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CANCER: A COMPREHENSIVE REVIEW

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Abstract: Cancer is a multifactorial, heterogeneous and chronic disease. Basically, cancer itself is a group of diseases, because of its frequency, reciprocal influences-even minor influence may lead to a major impact. Epidemiological studies clearly indicate thatrisk for several types of cancer (including pancreas cancer, liver cancer, breast cancer, urinary tract (colorectal) cancer is too high for mortality and morbidity. Obesity, hyperglycemia, and increased oxidative stress may also contribute to increased cancer risk. Despite many decades of basic research and clinical research and trials of promising new therapies, new drugs, new treatments, cancer is the main cause of morbidity and mortality. In conclusion cancer is a complex disease which is gaining more of its popularity in humans and so, it needs more clinical attention and better designed treatments, studies and drugs.

Keywords: Cancer, Oncogenes, Leukemia

INTRODUCTION

Cancer is a broad term; it is the disease which results when the cellular changes cause uncontrolled growth and division of the cells.[1,3,8,9] In simple terms, cancer is a group of more than 100 diseases that develops across time and involve the uncontrolled body cells. Cancer is a disease that can develop in any of the body tissue and from that each of the cancer type consists of its unique features, cancer begins when a cell breaks free from the normal restraints on cell division and begins to follow its own proliferation.

[1,2,3] The name cancer derives from an observation by *"Hippocrates"* more than 2,300 years ago. The term *"Korkinoma",* in Greek came then later, Cancer in Latin. The Hooke in 1600s, and Virchow in 1800s, came to an observation that the living tissues are composed of cells and all the cells arise as direct descendants of other cells. This understanding has raised more questions about cancer. [1,5,10,16] one of the important observations from early were made in 1775, an incidence of scrotal cancer was spread among

workers who worked as chimney sweeps as boys, and in the mid of 1800s, lung cancer was observed at alarmingly in high rates among the pitch blende miners in Germany.And by the end of the 19th century using cigarettes, cigars were thought by some physicians to be closely associated with cancers of the mouth and throat. These kind of observations and other observations too suggested that the origin and cause of cancer may lie outside the body and more important that cancer could be linked to identifiable and even preventable causes. [2,8] The 30 trillion cells of the normal, healthy body live in a complex regulating one another's proliferation. The normal cells reproduce only when they get instructed to do so by other cells, such unceasing collaboration ensures that each tissue maintains a size and architecture appropriate to the body's needs. [1,3] Cancer cells violate this scheme, they become deaf to the usual controls on proliferation and follow their own re-production agenda. [2] Tumors composed of such malignant cells and becomes more and more aggressive over time, and they become lethal when they disrupt the tissues and organs needed for the survival of the organism as a whole. Scientists have discovered set of some basic principles which governs the development of cancer that the cells in tumor descend from a common ancestral cells that at one point-usually decades before a tumor becomes palpable, initiated a program of the inappropriate reproduction, then the malignant transforms of a cell comes about through accumulation of mutations in specific classes of the genes within it.These genes provide the key to understand the process at the root of human cancer. Gene that are carried out in the DNA molecules of the chromosomes in cell nucleus. A gene specifies a sequence of amino acids that must be linked together to make particular protein; the protein then carries out the work of the gene, and when the gene is switched on then the cell responds by synthesizing the encoded protein. Mutations in a gene can perturb a cell by changing the amount or the activities of the protein product. Two of the gene classes, which together constitute only a small proportion of the full genetic set, which plays amajor role in triggering the cancer. The development of tumor occurs in three main stages first a genetically altered cell their tumor development begins when some cells within a normal population sustains a genetic mutation that increases its propensity to proliferate when it would normally rest. Then the second stage is called as hyperplasia where the altered cells and its descendants continue to look normal, but they re-produce too much-after years, one in a million of these cells suffers another mutation that further loosens controls on cell growth then the final stage is dysplasia where the off-spring of the cell appear abnormal in shape and in orientation; the tissue is now said to exhibit dysplasia once again, after a time a rare mutation that alters cell behavior occurs. Then after these three stages cancer or in-situ cancer begins to develop from the fourth stage where the affected cells become still more abnormal in growth and appearance. If the tumor has not broken into tissues, then it is called as in-situ cancer. This tumor may remain contained indefinitely, however, some cells may eventually acquire additional mutations, then in the fifth stage if the genetic changes allows tumor to perform invading underlying tissue and to shed cells into the blood or lymph, the mass is considered to have become malignant. The renegade cells are likely to establish new tumors (metastases) in the body; these may become lethal by disrupting a vital organ.

Some genes involved in human Cancers

[1.2,3,8] Genes are known as proto-oncogenes code for proteins whichstimulates the cell division; mutated forms, called oncogenes, can cause the stimulatory proteins to be over-active, with the result that cells proliferate excessively. Tumor suppressor genes code for proteins that inhibit the cell division. Mutations can cause the proteins to be inactivated and may thus deprive cells of needed restraints on proliferation. Investigators are still trying to decipher the specific functions of many tumor softener genes.

Table 1: Tumor Softener genes

• **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 in a broad range of cancers
2) RB	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 yet clear**	
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.

• **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 signaling pathways**	
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
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 cancers today but, some of the common types of cancers are: [2,8,14,15,16,19]

- 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

Basically, cancer is named after the part of that particular body from which it is originated.

For example:if kidney cancer spreads to the lungs, that time it is still known as kidney cancer not lung cancer in this case lung cancer would be an example of a secondary tumor. Caner is not just one disease it isa group of diseases, all of which causes cells in the body to change and grow out of control.

Categories of Cancer

There are five broad categories which indicates the tissue and blood classifications of cancer. [1,2,8,15,16]

1) Carcinoma: It is the cancer which is found in the tissue known as *"Epithelial tissue"*that covers surfaces of organs, glands, or body structures and there are four main types of carcinomas they are Melanoma, Basal cell carcinoma, Squamous cell skin cancer and Merkel cell carcinoma.

2) Sarcoma: It is a malignant tumor growing from connective tissues, such as cartilage, fat, muscles, tendons and bones. Most common sarcoma is of bone, example- osteosarcoma (occurs in bone) and chondrosarcoma (occurs in cartilage), there are somefour types of sarcomas they are soft tissue sarcoma, osteosarcoma, chondrosarcoma and Ewing's sarcoma.

3) Lymphoma: The cancer that originates in the nodes or glands in the lymphatic system, there are three types of lymphoma they are Hodgkin's lymphoma, non-Hodgkin's lymphoma and Cutaneous lymphoma.

4) Leukemia: Also called as "Blood Cancer" or cancer of bone marrow, that keeps bone marrow from producing normal red and white, blood cells and platelets. Types of leukemia includes Acute lymphocytic leukemia, Acute myeloid leukemia, Agnogenic myeloid leukemia, Chronic myeloid leukemia, Essential thrombocythemia (ET), Hairy cell leukemia and Myelodysplastic syndromes (MDS).

5) Myeloma: It grows in the plasma cells of bone marrow; in some cases, the myeloma cells collect in one bone and forms a single tumor that is called a plasmacytoma. However, in some other cases, the myeloma cells collect in many bones, forming many bone tumors, that is called multiple myeloma.

Causes of Cancer

There is not a single cause of cancer. Researchers believes that it is the interactivity of multiple factors together that generates the cancer. The factors maybe environmental, genetic or many others. The overall five-year survival rate for childhood cancer is about 80%, while in adult's cancers the surviving rate is 68%, as per researchers there are many and repetitive risk factors or exposures, which includes: [2,5,9,17,21,24]

- Genetic disorders: for example, Wiskott-Aldrich and Beckwith-Wiedemann syndrome alsocalled to change the immune system. One another theory suggests that cell in the stem cells, bone marrow becomes damaged, so when they replicate to make more cells, they make abnormal cells which are also known as cancer cells.
- Genetics, Inheritance and Family historymay play an important role in childhood cancers.
- Lifestyle factors: such as smoking, a high-fat diet and working with some of the toxic chemicals are examples of lifestyle choices that may berish factors for some adult cancers. Most children with cancer.

How Cancer is diagnosed?

There is not a single/ specific test to diagnose cancer. Many tests are needed to find out whether a person has cancer, or if any other condition or an infection is imitate the symptoms of cancer. [2,6,15,16,17,23] The complete evaluation of a patient requires a throughout history and physical examination along with diagnostic testing. Effective testing for diagnosis is used to confirm and eliminate the presence of disease, monitor the disease process and to effectively plan for its treatment. Diagnostic procedures for cancer may include Laboratory tests, tumor biopsy, imaging, surgery, endoscopic examinationor genetic testing. Some of the common tests to check the chemical components in bodily fluids and tissues are blood tests, (CBC), urinalysis, tumor markers. Diagnostic imaging includes X-rays, computed tomography scans (also known as CT scans or computer axial tomography or CAT scan), bone scanning, lymphangiogram (LAG), mammogram. Reflection imaging which includes ultrasound. Magnetic resonance imaging (MRI). Even there are some different types of endoscopic examinations used to diagnose cancer which includes cystoscopy (also called as cystourethroscopy), colonoscopy, endoscopic retrograde cholangiopancreatography (ERCP), esophagogastroduodenoscopy (also called as EGD or upper endoscopy), sigmoidoscopy. There are many different types of tumor biopsies used in the diagnosis of cancer, a biopsy is a procedure performed to remove tissue or cells from the body for examination under a microscope.

While others need to be done in a hospital. Some biopsies require use of an anesthetic, to numb the area, while other do not requires any kind of sedation. It is performed to determine whether tumor is cancerous or to determine the cause of an inflammation and infection. There are some frequent types of biopsies they are endoscopic biopsy, excisional or incisional biopsy, bone marrow biopsy, fine needle aspiration biopsy, punch biopsy, shave biopsy, and skin biopsy.

How Cancer is treated?

Depending on each person's medical history, condition and variety of cancer, the cancer is treated. [1,2,6,7,16,17] The most repeatedtreatments in today's world involve chemotherapy and radiation therapy and some of the other treatments includes surgery and biological therapies. There are some terms in treatment of cancer and they are:

- Neoadjuvant therapy: when doctors choose to use more than one therapy in treating a patient. Both to neutralize any cancer cells and donate to the efficacy of the principal therapy.
- Combined modality therapy: when doctors choose more than one remedy in treatment of a patient for example, a combination of radiation and chemotherapy.
- Adjuvant therapy: in this term more than one therapy in treating a patient. the treatment given after the primary cancer treatment is completed to improve the chance of a cure for example, sometimes the patient may be prescribed with multiple treatments.

The common treatments include:

1) Radiation therapy: In this the use of high-poweremission is used to kill or damage cancer cells, tumors and non-cancerous diseases, and it also has some disadvantages like side effects.

2) Chemotherapy: The most common treatment for a cancer nowadays is the chemotherapy. In this the use of anticancer agents to damage or kill cancerous cells and reduce cancer spreading to other parts of the body. It too has many side effects such as loss of hairs, tiredness (fatigue) is more primary side effect of chemotherapy, feeling and being sick, infections, anemia, bruising and bleeding, sore mouth, loss of appetite, skin and nail change, memory and concentration problems, sleep problems, sex and fertility issues, diarrhea and constipation, etc.

3) Hormone therapy: This technique includes the use of supplemental hormones to prevent or stop the growth or spread of tumors. And the type of therapy depends upon factors such as age of patient, the type and size of the tumor, and many of the other factors as well.

4) Bone marrow and blood transplant: This is a rare and specialized therapy in which transfer of health bone marrow cells into a patient after their own unhealthy bone marrow has been eliminated.

5) Biologic therapy: Treatments with substances which are produced naturally in the patient's own body or which can be used to block the cancer cells growth.

6) Immunotherapy: Also known as biotherapy, biological response therapy and biological therapy, is outline to improvethe body's immune system or in order to eliminate cancer. The organs, antibodies and cells of the immune management work to defend and protect the body against foreign invaders, such as viruses or bacteria. Researchers and scientists have found that the immune system can both determine the difference between cancerous cells and healthy cells in the body, and to kill the cancer cells.

7) Angiogenesis inhibitors: These are the substances which prevents the formation of blood vessels. In therapy, an angiogenesis inhibitor prevents the growth of new blood vessels that tumors need to grow.

CONCLUSION

Long way to go in optimizing the utilization of these therapies minimizing their complexity and toxicities and to learn how to integrate them into the current standard of care. Furthermore, there are many challenges ahead in incorporating them into the healthcare systems of an economically sustainable manner. Therefore, clinical researchers are beginning to crisp on managing and predicting these toxicities and monitoring their long-term outcomes. This may lead to guideline that how to manage these new therapies and should encourage clinicians to use them as early as possible in treatment pathways. However, currently not a specific treatment which for the disease there is a need in today's world to build a treatment which can cure the disease without promoting side effects or toxicity and long-term study are obligatoryfor the novel treatment of cancer.

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