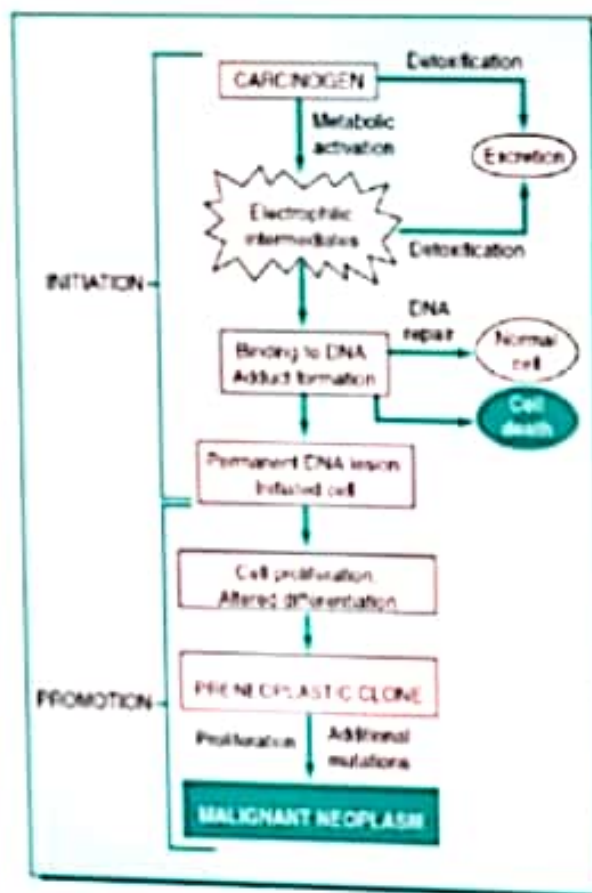


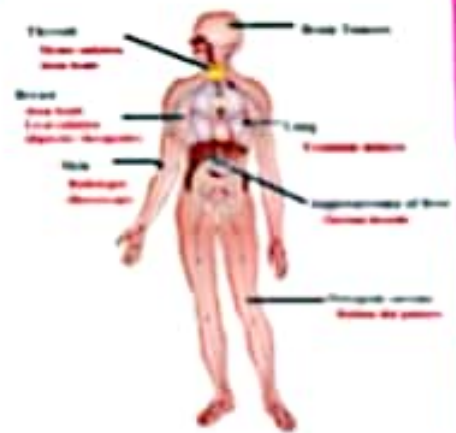
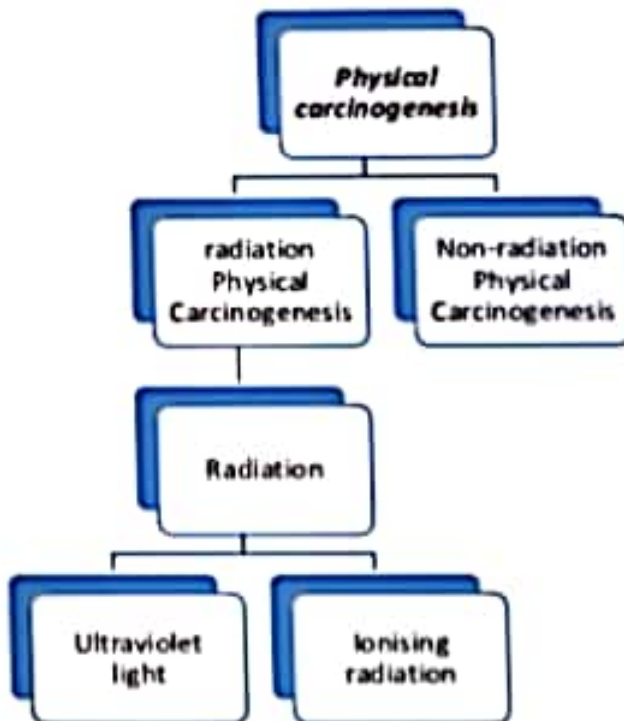
# Chemical Carcinogenesis:-

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 malignant melanoma
- 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.

- Nitrilotriacetate, BHA, BHT.

• Tumor promoters.

- 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 & B- 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