**Lecture 8**

**CARCINOGENS**

Several agents have been shown to be associated with cancer, carcinogens.

**Carcinogens** are substances that are capable of producing neoplastic growth. They are known to increase the likelihood that exposed individuals will develop a neoplasm. There are three broad classes of carcinogens.

*Chemical carcinogens*

1. Polycyclic aromatic hydrocarbons include tobacco smoke, exhaust fumes, and products of combustion. They may cause cancers of the lip, tongue, oral cavity, head, neck, larynx, lungs and bladder.
2. Aromatic amines and azodyes include certain foods; naphthalene (used in some moth repellants and insecticides). They may cause cancer of the bladder.
3. Alkylating agents include nitrogen mustard and mustard gas.

They may cause leukemia or lymphoid neoplasms.

1. Nitrosamines include food converted to nitrosamines gastric carcinoma.
2. Naturally occurring products such as Aflatoxin B, (Aspergillus fLavus) found on corn, barley, peas, milk, and cheddar cheese, may cause cancer of the nuts may cause cancer of the oral cavity.
3. Several drugs, such as griseofulvin and flagyl, may affect certain carcinomas as shown in laboratory rats. DES may cause cancer of the vagina in female offspring and testicular cancer in male offspring.

Alcohol may cause cancers of the mouth, pharynx, esophagus, larynx and liver.

1. Metals such as asbestos, cadmium, chromium. and nickel may cause cancer of the lung. nasal cavity, prostate, pleural cavity, and gastrointestinal tract.
2. Industrial compounds such as polyvinylchloride (used to manufacture plastics) may cause angiosarcoma of the liver.

*Physical carcinogens*

Ionizing radiation from the atomic bomb may cause direct or indirect damage to DNA resulting in leukemia.

Ultraviolet radiation from sun exposure may cause skin cancer.

*Biologic carcinogens*

Oncogenic viruses. Many viruses are implicated in human cancers including; Epstein-Barr virus in association with Burkitt's lymphoma and cancer of the nasopharynx, Human Papilloma virus in association with penile and cervical cancer

Schistosoma haematobium is a parasitic infestation may cause squamous cell cancer of the bladder.

*Other factors in carcinogenesis*

Injections of mineral oil into the peritoneal cavity may cause granulomatous inflammation, which may be followed by plasma cell tumors.

Asbestos fibers exposure may lead to mesothelioma of the lung.

Cigarette smoking may cause bronchogenic or gastric carcinoma with continuous exposure.

Pipe smoking may cause oral cancer.

Diet: High-fat and low-fiber diets are linked to cancer of the colon and breast while some food preservatives (e.g., those used for salting, drying or charring) may increase the risk of stomach cancer.

Sexual exposure: Women who become sexually active at an early age or who have multiple sexual partner are at an increased risk of developing cervical cancer.

Jewish men, circumcized shortly after birth, have low rates of cancer of the penis.

Early menarche, nulligravida,or late menopause may increase the risk of breast cancer in women.

Social habits: Heavy drinkers have an increased risk of cancer of the esophagus and cigarette smokers have an increased risk of lung cancer.

Hormones: Increased hormone levels over a period of time may cause cancer of the breast, endometrium, vagina, prostate, thyroid, or adrenal cortex.

Premalignant lesions: Fibrocystic disease of the breast may increase the risk of breast cancer. Adenomatous colon and rectal polyps may be precancerous.

*Staging of Neoplasms*

* To determine the extent of the tumor.
* To ascertain proper treatment.
* To evaluate survival rates.
* To establish the relative merits of different methods of treatment.
* To facilitate an exchange of information among treatment centers.

*Dissemination*. The most common routes of metastasis are through the lymphatic and blood vessels.

***Lymphatic dissemination*** - tumor penetrates small lymphatic vessels where emboli are shed and trapped in the first lymph node encountered. The lymph node often enlarges and the body's immune defense system is called upon to filter the tumor cells from circulation. The main venous-lymphatic communication is the thoracic duct where lymphatic fluid empties into the venous circulation.

 ***Bloodstream dissemination*** - Metastasis requires entrapment in the capillary bed of distant organs.

 Fibrin deposits protect the newly formed tumor from destruction by immune defensive cells. After the tumor reaches the lungs, it may break into branches of the pulmonary veins and be released into the systemic circulation to travel to the brain or viscera. Shedding into the portal venous system may lead to liver metastasis. Arrest and establishment:

* The growth of the spreading malignant cells is arrested once the clump exceeds 2 cm in diameter.
* In order to ensure further development. the clump establishes its own blood supply.
* This blood supply is the factor that changes a self-contained clump of malignant cells into a rapidly growing metastatic tumor.
* New capillaries are formed and they grow toward and penetrate the malignant cells creating their own blood supply.
* Proliferation. The malignant cells adjust their environment to further their own growth by establishing their own nutritional and waste system.

***Sites of metastasis***

The patterns of metastasis are determined by individual cellular characteristics and by environmental factors. Certain neoplasms metastasize more readily to specific sites (e.g breast cancer to lungs and brain). The site of metastasis may be similar to the primary growth site.

***Host Defense Mechanisms in the Control of Neoplasia:*** Some human tumors have tumor-specific antigens on their cell surfaces, or some other substances. These substances may be produced by the tumour cells or by the host cells in response to the presence of the tumour. These include the following.

***Oncofetal antigens***. These antigens are normally present during embryonic development and are reexpressed in neoplastic tissue. The markers include the following.

CEA--carcinoembryonic antigen.

AFP--alphafetoprotein.

GCDP--gross cystic disease protein.

***Lineage-associated antigens***. These antigens are noted in several solid tumors. They may prove useful for monitoring gastrointestinal and ovarian tumors.

***Differentiation antigens***. These antigens are still being studied to determine the significance of their presence in lymphocytic and

lymphoblastic leukemia.

***Histocompatibility antigens***. These antigens are being studied in neoplastic tissue in order to use a host-versus-tumor reaction to destroy the tumor or metastasis.

These compounds may be used to indicate the presence of a tumour in the following ways:

* Screening: detection of subclinical cancer
* Diagnosis: detection of symptomatic cancer
* Monitoring treatment
* Monitoring the course of the cancer
* Prognosis: to determine the possible outcomes from the cancer

*Clinical Manifestations of Neoplasms*. The earliest stages of both benign and malignant neoplasms are asymptomatic. As size increases, local alterations in function occur. As malignant neoplasms metastasize, function at these sites is impeded and biochemical balance within the body is disrupted. Local manifestations depend on the location and size of the space that is occupied and systemic features may be experienced generally in the whole body.