CANCER- BETWEEN LIFE AND DEATH

ABSTRACT

Cancer is a group of diseases characterized by the uncontrolled division and growth of abnormal cells in the body. These cells can form tumors, invade surrounding tissues, and metastasize to other organs through the bloodstream or lymphatic system. Cancer can affect almost any tissue in the body and is classified into over 100 types, with the most common being breast, lung, prostate, and colorectal cancers. The development of cancer is influenced by genetic mutations, environmental factors, and lifestyle choices, with risk factors such as smoking, exposure to radiation, and poor diet contributing to its onset. Early detection through screenings and advancements in personalized medicine, such as targeted therapies and immunotherapies, have significantly improved survival rates. However, cancer remains a leading cause of death worldwide due to its complex biology and resistance to treatment. This chapter explores the causes, symptoms, diagnosis, TNM staging and treatment of cancer.

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I. INTRODUCTION

Uncontrolled cell development is a hallmark of this multifaceted disease called cancer, which can potentially infiltrate or spread to other body parts. Since cancer is now the world's largest cause of death, it has grown to be a serious public health issue. From a broad standpoint, cancer is a group of connected diseases that can arise in virtually any place in the body rather than a single illness. The term "cancer" refers to the 277 distinct forms of the illness.[1] It is a genetic disorder that affects our body's cells. Our cells are controlled by our genes, however, when these genes are altered, the cells malfunction, proliferating and eventually becoming a tumor. Carcinogens are the substances that can cause cancer, and carcinogenesis is the process by which cancer develops. When the cell's function suddenly stopped, it turned malignant. [2] According to the Global Cancer Observatory (Globocan), in 2022, there were an estimated 9.74 million cancer-related deaths and 19.98 million new cancer cases worldwide. Asia was the continent with the highest number of new cancer cases, approximately 9.83 million, and the highest number of cancer-related deaths, around 5.46 million. Men generally experience higher rates of both new cancer cases and mortality compared to women. In men, the most commonly diagnosed cancers include lung, prostate, colorectal, stomach, liver, bladder, lip and oral cavity, and gallbladder cancers. In women, the most prevalent cancers are breast, cervical, colorectal, thyroid, and ovarian cancers. Among young individuals, cancers of the blood, brain, and lymph nodes are most frequently observed. [4]

II. HOW DOES A NORMAL CELL DIFFER FROM A CANCER CELL?

Cancer can develop from normal cells in a variety of ways. A series of significant genetic alterations in a normal cell cause unregulated growth and division.[5]

Table 1: Difference between Normal cells and Cancer Cells

Characteristic	Normal Cell	Cancer Cell
Structure	Well-defined structure, uniform shape, and size	Irregular shape, uneven size, distorted structure
Growth	Growth is regulated and stops when space is limited	Uncontrolled growth, can form tumors and continue dividing without limits
Division	Divides in a regulated manner (under checkpoints)	Divides uncontrollably due to mutations and loss of control mechanisms

Cell Cycle	Well-regulated cell cycle with checkpoints	A dysregulated cell cycle, often bypasses checkpoints
Apoptosis (Programmed Cell Death)	Normal cells undergo apoptosis when damaged	Cancer cells evade apoptosis, allowing survival despite damage
DNA Damage Repair	Efficient DNA repair mechanisms	Impaired DNA repair mechanisms allow mutations to accumulate
Cell Communication	Communicate properly with other cells	Impaired cell signaling, leads to uncontrolled proliferation and metastasis
Adherence	Adhere strongly to surrounding tissue and structures	Poor adhesion, can invade surrounding tissues and metastasize
Morphology	Uniform size and shape, distinct boundaries	Pleomorphic (variable size and shape), less distinct boundaries
Energy Metabolism	Aerobic metabolism (efficient ATP production)	Often rely on glycolysis (Warburg effect), even in the presence of oxygen
Angiogenesis (Blood Vessel Formation)	No excessive blood vessel formation	Stimulates the formation of new blood vessels to supply the tumor (angiogenesis)
Chromosomal Stability	Maintains chromosomal integrity and stability	Chromosomal instability, frequent mutations, and abnormalities
Immune Evasion	Normally recognized and targeted by the immune system	Often evade immune surveillance through various mechanisms
Senescence	Cells enter senescence (halt division) after a certain number of divisions	Cells bypass senescence and continue to divide indefinitely (immortality)

The link between genes and cancer is well-established. Cancer-causing genetic changes can arise due to:

- Errors during cell division
- DNA damage from environmental factors
- Genetic inheritance [5]

The body eliminates cells with damaged DNA by either repair mechanisms or apoptosis; the efficiency of these processes reduces with age. This reduction, in turn, is considered one of the factors leading to a higher susceptibility to cancer

in older people. Every individual's cancer often carries its unique combination of genetic changes, and the more a cancer progresses, the greater an accumulation of these changes. There are also differences in genetic alterations between different cells of the same tumor. [6]

III. TYPES OF GENES THAT CAUSE CANCER: “DRIVERS OF CANCER”

The three major types of genes contribute to the growth and development of cells are proto-oncogene, tumor suppressor genes, and DNA repair genes. Alterations in these genes can lead to uncontrolled cell proliferation and the development of cancer.

Proto-Oncogenes

Proto-oncogene are normal genes involved in cell growth, differentiation, and division. They transform into oncogenes by mutations such as point mutations, amplifications, or translocations. Mutation or overexpression of proto-oncogenes results in the formation of oncogenes, which drive uncontrolled cell division.

Examples

RAS: Genetic alterations in the RAS family of proto-oncogenes, such as KRAS, are common in cancers, including lung, colorectal, and pancreatic cancer.

HER2: Amplification of the HER2 gene is a common feature in breast cancers, leading to over production of the HER2 protein. This over production encourages cell growth and division. [7,8]

Tumor Suppressor Gene

Tumor suppressor genes are anti oncogene act as brakes on cell division. They regulate the cell cycle, promote DNA repair, and initiate apoptosis (programmed cell death) when cells are defective. Mutations or deletions of tumor suppressor genes lead to the loss of these "brakes," enabling unchecked cell proliferation.

Examples

TP53: This gene is commonly known as the "guardian of the genome" because it prevents the spread of cells containing damaged DNA. More than 50% of cancers carry mutations in TP53, including lung, breast, and colorectal cancers.

BRCA1/BRCA2: These genes are involved in DNA repair and, when mutated, result in increased risk of breast, ovarian, and other cancers. Inherited mutations in BRCA1/BRCA2 confer hereditary breast cancer. [9,10]

DNA Repair Gene

DNA repair genes are responsible for detecting and fixing DNA damage during cell cycle. Proper DNA repair maintains genetic stability. Mutations in DNA repair genes impair the cell's ability to fix DNA errors, leading to an accumulation of mutations, some of which may contribute to cancer.

Examples

MLH1, MSH2: These genes belong to the mismatch repair pathway and are responsible for Lynch syndrome, which is a hereditary condition linked with an increased susceptibility to several cancers, primarily colorectal.

XPA, XPC: Mutations of these two genes disturb nucleotide excision repair and can lead to the rare genetic disorder called xeroderma pigmentosum disease that results in increased sensitivity to external UV light, hence increasing this DNA damage leading to potential skin cancers. [11,12]

IV. CAUSES OF CANCER

The causes of cancer are multi-factorial and can be categorized in several risk factors:

1. **Lifestyle Factors:** The primary factors contributing to cancer include alcohol consumption, tobacco use, and smoking, all of which significantly increase the risk of cancer. Furthermore, an unhealthy diet and lack of physical activity are believed to play a substantial role in its development. [13]

2. **Genetic Factors:** Cancer is a result of successive gene mutations. Some gene mutations are inherited, and these can predispose individuals to certain

cancers. Examples include mutations in the BRCA1 and BRCA2 genes that increase the risk for breast and ovarian cancers. [14,15]

3. **Infectious Agents:** For example, human papilloma virus (HPV) is linked to cervical cancer, while the hepatitis B and C viruses are linked to liver cancer. Other infections include the Epstein Barr virus (EBV), Heliobacter pylori, Streptococcus bovis, and HIV. The hepatitis B virus can cause chronic inflammation and carcinogenesis to the liver and promote the initiation of hepatocellular carcinoma. The Epstein Barr virus can cause Hodgkin lymphoma, B cell lymphoma, & Nasopharyngeal Carcinoma. [14]

4. **Environmental Factors:** By exposing individuals to different carcinogens, environmental factors significantly trigger the occurrence of cancer. These elements fall into three categories: physical, chemical, and biological agents. Here's a detailed overview of the key environmental contributors to cancer risk:

Major Environmental Carcinogens

- **Asbestos:** A widely recognised carcinogen that mostly affects workers in manufacturing and construction and is connected to mesothelioma and lung cancer.
- **Arsenic:** It raises the risk of bladder, lung, and skin cancers and is present in tainted drinking water.
- **Benzene:** Many industrial operations expose workers to benzene, which is linked to leukemia and other blood malignancies.
- **Formaldehyde:** Connected to several cancers of the lymphatic system and nasopharyngeal carcinoma
- **Radon:** It is the second most common cause of lung cancer in the United States and is a naturally occurring radioactive gas that can build up in residences.
- **Ultraviolet (UV) Radiation:** Sunlight is a major source of UV radiation and sunlight exposure is one of the main causes of melanoma and other skin cancers.
- **Ionizing Radiation:** A kind of high-energy radiation that can cause cancer by damaging DNA. It can harm DNA and cause the development of cancer; sources include radon gas and medical imaging treatments. [14]

V. SYMPTOMS OF CANCER

Many symptoms can be caused by cancer; however, the most common causes are disease, trauma, benign tumors, or other issues.[16]

Below is the list of symptoms that can be observed in cancer are:

Table 2: List of Symptoms of Cancer

Symptom Category	Description	Examples	References
Local Symptoms	Caused by the growth of a tumor in a specific location, leading to the invasion of surrounding tissues.	Persistent cough (lung cancer) Lumps or swelling (breast or lymphatic cancers)	American Cancer Society (ACS), 2024; Cancer Research UK
Systemic Symptoms	Caused by cancer affecting multiple systems or releasing substances into the bloodstream.	Unexplained weight loss Fatigue Fever Night sweats	National Cancer Institute (NCI), 2024; Mayo Clinic
Metastatic Symptoms	Caused by cancer spreading to distant organs.	Bone pain (bone metastasis) Neurological symptoms (brain metastasis)	World Health Organization (WHO), 2023
Paraneoplastic Syndromes	Caused by substances secreted by tumors or an immune response to cancer.	Hypercalcemia Cushing syndrome Neurological syndromes	UpToDate, 2024; New England Journal of Medicine
Hematologic Symptoms	Involvement of blood or bone	Anemia Easy bruising or	American Society of

	marrow leading to related symptoms.	bleeding Frequent infections	Hematology (ASH), 2024; MedlinePlus
Psychological Symptoms	Emotional and psychological effects of cancer diagnosis or progression.	Depression Anxiety Cognitive dysfunction	National Comprehensive Cancer Network (NCCN) Guidelines for Distress Management
Treatment-Related Symptoms	Side effects of cancer therapies such as chemotherapy, radiation, or surgery.	Nausea and vomiting Hair loss Fatigue Neuropathy	Oncology Nursing Society (ONS), 2023; ASCO Guidelines

VI. HOW NORMAL CELLS CONVERT TO CANCER CELLS

Cancer develops when a sequence of genetic alterations occurs in healthy cells. Tissue is a mass of related cells that carry out related tasks. If left untreated, certain tissues might alter, become aberrant, and develop cancer. Tissue changes that are not considered as cancer are as follows:

Hyperplasia: When cells in a tissue proliferate more quickly than they should and accumulate in excess, this is known as hyperplasia. Under a microscope, however, the cells and the structure of the tissue still appear normal. Chronic irritation is one of the instances or factors that can lead to hyperplasia.

Dysplasia: Dysplasia refers to the abnormal development or growth of cells, tissues, or organs. It typically involves changes in the size, shape, and organization of cells within a tissue.

Carcinoma in Situ: The disease known as cancer in-situ is significantly more severe. Despite being referred to as stage 0 cancer, it is not cancer because the aberrant cells do not spread to neighbouring tissue as cancer cells do. However, certain carcinomas in situ are typically treated since they have the potential to develop into cancer**.**[27]

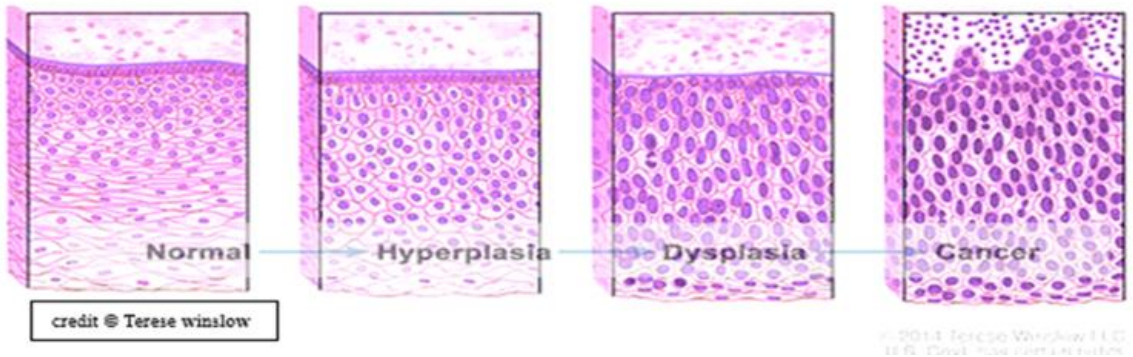

Figure 34: The Tissue Transformation in Abnormal to become a cancer

VII. TYPE OF CANCER

The organ and tissue in which the cancer is growing determine the type of cancer. For example, lung cancer begins in the lungs and their sub-organs, whereas breast cancer originates in the breast. Additionally, the cancer is classified by the tissue it affects, such as non-squamous cells and transitional cells. [1] These are a few types of malignancies that start in particular cell types:

Carcinoma

Carcinoma is the most common word used for cancer of epithelial origin. Under a microscope, epithelial cells, which come in a variety of forms, frequently resemble columns. [1] Carcinomas of different epithelial origin have specific names:

Adenocarcinoma: This is cancer of glandular epithelial tissue. e.g., Breast, colon & prostate cancer

Basal Cell Carcinoma: Arising from the basal cells in the epidermis (the outer layer of the skin)

Squamous Cell Carcinoma: This is a type of skin cancer that originates in the squamous cells, which make up the outer layer of the skin. Squamous cells also found in lungs, bladder, stomach& intestinal lining.

Transitional Cell Carcinoma: This is a type of cancer that arises from the transitional epithelial cells, which line the urinary tract, including the bladder, ureters, and kidneys. [7]

Sarcoma

Sarcoma is a type of cancer that originates from mesenchymal tissue. E.g., Osteosarcoma, Leiomyosarcoma, Liposarcoma, Kaposi sarcoma, etc. [29]

Types of Sarcoma

Soft Tissue Sarcomas: These cancers develop in soft tissues like fat, muscle, blood vessels, nerves, or deep skin tissues. Some examples of soft tissue sarcoma are –

- **Liposarcoma:** Arises from adipocytes.
- **Leiomyosarcoma:** Arises from smooth muscle.
- **Rhabdomyosarcoma:** Affects skeletal (striated) muscle, commonly seen in children.
- **Angiosarcoma:** Arise from blood vessels or lymph vessels.

Bone Sarcomas: These cancers develop in the bones. The two main types are:

Osteosarcoma: The most common bone cancer, typically found in the long bones (like the arms or legs), often in children and adolescents.

Chondrosarcoma: Originates in cartilage, often occurring in older adults.

Lymphomas

Cancer that originates in lymphocytes, a type of white blood cell (WBC), is known as lymphoma. This condition leads to the abnormal build up of lymphocytes in lymph nodes, lymphatic vessels, and other organs in the body. Lymphoma is classified into two main types: Hodgkin lymphoma and non-Hodgkin lymphoma. [30]

Leukemia

The term leukaemia refers to cancers that start in the bone marrow (blood-forming tissue). Solid tumours are not formed by these cancers. Rather, immature leukocytes proliferate in bone marrow and blood, displacing healthy blood cells.

Multiple Myeloma

Multiple myeloma originates in plasma cells, a type of immune cell. In this condition, abnormal plasma cells, known as myeloma cells, build up in the bone marrow and form tumors in bones across the body. This disease is also referred to as plasma cell myeloma or Kahler's disease. [31]

Melanoma

A tumor of melanocytes, the specialized cells responsible for producing melanin (the pigment that gives skin its color), is called melanoma. While melanoma primarily develops on the skin, it can also arise in other pigmented tissues, such as the eye.[15]

Brain and Spinal Cord Tumors

Tumours of the brain and spinal cord come in several varieties. Based on the kind of cell they originated in and the initial location of the tumour in the central nervous system, these tumours are given names. For instance, astrocytes, which are star-shaped brain cells that support the health of nerve cells, are where an astrocytic tumour starts. Both benign (not cancer) and malignant (cancer) brain tumours are possible.

Other Types of Tumors

Germ Cell Tumors

One kind of tumour that starts in the cells that produce sperm or eggs is called a germ cell tumour. These tumours can be benign or malignant, and they can appear practically anywhere in the body.[1]

Neuroendocrine Tumors

Cells that respond to a signal from the nervous system by releasing hormones into the blood are the source of neuroendocrine tumours. Due to their potential to produce more hormones than usual, these tumours can produce a wide range of symptoms. Malignant or benign neuroendocrine tumours are also possible.

Carcinoid tumor are slow growing neuroendocrine tumor. These tumors usually occur in the gastrointestinal system (most often in the rectum and small intestine). [31]

VIII. DIAGNOSIS OF CANCER

Cancer screening tests, such as MRIs, CT scans, and X-rays, should be performed if someone feels they may have cancer symptoms. These tests aid in determining whether a person has cancer or another illness. Cancer cannot be diagnosed with a single test. If a person inherits those genes, their risk of developing cancer increases because aberrant gene expression is also one of the causes of cancer. The gold standard test, which frequently serves as the sole means of confirming the existence of cancer, is the biopsy. [32-34]

Some common types of lab tests used to help diagnose cancer are listed below.

1. **Complete Blood Test (CBC):** CBC evaluates the blood's red, white, and platelet components. It gauges the amount of haemoglobin, a protein involved in the delivery of oxygen, in human blood. The CBC is useful in the treatment of cancer and helps with some types of cancer, such as blood cancer, such as leukaemia. [35]

2. **Immunophenotyping:** Antibodies specific to or associated with cancer are primarily located on the surface of cells and are monitored by immunophenotyping. Blood and bone marrow are the most common samples used for this test; however other body fluids and tissues may also be used. Leukaemias, lymphomas, myelodysplastic syndromes, and myeloproliferative disorders are among the blood disorders it aids in diagnosing, staging, and tracking.

3. **Tumor Markers:** Tumor markers are substances produced at higher levels by cancer cells compared to normal cells or in response to certain diseases. These markers can aid in diagnosing cancer, guiding treatment decisions, evaluating the effectiveness of therapies, and monitoring for cancer recurrence. [34]

4. **Cytogenetic Analysis:** In certain cancers, the arrangement of chromosomes got disturbed. For example, leukaemia is a blood cancer where such condition is seen. Chromosome changes may include broken, missing, rearranged, or extra chromosomes. Cytogenetic analysis may be used to diagnose cancer; plan treatment&find out how well treatment is working. [31]

5. **Liquid Biopsy.** Liquid biopsies search for cancerous cells or fragments of tumour cell DNA that are occasionally discharged into bodily fluids. A liquid

biopsy could aid in the early detection of cancer. Additionally, it can be used to help plan treatment, assess the effectiveness of treatment, and determine whether cancer has returned. [6]

Imaging Techniques

1. **Computer Tomography (CT)-Scan.** Because CT scans provide fine-grained views of the body's internal components, they are essential for the detection and treatment of cancer. Furthermore, it aids in determining the effectiveness of treatment and directing biopsies to accurately retrieve tumour samples. The stage, recurrence, and extent of the cancer's dissemination were all determined.

2. **Magnetic Resonance Imaging.** An invaluable tool in cancer diagnosis due to its ability to produce detailed images of soft tissues without radiation exposure. Its effectiveness in detecting tumors, assessing their extent, monitoring treatment response, and guiding biopsies makes it a critical component of modern oncology practice. [36]

3. **Nuclear Scans** Using radioactive material, nuclear scans create images of the interior of the body. Another name for this kind of scan is a radionuclide scan. A tracer—a little quantity of radioactive material—is injected into you prior to this scan. It travels through your circulation and gathers in specific organs or bones.

    - **Bone Scan:** Nuclear scans that look for abnormalities or injury to the bones are called bone scans. They can detect whether cancer has migrated to the bones from other parts of the body (known as metastatic bone tumours) or be used to diagnose bone cancer. [34]
    - **PET-Scan:** A particular kind of nuclear scan called a PET-Scan creates finely detailed three-dimensional images of the parts of your body where glucose is absorbed. Cancer in the body can be identified by the images because cancer cells frequently absorb more glucose than healthy cells.

4. **Other test** such as Ultrasound & X-rays are also used to get the location of cancer and describe its growth too.

Biopsy

The process by which the physician takes a sample of aberrant tissue is called a biopsy. Under a microscope, a pathologist examines the tissue and performs

additional tests on the sample's cells. In a pathology report, which includes information regarding your diagnosis, the pathologist details the findings. A biopsy is regarded as the gold standard for cancer diagnosis. [16]

IX. CANCER STAGING

Cancer staging aids in determining the size of the tumour or the extent to which the cancer has spread. It helps in:

- How advanced is the cancer?
- The stage-based optimal treatment approach for each individual. [32]

Various staging systems exist, depending on the specific cancer kind. The TNM staging system is utilised for the majority of malignancies.

The TNM Staging System

The TNM system is the most popular method for staging cancer. For reporting cancer, the TNM system is the primary approach used by the majority of hospitals and medical facilities. Unless different kinds of cancer has a different staging system, the cancer defined by this staging system is based on pathology report. [37] In the TNM system

- The T refers to the size of tumor and extent of the primary tumor.
- The N refers to the number of nearby lymph nodes that have cancer.
- The M refers to whether the cancer has metastasized (spread from the primary tumor to other parts of the body).

The term "metastasis" refers to the spreading of disease from one area to another. When malignant cells spread and develop into secondary tumours, the cells in the metastatic tumour resemble those in the main tumour. The metastatic cancer is also called stage IV cancer.[1]

X.CANCER TREATMENT

There are numerous options for treating cancer. The type and stage of the cancer determine the course of treatment. Combining chemotherapy, radiation, and surgery is the most effective way to remove cancer cells from the body and reduce the risk of recurrence in the majority of cases. [38]

1. **Surgery:** One way to eradicate cancer from the body is through surgery. Solid tumours, for instance, oral cancer, stomach cancer, ovarian cancer, and brain cancer that are localised in one location respond best to surgery. Leukaemia, a form of blood cancer, and tumors that have spread are not treated with it. [33]

2. **Chemotherapy:** Chemotherapy, which is used to eradicate cancer cells, functions by halting or delaying the rapid development and division of cancer cells. Chemotherapy can be used to reduce tumours that are causing pain and other issues, cure cancer, lower the possibility that it will return, or stop or limit its growth. In addition to killing rapidly proliferating cancer cells, chemotherapy also destroys or inhibits the growth of rapidly proliferating and dividing healthy cells. For instance, the cells are responsible for hair growth and the lining of your mouth and intestines. Effects including mouth sores, nausea, and hair loss might result from damage to healthy cells. The side effects usually improve or disappear once treatment is over. [7]

3. **Radiotherapy:** Radiotherapy, is a common treatment for cancer that uses high-energy radiation to kill or damage cancer cells. It works by damaging the DNA inside the cells, preventing them from growing or dividing. Cancer cells are not immediately killed by radiation therapy. Treatment must be administered for days or weeks under the supervision of oncologist. [28]

4. **Other Therapies for Cancer:** Varieties of other treatments options available for cancer treatment.

    - **Hormonal Therapy** decreases the growth of cancer, including prostate and breast cancer by the use of hormones.
    - **Hyperthermia** is a treatment helps to destroy cancer cells with minimal to no damage to healthy tissue, in this, the body tissue is heated to 113 °F.
    - **Immunotherapy** is a cancer treatment that boosts your immune system's ability to fight cancer.
    - **Photodynamic Therapy** a method in which alight is used to initiate or activate drug to kill cancer and other abnormal cells.
    - **Targeted Therapy** is one kind of cancer treatment that focusses on the alterations in cancer cells that promote their growth, division, and metastasis.

- **Stem Cell Transplants** are methods used to fix stem cells that develop into blood cells. In basically, blood cancer and other blood-related diseases are treated using this treatment. Additionally, those whose genes have been damaged by severe doses of radiation therapy or chemotherapy.

Clinical trials are now being conducted on a number of innovative technologies. There is hope that new cancer treatments may either cure or eradicate the disease. There is enormous optimism for the treatment of cancer with treatments like CAR-t therapy and Nano medicines.

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