Review Article CODEN: IJPRNK IMPACT FACTOR: 4.278 ISSN: 2277-8713
Martin A, IJPRBS, 2014; Volume 3(5): 249-257 IJPRBS

INTERNATIONAL JOURNAL OF PHARMACEUTICAL RESEARCH AND BIO-SCIENCE

RISK FACTORS AND TYPES OF TREATMENT ASSOCIATED WITH CANCER: AN OVERVIEW

MARTIN A[1], MARTIN R[2]

1. Department of Pharmaceutical Chemistry, Spectrum Institute of Pharmaceutical Sciences and Research, Greater Noida, India.
2. Department of Pharmaceutical Chemistry, Acharya and B.M. Reddy College of Pharmacy, Bengaluru, India.

Accepted Date: 24/09/2014; Published Date: 27/10/2014

Abstract: Cancer also known as a malignant tumor, is a group of diseases involving abnormal cell growth with the potential to invade or spread to other parts of the body. It can spread to other parts of the body through the blood and lymph systems. Cancers figure among the leading causes of death worldwide, accounting for 8.2 million deaths in 2012. There are more than 100 different types of cancer. However they are broadly categorized as Carcinoma, Sarcoma, Luekemia, Lymphoma and myeloma and Central Nervous system cancers. This review article gives an insight into types of cancer, its origin, risk factors associated with cancer and the types of treatment available for cancer.

Keywords: Cancer, types, origin, risk factors and types of treatment

PAPER-QR CODE

Corresponding Author: MR. ALEX MARTIN

Access Online On:

www.ijprbs.com

How to Cite This Article:

Martin A, Martin R; IJPRBS, 2014; Volume 3(5): 249-257

INTRODUCTION

Cancer is a term used for diseases in which abnormal cells divide without control and are able to invade other tissues. Cancer cells can spread to other parts of the body through the blood and lymph systems. Cancer is not just one disease but many diseases. There are more than 100 different types of cancer. Most cancers are named for the organ or type of cell in which they start - for example, cancer that begins in the colon is called colon cancer; cancer that begins in basal cells of the skin is called basal cell carcinoma.[1]

TYPES OF CANCER

Cancer types can be grouped into broader categories. The main categories of cancer include:

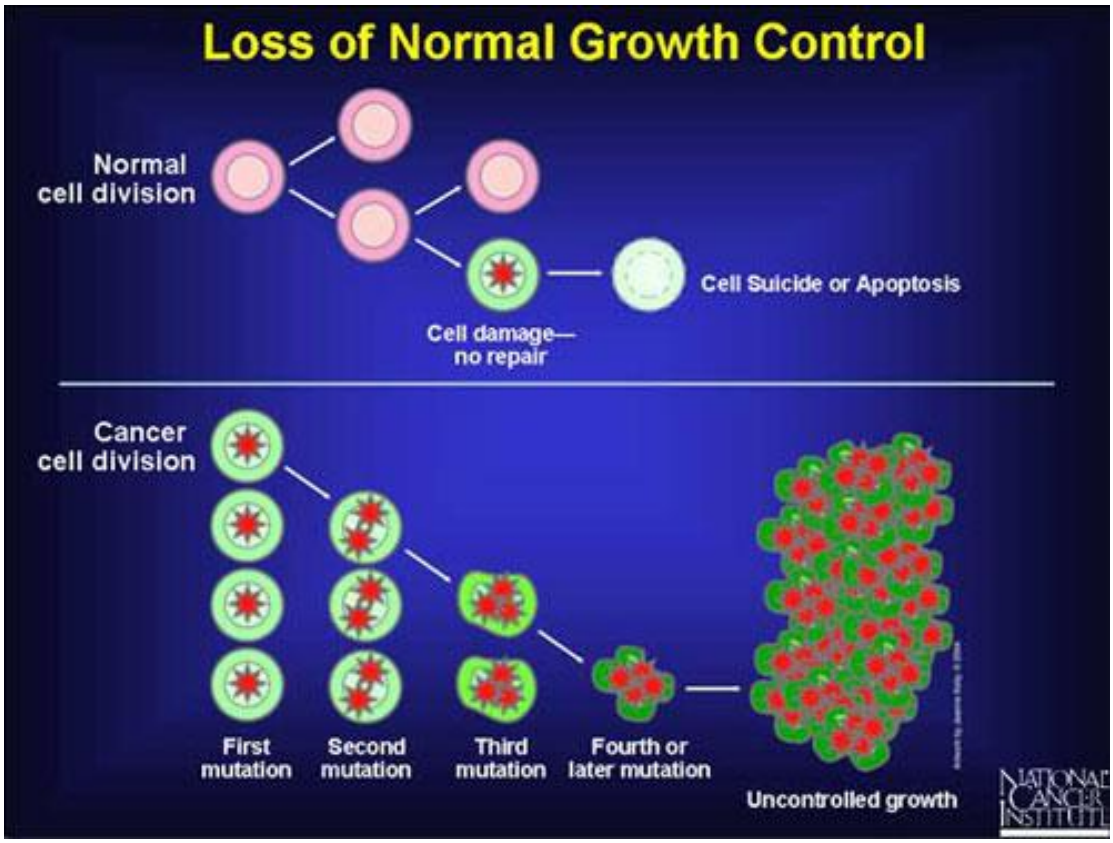
- **Carcinoma** - cancer that begins in the skin or in tissues that line or cover internal organs.
- **Sarcoma** - cancer that begins in bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.
- **Leukemia** - cancer that starts in blood-forming tissue such as the bone marrow and causes large numbers of abnormal blood cells to be produced and enter the blood.
- **Lymphoma and myeloma** - cancers that begin in the cells of the immune system.
- **Central nervous system cancers** - cancers that begin in the tissues of the brain and spinal cord.

ORIGINS OF CANCER

All cancers begin in cells, the body's basic unit of life. To understand cancer, it's helpful to know what happens when normal cells become cancer cells. The body is made up of many types of cells. These cells grow and divide in a controlled way to produce more cells as they are needed to keep the body healthy.

When cells become old or damaged, they die and are replaced with new cells. However; sometimes this orderly process goes wrong. The genetic material (DNA) of a cell can become damaged or changed, producing mutations that affect normal cell growth and division. When this happens, cells do not die when they should and new cells form when the body does not need them. The extra cells may form a mass of tissue called a tumor.

Figure: Growth pattern of Normal and Cancer cell



Not all tumors are cancerous; tumors can be benign or malignant.

- **Benign tumors** aren't cancerous. They can often be removed, and, in most cases, they do not come back. Cells in benign tumors do not spread to other parts of the body.
- **Malignant tumors** are cancerous. Cells in these tumors can invade nearby tissues and spread to other parts of the body. The spread of cancer from one part of the body to another is called metastasis.

Some cancers do not form tumors. For example, leukemia is a cancer of the bone marrow and blood.

RISK FACTORS ASSOCIATED WITH CANCER

- **Cigarette smoking/tobacco use**

Decades of research have consistently established the strong association between tobacco use and cancers of many sites. Specifically, cigarette smoking has been established as a cause of cancers of the lung, oral cavity, esophagus, bladder, kidney, pancreas, stomach, cervix, and acute myelogenous leukemia. Smoking avoidance and smoking cessation result in decreased incidence and mortality from cancer.

- **Infections**

Globally, infectious agents have been estimated to cause 18% of all cancer cases. The burden of cancers caused by infections is much greater in developing nations (26%) than in developed nations (8%). Infection with an oncogenic strain of human papilloma virus (HPV) is considered a necessary event for subsequent cervix cancer, and vaccine-conferred immunity results in a marked decrease in precancerous lesions. Oncogenic strains of HPV are also linked with cancers of the penis, vagina, anus, and oropharynx. Other examples of infectious agents that cause cancer are hepatitis B and hepatitis C viruses (liver cancer), Epstein-Barr virus (Burkitt lymphoma), and *Helicobacter pylori* (gastric cancer).

- **Radiation**

Radiation is energy in the form of high-speed particles or electromagnetic waves. Exposure to radiation, primarily ultraviolet radiation and ionizing radiation, is a clearly established cause of cancer. Exposure to solar ultraviolet radiation is the major cause of nonmelanoma skin cancers, which are by far the most common malignancies in human populations.[2]

Ionizing radiation is radiation with enough energy to remove tightly bound electrons from their orbits, causing atoms to become charged or ionized. Ions formed in the molecules of living cells can go on to react with and potentially damage other atoms in the cell. At low doses (e.g., those associated with background radiation), the cells repair the damage rapidly. At moderate doses, the cells may be changed permanently or die from their inability to repair the damage. Cells changed permanently may go on to produce abnormal cells when they divide, and in some circumstances, these altered cells may become cancerous or lead to other abnormalities (e.g., birth defects).

RISK FACTORS WITH UNCERTAIN ASSOCIATIONS WITH CANCER

- **Diet**

An assessment of the overall evidence of diet in relation to cancer prevention published by the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) [3] was based on systematic reviews of the epidemiologic evidence. With respect to dietary factors that may protect against cancer, the greatest consistency was seen for fruits and nonstarchy vegetables. In the WCRF/AICR report, conclusions were reached that both fruits and nonstarchy vegetables were associated with “probable decreased risk” for cancers of the mouth, esophagus, and stomach.

Life-long dietary patterns or dietary intake during specific life stages may be important in inducing or preventing cancer but would not be detected by relatively short-term randomized clinical trials.

- **Alcohol**

With respect to dietary factors that may increase cancer risk, the strongest evidence in the WCRF/AICR report was for drinking alcohol. The evidence was judged to be "convincing" that drinking alcohol increased the risk of cancers of the mouth, esophagus, breast, and colorectum (the latter in men). Further, the evidence was judged to be "probable" that drinking alcohol increased the risk of liver cancer and colorectal cancer (CRC) (the latter in women).

- **Physical activity**

A growing body of epidemiologic evidence suggests that people who are more physically active have a lower risk of certain malignancies than those who are more sedentary. In the WCRF/AICR report, the evidence was judged to be "convincing" that increased physical activity protects against CRC.

- **Obesity**

Obesity is being increasingly recognized as an important cancer risk factor. The study results revealed that obesity was associated with an increased risk of dying from obesity-associated malignancies, but obesity was not associated with overall cancer mortality.[4]

TYPES OF TREATMENT

- **Chemotherapy**

Chemotherapy (also called chemo) is a type of cancer treatment that uses drugs to destroy cancer cells. Chemotherapy works by stopping or slowing the growth of cancer cells, which grow and divide quickly. But it can also harm healthy cells that divide quickly, such as those that line your mouth and intestines or cause your hair to grow. Damage to healthy cells may cause side effects. Often, side effects get better or go away after chemotherapy is over.

- **Radiation therapy**

Radiation therapy uses high-energy radiation to shrink tumors and kill cancer cells.[5] X-rays, gamma rays, and charged particles are types of radiation used for cancer treatment. The radiation may be delivered by a machine outside the body (external-beam radiation therapy), or it may come from radioactive material placed in the body near cancer cells (internal radiation therapy, also called brachytherapy).Systemic radiation therapy uses radioactive substances, such as radioactive iodine, that travel in the blood to kill cancer cells.

- **Cryosurgery**

Cryosurgery (also called cryotherapy) is the use of extreme cold produced by liquid nitrogen (or argon gas) to destroy abnormal tissue. Cryosurgery is used to treat external tumors, such as those on the skin. For external tumors, liquid nitrogen is applied directly to the cancer cells with

a cotton swab or spraying device. Cryosurgery offers advantages over other methods of cancer treatment. It is less invasive than surgery, involving only a small incision or insertion of the cryoprobe (a hollow instrument) through the skin.

- **Transplantation**

a) Childhood Hematopoietic Cell Transplantation (PDQ)

Blood and marrow transplantation (BMT) or HCT is a procedure that involves infusion of cells (hematopoietic stem cells [HSCs]; also called hematopoietic progenitor cells [HPCs]) that reconstitute the hematopoietic system of a patient. The infusion of HSCs generally follows a preparative regimen given to the patient consisting of agents designed to do the following:

- Suppress the patient's immune system to prevent rejection.
- Intensively treat malignant cells in patients with cancer

b) **Bone Marrow Transplantation and Peripheral Blood Stem Cell Transplantation**

Bone marrow transplantation and peripheral blood stem cell transplantation are procedures that restore stem cells that were destroyed by high doses of chemotherapy and/or radiation therapy. After being treated with high-dose anticancer drugs and/or radiation, the patient receives the harvested stem cells, which travel to the bone marrow and begin to produce new blood cells.

c) **Other treatment methods**

i) Angiogenesis inhibitors

Angiogenesis is the formation of new blood vessels. This process involves the migration, growth, and differentiation of endothelial cells, which line the inside wall of blood vessels. The process of angiogenesis is controlled by chemical signals in the body. Angiogenesis plays a critical role in the growth and spread of cancer.

Angiogenesis requires the binding of signaling molecules, such as vascular endothelial growth factor (VEGF), to receptors on the surface of normal endothelial cells. When VEGF and other endothelial growth factors bind to their receptors on endothelial cells, signals within these cells are initiated that promote the growth and survival of new blood vessels.

Angiogenesis inhibitors interfere with various steps in this process. For example, **bevacizumab** is a monoclonal antibody that specifically recognizes and binds to VEGF.[6]

ii) **Biological therapy**

Biological therapy is a type of treatment that works with your immune system. It can help fight cancer or help control side effects from other cancer treatments like chemotherapy.

iii) **Gene therapy**

Gene therapy is an experimental treatment that involves introducing genetic material (DNA or RNA) into a person's cells to fight disease. A gene can be delivered to a cell using a carrier known as a "vector." The most common types of vectors used in gene therapy are viruses

iv) Hyperthermia

Hyperthermia (also called thermal therapy or thermotherapy) is a type of cancer treatment in which body tissue is exposed to high temperatures (up to 113°F). Hyperthermia is almost always used with other forms of cancer therapy, such as radiation therapy and chemotherapy.[7]

v) Laser therapy

Laser light can be used to remove cancer or precancerous growths or to relieve symptoms of cancer. It is used most often to treat cancers on the surface of the body or the lining of internal organs. Laser therapy is often given through a thin tube called an endoscope, which can be inserted in openings in the body to treat cancer or precancerous growths inside the trachea (windpipe), esophagus, stomach or colon.

vi) Photodynamic therapy

Photodynamic therapy (PDT) is a treatment that uses a drug, called a photosensitizer or photosensitizing agent, and a particular type of light. When photosensitizers are exposed to a specific wavelength of light, they produce a form of oxygen that kills nearby cells.[8-10] The U.S. Food and Drug Administration have approved the photosensitizing agent called porfimer sodium, for use in PDT to treat or relieve the symptoms of certain cancers.

vii) **Targeted cancer therapy**

Targeted cancer therapies are drugs or other substances that block the growth and spread of cancer by interfering with specific molecules involved in tumor growth and progression. By focusing on molecular and cellular changes that are specific to cancer, targeted cancer therapies may be more effective than other types of treatment, including chemotherapy and radiotherapy, and less harmful to normal cells.

viii) **Chemoprevention**

Chemoprevention refers to the use of natural or synthetic compounds to interfere with early stages of carcinogenesis, before invasive cancer appears[11]**.** Chemoprevention trials have had some positive results. Daily use of selective estrogen receptor modulators (tamoxifen or raloxifene) for up to 5 years reduces the incidence of breast cancer by about 50% in high-risk women. Finasteride (an alpha-reductase inhibitor) lowers the incidence of prostate cancer; this finding was complicated by a greater cumulative incidence of high-grade cancers in the finasteride-versus-placebo-group. Further analysis suggests this was due to finasteride's

shrinking the prostate but not the cancer, thereby increasing the ability to diagnose high-grade cancer without contributing to progression of prostate carcinogenesis. Dutasteride has also been shown to reduce the incidence of prostate cancer.[12] The impact of finasteride on prostate cancer mortality is uncertain.

Other chemoprevention candidates include COX-2 inhibitors and aspirin. COX-2 inhibitors inhibit the cyclooxygenase enzymes involved in the synthesis of proinflammatory prostaglandins. There is evidence to suggest that COX-2 inhibitors prevent colon and breast cancer, but the possibility of increased cardiovascular events may preclude their usefulness. In secondary analyses of pooled data from seven randomized placebo-controlled trials whose primary endpoints were vascular events, aspirin taken daily for 4 or more years was associated with an 18% reduction in overall cancer deaths (odds ratio, 0.82; 95% confidence interval [CI], 0.70–0.95).[13] Whether or not aspirin would have the same impact in reducing cancer incidence remains an open question, but the evidence for colon cancer suggests it may. Also, assessment of the risk-benefit profile needs to account for the effect of aspirin on the risk of bleeding.

CANCER DRUG DISCOVERY

Thirty-five years after the 'war on cancer' was declared, the discovery of anticancer drugs remains a highly challenging endeavour.[14] Cancer drug development is leading the way in exploiting molecular biological and genetic information to develop 'personalized' medicine. The new paradigm is to develop agents that target the precise molecular pathology driving the progression of individual cancers. Drug developers have benefited from decades of academic cancer research and from investment in genomics, genetics and automation; their success is exemplified by high-profile drugs such as Herceptin (trastuzumab), Gleevec (imatinib), Tarceva (erlotinib) and Avastin (bevacizumab). However, only 5% of cancer drugs entering clinical trials reach marketing approval. Cancer remains a high unmet medical need, and many potential cancer targets remain undrugged.[15]

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