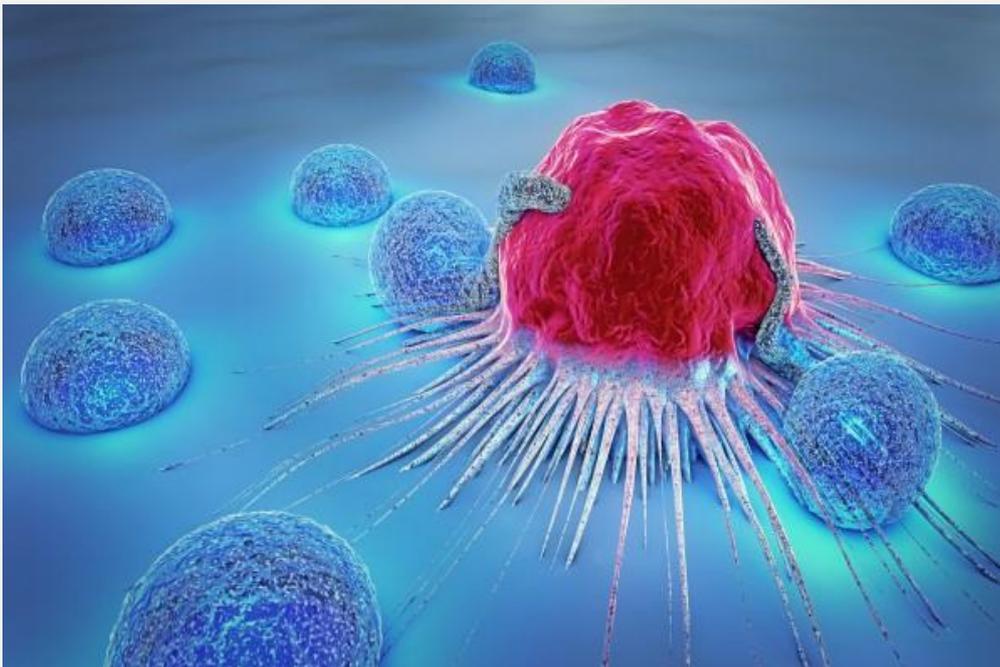# CANCER

1. Introduction

- **Cancer** is a group of diseases characterized by **uncontrolled, abnormal growth and division of cells** that can **invade surrounding tissues** and **metastasize** (spread) to distant sites.

- It arises when **normal regulatory mechanisms of cell growth, differentiation, and death** are disrupted.

2. Basic Terminology

Term	Meaning
Tumor / Neoplasm	An abnormal mass of tissue formed by excessive cell proliferation
Benign tumor	Localized, slow-growing, non-invasive, usually non-fatal
Malignant tumor (Cancer)	Rapidly growing, invasive, metastasizing, potentially fatal
Metastasis	Spread of cancer cells from the original (primary) site to distant organs
Oncology	Branch of medicine that studies and treats cancer

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3. Characteristics of Cancer Cells

Cancer cells differ from normal cells in several key ways:

Normal Cells	Cancer Cells
Controlled growth (regulated cell cycle)	Uncontrolled, continuous proliferation
Contact inhibition (stop dividing when crowded)	Loss of contact inhibition
Require growth factors	Grow independently of growth factors
Undergo apoptosis when damaged	Evade apoptosis
Limited cell divisions	Become "immortal" (limitless replication)
Organized tissue structure	Disorganized mass
Depend on anchorage for growth	Can grow without anchorage (anchorage-independent)
Non-invasive	Invasive and metastatic

4. Types of Cancer (Based on Tissue Origin)

Type	Origin	Examples
Carcinoma	Epithelial tissues (skin, glands, lining of organs)	Lung cancer, breast cancer, prostate cancer
Sarcoma	Connective tissues (bone, cartilage, muscle)	Osteosarcoma, chondrosarcoma
Leukemia	Blood-forming tissues (bone marrow)	Acute lymphoblastic leukemia (ALL)
Lymphoma	Lymphatic system	Hodgkin's lymphoma, Non-Hodgkin's lymphoma
Melanoma	Pigment-producing melanocytes	Skin melanoma
Glioma	Glial cells of the nervous system	Astrocytoma, glioblastoma

5. Causes of Cancer (Carcinogenesis)

- Cancer is **multifactorial** — caused by a combination of **genetic and environmental factors**.

A. Genetic Causes

1. **Oncogenes activation:**
   - Normal genes (**proto-oncogenes**) regulate cell growth.
   - Mutation → **oncogene** → uncontrolled proliferation.
   - Example:
     - *ras*, *myc*, *erbB*, *sis*.

2. **Tumor suppressor gene inactivation:**
   - Normally suppress cell division or promote DNA repair.
   - Loss of function → cancer.
   - Example:
     - *p53*, *Rb*, *BRCA1/2*, *APC*.

3. **DNA repair gene defects:**
   - Failure to correct mutations → genomic instability.
   - Example: *MSH2*, *MLH1* (colon cancer).

4. **Telomerase reactivation:**
   - Cancer cells express **telomerase**, enabling unlimited replication.

B. Environmental and Lifestyle Factors

Factor	Examples / Effects
Chemical carcinogens	Tobacco (benzopyrene), aflatoxins (liver cancer), nitrosamines
Radiation	UV rays (skin cancer), ionizing radiation (leukemia, thyroid cancer)
Viral infections	HPV → cervical cancer; EBV → Burkitt's lymphoma; HBV/HCV → liver cancer; HTLV-1 → T-cell leukemia
Diet	High-fat, low-fiber diets linked to colon and breast cancer
Occupational exposure	Asbestos → mesothelioma; benzene → leukemia
Hormonal factors	Estrogen → breast, endometrial cancers

6. Molecular Basis of Cancer

A. Hallmarks of Cancer (Hanahan and Weinberg, 2000; updated 2011)

1. **Sustaining proliferative signaling**

2. **Evading growth suppressors**

3. **Resisting cell death (apoptosis)**

4. **Enabling replicative immortality**

5. **Inducing angiogenesis (new blood vessel formation)**

6. **Activating invasion and metastasis**

7. **Deregulating cellular energetics**

8. **Avoiding immune destruction**

B. Important Genes in Cancer

Gene	Normal Role	Effect of Mutation	Associated Cancers
p53	DNA repair, apoptosis	Loss → genomic instability	Many cancers
Rb	Inhibits cell cycle (G1 → S)	Loss → uncontrolled division	Retinoblastoma
ras	Growth signal transduction	Gain → constant activation	Colon, pancreatic cancer
myc	Transcription factor	Overexpression	Lymphoma
BRCA1/2	DNA repair	Loss → defective repair	Breast, ovarian cancers
APC	Cell adhesion, signal control	Loss → polyp formation	Colon cancer

7. Process of Carcinogenesis

Cancer development is **multi-step** and includes:
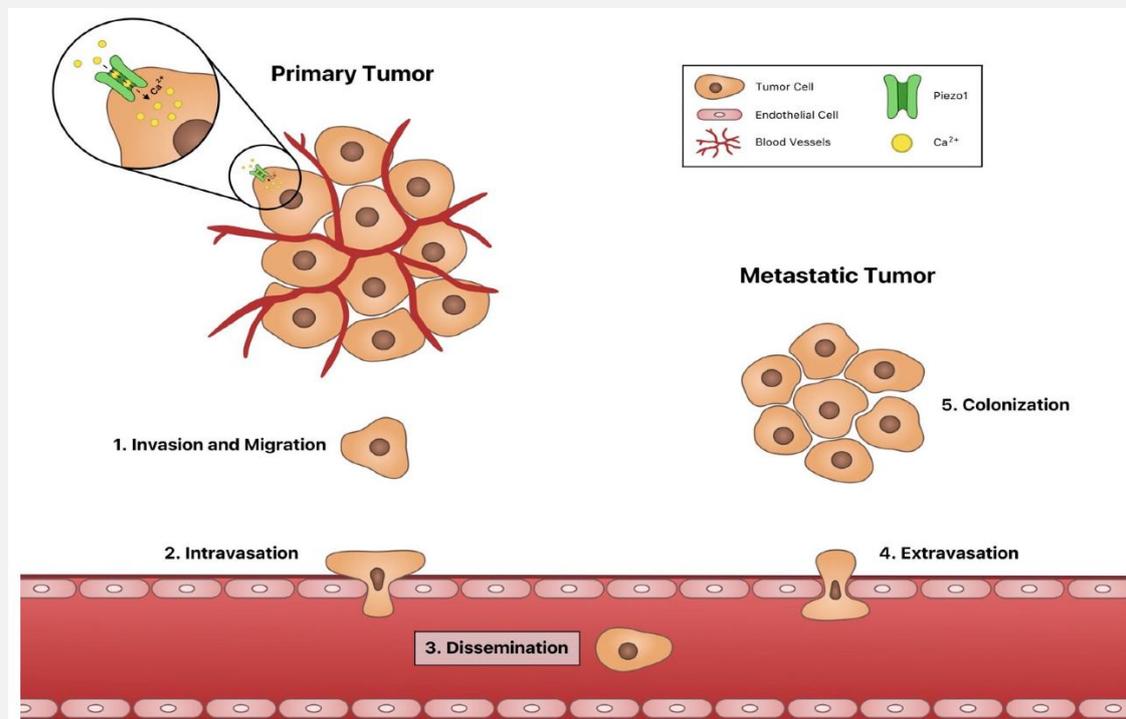
1. **Initiation:**
   - Irreversible genetic damage (mutation) caused by carcinogens.

2. **Promotion:**
   - Proliferation of initiated cells by promoters (e.g., hormones, inflammation).

3. **Progression:**
   - Acquisition of further mutations → malignant transformation → invasion/metastasis.


8. Metastasis

- The **spread of cancer cells** from the primary tumor to distant organs via:
  - **Bloodstream (hematogenous spread)**
  - **Lymphatic system**
  - **Direct invasion**
- Common metastatic sites: **lungs, liver, bones, brain**.

Steps in Metastasis:

1. Local invasion
2. Intravasation into blood/lymph
3. Transport and survival in circulation
4. Extravasation into new tissue
5. Colonization and growth at new site

9. Angiogenesis

- The formation of **new blood vessels** to supply nutrients and oxygen to the growing tumor.

- **Angiogenesis is the process of forming new blood vessels from existing ones, and it plays a critical role in cancer growth and metastasis by supplying tumors with the necessary nutrients and oxygen.**

- Stimulated by **VEGF (Vascular Endothelial Growth Factor)**.

- Target for anti-cancer therapy (e.g., Bevacizumab).
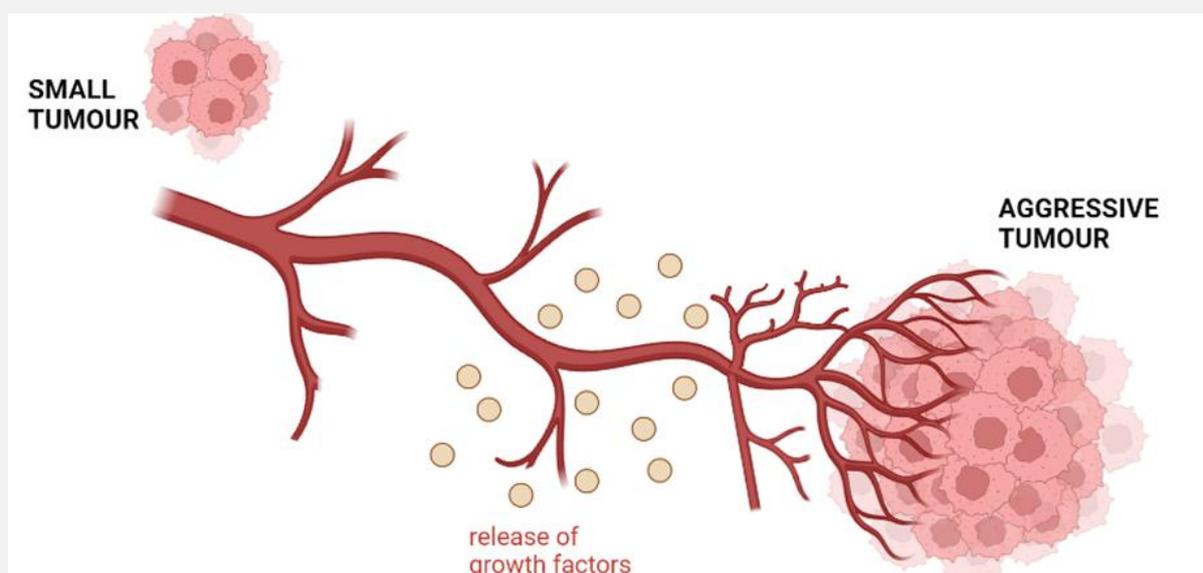
10. Diagnosis of Cancer

Diagnostic Method	Description / Purpose
Physical examination	Detect lumps, abnormal masses
Imaging	X-ray, CT, MRI, PET scan to detect tumors
Cytology	Pap smear (cervical cancer)
Histopathology	Biopsy — gold standard
Tumor markers	PSA (prostate), CEA (colon), AFP (liver), CA-125 (ovary)
Molecular tests	Gene mutation analysis (e.g., BRCA1/2, p53)

11. Treatment of Cancer

A. Surgery

- Removal of tumor (curative if localized).

B. Radiation Therapy

- Destroys DNA of rapidly dividing cells.

- Used alone or post-surgery.

C. Chemotherapy

- Cytotoxic drugs targeting dividing cells.

- Examples:

    - Alkylating agents: Cyclophosphamide

    - Antimetabolites: Methotrexate

    - Mitotic inhibitors: Vincristine, Paclitaxel

    - Topoisomerase inhibitors: Doxorubicin

D. Hormonal Therapy

- Used for hormone-dependent cancers:

    - Tamoxifen (anti-estrogen) → breast cancer

    - Flutamide (anti-androgen) → prostate cancer

E. Targeted Therapy

- Drugs target specific molecules involved in cancer growth:

    - Imatinib → inhibits BCR-ABL in CML

    - Trastuzumab → targets HER2 in breast cancer

    - Bevacizumab → anti-VEGF (angiogenesis inhibitor)

F. Immunotherapy

- Boosts the body's immune system to fight cancer.

    - Immune checkpoint inhibitors: Pembrolizumab (anti-PD-1)

    - CAR-T cell therapy

    - Interleukins and interferons

G. Gene Therapy (experimental)

- Replaces or modifies defective genes.

12. Prevention of Cancer

Primary Prevention

- Avoid tobacco, alcohol, and carcinogens

- Healthy diet (rich in fruits, vegetables, fiber)

- Regular exercise, maintain healthy weight

- Vaccination:

    - **HPV vaccine** (cervical cancer)

    - **Hepatitis B vaccine** (liver cancer)

Secondary Prevention

- Early detection and screening:
    - o Pap smear (cervical)
    - o Mammography (breast)
    - o Colonoscopy (colon)
    - o PSA (prostate)

13. Prognosis

- Depends on:
    - o Type and stage of cancer
    - o Presence of metastasis
    - o Patient's health and response to therapy
- **Early detection = better survival rate.**