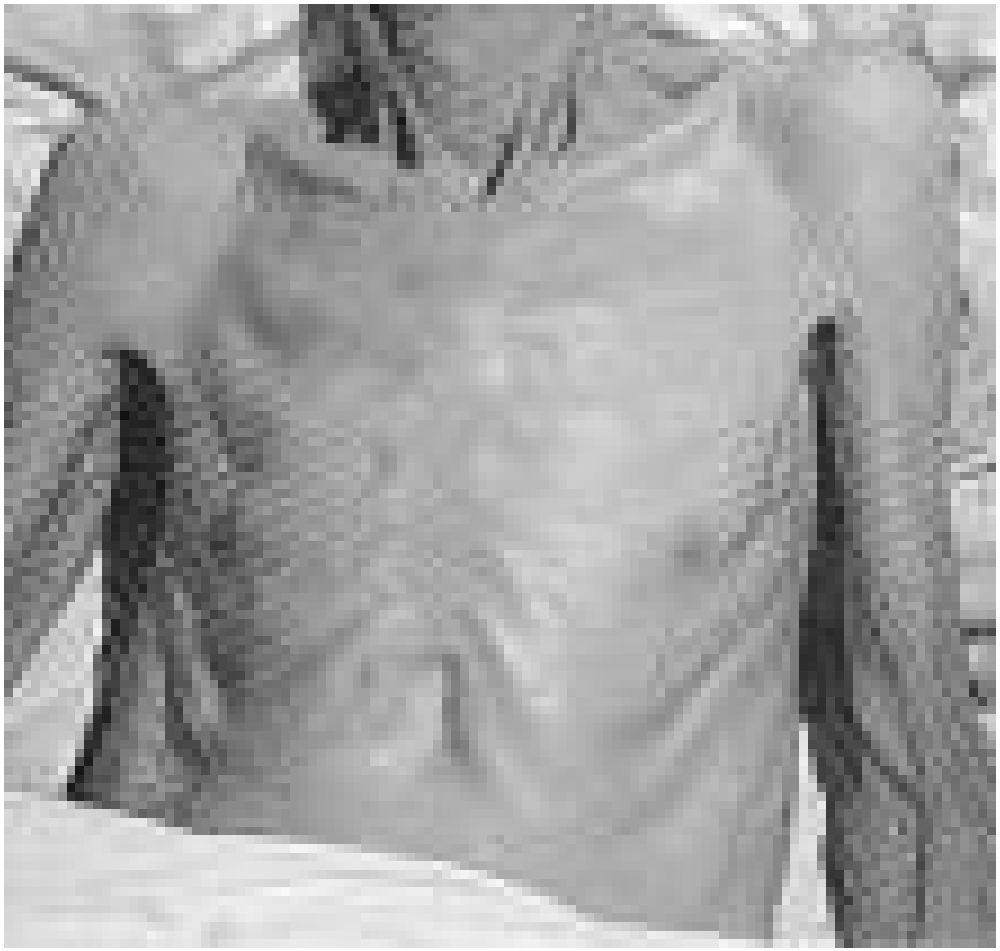
- **Tissue destruction**. Malignant tumors, both primary and metastatic, infiltrate and destroy the vital structures.

- **Infraction, ulceration, hemorrhage.** Cancers have a greater tendency to undergo infarction, surface ulceration and hemorrhage than the benign tumors. Secondary bacterial infection may supervene. Large tumors in mobile organs (e.g. an ovarian tumour) may undergo torsion and produce infarction and hemorrhage.

CANCER CACHEXIA

- Patients with advanced and disseminated cancers terminally have **asthenia (emaciation)** and **anorexia,** together referred to as cancer cachexia (meaning wasting).
- Possibly, cachectin or tumour necrosis factor $\propto$ (TNF- $\propto$) and interleukin-1 derived from macrophages play a contributory role in cachexia.
- The various other causes include necrosis, ulceration, hemorrhage, infection, malabsorption, anxiety, pain, insomnia, hyper-metabolism and pyrexia.

CANCER CACHEXIA



FEVER

- exact mechanism for fever is not known
- probably the tumour cells themselves elaborate pyrogens.
- Fever in Hodgkin's disease, adenocarcinoma kidney, osteogenic sarcoma

PARANEOPLASTIC SYNDROMES

- Paraneoplastic syndromes (PNS) are a **group of conditions** developing in patients with **advanced cancer** (10 to 15%) which are neither explained by direct and distant spread of the tumour, nor by the usual hormone elaboration by the tissue of origin of the tumor.

Endocrine Syndrome

- Elaboration of hormones or hormone-like substances by cancer cells of non-endocrine origin is called as ectopic hormone production.

- **Hypercalcaemia.** It occurs from elaboration of para-thormone-like substance by tumors such as squamous cell carcinoma of the lung, carcinoma kidney, breast
- **Cushing's syndrome** about 10% patients of small cell carcinoma of the lung elaborate ACTH or ACTH-like substance producing Cushing's syndrome.
- **Polycythaemia.** Secretion of erythropoietin renal cell carcinoma, hepatocellular carcinoma and cerebellar haemangioma may cause Polycythaemia.
- **Hypoglycemia**. Elaboration of insulin-like substance by fibro sarcomas, islet cell tumours of pancreas may cause hypoglycemia.

Neuromyopathic Syndromes

- About 5% of cancers are associated with **progressive destruction of neurons** throughout the nervous system without evidence of metastasis in the brain and spinal cord. This is probably mediated by **immunologic mechanisms**. The changes in the neurons may affect the muscles as well. The changes are: peripheral neuropathy, cortical cerebellar degeneration, myasthenia gravis syndrome.

Effect on osseous, joints and soft tissue

- E.g. hypertrophic osteoarthropathy and clubbing of fingers in cases of bronchogenic carcinoma by unknown mechanism.

Haematologic and vascular syndrome

- E.g. venous thrombotic (Trousseau's phenomenon), non-bacterial thrombotic endocarditis, disseminated intravascular coagulation (DIC), and normocytic normochromic anemia occurring in advanced cancers.
- Autoimmune hemolytic anemia may be associated with B-cell tumours.

Gastrointestinal syndromes

- Malabsorption of various dietary components
- hypoalbuminaemia

Renal syndromes

- Renal vein thrombosis or systemic amyloidosis may produce nephrotic syndrome in patients with cancer.

Cutaneous syndromes

- Acanthosia nigricans: appearance of black warty lesions in the axillae and the groins (adenocarcinoma of gastrointestinal tract.)
- seborrheric dermatitis in advanced malignant tumours
- exfoliative dermatitis in lymphomas and Hodgkin’s disease.

Acanthosia nigricans

Amyloidosis

- Primary amyloid deposits may occur in multiple myeloma whereas renal cell carcinoma and other solid tumours may be associated with secondary systemic Amyloidosis.

HOST RESPONSE AGAINST TUMOUR (IMMUNE SURVEILLANCE OF CANCER)

- **host defense mechanism in the form of immunological response exists so as to counter the growth and spread of cancer**

- Certain cancers evoke significant lymphocytic infiltrates composed of immuno competent cells and such tumors have somewhat better prognosis e.g. medullary carcinoma breast, seminoma testis.
- Rarely, a cancer may spontaneously regress partially or completely, probably under the influence of host defense mechanism. One such example is rare spontaneous disappearance of malignant melanoma from the primary site only to reappear as metastasis.
- It is highly unusual to have primary and secondary tumours in the spleen due to its ability to destroy the growth and proliferation of tumour cells.
- Immune surveillance exists is substantiated by increased frequency of cancers in immunodeficient host e.g. in AIDS patients, or in organ transplant recipients.

concept of immunology of cancer

- Tumour antigens
- Immune responses
- Prospects of immunotherapy

Tumour antigens

- **Tumour-specific antigens (TSA)**

Are located on tumour cells but not present on normal cells.

They are unique or specific antigens for particular tumour

Therefore, TSAs are targets of attack by tumour-specific cytotoxic CD8+T lymphocytes. The examples are:

- Over expressed antigens e.g.HER2 protein in cancer of the breast, ovary.
- Oncofoetal antigens e.g. ɷ - fetoprotein, carcinoembryonic antigen in cancers of liver, colon

- **Tumour associated antigen (TAA)**

Is present on tumour cells as well as on some normal cells.

TAA antigens shared by tumour cells and normal host cells from where the tumour originated.

It represent the stage at which the differentiation of tumour cells is arrested.

- Tissue specific antigens such as melanocyte specific proteins.
- Differentiation specific antigens prostate specific antigen (PSA) in carcinoma of prostate.

2)IMMUNE RESPONSES

- The nature of host immune response to tumours :
- Cell-mediated mechanism
- Humoral mechanism
- Inhibitory (regulatory) mechanism.

i) Cell-mediated mechanism

- cellular responses that can destroy the tumour cells and induce tumour immunity in humans:
- **Specifically sensitized cytotoxic T lymphocytes (CTL)** i.e. CD8+T cells which are directly cytotoxic requiring contact between them and tumour cell. They specifically attack the virally induced cancers e.g. in Burkitt's lymphoma (EBV – induced), invasive squamous cell carcinoma (HPV – induced).
- **Natural killer (NK) cells** are lymphocytes which destroy tumour cells without sensitization, either directly or by antibody-dependent cellular cytotoxicity (ADCC). They are the first line of defense against tumour cells.
- **Macrophages** are activated by interferon-γ secreted by T-cells and NK-cells, and therefore there is close collaboration of these lymphocytes with macrophages. Activated macrophages mediate cytotoxicity by production of oxygen free radicals or by tumour necrosis factor.

- **ii) Humoral mechanism.**
- Humoral antibodies may act by complement activation or by antibody-dependent cytotoxicity by NK cells.

- **iii) Inhibitory (Regulatory) mechanism.**
- In spite of host immune responses, most cancers grow relentlessly. This is due to some of the following controlling mechanisms:
- During progression of the cancer, immunogenic cells may disappear.
- Immunosuppression mediated by various acquired carcinogenic agents (viruses, chemicals, radiation).
- Immuno inhibitory role of factors secreted by tumours e.g. transforming growth factor-β.

PROSPECTS OF IMMUNOTHERAPHY

- The immune responses to be effective enough must eliminate the tumour cells more rapidly than their rate of proliferation
- **immunotherapy approaches:**
  - Cellular immunotherapy consists of infusion of tumour-specific cytotoxic T cells which will increase the population of tour-infiltrating lymphocytes.
  - The patient's peripheral blood lymphocytes are cultured with interleukin-2 which generates lymphokine-activated killer cells having potent anti-tumour effect.
  - Cytokine therapy is used to builds up specific and non-specific host defenses. These include: interleukin-2, interferon-α and -y, tumour necrosis factor- α , and granulocyte-monocyte , colony stimulating factor (GM-CSF).

DIAGNOSTIC METHODS

- **1) Histological Methods**

  Study of cytological feature of excised tumour mass or open / needle biopsy from the mass.

- **2) Cytological Methods**

a)exfoliative cytology

b)fine needle aspiration cytology, FNAC.

- **Histochemistry and Cytochemistry**
- help in identifying the chemical composition of cells, their constituents and their products by special staining methods
- E.g . For Basement membrane/collagen the stains used are
- Reticulin
- Van Gieson

Immunohistochemistry

- This is an immunological method of recognizing a cell by one or more of its specific components in the cytoplasm, cell membrane or nucleus. Also useful in classification or poorly-differentiated tumours of epithelial or mesenchymal origin
- Keratins:Carcinomas, mesotheliomas, some germ cells tumours
- Neurofilaments (NF) :Neural tumours

Electron Microscopy

- A few general features of malignant tumour cells by EM examination are:
- Cell junctions – their presence and type
- Cell shape and cytoplasmic extensions.
- Shape of the nucleus and features of nuclear membrane.
- Nucleoli – size and density.
- Cytoplasmic organelles – their number is generally reduced.
- Dense bodies in the cytoplasm.
- Any other secretory product in the cytoplasm e.g. melanosomes in melanoma and membrane-bound granules in endocrine tumours.

1) Tumour Markers (Biochemical Assays)

- Tumour markers are biochemical assays of products elaborated by the tumour cells in blood or other body fluids.
- Tumour markers include: cell surface antigens (or oncofoetal antigens)
- cytoplasmic proteins
- enzymes
- hormones and cancer antigens .

Important Tumour Markers

MARKER	CANCER
1. Omcofoetal antigens:	
i. Alpha-foetoprotein (AFP)	Hepatocellular carcinoma, non-seminomatous germ cell tumours of testis
ii. Carcinoma-embryonic antigen (CEA)	Cancer of bowel, pancreas, breast
1. Cytoplasmic proteins:	
i. Immunoglobulin	Multiple myeloma, other gammopathies
ii. Prostate specific antigen (PSA)	Prostate carcinoma
1. Enzymes:	
i. Prostate acid phosphates (PAP)	Prostatic carcinoma
ii. Neuron-specific enolase (NSE)	Neuroblastoma, oat cell carcinoma lung
1. Harmones:	
i. Human chorionic gonadotropin (HCG)	Trophoblastic tumours, non-seminomatous germ cell tumours of testis
ii. Calcitonin	Medullary carcinoma thyroid
iii. Catecholamines and vanillyl mandelic acid (VMA)	Neuroblastoma, pheochromocytoms
iv. Ectopic hormone production.	Paraneoplastic syndromses
1. Secreted cancer antigens:	Ovary
i. CA-125	Breast
ii. CA-15-3	

2) Modern Aids in Tumour Diagnosis

A) Flow cytometry.

- It can be employed on blood cells and their precursors in bone marrow aspirates and body fluids, and sometimes on fresh frozen unfixed tissue.
- The method employs either identification of cell surface antigen (e.g. in classification of leukemia's and lymphomas), or by the DNA content analysis (e.g. aneuploidy in various cancers).

B) In situ hybridization.

- In situ hybridization may be used for analysis of certain human tumours by the study of oncogenes aside from its use in diagnosis of viral infection

Molecular diagnostic techniques.

- **DNA/RNA-based molecular techniques:**
- here the DNA/RNA is extracted from the cell and then analyzed.
- Techniques include
- DNA analysis by Southern blot,
- RNA analysis by northern blot,
- polymerase chain reaction (PCR).
- **Application :**
- hematological as well as non-hematological malignancies by:
- analysis of molecular cytogenetic abnormalities;
- mutational analysis;
- antigen receptor gene rearrangement; and
- By study of oncogenic viruses at molecular level.

DNA microarray analysis of tumours.

- Molecular profiling of a tumour by use of gene chip technology which allows measurement of levels of expression of several thousand genes (up-regulation or down-regulation) simultaneously.

COMPLICATIONS OF CANCER

- **1) Malnutrition.**
- **2) Altered taste sensation..**
- **3) Infection** of the lungs, GU system, mouth, rectum, peritoneal cavity, and blood (septicemia).

ONCOLOGICAL EMERGENCIES

- **Obstructive Emergencies.**

  Obstructive emergencies are primarily caused by tumor obstruction of an organ or blood vessel. It includes:

- Superior vena cava syndrome
- Spinal cord compression syndrome
- Third space syndrome
- Intestinal obstruction.

- **a) Superior vena cava syndrome.**

  The most common cause are lung cancer, non-Hodgkin's lymphoma, and metastatic breast cancer.

- **b) Spinal cord compression syndrome**

  This is due to presence of a tumor in the epidural space of the spinal cord. The most common primary tumors that produces this problem are breast, lung, prostate, GI, and renal tumors and melanoma. Manifestations include intense, Localized, persistent back pain, motor weakness and dysfunction, sensory paresthesia and loss , autonomic dysfunction etc.

- **C) Third space syndrome**

  occurs secondary to extensive surgical procedures, bilologic therapy, or septic shock.

D) Intestinal obstruction.

- **Metabolic Emergencies.**
- This is caused by modulation of ectopic hormones directly from the tumor or secondary to metabolic alterations caused by the presence of the tumor or cancer treatment.
- It includes
  - syndrome of inappropriate antidiuretic hormone secretion
  - hypercalcaemia
  - tumor lysis syndrome
  - septic shock
  - disseminated intravascular coagulation.

Syndrome of Inappropriate antidiuretic Hormone secretion

- Syndrome of inappropriate antidiuretic hormone secretion results from abnormal or sustained production of ADH with resultant H_2O retention and hyponatremia.
- It can occur in lung cancer, cancers of pancreas, duodenum, brain, esophagus, colon, ovary, prostate, bronchus, leukemia, Hodgkin's lymphoma.
- Symptoms include weight gain, weakness, anorexia, nausea, vomiting, personality changes, seizures, and coma.

Hypercalcaemia

This occurs with metastatic disease of the bone, multiple myeloma, or when a parathyroid hormone- like substance is secreted by cancer cell in the absence of bony metastasis.

Signs and syndromes

- apathy
- depression,
- fatigue,
- muscle weakness,
- polyuria,
- nocturia,
- anorexia,
- nausea, vomiting,
- ECG changes.

- **Tumor Lysis syndrome.**
- rapid release of intracellular components in response to chemotherapy. The components released are potassium, phosphate, and DNA and RNA components (which are metabolized to uric acid by the liver)
- Four hallmark signs of TLS are hyperuricemia, hyperphosphatemia, hyperkalemia, and hypocalcemia.

- **Other Complications**
- **Septic Shock**
- **Disseminated intravascular coagulation.**

Infiltrative Emergencies.

- **I) Cardiac tamponade.**
- This result from fluid accumulation in the pericardial sac, constriction of the pericardium by tumor, or pericarditis secondary to radiation therapy to the chest.
- Manifestations include a heavy feeling over the chest, shortness of breath, tachycardia, cough, dysphagia, hiccups, hoarseness, nausea, vomiting, excessive perspiration, decreased level of consciousness, pulsus paradoxus, extreme anxiety.

- **II) Cardiac artery rupture.**

Rupture of the carotid artery occurs most frequently in patients with cancer of the head and neck secondary to invasion of the arterial wall by tumor or to erosion following surgery or radiation therapy.

PREVENTION AND HEALTH EDUCATION

- **Primary Prevention**
  Secondary Prevention
- **Cancer's seven warning signals**
- Change in bowel or bladder habits
- A sore that does not heal
- Unusual bleeding or discharge
- Thickening or lump in breast or elsewhere
- Indigestion or difficult in swallowing
- Obvious change in wart or mole
- Nagging cough or hoarseness

Cancer's seven safeguards

Lung: Don't smoke cigarettes.

Colorectum: Have a proctoscopic Exam as part of a regular Checkup after age 40.

Breast: Practice monthly breast self-examination.

Uterus: Have a Pap test as part of a regular checkup.

Skin: Avoid overexposure to the Sun.

Oral: Have a regular mouth examination by physician or dentist.

Complete body: Have an overall physical checkup annually or at 3-year intervals, depending on age.

Tertiary Prevention

- Organizations that can help meet the needs of cancer survivors .
- Reach to Recovery
- United Ostomy Association
- The National Coalition for Cancer Survivorship

MANAGEMENT

- **<u>COLLABORATIVE CARE</u>**
- Goals of cancer treatment :
- Cure
- Control
- Palliation

- **Curative Cancer Therapy**
- local cell carcinoma of the skin is usually used by surgical removal of lesion or by several weeks of radiation therapy.

- **Control Cancer Therapy**
- E.g.: Multiple myeloma, certain brain cancer, chronic lymphocytic leukemia. Patient may undergo are initial course of treatment followed by maintains therapy for as long as the disease is responding or until adverse effects warrant discontinuation.

- **Palliative cancer Therapy**
- With this treatment goal, relief or control of symptoms and the maintenance of satisfactory quality of life are the primary goals
- Radiation therapy or chemotherapy given to reduce tumor size and relieve subsequent symptoms such as the pain of bone metastasis or discomfort associated with lymph edema are examples

The goals of cure, control and palliation are achieved through the use of four treatment modalities for cancers:

- Surgery
- radiation therapy
- chemotherapy
- biologic and targeted therapy.

It can be used either as alone or in combination depending on disease process.

Surgical Therapy

- Diagnostic surgery
- Surgery as treatment
- Palliative surgery
- Reconstructive Surgery
- Preventive Surgery

- When surgery is performed with curative intent, the type of tumor determines the extent of the excision. For slow growing tumors such as squamous cell carcinoma, and adenocacinoma of the skin a wide local excision may be sufficient.
- Tumors of colon and breast that spread to the regional lymph nodes are removed with are block excision of tumor and regional lymph nodes.
- Large tumor such as sarcomas, which tend to spread locally without metastasis, is removed with radical excision such as amputation.

RADIATION THERAPY

- Radiation therapy is the local treatment modality for cancer.
- **Primary Radiation therapy:** is used to achieve local cure of the cancer. E.g.: early stage skin cancer, prostate cancer etc.
- **Adjuvant Radiation therapy:** this can be used either pre-operatively or postoperatively to aid in the destruction of cancer cells. (Colorectal cancer, early breast cancer)
- **Palliative Radiation therapy** it can be used to reduce pain caused by obstruction, pathologic features, spinal cord compression, and metastatic areas.

Principles of Radiation Therapy

- A highly radiosensitive tumor is greatly affected by radiation because it divides rapidly, well vascular bed and that high oxygen content.
- Radiation therapy is the use of high energy ionized radiation to treat a variety of cancers.
- Ionized radiation destroys a cells ability to reproduce by damaging its DNA, delaying mitosis to repair DNA or inducing apoptosis
- Rapidly dividing cells will oxygenated tumor shows a much greater response to radiation than poorly oxygenated tumors.
- Oxygen free radicals formed during ionization without rapidly with nearby movements careering cellules damage. A well visualized tumor may therefore be more responsible to radiation therapy.

Types of Radiation Therapy

- I) External- Beam radiation therapy:/ teletheraphy
- by high energy x-ray or Gamma-ray machines (e.g: cobalt, beta ion, or a machine containing a radioisotope)
- used to threat salivary gland tumors, sarcomas, prostate tumors, lung tumors.

- **II) Internal –Radiation therapy (Brachy therapy)**
- **Sealed –source RT:**
- It is used for intracavity and interstitial therapy.
- **Intra-cavity therapy:** the radio- isotope usually calcium 137, radiant 226 is put in an applicator which is then placed in the body correctly for carefully calculated time, generally 24-74 hours.
- It is used for cancer of uterus and cervix
- **In Interstitial therapy:**
- the radio isotopic of choice I e eg: iridium 192, iodine 125, cerium 137, gold198 or radon 222 is placed in needles, beads, seeds, ribbons, catheters which are these implanted directly into the tumor, either left there temporarily or permanently.

Unsealed-Source Radiation Therapy

- This is used in systemic therapy. These source are colloid suspensions that come into direct contact with body tissues. The radioisotopes can be used administered either as iv or oval or directly into body cavity. Eg; Iodine 131 is given orally

Radiation safety standards

- Distance: The intensity of radiation decreases universally with the square of the distance from the source e.g.: If you stand 4 feet from it source of radiation, you are exposed to about one forth of the amount of radiation you would receive at 2 feet.
- Time
- Shielding

Treatment Conditions

- Tumor locations should be specified and exposed to the radiation to prevent damage to normal tissue. This can be done by use of shielding “ block “ which protect normal tissue
- Pregnant ladies / health workers should not be exposed to radiation to prevent damage to fetus.

- **Dose of radiation:**
- The radiation dose is determined based on tumor volume, type of tumor and treatment setting.
- Once the total dose is determined, that dose is divided into daily “ fractions “ (generally between 180 and 200 cGY)
- Treatment is typically determined once a day Monday through Friday for a period of 2-8 weeks)

- **Tumors with high radio sensitivity:**
- ovarian dysgerminoma
- Testicular seminoma
- Hodgkin's lymphoma
- Non- Hodgkin's lymphoma
- Wilm's tumor
- Neuroblastoma

- **Poor radio sensitivity**:
- Osteosarcoma
- Malignant melanoma
- Malignant gliomas
- Testicular non seminoma

SIDE EFFECTS OF RADIATION THERAPY

- **GI system:**
- Stomatitis
- Mucositis
- Esophagitis
- Nausea and vomiting
- Anorexia
- Diarrhea
- Tenismus
- Xerostomia(dry mouth)
- Radiation caries

- **Hematological system:**
- Bone marrow suppression
- Anemia
- Leucopenia
- Thrombocytopenia

- **Integumentary system:**
- Alopecia
- Desquamation
- **Genitourinary system:**
- Hemorrhagic cystitis
- Urethritis
- Reproductive dysfunction
- **Nervous system:**
- Increased ICP

- **Respiratory system:**
- Pneumonitis

- **Cardiovascular system:**
- pericarditis
- Myocarditis

- **Psychoemotional**
- fatigue

CHEMOTHERAPY

Goals

- The goal of chemotherapy is to eliminate or reduce the number of malignant cells present in the primary tumor and metastatic tumor sites without extensive destruction of normal cells.
- **Types of chemotherapy**
- Adjuvant chemotherapy
- Neo-adjuvant chemotherapy

Types of chemotherapy drugs with their action and effect on cells:

- Action:
- The effect of chemotherapy is at the cellular level. Chemotherapy directly or indirectly disrupts reproduction of cells by altering essential biochemical process. The desired outcome is control or eradication of all malignant cells.

Types of chemotherapy drugs:

- **Cell-cycle phase –non-specific chemotherapeutic drugs:**
- These drugs have their effect on the cells during all phases of cell cycle- including those in the process of cellular replication and proliferation and those in the resting phase. GO)
- **Cell-cycle phase –specific chemotherapeutic drugs:**
- Exerts their most significant effects during specific phase of cell cycle i.e. when cells are in the process of cellular proliferation or replication during G1, S1, G2, or M.

Chemotherapeutic agents:

- cell specific
- Antimetabolites
- Vinka alkaloids
- Steroids
- Hormones

- cell cycle non-specific
- Alkylating agents
- Antibiotics

Methods of chemotherapy administration

- Intra-arterial chemotherapy
- Intraperitonial
- Intrathecal
- intraventricular
- Intracavitary
- Intravenous
- Intramuscular
- Oral
- Subcutaneous
- Topical
- Continuous infusion

SIDE EFFECTS OF CHEMOTHERAPY:

- **GI system:**
- Stomatitis
- Mucositis
- Esophagitis
- Nausea and vomiting
- Anorexia
- Diarrhea
- Constipation
- Hepato toxicity
- **Nervous system:**
- Increased ICP
- Peripheral neuropathy
- **Respiratory system:**
- Pneumonitis
- **Cardiovascular system:**
- pericarditis
- myocarditis
- cardio toxicity
- **Psycho emotional**
- Fatigue
- **Biochemical**
- Hyperuricemia

- **Hematological system:**
- Bone marrow suppression
- Anemia
- Leucopenia
- Thrombocytopenia
- **Integumentary system:**
- Alopecia
- Chemotherapy induced skin changes

- **Genitourinary system:**
- Hemorrhagic cystitis
- Reproductive dysfunction: sterility
- Nephrotoxicity

BIOLOGIC THERAPY AND TARGETED THERAPY

- Biologic therapy consists of agents that modify the relationship between the host and the tumor by altering the biological responses of the host to the tumor cells.
- Biologic agents may affect host tumor response in 3 ways:
- They have direct anti tumor effect.
- They restore, augment or modulate host immune system mechanisms.
- They interfere with the cancer cells ability to metastasize or differentiate.
- The biotherapy is useful in early stages of cancer.

- **Nonspecific immunostimulation**: uses biological agents such as BCG, and corynebacterium parvium which stimulates reticuloendothelial system and thus augment immune system.
- **Intralesional stimulation:**
- Injecting a biological agent directly into tumor .this initiates specific and non-specific response that triggers local cancer cell destruction.
- **Active specific immunostimulation**:
- uses specific tumor antigens vaccines to stimulate the patient's immune system to control or reject malignant cells by producing antibodies and lymphocytes.
- **Adoptive transfer of immunity:**
- Involves transferring immunologically active cells from a donor with established immunity to stimulate active immunity in the patient.

Targeted therapy

Interfere with the cancer growth by targeting specific cellular receptors and pathways that are important in tumor growth. The targeted therapies are more selective for specific molecular targets than cytotoxic anticancer drugs. Thus they are able to kill the cancer cells with out killing normal cells .it includes,

- Tyrosine kinase inhibitors
- Monoclonal antibodies
- Antiangiogenic agents
- Proteasome inhibitors

- **Tyrosine kinase inhibitors:**
- Tyrosine kinase is an important enzyme that activates the signaling pathways that regulate cell proliferation and survival.
- **Monoclonal antibodies:**
- Are capable of binding of specific target cells, including tumor cells. they function by being directed at specific binding sites
- **Human epidermal growth factor receptor 2 (HER-2)**
- (HER-2) is over expressed in certain cancers (especially breast cancers) and is associated with more aggressive disease and decreased survival. Trastuzumab (Herceptin) is a MoAb that binds to HER-2 and inhibits the growth of breast cancer cells that over express the HER-2 protein. Trastuzumab is used in the treatment of metastatic breast cancers that over express HER-2.

- **Angiogenesis inhibitors**
- work by preventing the mechanisms and pathways necessary for vascularization of tumors. Bevacizumab(Avastin), a recombainant human moAb, is indicated in combination with chemotherapy (e.g.5-FU) for the management of metastatic colorectal cancer.
- **Proteasome inhibitors :** **proteasomes** are intracellular multienzyme complexes that degrade proteins. Proteasome inhibitors can cause these proteins to accumulate, thus leading to altered cell function. Normal cells are capable of recovering from proteasome inhibition, but cancer cells undergo death when proteasomes are inhibited.

- Cytokines
- monokines
- Interferons.
- Tumor necrosis factor.
- Colony-stimulating factors.
- lymphokines
- Interleukin-2.
- Thymic factors

- **Interferons.**
- Interferons are a family of secretory glycoproteins produced by leukocytes in response to viral infections or to other stimuli. They appear to have an inhibitory effect on DNA synthesis and cell growth and may suppress the tumor directly.
- **Interleukin-2.**
- Interleukin-2 (IL-2) stimulates formulation of T cells and natural killer cells.
- **Tumor necrosis factor.**
- Tumor necrosis factor (TNF) is a monokine capable of causing necrosis in existing tumors by selectively killing neoplastic cells . TNF alters the vascular endothelium, resulting in a hemorrhagic tumor necrosis.

- **Colony-stimulating factors.**
- Colony- stimulating factors (CSFs), also called growth factors, are administered to cancer patients in hopes of decreasing the severity of neutropenia associated with chemotherapy. These monokines stimulated the maturation and production of blood cells. CSFs do not exhibit antitumor activity.
- There are four types of CSFs. I)
- Granulocyte-macrophage CSF (GM-CSF),
- II) Granulocyte CSF (G-CSF),
- III) Interleukin-3,
- IV) erythropoietin
- **Thymic factors**
- The two most common factors produced by the thymus gland are thymosin fraction 5 9 TF-5) and thymosin alpha 1 (Tα-1) thymic factors have immunostimulating capacities in immunosuppressed cancer patients.

HEMATOPOIETIC STEM CELL TRANSPLANTATION

- The goal of HSCT is cure.
- The approach is to eradicate tumor cells and / or clear the marrow of its components to make way for engraftment of the transplanted stem cells.
- This is the accomplished by administering higher than usual dosage of chemotherapy with or without radiation therapy,

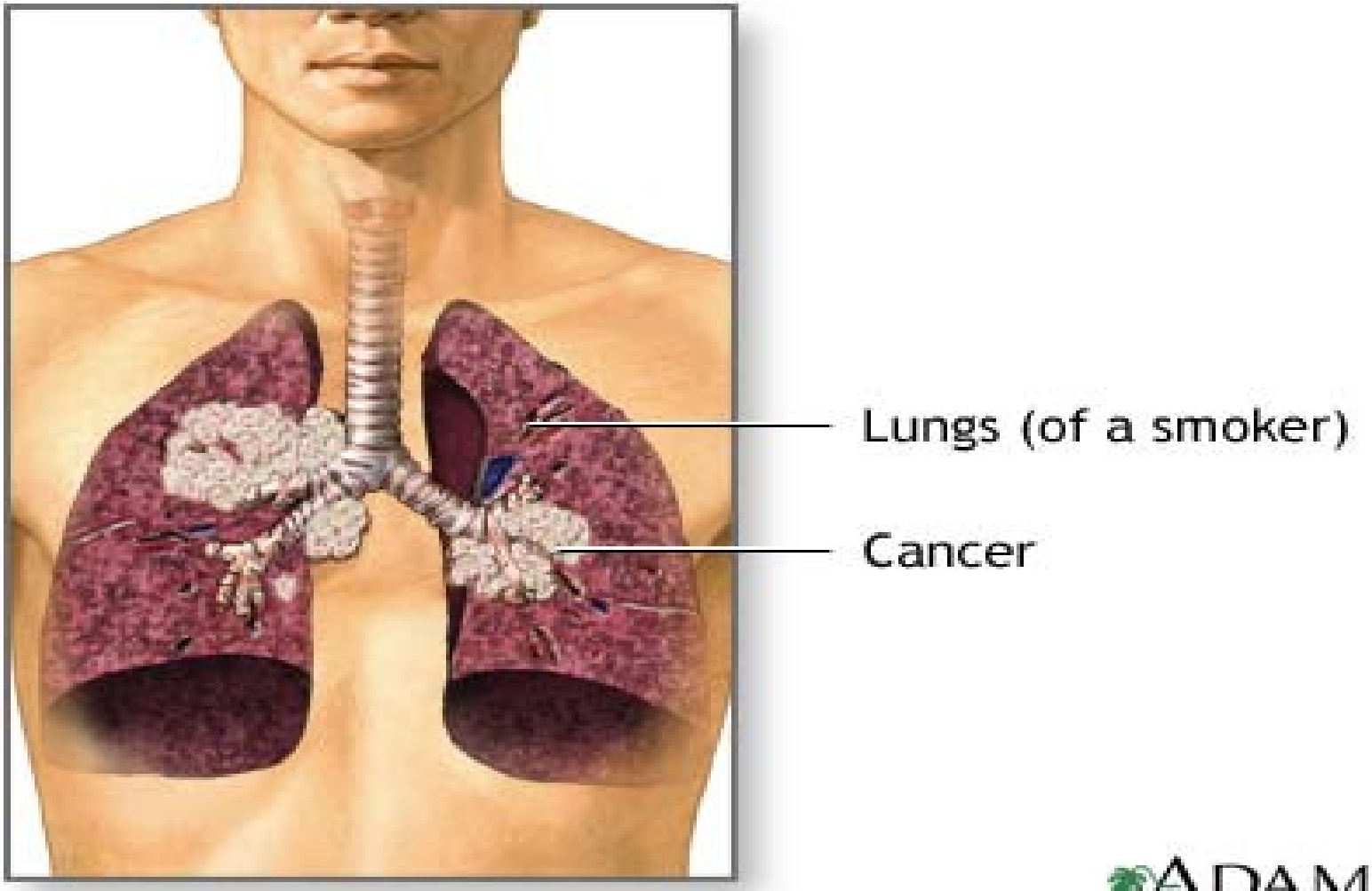
GENE THERAPY

- Gene therapy is an experimental therapy that involves introducing genetic material into a person's cell to fight disease. Researchers use many approaches to
- either target healthy cells to enhance their ability to fight cancer.
- target cancer cell to destroy them or prevent their growth.
- replace missing or altered genes with healthy genes.
- genes therapy is used to stimulate the body's natural ability to attack cancer cells.
- to prevent cancer cells from developing new blood vessels (angiogenesis).

Nursing interventions during advanced cancer stages

- **Counseling and guidance**
- **Encouraging social and vocational activities.**
- **Decreasing fear of helplessness.**
- **Facilitating activities of daily living.**
- **Promoting comfort**
- **Maintaining nutrition.**
- **Maintaining elimination**
- **Maintaining personal hygiene.**
- **Preventing effects of immobility.**
- **Teaching patient and family**
- **MANAGEMENT OF CANCER PAIN**
- **PSYCHOLOGIC SUPPORT**

LUNG CANCER



ETIOLOGY

- inhaled carcinogens-Radon gas , Asbestos
- Other inhaled carcinogens like nickle,iron,uranium, aromatic hydrocarbons, chromates, arsenic can also cause cancer.
- Petrolium manufacturing
- air pollution

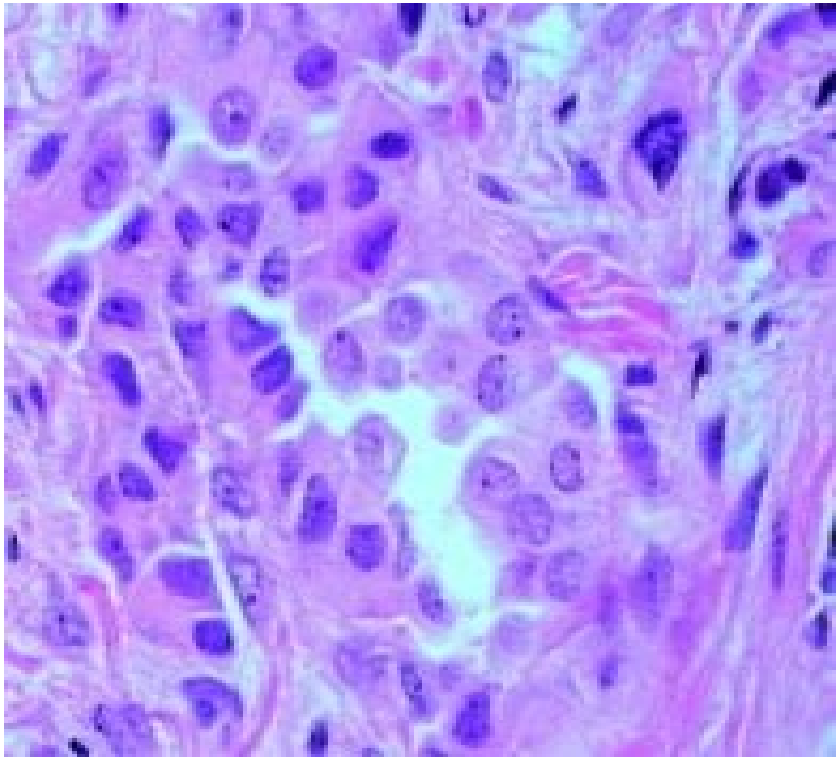
- Viruseshuman papillomavirus, JC virus, simian virus 40 (SV40), BK virus and cytomegalovirus. These viruses may affect the cell cycle and inhibit apoptosis, allowing uncontrolled cell division.

- Metastatic cancer: from primary colon and kidney malignancy can also occur.g

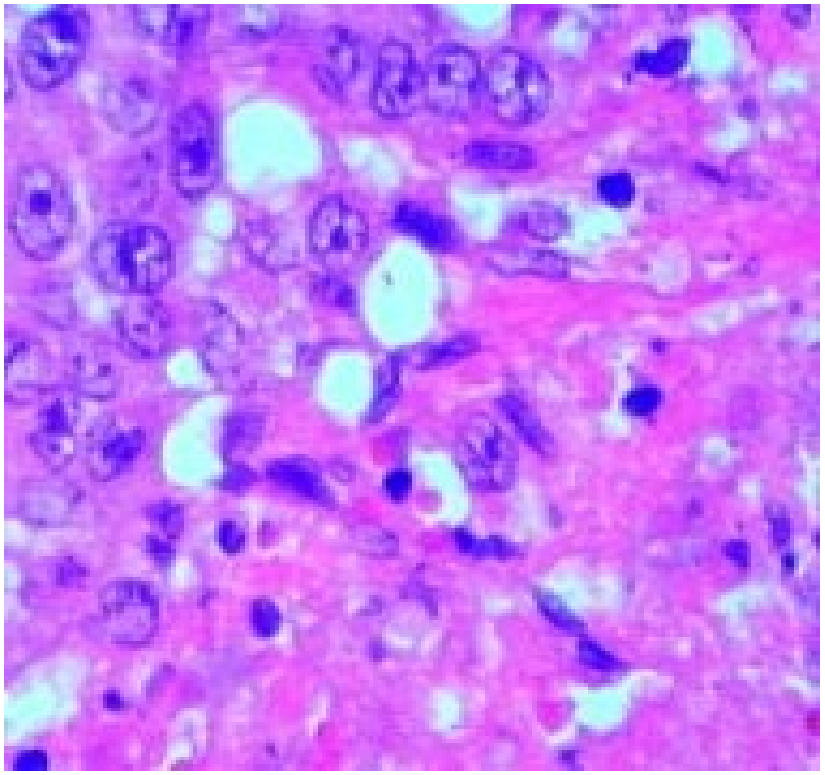
Pathology of lung cancer

- There are four main types of lung cancer based on the histological appearance of the cancer cells: (primary tumours)
- Adenocarcinoma (30% of cases)
- Squamous cell carcinoma (25% of cases)
- Small cell carcinoma (20% of cases)
- Large cell carcinoma (10% of cases)

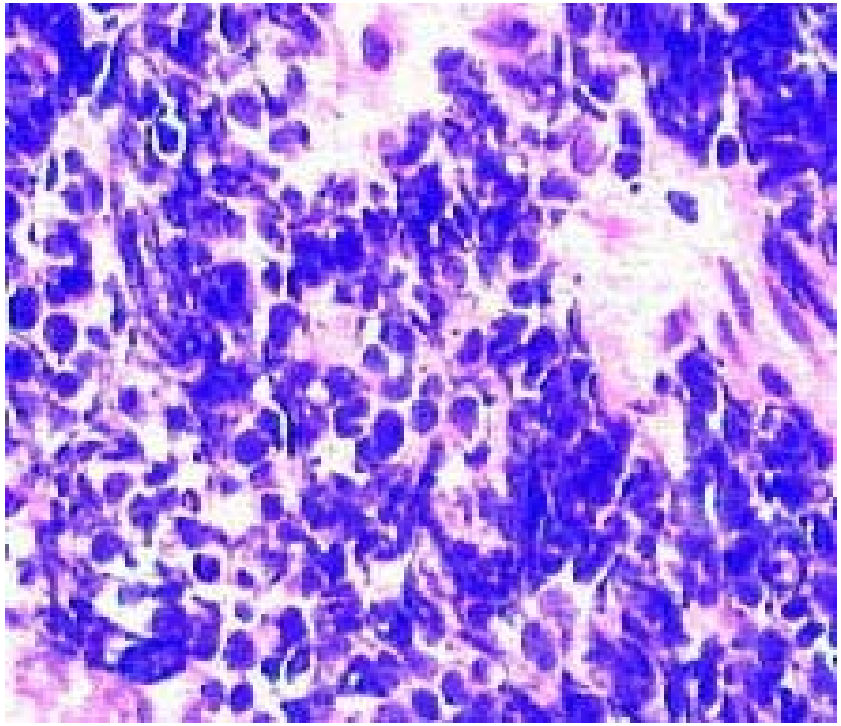
Adenocarcinoma



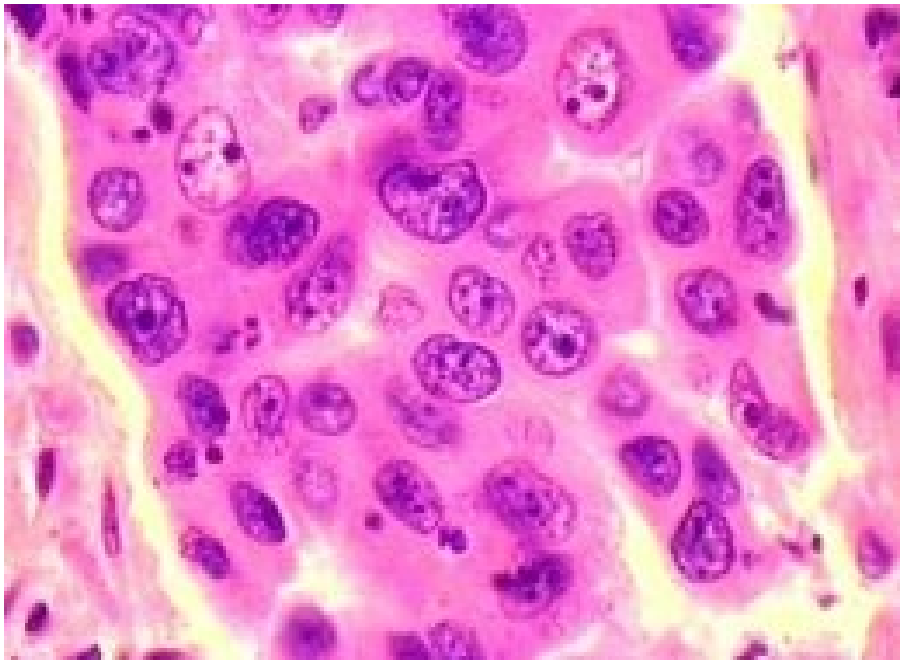
Squamous cell carcinoma



Small cell carcinoma



Large cell carcinoma



Secondary tumors

- Secondary tumors of the lung are very common, usually affecting the parenchyma, and often arise from primary tumors in; kidney, prostate, breast, bone, gastrointestinal tract, cervix or ovary.

Development of lung cancer

Chronic exposure to harmful substances is thought to cause bronchial mucosal cells to undergo changes. Pathologic changes in the bronchial system shows:

- Non specific inflammatory changes leading to
- Hypes secretion of mucus
- Desquamation of cells.
- Reactive hyperplasia of basal cells.
- Metaplasia of normal epithelium to stratified squamous cells.

- The injury elicits a compensatory and inflammatory response.
- Mucosal basal cells respond by proliferating to generate mucus-secreting goblet cells, and columnar epithelial cells are replaced by stratified squamous epithelium (metaplasia).
- Cellular atypia and increased mitotic activity which leads to mucosal dysplasia signals the development of neoplasia.
- Pre-invasive lesions are defined as morphological changes within the basal mucosa that are not invasive carcinomas but that may represent the initiation of carcinogenesis.

Growth and spread of lung cancer

- The first signs of invasive cancer are invasion of the basement membrane and infiltration of malignant cells into the underlying connective tissues and blood vessels. The process can take between 10 and 20 years or longer to develop.

- **Direct spread**
  Local spread of bronchial carcinoma destroys lung tissue and reduces ventilation capacity. The pleura and ribs may also be directly involved.
  Carcinoma in the apex of the lungs can erode ribs and involve the lower part of the brachial nerve plexus, causing severe pain in the shoulder and down the inner surface of the arm.

- Bronchial carcinoma can:
- Invade the phrenic nerve, paralysing the diaphragm
- Invade the oesophagus producing progressive dysphagia
- Invade the pericardium, leading to pericardial effusion/malignant dysrhythmias.

Metastasis

- Metastasis can occur by three main routes:
- Spread into body cavities
- Invasion of lymphatic vessels
- Haematogenous spread
- The lymphatic channels of the lungs are a common route for the spread of bronchial carcinoma. This leads to lymphangitis carcinomatosa and severe dyspnoea. There is frequent involvement of the lymph nodes of the lung, mediastinum, axillae and neck. Organs with a rich blood supply, such as the liver, are often affected. Secondary tumors are also common in the brain and adrenal gland.

  Metastasis from other primary tumours, such as renal carcimomas, often becomes established in the lungs.

Staging of Non small cell lung cancer

Stages	Characteristics
Tumor is small and localized to lung. No LN involvement	
A	Tumor < 3 cms
B	Tumor > 3cms invading surrounding local areas
II	
A	Tumor < 3cms with invasion of limp nodes on same side of chest
B	Tumor > 3cms involving the bronchus and lymph nodes on same side of the chest and tissue of other local organs
III	Tumor spread to the near by structures (chest vale, plera, percardiam,) and regional lymphnodes.
B	extensive tumor invol.involving heart, trachea, esophagus, mediastinum, malignant plural effusion, supra clavicular lymphnodes.
IV	distant metastasis

Signs and symptoms

- dyspnea
- hemoptysis
- chronic coughing or change in regular coughing pattern
- wheezing
- chest pain or pain in the abdomen
- cachexia (weight loss), fatigue and loss of appetite
- dysphonia (hoarse voice)
- clubbing of the fingernails (uncommon)
- dysphagia

- **paraneoplastic phenomena :**

  Lambert-Eaton myasthenic syndrome (muscle weakness due to auto-antibodies),

  hypercalcemia or syndrome of inappropriate antidiuretic hormone (SIADH).

  Tumors in the top (apex) of the lung, known as Pancoast tumors, may invade the local part of the sympathetic nervous system, leading to changed sweating patterns and eye muscle problems (a combination known as Horner's syndrome), as well as muscle weakness in the hands due to invasion of the brachial plexus.

DIAGNOSTIC STUDIES

- History and physical examination
- Chest X-ray –show lung mass and infiltrate ,helps in identifying metastasis,pleural effusion,pneumonia, atelectasis.
- Sputum for cytologic study
- Fibroptic bronchoscopy
- Computed tomography scan
- MRIscan
- Position emission tomography
- Spirometry
- Mediastinoscopy
- Video assissted thoracoscopy
- Pulmonary angiography
- Lung scan
- Fine needle aspiration

Complications of lung cancer

- Pneumonia
- Obstruction -breathlessness
- Mediastinal involvement include pericardial involvement ,cardiac tamponade, and dysrhythmias.
- Secondary metastasis to liver, kidney, adrenal glands, brain can occur.

Treatment

- **Surgery**
- **Exploratory thoracotomy**
- **wedge resection**
- **segmentectomy**
- **lobectomy (one lobe)**
- **bilobectomy (two lobes)**
- **pneumonectomy (whole lung)**

Chemotherapy

- Non-small cell lung carcinoma is often treated with cisplatin or carboplatin, in combination with gemcitabine, paclitaxel, docetaxel, etoposide or vinorelbine.
- In small cell lung carcinoma, cisplatin and etoposide are most commonly used. Combinations with carboplatin, gemcitabine, paclitaxel, vinorelbine, topotecan and irinotecan are also used.

Radiotherapy

- radical radiotherapy: non-small cell lung carcinoma
- Continuous hyperfractionated accelerated radiotherapy (CHART) :small cell lung carcinoma
- **Interventional radiology**
- **Radiofrequency ablation** :Bronchogenic carcinoma.

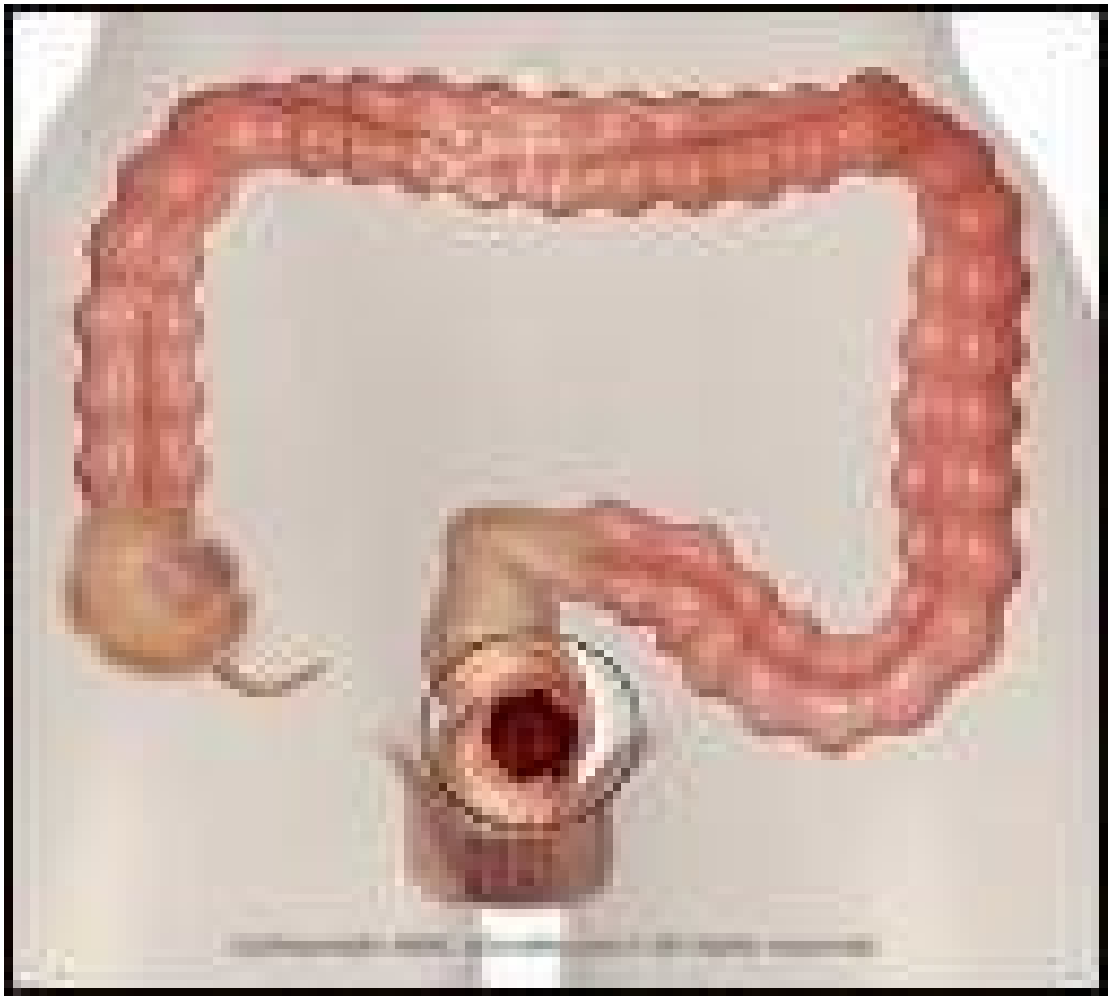
Targeted therapy

- Gefitinib (Iressa) is one such drug, which targets the tyrosine kinase domain of the epidermal growth factor receptor (EGF-R) which is expressed in many cases of non-small cell lung carcinoma.
- Erlotinib (Tarceva), another tyrosine kinase inhibitor, has been shown to increase survival in lung cancer patients
- The angiogenesis inhibitor bevacizumab (in combination with paclitaxel and carboplatin) improves the survival of patients with advanced non-small cell lung carcinoma.

Other therapies

- **Bronchoscopic lasor theraphy**. (for removing obstucting broncheal lesions)
- **Photodynamic theraphy-** which destory tumor cells
- **Airway Stenting** : This supports airway wall against collapse, or external compression and can inpede extention of tumor into airway
- **Cryotherapy**. Cryotherapy is a technique in which tissue is destroyed as a result of free using

COLORECTAL CANCER



COLORECTAL CANCER

PATHOGENESIS

ETILOGICAL FACTORS

- Increasing age(90% age more than 50 years)
- Family history of colorectal cancer
- Colorectal polyps
- Hereditory diseases i.e familial adenomatous polyposis (5%-10%)
- Hereditary non polyposis colorectal cancer syndrome
- Lifestyle factors: obesity
- Smoking
- Alcohol use
- Large intakes of red meat

PATHOPHYSIOLOGY

Adenomatous cancer begins at mucosal polyp present in luman of colon and rectum.

↓

Cancer progress down from tip of polyp to the body and atalk

↓

Becomes invasive and penetrates muscularis mucosa

↓

Gains access to the regional lymphnodes and vascular system

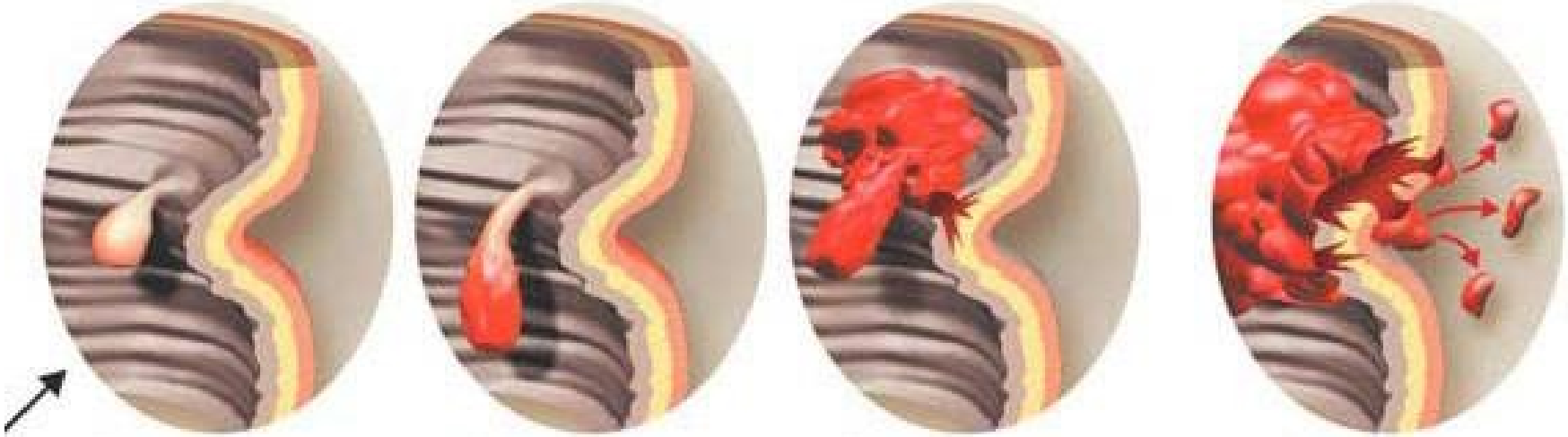
↓

Spread to the distant sites

(regional lymph nodes ,liver, lungs, peritoneum, bones,brain etc.)

↓

growing tumor can obstruct the bowel.



1 Cells that line the colon are very active, constantly dividing and creating buds, known as polyps. Most polyps are small, benign growths that eventually stop growing

2 But a tiny percentage of these polyps keep growing, sometimes for 10 years or more. Various genetic mutations can transform them into cancerous tumors

3 As these tumors grow larger, they gather more mutations and begin to burrow deeper and deeper into the muscle wall that surrounds the colon

4 Once the cancer invades the blood and lymph systems, malignant cells can break off and spread to other organs, such as the liver, lungs and stomach

CLINICAL MANIFESTATIONS

- Hematochezia (pasage of blood hrough rectum)
- Malena(black,tarry stools)
- Abdominal pain
- Changes in bowel patren
- Weakness
- Anemia,Weigt loss

left sided colon cancer

- rectal bleeding
- alternatinng constipation and /diarrhea
- change in the caliber of stool (narrow, ribbonlike)
- sensation of incomplete evacuation

- **right sided colon cancer**
- usually asymptomatic
- vague abdominal discomfort/cramping
- colicky abdominal pain
- iron deficiency anemia
- Occult bleeding
- anemia

DIAGNOSIS :TNM CLASSIFICATION

- **T PRIMARY TUMOR**
- T primary tumor cannot be assesed because of incomplete information
- T Carcinoma in situ cancer in eartiet stge, not grown beyond mucosa layer
- T Tumor grown beyond mucosa into sub mucosa
- T Tumor grown through submucosa into muscularis propria
- T Tumor has grown through muscularis propria into submucosa but not neighbouring organ/tissue
- T Tumor has sprerad oompletely through colon or rectalwall into nearby tissue/organ
- **N Lymph Node Involement**
- N Lymph node scan not be asssd.
- N No Regional lymph node involvement found
- N Cancr is found in one to three near by lymph nodes
- N Cancr is found in four or more near by lymph nodes
- **M metastasis**
- M presence of distant metastasis can not be assessed
- M no distant metastasis seen
- M distant metastasis is present

DIAGNOSIS

- History and physical examination
- Digital rectal examination(to identify rectal polyps)
- Testing of stool for occult blood
- Barium enema(every 5 years)
- Sigmoidoscopy
- Colonoscopy
- Biopsy
- Stool DNA test(not at sensitive)
- CBC- for anemia
- Coagulation studies
- Liver function tests
- Carcino embryonic antigen (CEA) is a complex glycometer produced by 90% of colorectal cancers ,it is useful in monitoring disease recurrence following surgery /chemotherapy
- Computed tomography scan of abdomen to detect metastasis
- MRI scan
- Ultrasound

COLLABORATIVE CARE

- **Surgical therapy:**
- It includes
- Polypectomy during colonoscopy
- Resection of bowel and reanastomosis
- Palliative surgery- when tumor is not resectable/ metastasis is present, Palliative surgery is done to control hemorrhage and to relieve obstruction
- Abdominal perineal resection following colostomy

Chemotherapy

- Combination of 5-fluorouracil plus leucovorin and irinotecan is approved as first line chemotherapy for patients with metastatic colorectal cancer.
- 5-fluorouracil and levamisole with or with out leucovorin
- Other drugs include, oxaliplatin and raltitrexed

Biologic and targeted therapy

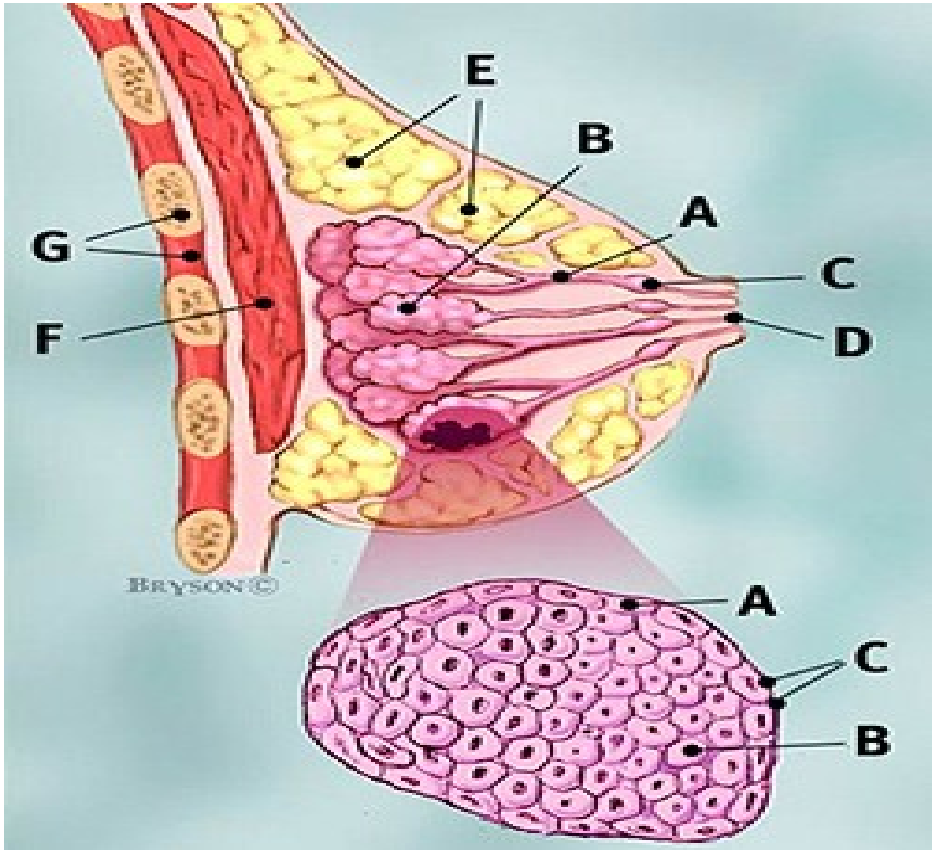
This includes use of three monoclonal antibodies.
Two drugs target epidermal growth factor receptor i.e. cetuximab and panitumumab.
Other drug targets vascular endothelial growth factor i.e bevacizumab

- **Radiation therapy:**
- post operatively as an adjuvant to surgery and chemotherapy
- as a palliative measure for patients with metastatic cancer.

COMPLICATIONS

- Bleeding
- Perforation
- Peritonotis
- Fistula formation

BREAST CANCER



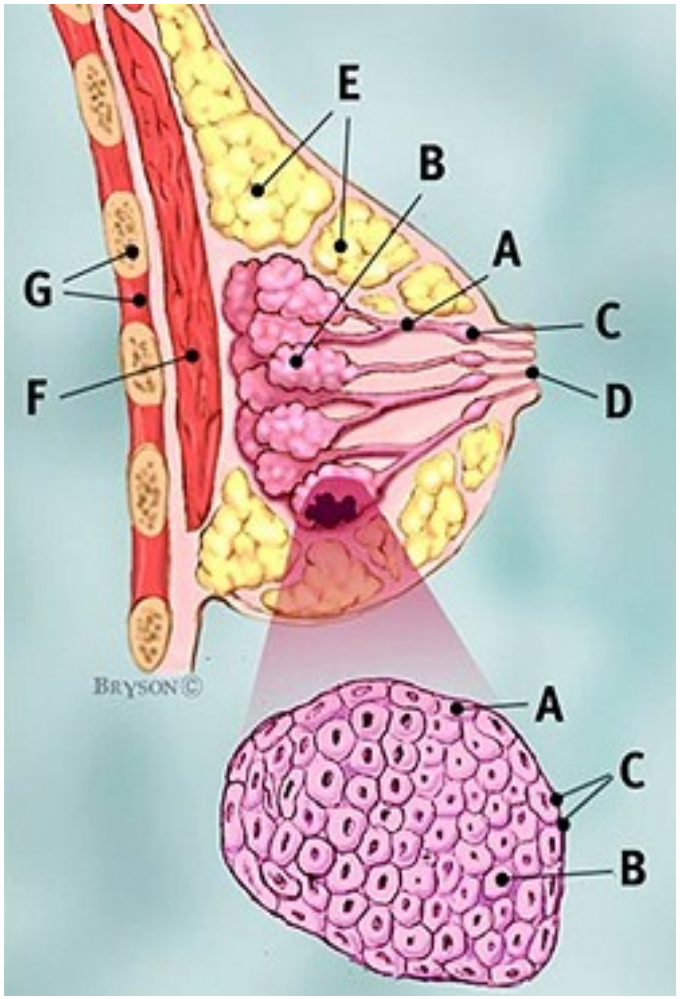
- **ETIOLOGY/RISKFACTORS**
- Female gender (90%)
- Age over 50 years
- Hereditary and genetically related susceptibility
- Gene mutations (BRCA-1 or BRCA -2) play a role in 5-10% of breast cancer cases. Genetic alteration in the tumor suppressor gene p53 is found.
- Personal history of colon cancer, endometrial cancer, ovarian cancer.
- Early menarche (before age of 12)
- Later menopause (after age of 55)
- First full term pregnancy after age 30years. (Prolonged exposure to estrogen)
- Null parity
- Benign breast disease
- Weight gain and obesity after menopause (fat cells store estrogen) exposure to ionizing radiation (radiation damages DNA)
- Use of oral contraceptives, alcohol intake

Patho-physiology
Types of Breast Cancer

- **Infiltrating ductal carcinoma (63% -68%)**
  - Colloid (mucinous)
  - Inflammatory
  - Pagets disease
  - Medullary
  - Papillary
  - Tubular
- **Infiltrating lobular carcinoma (10% -15%)**
- **Non invasive**
- Ductal carcinoma in situ

Normal breast with lobular carcinoma in situ (LCIS) in an enlarged cross–section of the lobule.

- **Normal breast with lobular carcinoma in situ (LCIS) in an enlarged cross–section of the lobule.**
- **Breast profile:**
- **A: ducts**
- **B: lobules**
- **C: dilated section of duct to hold milk**
- **D: nipple**
- **E: fat**
- **F: pectoralis major muscle**
- **G: chest wall/ rib cage**
- **Enlargement:**
- **A: normal lobular cells**
- **B: lobular cancer cells**
- **C: basement membrane**

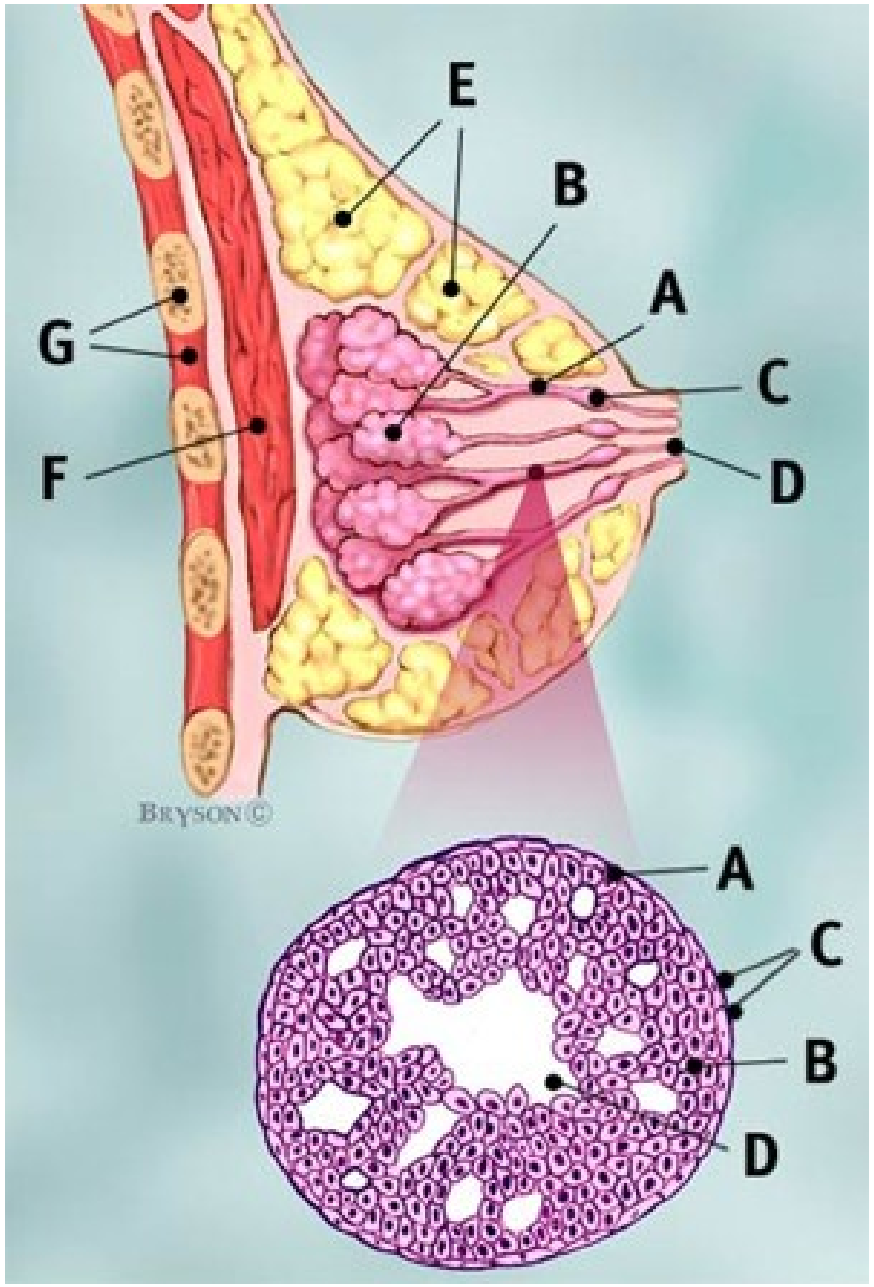


Normal breast with invasive ductal carcinoma (IDC) in an enlarged cross–section of the duct. Breast profile:

A: ducts
B: lobules
C: dilated section of duct to hold milk
D: nipple
E: fat
F: pectoralis major muscle
G: chest wall/ rib cage

Enlargement:

A: normal duct cells
B: ductal cancer cells breaking through the basement membrane
C: basement membrane



- Invasive lobular carcinoma
- Normal breast with invasive lobular carcinoma (ILC) in an enlarged cross–section of the lobule.
- Breast profile:
- A: ducts
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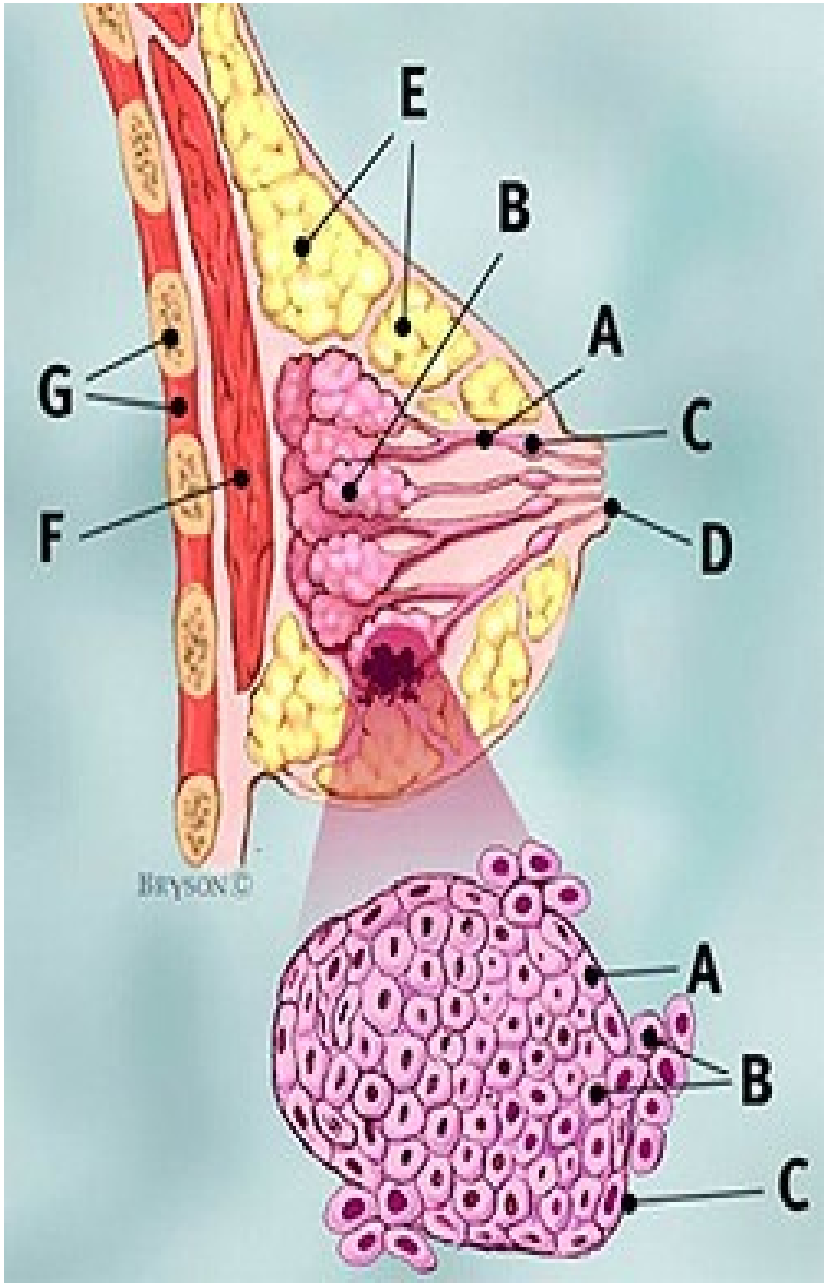

Clinical manifestations

- It occurs most often in the upper, outer quadrant of the breast because it is the location of most of the glandular tissue.
- The growth rate at which the lesion grows is considerably slow.
- The palpable breast cancer is characteristically hard and may be irregularly shaped, poorly delineated, non mobile and non tender.
- nipple discharge: usually unilateral and may be clear or bloody.
- Nipple retractions may occur.
- Peau d' orange may occur due to plugging of dermal lymphatic.
- In large cancers infiltration, indurations and dimpling (pulling in) of the over lying skin may also be noted.

Diagnosis

- Assessing axillary lymph node status
- Lymphatic mapping and sentinel lymph node dissection, by injecting radio isotope or blue dye.
- Cell proliferation indices: measures rate of tumor cell proliferation.
- Identification of marker HER-2
- Mammography
- Ultrasound
- Biopsy
- MRI scan
- **For staging work up,**
- CBC- for anemia
- Coagulation studies- platelet count
- Calcium and phosphorus levels
- Liver function tests
- Computed tomography scan of abdomen and pelvis to detect metastasis
- Chest X-ray
- Bone scan

COLLABORATIVE CARE

- **Surgical therapy**
- **Breast- conserving (lumpectomy) with sentinel lymph node:**
- **Biopsy / dissection and or axillary lymph node dissection.**
- Modified radical mastectomy which may include reconstruction.
- **Tissue expansion and breast implants**:

Adjuvant therapy

- 1. **Radiation therapy**
- It is used for breast cancer as,
- Primary treatment to prevent local breast recurrences after conservation surgery.
- Adjuvant treatment following mastectomy to prevent local and nodal recurrences.
- Palliative treatment for pain caused by local recurrence and metastasis.

Chemotherapy

- Preoperatively chemotherapy can be used to decrease the size of primary tumor,
- The most common combination protocols include:
- Cyclophosphamide, methotrexate, 5-fluorouracil(CMF)
- Doxorubicin, Cyclophosphamide, with or without addition of taxane.

THANKYOU