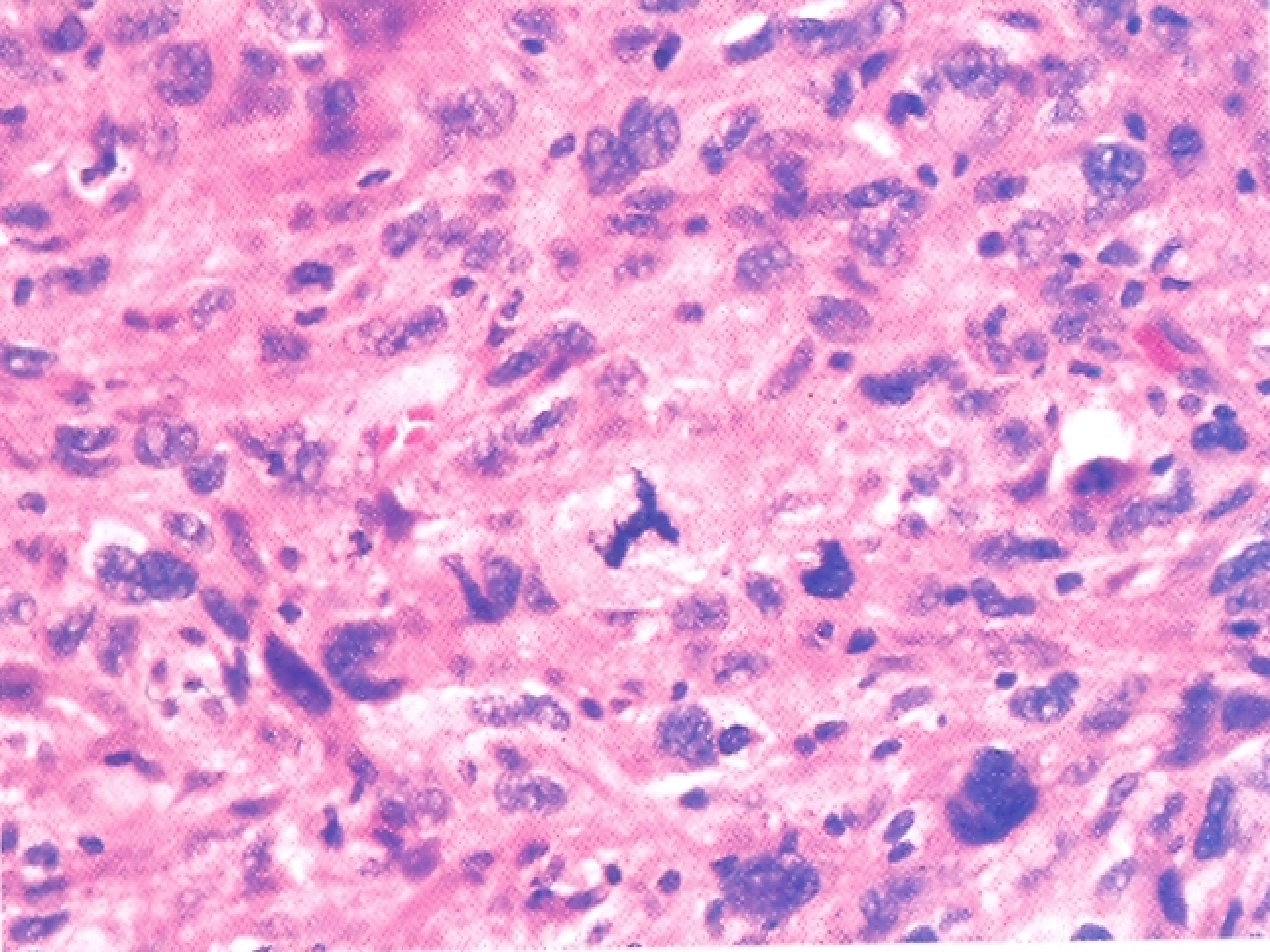
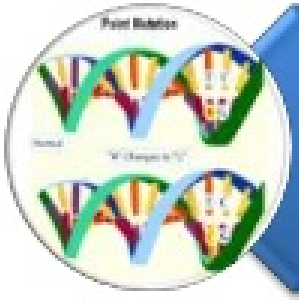


- (a) adenoma
- (b) Well diff. adenocarcinoma
- (c) Squamous cell carcinoma
- (d) Leiomyoma
- (e) Anaplastic carcinoma

- Which one of the following numbered sequences best illustrate the postulated sequence of events that precedes the formation of an infiltrating SCC of cervix
- 1. carcinoma in situ
- 2. Invasive ca
- 3. Mild dysplasia
- 4. Mod. Dysplasia
- 5. severe dysplasia
- 6. Sq. metaplasia

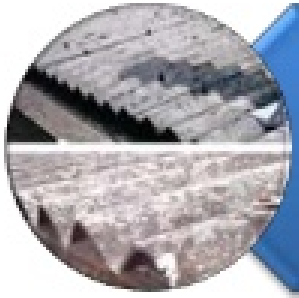
Causes of cancer

Three major type of carcinogens



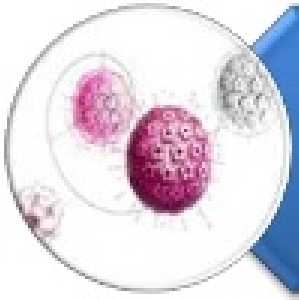
Chemical carcinogenesis

- Mutagens
- Chemical carcinogenesis and their metabolism



Physical carcinogenesis (radiation)

- Ultraviolet radiation, Asbestos



Infectious Pathogens (Viral)

- Human T-cell leukemia viruses, DNA viruses, Human papillomaviruses
- Epstein-Barr virus, Hepatitis B virus

CARCINOGENIC AGENTS

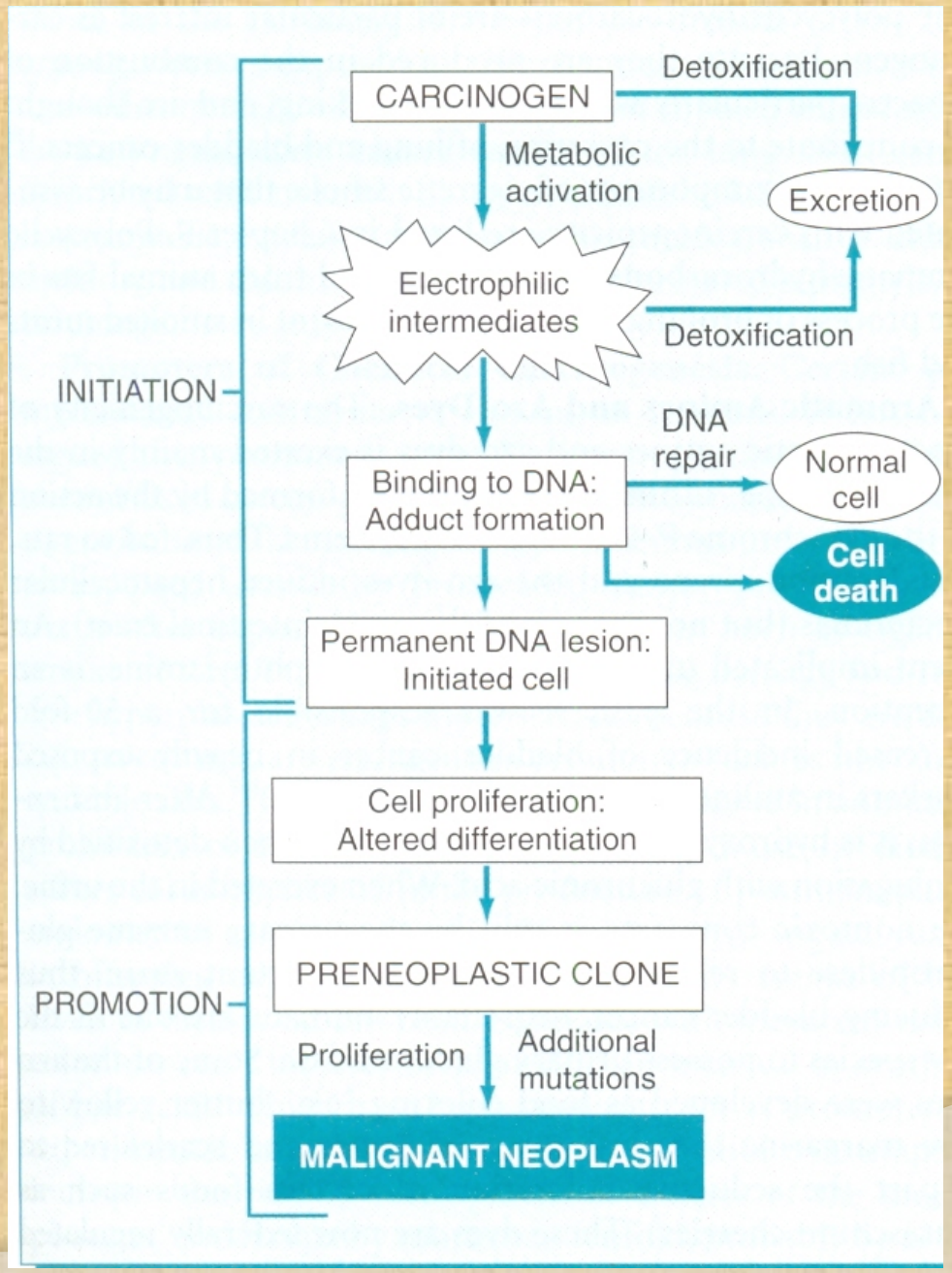
1. CHEMICAL CARCINOGENS
    1. Direct Acting
    2. Indirect Acting
2. RADIATION CARCINOGENS
3. MICROBIAL CARCINOGENS

CHEMICAL CARCINOGENS

- **1. DIRECT ACTING AGENTS**
- Require no metabolic conversion
- Weak carcinogens, imp b/c chemotherapeutic agents e.g; Alkylating agents---Evoke 2nd cancer, usually leukemia

2. INDIRECT ACTING AGENTS

- Requires metabolic conversion-**Procarcinogen**
- Polycyclic hydrocarbons e.g; Benzo(a)pyrine formed at high temp. from tobacco---leads to Ca lung
- Aromatic amines & azo dyes--β naphthalamine – Bladder ca
- Aflatoxin B1----------HCC
- Preservative- Nitrite...cause nitrosylation of amines in food---Carcinogenic


CARCINOGEN
Detoxification
Metabolic activation
Excretion
Electrophilic intermediates
Detoxification
INITIATION
DNA repair
Binding to DNA: Adduct formation
Normal cell
Cell death
Permanent DNA lesion: Initiated cell
Cell proliferation: Altered differentiation
PRENEOPLASTIC CLONE
PROMOTION
Proliferation
Additional mutations
MALIGNANT NEOPLASM

STEPS INVOLVED IN CHEMICAL CARCINOGENESIS

- Initiation results from exposure of cells to a sufficient dose of carcinogenic agent (initiator) an initiated cell is altered, making it potentially capable of giving rise to a tumor. Initiation alone, however, is not sufficient for tumor formation.
- Initiation causes permanent DNA damage (mutations). It is therefore rapid and irreversible and has memory.
- Promoters can induce tumors in initiated cell but they are nontumorigenic by themselves.

MOLECULAR TARGETS OF CHEMICAL CARCINOGENS

- Ames test, is used to check the ability of chemicals to induce mutations in microorganisms (70% to 90%).
- DNA is a primary target for chemical carcinogens and result is DNA damage which may be repaired by several enzymes if damage is beyond the repairing capacity of individual damage may initiate the tumorogenic effect by causing mutations in RAS and p53 (finger prints)

TABLE 7–11 Major Chemical Carcinogens

Direct-Acting Carcinogens

Alkylating Agents

β-Propiolactone
Dimethyl sulfate
Diepoxybutane
Anticancer drugs (cyclophosphamide, chlorambucil, nitrosoureas, and others)

Acylating Agents

1-Acetyl-imidazole
Dimethylcarbamyl chloride

Procarcinogens That Require Metabolic Activation

Polycyclic and Heterocyclic Aromatic Hydrocarbons

Benz(a)anthracene
Benzo(a)pyrene
Dibenz(a,h)anthracene
3-Methylcholanthrene
7,12-Dimethylbenz(a)anthracene

Aromatic Amines, Amides, Azo Dyes

2-Naphthylamine (β-naphthylamine)
Benzidine
2-Acetylaminofluorene
Dimethylaminoazobenzene (butter yellow)

Natural Plant and Microbial Products

Aflatoxin B_1
Griseofulvin
Cycasin
Safrole
Betel nuts

Others

Nitrosamine and amides
Vinyl chloride, nickel, chromium
Insecticides, fungicides
Polychlorinated biphenyls

RADIATION CARCINOGENESIS

- Radiation is an established carcinogen
- 10 fold inc. in Ca Lung in miners of radioactive elements
- Atomic bomb survivors—AML, CML- 7 yrs, thyroid, breast, colon & lung Ca.
- Therapeutic irradiation of H&N- papillary Thyroid ca

- Ionizing radiation causes chromosomal breakage, translocations & less frequently point mutations
- Radiation causes formation of pyrimidine dimers within DNA, leading to mutations
- SCC, BCC, Melanomas