

CANCER

TYPES OF CANCER

Cancer is not one single disease but a complex of many diseases. About two hundred distinct types of cancer have been recognized. These can be grouped into four main types: carcinomas, sarcomas, lymphomas and leukemias

1. **Carcinomas** - are tumours made up principally of epithelial cells of ectodermal or endodermal origin. The solid tumours in nerve tissue and in tissues of body surfaces, or their attached glands, are examples of carcinomas. These include cervical, breast, skin and, brain carcinomas. About 85 per cent of cancers are carcinomas.
2. **Sarcomas** are tumours made up principally of connective tissue cells, which are of mesodermal origin. They are solid tumours growing from connective tissue cartilage, bone and muscle. Although they account for most of the cancers studied in laboratory animals, they constitute only about 2 per cent of human cancers.
3. **Lymphomas** are, cancers in which there is excessive production of lymphocytes by the lymph nodes and spleen. Hodgkins disease is an example of a lymphoma. Lymphomas constitute about 5 per cent of human cancers.
4. **Leukemias** are neoplastic growths of leucocytes (W. B. C) and are characterized by excessive production of the cells.

CHARACTERISTICS OF CANCER CELLS

1. **Immortalization.** Normal cell cultures do not survive indefinitely. For example human cell cultures die after about 50 generations, and chicken cell cultures have a much shorter life expectancy. On the other hand transformed cell cultures are immortal and can grow indefinitely.
2. **Loss of contact inhibitions.** Normal cells in a culture stop growing when their plasma membranes come into contact with one another. When two normal cells come into

contact, one or both will stop moving and then begin to move in another direction. This inhibition of growth after contact is called contact inhibition.

3. **Reduced cellular adhesion**

When normal cells become cancerous there is a change in the 'stickiness' of their cell membranes. Normal cells show stickiness or adhesiveness. If grown in a nutrient medium kept in a glass vessel, the cells stick to the glass rather than float in the medium. Transformed cells show a decreased adhesiveness, and if grown in solid media stick to each other less than do normal cells.

4. **Invasiveness.** One of the most important characteristics of transformed cells is their invasiveness, i.e. the ability to invade other tissues.

5. **Loss of anchorage dependence**

Most normal cells must be attached to a rigid substratum (i.e. they must be anchored) in order to grow. Transformed cells can grow even when they are not attached to the substratum, as for example when they are suspended in a semisolid medium containing agar or methyl cellulose.

6. **Disorganisation of the Cytoskeleton** - Normal cells have a cytoskeleton (very much like muscle fibres) which consists of microtubules and microfilaments. These fibres have a regular arrangement and bring about coordinated cell movement. In transformed cancer cells the fibres are much fewer in number and usually much thinner. It has been suggested that in transformed cells the cytoskeleton undergoes depolymerization.

THEORIES OF CAUSES OF CANCER

Somatic Mutation Hypothesis - According to this hypothesis cancer is the result of somatic mutations (i.e. mutations not involving germ cells), without viral infection occurring in a cell. Such a mutation may alter the control mechanism of the cell, leading to unregulated division or cancer. The mutations may involve the activation of normally repressed genes. This could take place by.

(i) Mutations in the repressed genes themselves, or

(ii) Mutations that block the production of repressor proteins, thus unblocking inactive genes and making them active. Most cancerous cells have abnormal chromosomal components. Often there are different numbers of chromosomes in different cells of one tumour.

Viral Gene Hypothesis- There is convincing evidence that viruses cause a number of specific cancers in animals. Viruses causing malignant tumours have been isolated from many animals including fish, frogs, mice, rats, squirrels, dogs, deer and horses. The polyoma virus has been isolated from mice and the simian virus 40 (SV 40) from monkeys. Tumour producing viruses are called oncoviruses.

Defective Immunity Hypothesis - According to the defective immunity hypothesis the defense mechanism fails under certain conditions and tumours are formed. This may be because the number of immune lymphocytes may not be large enough to block tumour development.

EXTRINSIC CAUSES

Physical Causes

Physical Agents Ultraviolet and high-energy radiation are causative agents for human and animal cancer. High levels of radiation like those from radiation therapies and x-rays (repeated exposure) can damage normal cells and increase the risk of developing leukemia, as well as cancers of the breast, thyroid, lung, stomach and other organs. A correlation exists between exposure to the Sun's ultraviolet rays and the occurrence of skin cancer in humans. Cancers caused by radiation include leukemia, and cancer of the thyroid, breast, stomach, uterus, and bone. Routine diagnostic tools such as X rays are used with care so that a person is not overexposed. UV radiations from the sun are directly linked to melanoma and other forms of skin cancer. These harmful rays of the sun cause premature aging and damage the skin. Artificial sources of UV radiation, such as sun lamps and tanning booths, also increase the risk of skin cancer. By wearing protective clothing and sunscreens and by avoiding prolonged exposure to the sun, one may reduce the risk of skin cancer.

Chemical causes

A chemical carcinogen is an environmental chemical that can interact with cells to initiate cancer, usually by chemically altering the chromosomes or genes in cells. Genes are responsible for manufacturing the enzymes and other proteins a cell needs to function properly. An altered gene usually makes an abnormal protein that may change the growth properties of a cell and cause it to become a cancer cell.

Many chemicals that are developed are now tested to determine their cancer-causing potential. Unfortunately, many thousands of chemical substances already in use have not been adequately tested. Of the thousands of chemical substances that have been tested, many have been found to be carcinogenic and should be avoided if at all possible. Carcinogens include cigarette smoke, pesticides, asbestos, heavy metals (lead, mercury, cadmium), benzene, and nitrosamines.

Some of the chemicals that cause cancer are:

Asbestos	- Lung
Benzene	- Leukemia
Carbon tetra chloride	- Liver
Mustard Gas	- Lung, Larynx
Vinyl Chloride	- Liver, Lung, brain
Soot & Tar	-Skin, Lung, Bladder
Tobacco	- Lung, oral, larynx, oesophagus, stomach, pancreas,

Biological Causes (Virus)

There are many viruses which are capable of causing tumours in animals. These viruses are called as oncoviruses or tumour viruses. Some tumour viruses have RNA genome and are called as RNA viruses or Retroviruses. Some have DNA genome and are called as DNA viruses.

The DNA tumour viruses are collectively known as PAPOVA viruses. The name PAPOVA has been derived from the first two letters of three types: **P**apilloma virus, **P**olyoma virus and **V**acuolating virus.

Some of the DNA tumour viruses, their genome size and the tumours caused are summarized in the table below:

Sr. No.	Name of the virus	Genome size	Tumour caused
1.	Herpes Virus	100-200 Kb	Burkitt's Lymphoma by Epstein Barr virus
2.	Papilloma Virus	8Kb	Warts, cervical cancers
3.	Polyoma Virus	5Kb	Tumours in mice
4.	Hepatitis B virus	3 Kb	Liver cells

The RNA tumour viruses are classified as retroviruses. The RNA genome makes a DNA copy with the help of an enzyme called as *reverse transcriptase*. All retroviruses do not cause cancer.

The first cancer causing gene was found in the retrovirus called **RSV, Rous Sarcoma Virus**, that produces sarcoma in chicken.

INTRINSIC CAUSES

Somatic mutations:

The majority of human cancers result from an accumulation of somatic mutations. Somatic mutations are not passed on to the next generation. These changes are acquired during a person's lifetime from exposures to carcinogens and other mutagens, or from random unrepaired errors that occur during routine cell growth and division. Occasionally, one of these somatic mutations alters the function of some critical genes, providing a growth advantage to the cell in which it has occurred. Genes known as Tumour Suppressor Genes are known to control the multiplication of cells under normal conditions. It is believed that mutation in these tumour suppressor genes may lead to removal of that control and hence cancer.

Oncogenes:

Oncogenes are the genes that promote the loss of growth control and malignancy. Oncogenes arise from proto-oncogenes. **Proto-oncogenes** are the genes that encode the proteins having a role in cell's normal activities. Mutations in proto-oncogenes cause them to act abnormally and promote the formation of tumour. Most of the known oncogenes are derived from proto-oncogenes that play a role in transmitting signals to the nucleus. Oncogenes encode proteins that control cell proliferation, apoptosis, or both. The products of oncogenes can be classified into six broad groups: transcription factors, chromatin remodelers, growth factors, growth factor receptors, signal transducers, and apoptosis regulators.

Ageing

The aging of the body may not directly affect cancer risk, but instead it may be that the cumulative exposure to cancer-causing substances over time eventually leads to the disease in some individuals.

With some exceptions, most types of cancer become increasingly common with age. In animals, there is a sudden dramatic rise in cancer incidence when they reach half their maximum possible life span, yet most individual animals die of other causes before cancer can develop.

It is believed that telomeres play important role in ageing and hence cancer. At the ends of the chromosomes are stretches of DNA called telomeres, which protect our genetic data, make it possible for cells to divide and hold some secrets to how we age and get cancer. Each time a cell divides, the telomeres get shorter. When they get too short, the cell no longer can divide and becomes inactive or "senescent" or dies. This process is associated with aging, cancer and a higher risk of death.

The cancerous cells produce enzyme telomerase which does not allow the shortening of telomeres with cell division. Studies have found shortened telomeres in many cancers, including pancreatic, bone, prostate, bladder, lung, kidney, and head and neck.