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Cancer: A Comprehensive Review

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ABSTRACT:
Cancer is a condition where cells divide uncontrollably, starting in cells, the body's basic building blocks. Under normal circumstances, the body produces new cells as needed, and old cells die when they should. However, cancer disrupts this process, leading to the formation of extra cells that can form a mass called a tumor. Benign tumors are masses that do not spread, while malignant tumors are those that divide uncontrollably and can invade nearby tissues. A defining feature of malignant cancer is its ability to spread from one part of the body to another, a process known as metastasis. Cancers are often named based on their origin, such as lung cancer or brain tumors. Carcinogens, which can be physical, chemical, or biological, are agents that cause cancer. Cancer often goes undetected for a long time, but advances in technology now allow for molecular analysis of different cancer types. Symptoms and treatments vary based on the type and stage of cancer, with common treatments including surgery, radiation, and chemotherapy. Newer treatments may involve hormone therapy or stem cell transplantation.

Key Words: Cancer, Malignant Tumor, Cell Division, Stem Cell.

I. INTRODUCTION:

Cancer is a term that encompasses a broad spectrum of diseases characterized by uncontrolled cell growth and division. It refers to more than 100 distinct diseases that can develop in any body tissue, each with unique features. Cancer begins when a cell escapes the normal regulatory mechanisms of cell division and initiates its own proliferation (1). The term "cancer" originates from an observation made by Hippocrates over 2,300 years ago, who used the Greek word "karkinoma," later translated to "cancer" in Latin. In the 1600s, Hooke, and in the 1800s, Virchow, observed that living tissues are composed of cells, all of which arise from pre-existing cells. This understanding led to further inquiries into the nature of cancer. Significant early observations in cancer research include the incidence of scrotal cancer among chimney sweeps in 1775 and high rates of lung cancer among pitchblende miners in Germany during the mid-1800s. By the late 19th century, some physicians suspected a link between tobacco use and cancers of the mouth and throat. These observations suggested that cancer could have external causes and might be preventable (2). A healthy body contains approximately 30 trillion cells, which regulate each other's proliferation to maintain appropriate tissue size and architecture. Normal cells reproduce only when instructed by other cells, ensuring coordinated growth. In contrast, cancer cells ignore these controls and follow their own agenda for reproduction. Tumors formed by these malignant cells become more aggressive over time and can be lethal if they disrupt essential tissues and organs. Scientists have identified basic principles governing cancer development. Tumor cells descend from a common ancestor that, often decades before the tumor becomes detectable, initiated abnormal reproduction due to mutations in specific genes. These genes, carried in the DNA of chromosomes, are crucial for understanding cancer. Genes specify amino acid sequences to form proteins, which perform cellular functions. Mutations can alter the quantity or activity of these proteins, disrupting normal cell behavior (3).

Two main classes of genes play a critical role in triggering cancer. Tumor development occurs in three main stages:

I. Genetically altered cell: Tumor development begins when a cell in a normal population acquires a genetic mutation that increases its propensity to proliferate.
II. Hyperplasia: The altered cell and its descendants reproduce excessively but still appear normal. After years, a rare mutation may occur, further loosening growth controls.
III. Dysplasia: The offspring of the mutated cell appear abnormal in shape and orientation, exhibiting dysplasia. Another

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mutation may then occur, altering cell behavior.

The fourth stage is when in-situ cancer develops. The affected cells become more abnormal in growth and appearance, but the tumor remains contained within the tissue. Some cells may acquire additional mutations, leading to the fifth stage:

Malignancy: The tumor invades underlying tissue and sheds cells into the blood or lymph, becoming malignant. These renegade cells can establish new tumors (metastases) elsewhere in the body, potentially disrupting vital organs and becoming lethal(2).

Some genes involved in human Cancers

Some genes involved in human cancers include proto-oncogenes and tumor suppressor genes. Proto-oncogenes code for proteins that stimulate cell division. When these genes mutate, they become oncogenes, which can cause the stimulatory proteins to become overactive, leading to excessive cell proliferation. Tumor suppressor genes, on the other hand, code for proteins that inhibit cell division. Mutations in these genes can inactivate the proteins, removing necessary restraints on cell proliferation. Researchers are still working to understand the specific functions of many tumor suppressor genes (4).

Table 1: Tumor Softener genes (5)

Genes for proteins in the Cytoplasm	
1) APC	Involved in colon and stomach cancers
2) DPC 4	Codes for a relay molecule in a signaling pathway that inhibits cell division, involved in pancreatic cancer
3) NF-1	Codes for a protein that inhibits a stimulatory (Ras) protein. Involved in neurofibroma and pheochromocytoma (cancers of the peripheral nervous system) and myeloid leukemia
4)NF-2	Involved in meningioma and ependymoma (brain cancers) and schwannoma (affecting the wrapping around peripheral nerves)
Genes for proteins in the nucleus	
1) MTS 1	Codes for the p16 protein, a braking component for the cell cycle clock, involved
2) RB	in a broad range of cancers Codes for the pRB protein, a master brake for the cell cycle, involved in retinoblastoma and bone, bladder, small cell lung and breast cancer
3) P53	Codes for the P53 protein, which can halt cell division and induce abnormal cells to kill themselves, involved in a wide range of cancers
4) WT 1	Involved in Wilms "Tumor of the kidney"
Genes for proteins whose cellular location is not yetclear	

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1) BRCA 1	Involved in breast and ovarian cancers
2) BRCA 2	Involved in breast cancer
3) VHL	Involved in renal cell cancer

Table 2: Oncogenes (6)**.**

Genes for the growth factors or their receptors	
1) PDGF	Codes for platelet-derived growth factor, involved in glioma (a brain cancer)
2) erb-B	Codes for the receptor for epidermal growth factor, involved in glioblastoma (a brain cancer) and breast cancer
3) erb-B2	Also called HER-2 or nev. codes for a growth factor receptor, involved in breast, salivary gland and ovarian cancers
4) RET	Codes for a growth factor receptor, involved in thyroid cancer
Genes for cytoplasmic relays in stimulatory signalingpathways	
1) Ki-ras	Involved in lung cancer, ovarian cancer, colon cancer and pancreatic cancers
2) N-ras	Involved in leukemias
Genes for transcription factors that activates growth-promoting genes	
1) C-myc	Involved in leukemias and breast cancer, stomach cancer and lung cancer
2) N-myc	In neuroblastoma (a nerve cell cancer) and glioblastoma
3) L-myc	In lung cancer
Genes for some other kinds of molecules	
1) BCL2	Codes for a protein which normally block cell suicide, involved in follicular B cell lymphoma
2) BCL1	Called as PRAD1. Codes for cyclin D1, a stimulatory component of the cell cycle clock, involved in breast cancer, head cancer and neck cancer

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3) MDM-2	An antagonist of the p-53 tumor suppressor protein, in sarcomas (connective tissue cancers) and other cancers

Types of Cancers:
There are multiple types of cancer today, with some of the most common including:

- Bladder cancer
- Thyroid cancer
- Breast cancer
- Prostate cancer
- Colon and rectal cancer
- Pancreatic cancer
- Endometrial cancer
- Non-Hodgkin lymphoma
- Kidney cancer
- Melanoma
- Lung cancer
- Liver cancer
- Leukemia
- Skin cancer

Cancer is typically named after the part of the body where it originates. For example, if kidney cancer spreads to the lungs, it is still referred to as kidney cancer. In this scenario, the lung involvement is considered a secondary tumor. Cancer is not a single disease; rather, it is a group of diseases characterized by uncontrolled cell growth and changes in cell behavior (7).

Categories of Cancer
There are five broad categories that indicate the tissue and blood classifications of cancer:

1. **Carcinoma**:
   - This type of cancer is found in epithelial tissue, which covers the surfaces of organs, glands, or body structures.
   - The main types of carcinomas include:
     - Melanoma
     - Basal cell carcinoma
     - Squamous cell skin cancer
     - Merkel cell carcinoma
2. **Sarcoma**:
   - Sarcomas are malignant tumors that grow from connective tissues such as cartilage, fat, muscles, tendons, and bones.
   - Common sarcomas include:
     - Osteosarcoma (occurs in bone)
     - Chondrosarcoma (occurs in cartilage)
     - Other types include soft tissue sarcoma and Ewing's sarcoma
3. **Lymphoma**:
   - This type of cancer originates in the nodes or glands of the lymphatic system.
   - Types of lymphoma include:
     - Hodgkin's lymphoma
     - Non-Hodgkin's lymphoma
     - Cutaneous lymphoma
4. **Leukemia**:
   - Also known as "blood cancer," leukemia is a cancer of the bone marrow that prevents the production of normal red and white blood cells and platelets.
   - Types of leukemia include:
     - Acute lymphocytic leukemia
     - Acute myeloid leukemia
     - Agnogenic myeloid leukemia
     - Chronic myeloid leukemia
     - Essential thrombocythemia (ET)
     - Hairy cell leukemia
     - Myelodysplastic syndromes (MDS)
5. **Myeloma**:
   - This cancer grows in the plasma cells of the bone marrow.
   - In some cases, myeloma cells collect in one bone, forming a single tumor called a plasmacytoma.
   - In other cases, myeloma cells collect in many bones, forming multiple tumors, a condition known as multiple myeloma.

Causes of Cancer
Cancer is not caused by a single factor; instead, it is believed to result from the interplay of multiple factors. These factors can be environmental, genetic, or related to lifestyle. Researchers have identified several risk factors and exposures that contribute to the development of cancer (8).

1. **Genetic Disorders**:
   - Certain genetic disorders, such as Wiskott-Aldrich and Beckwith-Wiedemann syndrome, can alter the immune system and increase the risk of cancer.
   - Another theory suggests that damage to stem cells or bone marrow cells can lead to the replication of abnormal, cancerous cells.
2. **Genetics, Inheritance, and Family History**:
   - Genetics and family history can play a significant role in the development of

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childhood cancers. Children with a family history of cancer may have a higher risk.

3. **Lifestyle Factors**:
- Lifestyle choices are important risk factors for many adult cancers. Examples include:
  - Smoking
  - A high-fat diet
  - Exposure to toxic chemicals

The overall five-year survival rate for childhood cancer is about 80%, while for adult cancers, the survival rate is approximately 68%. These factors highlight the complexity of cancer development and the importance of considering both genetic and environmental influences.

How Cancer is diagnosed?

Cancer diagnosis involves multiple tests to confirm the presence of the disease, as no single test can definitively diagnose cancer. A thorough patient evaluation includes a detailed medical history, physical examination, and various diagnostic tests. These tests help confirm or rule out cancer, monitor disease progression, and plan effective treatment (9).

Diagnostic procedures for cancer include:

1. **Laboratory Tests**: These tests check the chemical components in bodily fluids and tissues, such as:
- Blood tests (e.g., Complete Blood Count, CBC)
- Urinalysis
- Tumor markers
2. **Imaging Tests**: These visualize the inside of the body to detect abnormalities, such as:
- X-rays
- Computed Tomography (CT) scans
- Bone scanning
- Lymphangiogram (LAG)
- Mammogram
- Ultrasound
- Magnetic Resonance Imaging (MRI)
3. **Endoscopic Examinations**: These involve inserting a flexible tube with a light and camera to view internal organs, including:
- Cystoscopy (cystourethroscopy)
- Colonoscopy
- Endoscopic Retrograde Cholangiopancreatography (ERCP)
- Esophagogastroduodenoscopy (EGD or upper endoscopy)
- Sigmoidoscopy
4. **Biopsies**: A biopsy involves removing tissue or cells for examination under a microscope to determine if a tumor is cancerous or to identify the cause of inflammation and infection. Types of biopsies include:
- Endoscopic biopsy
- Excisional or incisional biopsy
- Bone marrow biopsy
- Fine needle aspiration biopsy
- Punch biopsy
- Shave biopsy
- Skin biopsy

Some biopsies are performed in a hospital and may require anesthesia to numb the area, while others can be done without sedation. Each type of biopsy is chosen based on the location and nature of the suspected cancer.

Treatments of Cancer

1. **Surgery**: Surgery is a common treatment for most cancers, except for blood cancers. Specialized cancer surgeons aim to remove all or most of the tumor. This method is particularly effective for early-stage cancers that haven't spread to other parts of the body. According to Marta Batus, MD, a medical oncologist at Rush, "It depends on the size of the tumor and other factors, but many patients with stage one cancers do not need any other treatment except for surgery. Surgery can also play a role in cancer treatment even when a tumor has spread beyond its original site." Another oncologist, Busts, adds, "Our options for treating cancer even at later stages have grown, and surgery is a big part of that. The role of surgery has expanded, and it is very encouraging."

Depending on the cancer and its stage, minimally invasive surgery may be an option. For example, thoracic surgeons at Rush often use video-assisted thoracoscopic surgery (VATS), a minimally invasive procedure, to remove early-stage lung cancer tumors. VATS uses smaller incisions than open surgery, typically offering patients less pain, shorter hospital stays, and fewer complications (10).

2. **Immunotherapy**: Immunotherapy is a relatively new type of cancer treatment that uses medications to rev up the patient's immune system to fight cancer. These treatments can work across different cancer types and may be effective in treating even the most advanced and hard-to-treat cancers.

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Researchers continue to explore the potential of immunotherapy, and several effective FDA-approved drugs are now commonly used to treat certain cancers.

Immunotherapy has opened up more options for many patients and is now the frontline treatment for certain conditions. According to Batus, "Patients don't lose their hair, they don't have nausea or vomiting, and most of the time they experience minimal side effects, if any." Some patients may experience side effects depending on the drug administered and the type of cancer being treated. Immunotherapy is administered through IV infusion and offers some patients with late-stage cancers a treatment option they previously didn't have, sometimes allowing them to live longer than expected.

For instance, immunotherapy has redefined how doctors treat melanoma, the most dangerous and deadly form of skin cancer. Five years ago, the overall survival for a patient diagnosed with metastatic melanoma (cancer that has spread to other parts of the body) was about nine months. Today, thanks to a combination of immunotherapies, the majority of patients with metastatic melanoma are alive and doing well at least one year later, and many are living several years beyond that (11).

3. Targeted Therapies

Oncologists use targeted therapies, also known as precision medicine, to tailor medications for each individual patient and cancer type. Initially, a tumor or blood sample is tested to identify its genetic profile, allowing clinicians to administer medications that specifically target the genes causing the cancer. There may be five or six gene processes that can turn cancer on or off. With genetic testing, doctors can determine which medicines to use and which ones to avoid. These medications, delivered in pill or IV form, either destroy cancer cells or stop them from continuing to grow. Like immunotherapy, targeted therapies can be used at any stage: as a first treatment, to keep the cancer from returning, or if the cancer recurs.

For instance, patients with breast cancer are typically tested to see if they carry the HER2 gene, which can cause breast cancer cells to grow. If a patient tests positive for HER2, oncologists use medications or a combination of medications developed to target the gene, such as trastuzumab or pertuzumab. These medications help stop the growth of cancer cells, often without harming healthy cells. Nowadays, a cancer diagnosis doesn't necessarily mean chemotherapy with its associated nausea, vomiting, and hair loss (12).

4. Active Surveillance

Active surveillance, also called watchful waiting, may be sufficient for certain types of cancers. Doctors may recommend this approach if the cancer is at an early stage and is growing slowly or not at all. For example, doctors often recommend active surveillance for prostate cancer, which tends to grow very slowly. Doctors monitor the patient's prostate-specific antigen (PSA) levels with blood tests and watch for symptoms. If or when symptoms worsen or tests show that the cancer is growing more rapidly, they then discuss additional treatments. Often, patients undergoing active surveillance have no symptoms and continue living their lives as usual. Surveillance may also be an option for patients who want a break from treatment side effects or for those who have exhausted all other treatment options (13).

5. Supportive Care

Supportive cancer care can effectively complement standard treatment, helping to minimize the physical and emotional stress of cancer treatment. For example, psychotherapy and massage therapy can help ease a patient's anxiety as they cope with a diagnosis. Acupuncture can be beneficial for pain relief, and nutrition counseling can help prevent significant weight loss during treatment and keep the body as healthy as possible (14). Types of integrative medicine include:

- Aromatherapy
- Fitness classes
- Hypnosis
- Mindfulness meditation

Immune System After Treatment

Most cancer patients know that chemotherapy weakens their immune systems, putting them at risk for viral and bacterial infections. Many assume their immune system has returned to normal a month or 100 days after chemo ends. However, new research suggests that the effects of chemotherapy can compromise part of the immune system for up to nine months post-treatment, leaving patients vulnerable to infection (15).

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A small observational study conducted by the UK's University of Leeds and Leeds Teaching Hospitals NHS Trust demonstrated this prolonged impact. Researchers measured the levels of lymphocytes (white blood cells that fight infections) in breast cancer patients before and up to nine months after receiving chemotherapy. The study found that lymphocyte levels, including various natural killer cells, T cells, and B cells, dropped significantly after chemo. While most immune cells returned to pre-chemo levels after nine months, certain types of NK, T, and B cells did not (16).

Specifically, B cells (crucial for creating antibodies) and CD4+ T cells (helper T cells) only partially recovered, reaching only 69% of pre-chemo levels. This partial recovery potentially leaves patients vulnerable. In smokers, recovery was substantially impaired, with levels reaching only 51% of pre-chemo levels after nine months (16).

II. CONCLUSION:

It's clear that there is still a long road ahead in optimizing the use of these therapies, reducing their complexity and side effects, and integrating them effectively into current standards of care. Challenges remain in making these treatments economically sustainable within healthcare systems. Clinical researchers are increasingly focusing on managing and predicting toxicities, as well as monitoring long-term outcomes. This effort may lead to guidelines on how to effectively incorporate these new therapies into treatment pathways. However, the search continues for specific treatments that can cure diseases without causing significant side effects or toxicity. Ongoing long-term studies are essential for advancing novel cancer treatments.

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