# CHILDREN AND CANCER

**KAMALA KANT PARASHAR**
Asstt. Prof. (Panna Dhi Maa Subharti Nursing College,
Swami Vivekananda Subharti University, Meerut, UP, INDIA
Email: kkparashar.kant@gmail.com

**Abstract:** Cancer is an abnormal growth of cells which tend to proliferate in an uncontrolled way and, in some cases, to metastasize (spread). Cancer can involve any tissue of the body and have many different forms in each body area. Most cancers are named for the type of cell or organ in which they start. If a cancer spreads (metastasizes), the new tumor bears the same name as the original (primary) tumor. Cancer is the Latin word for crab. The ancients used the word to mean a malignancy, doubtless because of the crab-like tenacity a malignant tumor sometimes seems to show in grasping the tissues it invades. Cancer may also be called malignancy, a malignant tumor, or a neoplasm (literally, a new growth).

**Key words:** Cancer HBV, EBV, Chemotherapy, Radiotherapy, BONE MARROW.

## INTRODUCTION:

A cancer diagnosis is upsetting at any age, but especially so when the patient is a child. Childhood cancer is the second leading cause of death in children aged 1 to 14 years. During childhood there are changing incidences for various types of cancer. For children in all pediatric age-group, leukemia is the most frequent type of cancer, followed by brain tumors and lymphoma.

## RISK FACTORS:

Familial and genetic factors are identified in 5-15% of childhood cancer cases. In <5-10% of cases, there are known environmental exposures and exogenous factors, such as prenatal exposure to tobacco, X-rays, or certain medications. For the remaining 75-90% of cases, however, the individual causes remain unknown. In most cases, as incarcinogenesis in general, the cancers are assumed to involve multiple risk factors and variables.

Aspects that make the risk factors of childhood cancer different from those seen in adult cancers include:

- Different, and sometimes unique, exposures to environmental hazards. Children must often rely on adults to protect them from toxic environmental agents.
- Immature physiological systems to clear or metabolize environmental substances
- The growth and development of children in phases known as "developmental windows" result in certain "critical windows of vulnerability".
  - Life style
  - Passive smoking
  - Neglect child
  - Broken family
  - Parental relationship
  - Dietary pattern

## ETIOLOGY:

Cancer-causing agents can be categorized into three groups:

1. oncogenic viruses,
2. chemicals, and
3. Radiation.

All three lead to the molecular mechanisms of cancer described in the section

### 1. Oncogenic viruses

A large number of DNA and RNA viruses cause tumours in animals, but in humans it is the DNA viruses that are implicated in most forms of cancer. Only one RNA virus is known to cause cancer in humans.

- DNA viruses: Three DNA viruses
    a. human papillomaviruses,
    b. Epstein-Barr virus, and
    c. Hepatitis B virus is linked to tumors in humans.

a. **Human papillomaviruses**: - More than 70 types of human papillomaviruses (HPV) have been described. Some cause benign papillomas of the skin (warts). Other strains, particularly HPV-16 and HPV-18, are linked to genital and anal cancers.
b. **Epstein-Barr virus**: - Epstein-Barr virus (EBV) is a type of herpes virus that is well known for causing mononucleosis. It also contributes to the pathogenesis of four human tumors: 1.Burkitt lymphoma, 2.B-cell lymphomas in individuals whose immune systems are impaired from human immunodeficiency virus (HIV, the causative virus of AIDS) infection or the use of immunosuppressant drugs in organ transplantation, 3.nasopharyngeal carcinoma, and some kinds of 4.Hodgkin disease.
c. **Hepatitis B virus**: - Hepatitis B virus (HBV) is endemic in Southeast Asia and sub-Saharan Africa, areas that have the world's highest incidence of hepatocellular carcinoma (liver cancer). The precise role of hepatitis B virus in causing liver cancer is not yet understood, but evidence suggests that viral proteins disrupt signal transduction and thereby deregulate cell growth.

- **RNA viruses**

    Only one human retrovirus, the human T-cell leukemia virus type I (HTLV-I), is linked to a human tumor. This virus is associated with a T-cell leukemia/lymphoma. When cells are constantly dividing, they are at greater risk from secondary transforming events (mutations) that will ultimately lead to the development of cancer.

**2. Chemicals**

Numerous chemicals are known to cause cancer in laboratory animals, and some of these substances have been shown to be carcinogenic for humans as well. Many of these chemicals carry out their effects only on specific organs.

Direct-acting carcinogens include organic chemicals such as nitrogen mustard, benzoyl chloride, and many metals.

There also are chemical carcinogens that occur naturally in the environment. One of the most important of these substances is aflatoxin B 1; this toxin is produced by the fungi Aspergillus flavus and A. parasiticus, which grow on improperly stored grains and peanuts. Aflatoxin B is one of the most potent liver carcinogens known.

Fats, too, may act as promoters of carcinogenesis, which possibly explains why high levels of saturated fat in the diet are associated with an increased risk of colon cancer.

**3. Radiation**

Among the physical agents that give rise to cancer, radiant energy is the main tumor-inducing agent in animals, including humans.

- **Ultraviolet radiation**

    Ultraviolet (UV) rays in sunlight give rise to basal-cell carcinoma, squamous-cell carcinoma, and malignant melanoma of the skin. The risk of developing UV-induced cancer depends on the type of UV rays to which one is exposed (UV-B rays are thought to be the most dangerous), the intensity of the exposure, and the quantity of protection that the skin cells are afforded by the natural pigment melanin. Fair-skinned persons exposed to the sun have the highest incidence of melanoma because they have the least amount of protective melanin.

- **Ionizing radiation**

    Ionizing radiation, both electromagnetic and particulate, is a powerful carcinogen, although several years can elapse between exposure and the appearance of a tumor.

The atomic explosions in Japan at Hiroshima and Nagasaki in 1945 provided dramatic examples of radiation carcinogenesis: after an average latency period of seven years, there was a marked increase in leukemia.

**Inherited susceptibility to cancer**

Not everyone who is exposed to an environmental carcinogen develops cancer. This is so because, for a large number of cancers, environmental carcinogens work on a background of inherited susceptibilities. It is likely in most cases that cancers arise from a combination of hereditary and environmental factors.

**Familial cancer syndromes**

Although it is difficult to define precisely which genetic traits determine susceptibility, a number of types of cancer are linked to a single mutant gene inherited from either parent. Hereditary cancer syndromes include hereditary retinoblastoma, neurofibromatosis.

**Chromosomal translocation**

Chromosomal translocation has been linked to several types of human leukemias and lymphomas. Through chromosomal translocation one segment of a chromosome breaks off and is joined to another chromosome. As a result of such an event, two separate genes can be fused. In some cases the newly created gene leads to tumor development.

**DNA repair defects**

DNA repair mechanisms are involved in maintaining the integrity of DNA, which often acquires errors during replication. When the cellular mechanisms that repair errors in the DNA are damaged—through acquired or inherited alterations—the rate of genetic mutation increases by several orders of magnitude.

DNA repair mechanisms maintain the integrity of DNA, which often acquires mutations during replication. If these mechanisms fail, or if the cell does not undergo apoptosis (a genetically encoded cell "suicide"), more mutations may occur, and the cells will proliferate. If the proliferation is slow and localized to the area in which it begins, the result is a benign tumor. With fast, uncontrolled growth and the invasion of other tissues, a malignant tumor arises.

**Types of child cancer:**

The most common cancers in children are (childhood) leukemia (34%), brain tumors (23%), and lymphomas (12%).[7] In 2005, 4.1 of every 100,000 young people under 20 years of age in the U.S. were diagnosed with leukemia, and 0.8 per 100,000 died from it. The number of new cases was highest among the 1–4 age group, but the number of deaths was highest among the 10–14 age group.

In 2005, 2.9 of every 100,000 people 0–19 years of age were found to have cancer of the brain or central nervous system, and 0.7 per 100,000 died from it.[8] These cancers were found most often in children between 1 and 4 years of age, but the most deaths occurred among those aged 5–9. The main subtypes of brain and central nervous system tumors in children are: astrocytoma, brain stem glioma, craniopharyngioma, desmoplastic infantile ganglioglioma, ependymoma, high-grade glioma, medulloblastoma andatypical teratoid rhabdoid tumor.

Other, less common childhood cancer types are:

- Neuroblastoma (7%, nervous system)
- Wilms tumor (5%, kidney)
- Non-Hodgkin lymphoma (4%, blood)
- Childhood rhabdomyosarcoma (3%, many sites; a form of rhabdomyosarcoma)
- Retinoblastoma (3%, eye)
- Osteosarcoma (3%, bone cancer)
- Ewing sarcoma (1%, many sites)
- Germ cell tumors (many sites)
- Pleuropulmonary blastoma (lung or pleural cavity)
- Hepatoblastoma and hepatocellular carcinoma (liver cancer)

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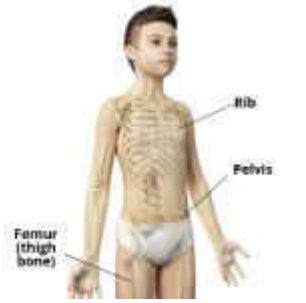
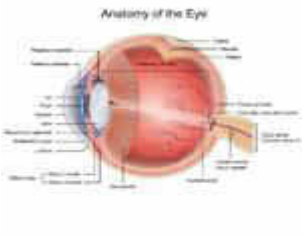
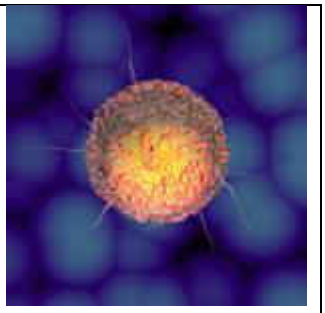
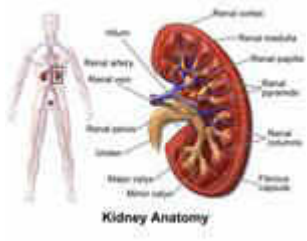
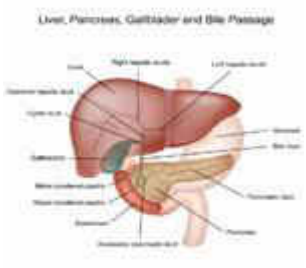
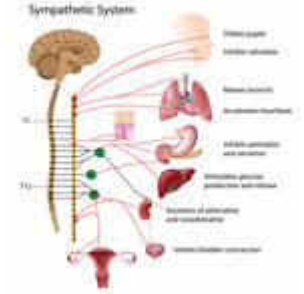
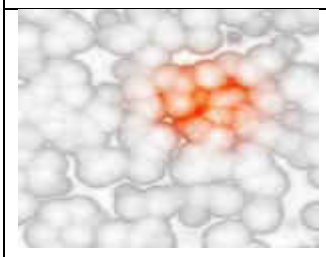
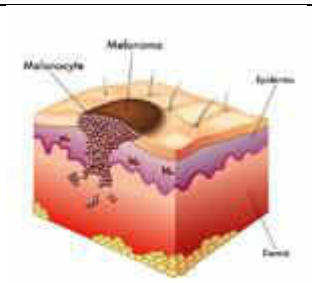
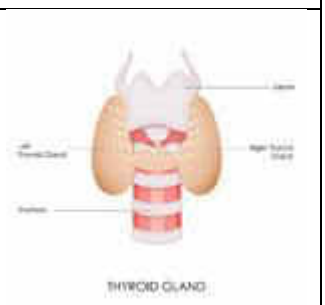
|  BRAIN TUMOR |   EWING SARCONOMA |   EYE CANCER |  GERM CELL TUMORS |
|   WILMS TUMORS |   LIVER CANCER |   NEUROBLASTOMA |   OSTEOSARCOMA |
|  RHABDOMYOSARCOMA |   SKIN CANCER |  SOFT-TISSUE SARCOMA |   THYROID CANCER |

**DIAGNOSTIC EVALUATION**

In order for cancer to be diagnosed as early as possible, an individual should be aware of symptoms that may be related to the disease. The American Cancer Society lists seven basic warning signs of cancer:

1. Unusual bleeding or discharge,
2. Persistent hoarseness or cough,
3. Changes in bowel or bladder habits,
4. A persistent thickening or lump,
5. A sore that does not heal within two weeks,
6. Indigestion or trouble swallowing, and
7. A change in the appearance of a mole or wart.

The evaluation of a child suspected of having cancer may take several days to complete. Sign and symptoms depend on the type of cancer and its location. The following are the essential component of a comprehensive evaluation for childhood cancer.

**IMAGINE STUDIES:**

- Computed tomography (CT),
- Ultrasound,
- Nuclear scan,
- Magnetic resonance imaging (MRI)

**BIOPSY:**

Biopsies, the most definitive diagnostic tests for cancer, can be performed by the physician in the operating room. There are different techniques.

- **excisional biopsy,**
- **Incisional biopsies**,
- **fine-needle aspiration biopsy**,

**BONE MARROW:**

**Bone marrow** may be accomplished by-

1. **Aspiration**: obtaining marrow through a large or fine bore needle, or
2. **Biopsy**: obtaining a piece of bone through a special type of needle.

**MEDICAL MANAGEMENT:**

**TREATMENT**

Once a diagnosis of cancer has been established, a plan for treatment is needed. A therapeutic strategy is best achieved by a multidisciplinary team of physicians that includes surgeons, medical and radiation oncologists, diagnostic radiologists, pathologists, and depending on the operations planned plastic and reconstructive surgeons or physical rehabilitation specialists, trained nursing staff and social workers.

Therapeutic strategies must be tested in experimental trials using specific scientific methods and standards before they are proven effective. The largest risk in using unproven approaches is that they may cause a delay in treatment with a proven method.

**Conventional therapies**

Surgery, radiation, and chemotherapy alone or in combination, bone marrow transplantation and immunotherapy are the most common methods used to treat cancer. The specific treatment will vary depending on the kind of cancer, the extent of the disease, its rate of progression, the condition of the patient, and the response to therapy.

**SURGERY**

The main goal of surgery, besides obtaining biopsies, is to remove all traces of tumor and restore normal body functioning. Surgery is the oldest form of cancer therapy and was until recently the only method that could actually cure cancer. It is still the principal cure.

Although new advances in surgical techniques have allowed for the successful removal of many cancers, the development of other treatment strategies has reduced the extent of surgical intervention in treating some cancers.

**RADIATION THERAPY**

Radiation therapy can be used for curative purposes and is often employed for palliation to relieve the symptoms by shrinking the size of tumor. Radiation therapy is the use of ionizing radiation X-rays, gamma rays, or subatomic particles such as neutrons to destroy cancer cells. Approximately 50 percent of all individuals diagnosed with cancer receive radiation therapy.

Cells are destroyed by radiation either because they sustain so much genetic damage that they cannot replicate or because the radiation induces apoptosis (or programmed cell death). Cancer cells are more sensitive to radiation than are healthy cells because they are continuously proliferating. This factor renders them less able to recover from radiation damage than normal cells, which are not always reproducing.

Different ranges, or voltages, of radiation are used in clinical practice.

- The lowest range is called superficial radiation;
- The medium range is called orthovoltage; and
- The high range is called supervoltage.

Two techniques are used to deliver radiation therapy in the clinic:

1. Brachytherapy (internal radiation)and
2. Teletherapy (external radiation)

1. In **brachytherapy**, also called internal radiation therapy, the source of radiation is placed directly into the tumour or within a nearby body cavity. Some of the substances used are radioactive isotopes of iridium, cesium, gold, and iodine. The devices used to contain the radioactive substances are diverse in form (e.g., tubes, needles, grains, and wires). Sometimes the radioactive source is delivered to the tumour through tubes and then withdrawn an approach called remote brachytherapy.
2. **Teletherapy**, or external radiation therapy, uses a device such as a clinical linear accelerator to deliver orthovoltage or supervoltage radiation at a distance from the patient. The energy beam can be modified to adapt the dose distribution to the volume of tissue being irradiated.

## CHEMOTHERAPY

Chemotherapy is the administration of chemical compounds, or drugs, to eliminate cancer cells. Chemicals destroy cancer cells by preventing them from multiplying. Unlike surgery or radiation therapy, which cannot treat widespread metastases, anticancer drugs can disperse throughout the body via the bloodstream and attack tumor cells.

### Chemotherapy agents used in the treatment of childhood cancer

| AGENT/ ADMINISTRATION | SIDE EFFECT AND TOXICITY | SPECIFIC NURSING CONSIDERATION |
|---|---|---|
| **Alkylating agents**<br>• Mechlorethamine (nitrogen mustard, mustargen) IV<br>• Cyclophosphamide (cytoxan, CTX, neosar) PO, IV, IM<br>• Ifosfamide(ifos, IFF) IV<br>• Melphalan, PO, IV<br>• Procarbazine, PO<br>• Dacabazine, IV<br>• Cisplatin, IV<br>• Carboplatin, IV<br>• Chlorambucil, PO<br>**Antimetabolites**<br>• Cytosine arabinoside, IV, IM, SC, IT<br>• 5-Azacytidine, IV<br>• Mercaptopurine, PO, IV<br>• Methotrexate, PO, IV, IM,IT<br>**Plant alkaloids**<br>• Vincristine, IV<br>• Vinblastine, IV<br>• VP-16, IV<br>• VM-26, IV<br>**Antibiotic**<br>• Actinomycin-D, IV<br>• Doxorubicin, IV<br>• Daunorubicin, IV<br>• Bleomycin, IV, IM, SC<br>**Hormones**<br>• Corticosteroid (prednisolon), PO, IM, IV but rarely used<br>**Enzymes**<br>• L- Aspiraginase IV, IM<br>**Other agents**<br>• Hydroxyurea, PO | • Nausea and vomiting<br>• Bone marrow depression<br>• Alopecia<br>• Local phlebitis<br>• Hemorrhage cystitis<br>• Severe immunosupression<br>• Stomatitis<br>• Hyperpigmentation<br>• Infertility<br>• Neurotoxicity<br>• Dermitis<br>• Azoospermia<br>• Burning sensation in vein during infusion<br>• Renal toxicity<br>• Electrolyte imbalance<br>• Anaphylactic reaction<br>• Mild hepatotoxicity<br>• Mucosal ulceration<br>• Hepatitis<br>• Diarrhea<br>• Anorexia<br>• Photosensititivity<br>• Fever<br>• Hypotension with rapid infusion<br>• Bradicardia<br>• Abdominal cramps<br>• Acne<br>• ECG changes<br>• Mood change<br>• Muscle wasting | • Give dose early in day to allow adequate fluid afterward<br>• Warn parents toreport sign of burning on urination<br>• Must be given cautiously in patient with renal dysfunction<br>• Decrease IV rate or use cold pack along vein to decrease burning<br>• Renal function must be assessed before giving drugs<br>• Must maintain hydration before and during therapy<br>• Monitor intake and output<br>• Do not use aluminium needle; reaction with aluminium decrease potency of drug<br>• Monitor sign of electrolytes loss<br>• Have emergency drug beside<br>• Infuse slowly via IV drip to decrease sensitivity of nausea and vomiting<br>• Use sunscreen<br>• Report sign of neurotoxicity<br>• Observe for any change in vital sign<br>• Warn patient that drug cause urine to turn red<br>• Follow pulmonary function test |

## BONE MARROW TRANSPLANTATION

One of the most life-threatening effects of high doses of chemotherapy and of radiation as well is damage that can be done to bone marrow. Found within the cavities of bones, marrow is rich in blood-forming (hematopoietic) stem cells, which develop into oxygen-bearing red blood cells, infection-fighting white blood cells, and clot-forming platelets. Chemotherapy can decrease the number of white blood cells and reduce the platelet count, which in turn increases susceptibility to .There are two common approaches to marrow transplantation:

1. **Autologous transplants** and
2. **Allogeneic transplants**.
    1. An **autologous transplant** involves the harvesting and storage of the patient's own stem cells before therapy. After the patient has received high levels of chemotherapy or radiation to destroy the cancer cells, the stem cells are injected into the bloodstream to speed recovery of the bone marrow.
    2. If an individual's marrow is diseased—from leukemia, for example—a person with a matching tissue type is found to donate stem cells. This type of transplant, called an **allogeneic transplant**, carries the risk of mismatch between tissues—a situation that can stimulate immune cells of the host to react with the donated cells and cause a life-threatening condition called graft-versus-host disease.

## IMMUNOTHERAPY

Tumor-associated antigens are present on tumor cells, but they also are found on the surface of normal cells; in addition, these antigens are not specific to a certain type of tumor but are seen in a variety of cancers. Despite the lack of tumors specificity, some tumor-associated antigens can serve as targets for attack by components of the immune system. For instance, antibodies can be produced that recognize a specific tumor antigen, and these antibodies can be linked to a variety of compounds—such as chemotherapeutic drugs and radioactive isotopes—that damage cancer cells. In this way the antibody serves as a sort of “magic bullet” that delivers the therapeutic agent directly to the tumor cell. In other cases a chemotherapeutic agent attached to an antibody destroys cancer cells by interacting with receptors on their surfaces that trigger apoptosis.

## COMPLICATION:

Although tremendous advances have been achieved through current method of cancer therapy, the successes are not without consequences. Numerous side effects are expected with chemotherapy and radiotherapy.

- Acute tumor lysis is cause by the rapid release of intracellular metabolites during the initial treatment of malignancies such as T-cell lymphoma and acute leukemia. Rapid tumor lysis lead to- hyperuricemia, hypocacemia, hyperphosphotemia, and hyperkalemia.
- Hyperleukocytosis, defined as a peripheral white blood cell count >100,000/$mm^3$, can lead to capillary obstruction, microinarction, and organ dysfunction. Children experience respiratory distress and cyanosis, neurological changes include altered level of consciousness, visual disturbaces, agitation, confusion, ataxia, and delirium.
- Obstruction may lead an oncologic emergency for child with cancer.space occupying lesion, especially from Hodgkin disease and NHL, located in the chest may cause superior vena cava syndrome (SVCS) leading to airway compromise and potentially to respiratory failure.
- Overwhelming infection in the immunocompramised child constitute an emergency situation. Gram negative sepsis can result in numerous complication, including disseminated intravascular coagulation (DIC), created by bacteria or fungus causing damaged to the endothelial system. Life threatening hemorrhage can occure from DIC, thrombocytopenia (platelet count > 20,000/$mm^3$) and Leukocytosis (leukocyte > 100,000/$mm^3$). Leukocytosis may cause intracranial bleeding from increased viscosity of the blood.

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