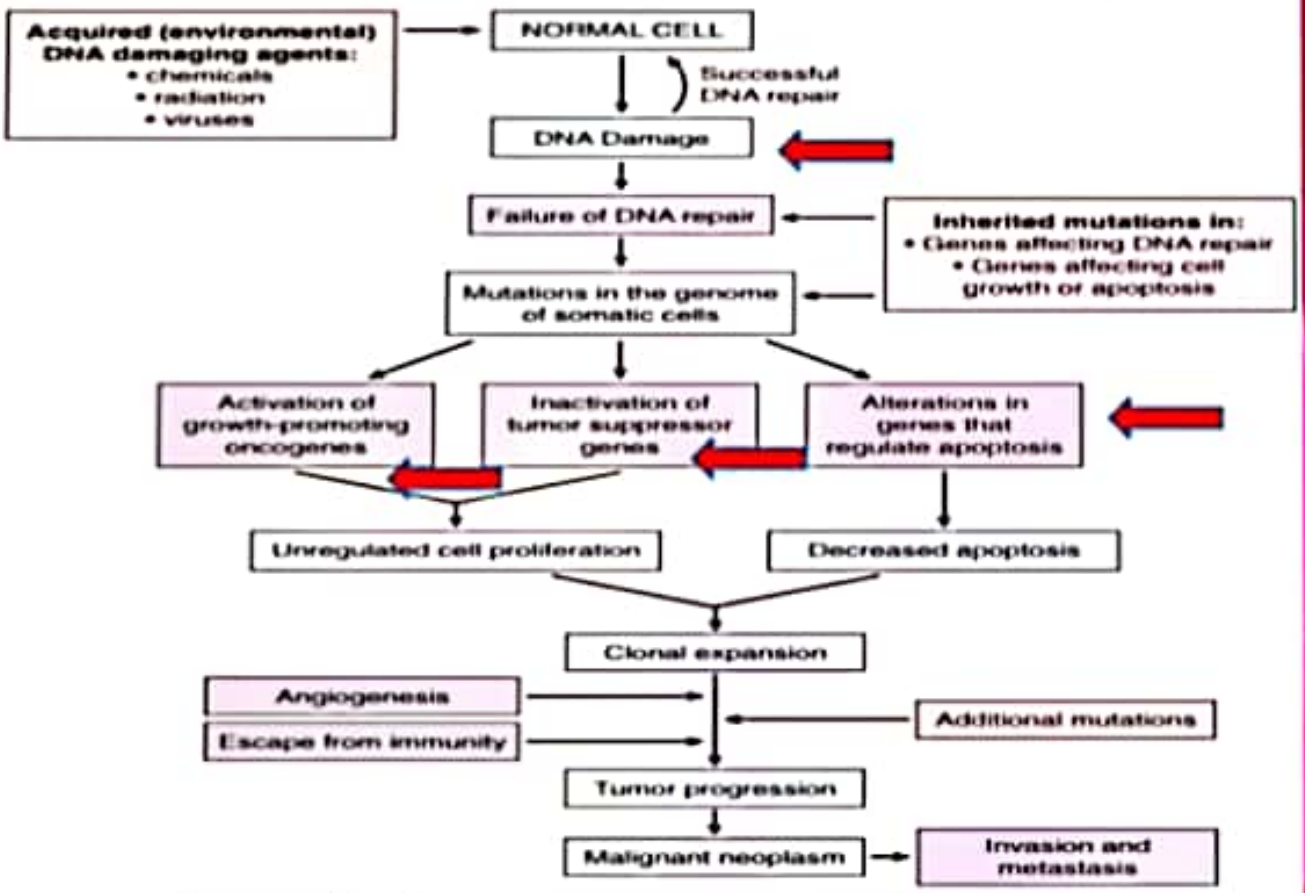
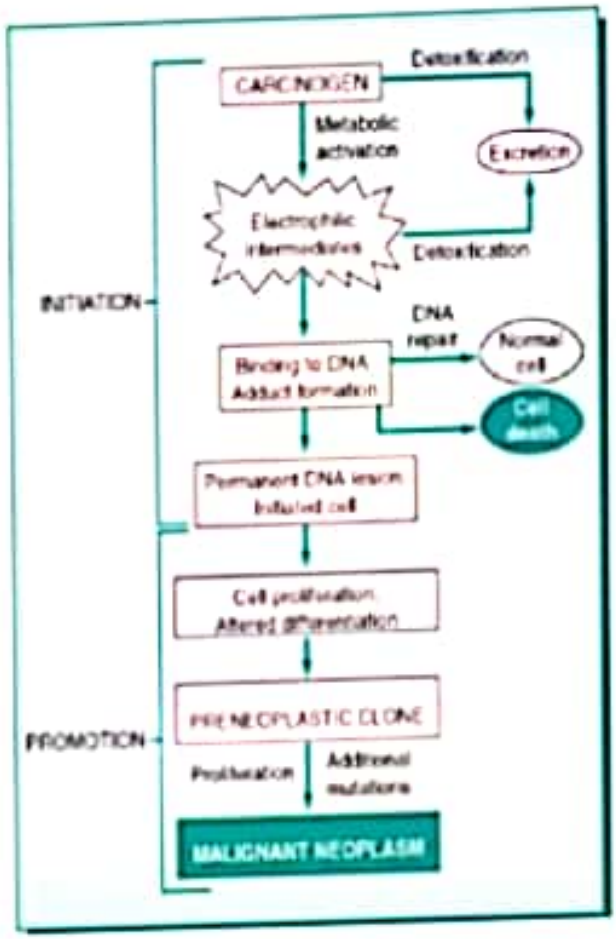
## Molecular Basis of Carcinogenesis:-

- Genes control <u>cell division</u> by cytokines.
- Four important classes of regulatory genes (for cell division):
  1. Promotors - Proto-oncogenes
  2. Inhibitors - Tumor or Cancer-suppressor genes - p53
  3. Genes regulating Apoptosis.
  4. DNA repair genes.



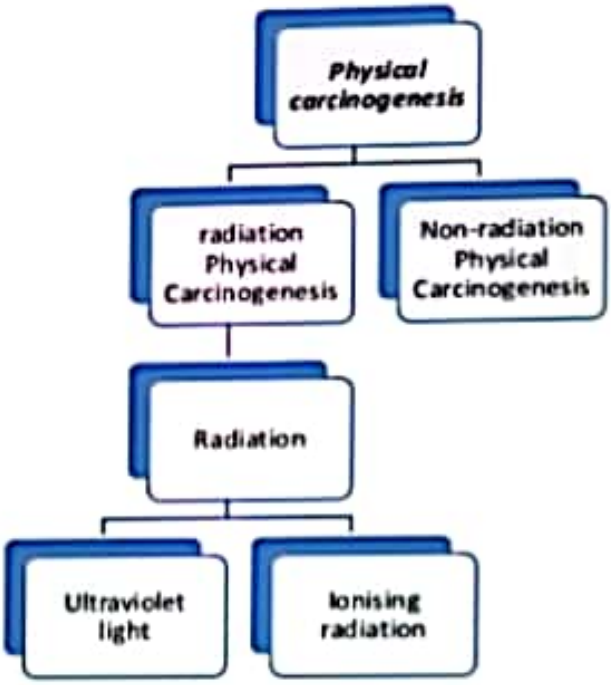
# Chemical Carcinogenesis:-

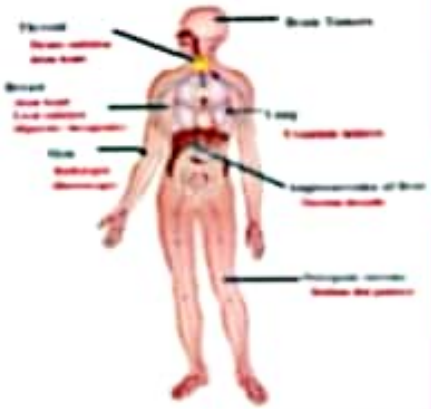
1. Biotransformation
2. Initiation: Covalent binding to DNA
3. Fixation: Mutation stabilized by mitosis
4. Gene expression, transformation
5. Neoplastic growth, proliferation
6. Progression, local effects
7. Metastasis




**Chemical Carcinogenesis**

# Physical carcinogenesis



## Radiation Carcinogenesis-

▶ **Ionizing radiation** → Carcinogenesis can result from ionizing radiation and may develop from 2 different mechanisms;

1. **Direct ionization** – damages DNA and other molecules can cause direct somatic mutations
2. **Secondary effectors** such as oxygen radicals can be formed by ionizing radiation. Oxygen free radicals can damage and kill cells and also induce mutations.

▶ **X Ray workers** - Leukemia

▶ **Radio-isotopes** - Thyroid carcinoma

▶ **Atomic explosion** - Skin cancer, Leukemia

## *Physical carcinogenesis*

- **Radiation- Ultraviolet light**
  - Causes: mutation, inhibits cell division and cell death
  - MOA: formation of pyrimidine dimer
  - Main source of UV light is sunlight, UV lamp and welder's arcs
  - Penetration of UV light protected by **melanin** pigmentation of the skin.

- Sun light → white race → basal cell carcinoma, squamous carcinoma and malignantmelanoma
- Sun light → darker races → protected by melanin pigment, which absorbs UV radiation
- Lifetime risk of 1 rad of whole-body x ray or gamma-ray radiation is one excess cancer death per 10,000 person

# Viral Oncogenesis

- Viruses contribute to the pathogenesis of human malignancies through the integration of viral genetic elements into the host DNA. These new genes are expressed by the host; they may

- Disrupt normal host genes required for control of cell growth and division (Alterations in Oncogenes, cancer suppressor genes and genes regulating DNA repair resulting in up-regulation of cell division → Carcinogenesis).

- Alternatively, viral infection may result in immune dysfunction, leading to decreased immune surveillance for early tumors.

- Human Papilloma Virus
  - Cervical neoplasia – warts, papilloma, ca cx
- Epstein-Barr virus –
  - Burkitts Lymphoma, Nasopharyngeal ca.
- Hepatitis B & C virus
  - Hepatocellular carcinoma.

## Classification of Carcinogens :-

### Genotoxic Carcinogen:-

Chemical capable of producing cancer by directly altering the genetic material of target cells.

- • DNA replication errors.
- • Point mutations.
- • Chromosomal aberration.

**1- Direct carcinogens** (no metabolic activation).

- Alkylating agents.

**2-Indirect carcinogens** (metabolic activation).

- Polycyclic aromatic hydrocarbons.
- Aromatic amines.
- Nitrosamines.
- Natural substances.

**3- Inorganic carcinogens.**

**4- Ni, Cr, Cd, As.**

### Epigenetic Carcinogen:-

- Non-DNA reactive.
- - Potentiators.
- - Ex.: hormone, immune function modifiers

**Cytotoxic carcinogens.**

- Nitrillotriacetate, BHA, BHT.

**• Tumor promotors.**

- DDT, Dioxin

**• Hormones.**

- Estradiol,

**• Immunosuppressants.**

- Cyclosporin A

**• Particulates.**

- Asbestos.

## Diet & nutrients protecting from cancer ;

- Fruits & vegetables
  - High level of fibers
  - Antioxidants which decrease damaging effects caused by free radicals and reactive oxygen species on DNA

Examples:

a- Tocopherol & β- carotene ( carotenoids), vit C : decrease tumor incidence.

b- Tomatos : contain lycopene protect against prostate cancer .

c- Green tea : contain polyphenols which act as antioxidants.

d- Red grapes : contain resveratrol which acts an antioxidant.

## Principle of Treatment :-

- Surgical therapy - early stage/debulk
- Chemotherapy
- Radiotherapy
- Immunotherapy