NEOPLASIA III

WHAT IS THE PREVALENCE OF CANCER?

- Cancer occurs in all parts of the world. It affects animals as well as humans. However, the types of cancer most prevalent in a community will vary with the age, sex distribution and race, geographical situation, the economic and environmental situation and habits of the people including their diets.

- In developed countries cancer is responsible for about 25–30% of deaths. It is second to cardiovascular disease as a cause of death.
- Although cancer can occur at any age it is relatively uncommon before the age of 40 years but as people grow older the risk of cancer progressively increases.

What is a carcinogen?

- A carcinogen is any substance or agent that, because of the way it affects cell DNA, can cause cancer
- Carcinogens may be *chemical substances*; *physical agents*, such as asbestos dust; or *biological agents*, such as certain viruses and bacteria
- In the workplace, carcinogenic substances may be inhaled, absorbed through the skin or even ingested in some cases

WHAT ARE CARCINOGENS?

- Carcinogens are cancer-inducing factors that can be classified as:
- & Physical forces—UV light, x-rays, and gamma radiation
- & Chemicals
- & Viruses
- & Endogenous oncogens

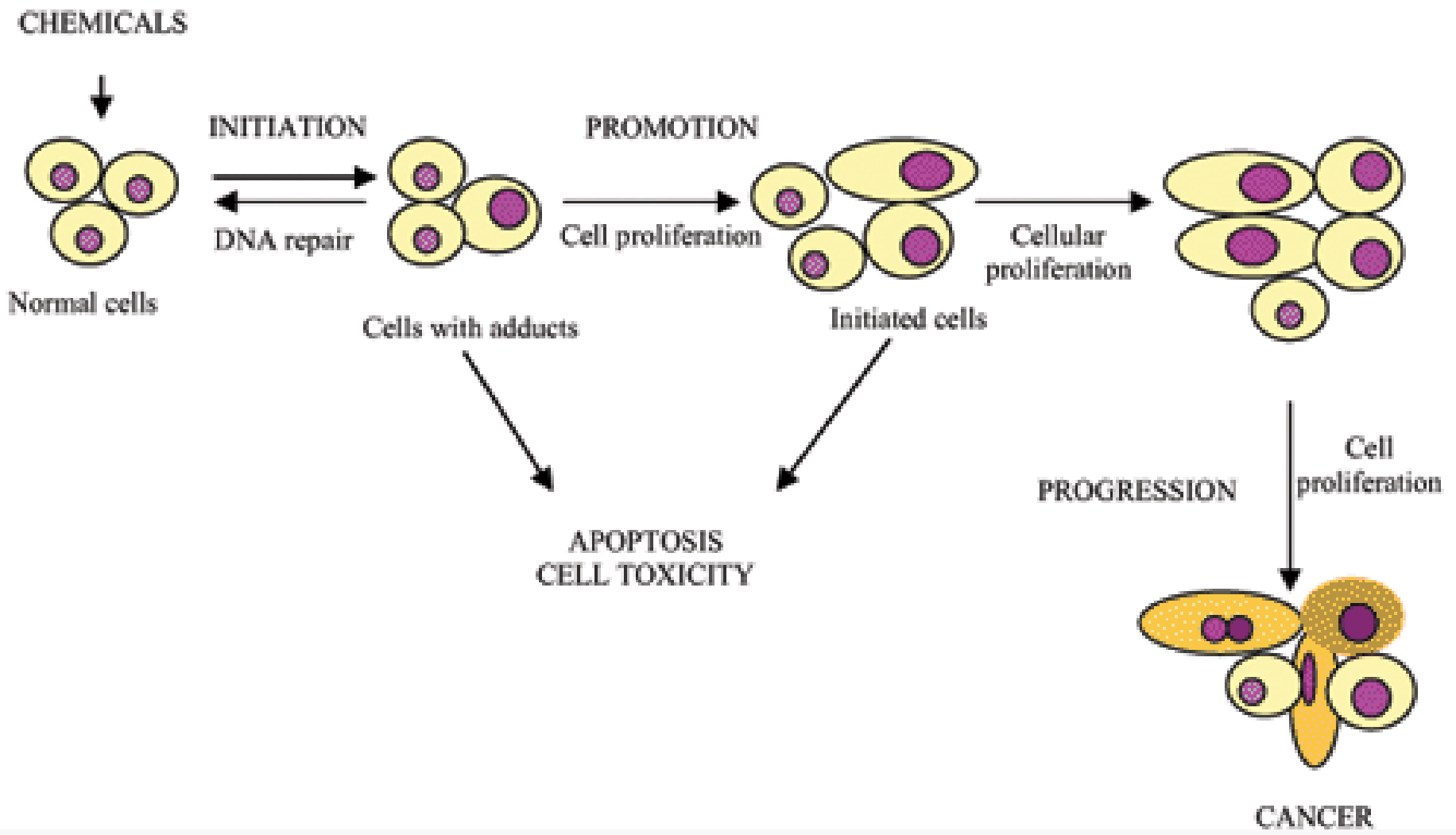
- Initiation: This is the first step that will induce the irreversible but not lethal change in the genetic material of the affected cell.
- Promotion: This is the second step required for the formation of tumor. It promotes the replication of the initiated cells. Promoters cannot induce cancer on their own. Some carcinogens may act as initiators and promoters.
- Progression: This is the third phase of tumor formation in which the growth of tumor
- becomes autonomous.

WHAT IS THE DIFFERENCE BETWEEN DIRECT-ACTING AND INDIRECT CARCINOGENS?

- Direct-acting carcinogens (e.g., some metals such as nickel): they capable of binding to the DNA and directly causing genetic damage.
- Indirect carcinogens: must be metabolized into an active form that can bind to the DNA. Typical examples are:

- ○ Polycyclic hydrocarbons from cigarette smoke are metabolized by cytochrome P450 into DNA-binding epoxides in the bronchial epithelium.
- ○ Aromatic amines ingested in food are metabolized in the liver, and are excreted in urine. These carcinogens act on the transitional epithelium of the urinary bladder.

STAGES OF CARCINOGENIC AGENTS EFFECT



- Polycyclic aromatic hydrocarbons: lung cancer and skin cancer
- Benzene: leukemia
- Aflatoxin B-1: toxin produced by Aspergillus flavus that grows on moldy grains and peanuts; cause of liver cancer
- Nickel: cancer of nasal cavity and lungs
- Arsenic: skin cancer
- Asbestos: mesothelioma

RADIATION CARCINOGENESIS

- UV rays of sunlight, x-rays, nuclear fission, radionuclides are sources of carcinogenic agents.
- Ionizing radiation causes chromosome breakage, translocations, and, less frequently, point mutations, leading to genetic damage and carcinogenesis.
- UV rays induce the formation of pyrimidine dimers within DNA, leading to mutations. Therefore, UV rays can give rise to squamous cell carcinomas and melanomas of the skin.

VIRAL AND MICROBIAL ONCOGENESIS

- Human papilloma virus (HPV) subtypes 16 and 18 are implicated in the pathogenesis of carcinoma of the cervix and the lower female genital tract.
- Epstein-Barr virus has been associated with Burkitt lymphoma and nasopharyngeal carcinoma.
- Hepatitis virus B and C chronic liver disease has been associated with hepatocellular carcinoma.
- Herpes virus 8 has been isolated from cells of Kaposi sarcoma.

HELICOBACTER PYLORI INFECTION

- H. pylori–induced gastric cancers by chronic inflammation, stimulation of gastric cell proliferation, and production of reactive oxygen species that damage DNA.
- H. pylori infection leads to polyclonal B cell proliferations and that eventually a monoclonal B cell tumor (MALT lymphoma) emerges as a result of accumulation of mutations.

ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

- It attackes immune defences mechanism against infection resulting in a higher incidence of cancer developing in affected people.
- Several cancers are now commonly associated with HIV infection or AIDS. These include Kaposi's sarcoma, lymphomas ,non-Hodgkin lymphoma and cancer of the cervix

CONDITIONS RELATED TO CANCER DEVELOPMENT

- **Pre-Existing Abnormalities** chronically inflamed or ulcerated tissues, or severely scarred tissues (Ex; chronic ulcer, severe burn,polyps, papillomas and adenomas)
- **Nutritional Deficiencies and Food Habits:** High animal fat content of food appears to be associated with increased risk of some cancers; whilst a diet rich in fresh fruit and vegetables appears to be protective.

HOW DOES THE HOST REACT TO NEOPLASIA?

- Host reaction can be considered under two headings:
- Local tissue reaction, such as formation of tumor stroma & Systemic reaction, such as immune response

- Desmoplasia is a term for the formation of connective tissue in response to tumors. It may be a defense mechanism used by the body to wall off the tumor and limit the invasive growth of tumor cells. On the other hand, the connective tissue stroma provides a framework for the growth of tumors and protects them mechanically from outside damage. Stroma also contains blood vessels that are essential for the nourishment of tumor cells.

What are tumor markers?

They are substances that are secreted by tumor cells or released from the surface of tumor cells into the circulation.

These substances can be classified as:

& carcinoembryonic antigen

& alpha-fetoprotein

& Enzymes (e.g., lactate dehydrogenase and prostate-specific antigen)

Hormones (e.g., insulin, and calcitonin)

& Biogenic amines (e.g., norepinephrine)

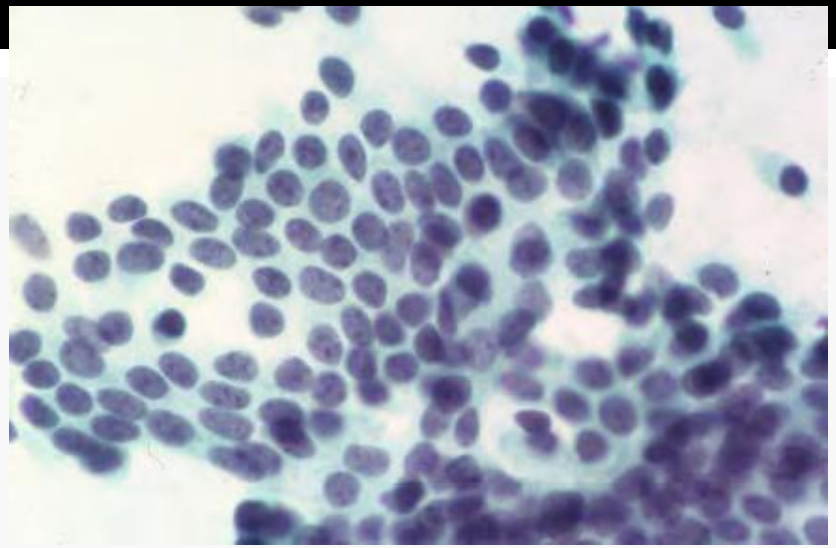
CLINICAL ASPECTS OF TUMORS

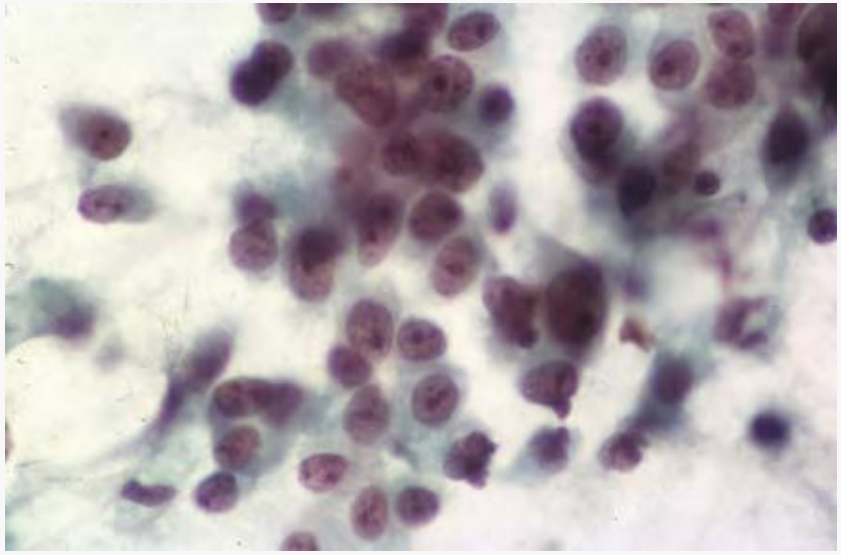
- Cachexia is loss of body weight accompanied by weakness and exhaustion. It may be caused by large tumors that act as parasites draining energy and nutrients. In other cases, tumors inhibit nutrition (e.g., carcinoma of the esophagus prevents swallowing). Other tumors secrete cytokines, such as tumor necrosis factor, which promote catabolism and loss of fat tissue and muscles.

- Paraneoplastic syndromes include signs and symptoms caused by tumor effects:
- Unrelated to the mechanical effects of the tumor mass or distant metastases
- May result from substances released from tumor cells but not found in the normal cells from which the tumor has originated
- May result from a series of immunologic and other host reactions to tumor
- May have a complex and not fully understood pathogenesis

- Grading of tumors is determined by cytological appearance and is based on the idea that behavior and differentiation are related, with poorly differentiated tumors having more aggressive behavior.
- Staging, determined by surgical exploration or imaging, is based on size, local and regional lymph node spread, and distant metastases. Staging is of greater clinical value than grading.

LABORATORY DIAGNOSIS OF CANCER





- Biopsy
- cytology
- Immunohistochemis try
- DNA microarray
- Immunofluorescent
- polymerase chain reaction

- Cancer grading gives an indication of the likely aggressiveness of the cancer, Grading of tumors is determined by cytological appearance and is based on the idea that behavior and differentiation are related, with poorly differentiated tumors having more aggressive behavior.

- • Staging, determined by surgical exploration or imaging, is based on size, local and regional lymph node spread, and distant metastases. Staging is of greater clinical value than grading because it determine type of treatment modalities and the extent of surgical intervention.

Suggestive Reading

Vinay Kumer, Apul L. Abbass, Jon C. Aster. Rubbin Basic pathology, Elsevier, 9th edition, 2013

THANK YOU