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## CANCER CAUSES AND TREATMENTS

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**ABSTRACT:** Cancer is a genetic disorder that results from genetic or epigenetic alterations in the somatic cells and has abnormal cell growth which may be spread to other body parts. In 2018, 18 million cancer was recorded globally in which 9.5 million cancer cases in men, 8.5 million cases in women, and 9.6 deaths were also recorded in the same year. The most spreading cancer globally is prostate, breast, lung stomach, colorectal cancer, non-melanoma skin malignancies but there are 100 types of cancers that affect humans. The impact of cancer is increasing significantly day by day. Tobacco is 22% responsible for causing cancer, 15% cancer is caused due some infections like HIV, hepatitis b, Epstein-Barretc, and 10% is due to poor diet, obesity, excessive consumption of alcohol, exposure to ionizing radiation, *etc.* In this review article, we try to shed a light on various cancer-causing factors, type of cancer, how the cancer starts, sign or symptom of cancer, diagnosing tests, the treatments of cancer and problems related to cancer treatments. Nowadays, a lot of research is going on precision medicine for a better future of cancer treatments. The common therapies are given to patient's chemotherapy, radiation therapy, immunotherapy, surgery and hormone therapy and combinations of these therapies. Stem cell transplant is also the best therapy for cancer but it given after the common therapies to recover the patient from blood loss and help in making the patient healthy.

**INTRODUCTION: Cancer:** Cancer is a disorder that results from genetic or epigenetic alterations in the somatic cells and has abnormal cell growth which may be spread to other body parts. They form a subset of neoplasm. The unregulated growth of cells in a group called neoplasm or tumor and they form a lump or mass and may be distributed diffusely<sup>1-3</sup>.

It was predicted by Global demographic characteristics that about 420 million new cases of cancer by 2025 annually, which means increasing cancer incidence in years. Cases of cancer about 18 million in 2018 were recorded worldwide; in men, about 9.5 million and women about 8.5 million.

Globally about 9.6 million deaths were estimated in cancer<sup>4, 5</sup>. The commonest cancers are prostate cancer (1.28 million), female breast cancer (2.09 million), colorectal cancer (1.1 million), stomach cancer (1.03 million) and non-melanoma skin malignancies (1.04 million)<sup>6, 7</sup>. Cancer-related deaths, from most to least frequent, are due to lung cancer (1.76 million), colorectal cancer (862,000),

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and stomach cancer (783,000), liver cancer (782,000). Over 100 types of cancers affect humans<sup>8</sup>.

### Key Facts:

- ✓ Globally about 9.6 million in 2018 deaths were estimated in cancer which represents the cancer is the second leading cause of deaths and about 1 in 6 deaths are due to cancer<sup>4</sup>.
- ✓ About 70% of deaths in middle- income and Low Countries are due to cancer<sup>5</sup>.
- ✓ The main and the most important cause of cancer is tobacco use, approximately 22%<sup>10, 11</sup>.
- ✓ There are also some infections that cause cancer, like Human papilloma Virus (HPV), are causes 25% of cancer in middle and low-income countries<sup>11</sup>.
- ✓ In 2017, solely twenty-sixths of low-income countries reported having pathology services usually obtainable within the public sector.
- ✓ More than ninetieth of high-income countries reported treatment services square measure obtainable compared to but a half-hour of low-income countries<sup>12</sup>.
- ✓ The impact of cancer is increasing significantly day by day.
- ✓ The cancer policy is necessary for all countries, but many countries do not have these policies.

**Problems:** Globally, about 9.6 million in 2018 deaths were estimated in cancer, which represents the cancer is the second leading cause of deaths. The most common cancers are:<sup>4,8</sup>

- ✓ Lung (2.09 million cases)
- ✓ Breast (2.09 million cases)
- ✓ Colorectal (1.80 million cases)
- ✓ Prostate (1.28 million cases)
- ✓ Skin cancer (non-melanoma) (1.04 million cases)
- ✓ Stomach (1.03 million cases)

The most common causes of cancer death are cancers of:

- ✓ Lung (1.76 million deaths)
- ✓ Colorectal (862 000 deaths)
- ✓ Stomach (783 000 deaths)
- ✓ Liver (782 000 deaths)
- ✓ Breast (627 000 deaths)

### Causes of Cancer:<sup>13, 14</sup>

- There are many causes which may cause cancer in different body parts like mainly 22% deaths are due to tobacco consumption, 10% of deaths are due to poor diet, obesity, lack of physical activity, excessive drinking of alcohol or other facts include certain exposure to ionizing radiation, environmental pollutants, and infection.
- About 15% of cancer in the world is due to some infections like hepatitis b, hepatitis c, human papillomavirus infection, helicobacter pylori, and immunodeficiency virus (HIV), Epstein - Barr virus. These factors are at least partly responsible for changing the genes.
- Inherited genetic defects from patient's parents are also responsible for 5-10% of cancer.
- Cancer is caused by the interaction between genetic factors and 3 categories of agents which we consume externally including:
  - i. **Physical Carcinogens:** Ionizing radiation such as radon, ultraviolet rays from sunlight, uranium, radiation from alpha, gamma, beta, and X-ray-emitting sources.
  - ii. **Chemical Carcinogens:** Compounds like n-nitrosamines, asbestos, cadmium, benzene, vinyl chloride, nickel, and benzidine and contains about 60 known potent cancer-causing toxins or chemicals in cigarette smoking or tobacco consumption, a drinking water contaminant (arsenic), a food contaminant (aflatoxin)<sup>12</sup>.
  - iii. **Biological Carcinogens:** Infections from certain bacteria, viruses, or parasites and Pathogens like human papillomavirus (HPV), EBV or Epstein-Barr virus, hepatitis B and C,

Kaposi's sarcoma-associated herpesvirus (KSHV), Merkel cell polyomavirus, *Schistosoma* spp., and *Helicobacter pylori*.

Aging is also the cause of cancer. Age is the common incidence of cancer, which dramatically rises.

- **Genetics:** Genetic is the commonest cause for cancer or tumor-like Ovarian, breast, prostate, skin cancer, colorectal cancer. Individuals that eat heaps of cooked meat can also increase risk because of compounds fashioned at high temperatures. Proving that a substance doesn't cause or isn't associated with hyperbolic cancer risk is tough.

**Types of Cancer:** Cancers are divided into various types that are:<sup>15</sup>

- a. **Carcinomas:** It starts in the tissue or the skin, which covers the glands and internal organ surface. It forms a solid tumor. Breast cancer, prostate cancer, colorectal cancer, lung cancer.
- b. **Sarcomas:** It starts in the tissues which connect and support the body. It can be formed in nerves, tendons, joints, fat, blood vessels, bone, lymph vessels, muscles, or cartilage.
- c. **Leukemia's:** Leukemia is a cancer of the blood. It begins when healthy blood cells grow uncontrollably and change. It is divided into 4 types, that are acute myeloid leukemia, acute lymphocytic leukemia, chronic myeloid leukemia, and chronic lymphocytic leukemia
- d. **Lymphomas:** Lymphoma is cancer that begins in the lymphatic system and it is a network of glands and vessels that helps to fight with infection. Hodgkin lymphoma and Non-Hodgkin lymphoma.
- e. **Central Nervous System Cancers:** Cancer that starts in brain tissues and spinal cord called "brain and spinal cord tumors", and others primary CNS lymphomas, vestibular schwannomas, gliomas, pituitary adenomas, primitive neuro-ectodermal tumors, meningiomas, and vestibular schwannomas.
- f. **Multiple Myeloma:** Multiple myelomas is cancer that begins in plasma cells, another type

of immune cell. The myeloma cells which are plasma cells, are build up in bone marrow and make tumors in bones. It is called plasma cell myeloma and Kahler disease.

- g. **Melanoma:** It starts in cells that become melanocytes. These cells are specialized cells that make melanin, i.e., the pigment that gives the color to the skin. Mainly melanomas develop on the skin, but it can also develop in other pigmented tissue like an eye.

#### h. Other Types of Tumors:

**Germ Cell Tumors:** It is the type of tumor that starts in the cells which give rise to eggs or sperms. This can be occurring anywhere in the body and either malignant or benign.

**Neuroendocrine Tumors:** Neuroendocrine tumors form from cells that release hormones into the blood in response to a signal from the nervous system. It forms from those cells which release hormones in blood in response to signal from the nervous system. These tumors, which can create higher-than-normal amounts of hormones, will cause many various symptoms. It may be either benign or malignant.

**How it Begins:** There are several steps by which cancer begins in the body:<sup>16</sup>

1. **Cell Changes and Cancer:** Our body is made up of small units called cells and more than 100,000,000,000,000 cells combine to makes our body. All types of cancer firstly start in cells by changes. Usually, our body has the right number of cells because the cell produces signals. if any signal is missing than cells may start to multiply unnecessarily and make a lump which also called a tumor. But there are also other types of cancer which start from different pathways like blood cells this cancer is called leukemia, and they not make a solid lump.
2. **Genes and Cell Division:** Our body has different cells for a different job, but they all are similar. They all have nuclei that control the cell and the nucleus contains chromosomes which are made up of thousands of genes. A long string of DNA (Deoxyribonucleic acid) called genes, which

contain a coded message which tells the cell how to behave or divide. When the right time occurs for cell division, the cells divide and make the exact similar copies of them. One cell divides into 2 identical cells, and then 2 cells divide into 4, and so on.

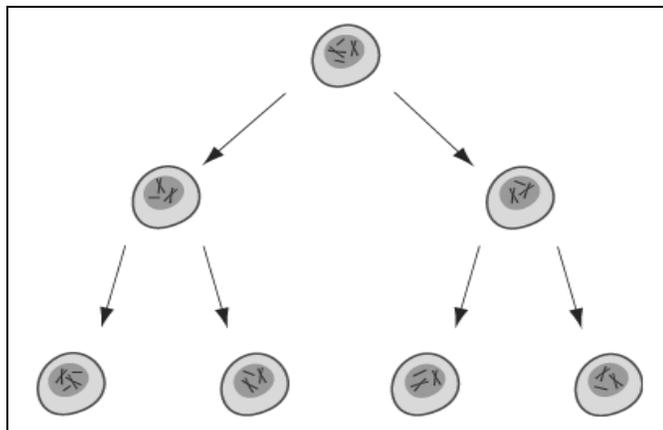


FIG. 1: CELL DIVISION

### 3. Gene Changes within Cells (Mutations):

When a cell is dividing mainly, a mutation occurs in this step but also by the chemical changes which are coming from outside like tobacco smoke, and it is happening by chance. Mutation means the gene is copied twice, damaged or lost. The meaning of mutation is that the cells are not growing by its instructions, and grow unnecessarily. Mutation of genes may mean that a cell stops producing proteins that require cell division and may produce too many proteins by which the cell division occurs rapidly and form lump or tumor, the tumor is made up of millions of cancer cells.

**4. How Cancer Grows:** A cancer can continue to grow because cancer cells act differently than normal cells. Cancer cells have the same needs as normal cells. Cancer cells need nutrients and oxygen from blood vessels to survive and grow. The tumor can easily grow by nutrients and oxygen. They need a blood supply to bring oxygen and nutrients to grow and survive. When a tumor is very small, it can easily grow, and it gets oxygen and nutrients from nearby blood vessels. Cancer cells are different from normal cells because of they:

- Divide out of control

- They are immature and don't develop into mature cells with specific jobs.
- Avoid the immune system.
- Ignore signals that tell them to stop dividing or to die when they should.
- Don't stick together very well, and through blood or lymphatic system, they can spread to other body parts.
- Grow into and damage tissues and organs.

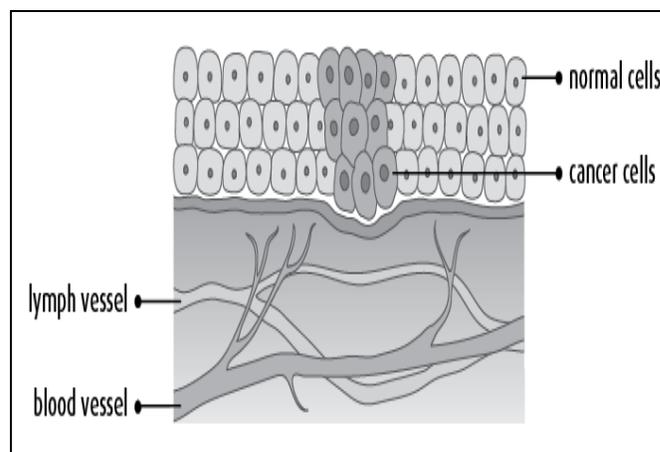


FIG. 2: HOW CANCER GROWS

**How it Spread:** As the tumor grows, the cancer cells are carried with the lymphatic system or bloodstream to other body parts, Then the cancer cells may be developed into new tumors and it is called metastasis. Cancer may spread to lymph nodes, which are bean-shaped organs and tiny that helps to fight with infection. Neck; underarms and groin area *etc.* these are the body parts where the lymph nodes are located. Cancer may also spread through the bloodstream to other body parts like the liver, bones, brain, or lungs. If cancer spreads to different body parts from that area where it began than it is named as metastatic cancer of that particular area where it starts.

For example, if lung cancer spreads to the breast than it is called metastatic lung cancer, not breast cancer.

**Common Cancers:** There are more than 100 cancers which affect humans but commonest among all are: Bladder, breast (female-male), endometrial, thyroid, colorectal cancer, leukemia, lung (including bronchus), melanoma, kidney (renal cell and renal pelvis) cancer, non-Hodgkin lymphoma, prostate, pancreatic cancer<sup>17-19</sup>.

**Symptoms and Signs of Cancer:**<sup>20</sup>

**Early Symptoms:** At the earliest stage cancer gives no sign or symptoms by which we cannot indicate the disease. Moreover, the symptoms or signs are shown in harm condition.

Some common symptoms that may occur with cancer are as follows:

1. **Persistent Cough or Blood-Tinged Saliva:** If anyone is having cough from a month or blood in the mucus, then these are the sign of bronchitis or sinusitis, but they could be symptoms of neck, head or lung cancer.
2. **A Change in Bowel Habits:** It usually depends on the diet of a person and fluid intake. People with cancer felt that they need to have a bowel movement and also feel the same if they had if this symptom lasts more than a few days than it is a symptom of cancer. Mainly in cancer, there is continuous diarrhea.
3. **Blood in the Stool:** It is also the early symptom of cancer by which we can examine cancer. The evaluation includes colonoscopy *etc.*
4. **Unexplained Anemia:** People with low RBC in their blood from normal, then this condition is called anemia. Bowel cancer can cause iron-deficiency anemia. The evaluation includes X-ray studies or endoscopy of your lower and upper intestinal tracts.
5. **Breast Lump or Breast Discharge:** Most breast lumps are noncancerous tumors like cysts or adenomas, but all lumps are needed to check. The evaluation includes Ultrasound and x-ray study included MRI of the breast. Discharge from the breast is also the sign of cancer, and it is quite common, but not from only one nipple or bloody.
6. **Lumps in the Testicles:** Men with cancer have an uncomfortable or painless lump on a testicle.
7. **Change in Urination:** The symptoms are slow urine flow, frequent urination, change in bladder function or small amounts of urine, caused by a urinary infection in women or by an enlarged prostate gland. Most men will suffer from enlargement of the prostate gland as they age, these may be the symptom of prostate

cancer. The evaluation includes PSA blood tests and the biopsy of the prostate.

8. Persistent back pain
9. Unexplained weight loss
10. Stomach pain and nausea
11. Bone pain

**Late Symptoms:** These symptoms are depending on cancer type, location or where the cancer cells have spread.

- Change in bowel or bladder habits
- Obvious change in the size, color, shape, or thickness of a wart or mole
- Indigestion or difficulty in swallowing
- Change in size, shape, color or thickness of mole.
- A sore throat that does not heal.
- Hoarseness
- Thickening or lump in the breast, testicles, or elsewhere

Other signs or symptoms may also alert you. These include the following:

- Unexplained loss of weight or loss of appetite
- Nausea
- Vomiting
- Fatigue
- Unexplained low-grade fevers may be either persistent or not.
- Recurring Infections
- Pain in the bones and other body parts

Many cancers will present in with general signs or symptoms, but they often have more than these symptoms, for more specifications. For example, lung cancers have a common symptom of pain in the chest. The patient may have a persistent cough with bleeding. Lung cancer patients are become very fatigued due to shortness of breath.

**Diagnosis:** Diagnosis of cancer is carried by doctors by taking screening tests of patients. For example, colonoscopy, mammography, and a pap test. Other tests are also performed before screening tests to check the abnormalities in the body. For example, CT scan, MRI scan, X-rays and ultrasound. In that area which is not clearly visualized like some lymph nodes or inside bones, radionuclide test is performed for this purpose.

Person with cancer who have no symptom then they diagnosed during tests of other condition or issues, and if any person has symptoms of cancer doctor will perform various tests<sup>21,22</sup>.

**Lab Tests:** Lab test include urine, blood and other body fluids to measures the substances which are responsible for the cancer in our body, like low and high levels of the substance which can cause cancer. Tumor markers are produced by the cancer cells and other cells in response to cancer. Lab tests are not the accurate result for cancer diagnosis, so doctor needs to clarify these tests by performing other cancer tests also.

**Imaging Tests:** In this test, the picture of the area inside the body are created which help to see the tumor present or not. It involves tests like:

**Ct Scan:** This scan is used to create 3-dimension images of your organs from different angles by X-ray machines which are linked to the computer. Usually, before the scanning, you may have to take a dye or other contrast material which helps to make the picture easier to identify certain areas of body. In the donut-shaped scanner machine the picture taken by moving around the body.

**MRI:** This scan is also used to take the picture of the body organs by taking pictures in slices and create detailed image. Radio waves and powerful magnet are used to take the slices. This scan shows the exact difference between unhealthy and healthy tissues. As in CT scan, before MRI scans also you have to take a dye for further scan. It is a round chamber machine in which the body is pushed and it makes rhythmic beats and loud thumping noise.

**Nuclear Scan:** It is also called a radionuclide scan because radioactive material is used to take the picture of body organs. As a CT and MRI scan, the person needs to receive a small amount of radioactive material in the injection form known as a tracer. It collects in the bones by flowing through blood. In this scanner measure the radioactivity and create pictures of organs or bones on film or on the screen of the computer. It includes 2 scans named as: Pet and bone scan.

**Bone Scan:** It is used to checking for damage to bones or abnormal areas. Before the scan person has to take the small radioactive material in his/her

vein, it travels through the blood and collects in an abnormal area in the bones. A special scanner pictured the material where it collects, and these areas are called hot spots.

**Pet Scan:** In this scan, the radioactive glucose material is used for the 3-D picture of body organs because cancer cells consume more glucose than healthy cells.

**Ultrasound:** In ultrasound, high energy sound waves are used for the echo of tissues because these waves, people cannot hear. The computer uses these echoes to create a picture of body organs where a device called transducer slowly moves on the skin and the picture is called a sonogram.

**X-rays:** In X-ray scan, x-rays are used in low doses of radiation to create a picture of body organs and you have to stay still withholding the breath for 1-2 seconds when the beam is directing on the body part.

**Biopsy:** Biopsy is the test in which the doctor removes a sample of tissue from the patient's body for diagnosing cancer. Then a pathologist does further test and looks tissue in the microscope and described all details in the pathology report. Sedative and anesthesia are given to patients before biopsy for relaxation. The biopsy sample is obtained in various ways:

- i. **With Needle:** Needle is used to withdraw fluid or tissue from the body. This method is used for spinal taps, bone marrow aspirations, prostate, and liver and breast biopsies.
- ii. **With Endoscopy:** In this method, the endoscope which is a thin and lighted tube, goes inside from natural body openings, such as anus or mouth to examine the areas inside the body. If the doctor sees any abnormal tissue during an examination, then he removes the abnormal tissue with normal tissues. For example, Colonoscopy, bronchoscopy.
- iii. **With Surgery:** Through surgery, the area of abnormal cells is removed. It may be excisional, in which the surgeon removes the entire area of abnormal cells with some

normal cells and incisional, in which a small part of an abnormal area is removed.

**Diagnosis:** After tests and reports if anyone having cancer then the doctor will figure out the stage of cancer for the best treatment.

**Side Effects of Cancer Treatments:** The treatment of cancer can affect also to the normal cells, tissue, and organs<sup>23</sup>. Side effects are the effects of treatment which are shown with therapeutic effect. Common side effects are shown below<sup>24-26</sup>

- Anemia
- Appetite loss
- Bruising and bleeding (thrombocytopenia)
- Constipation
- Delirium
- Diarrhea
- Edema
- Fatigue
- Fertility issue in boys and men
- Fertility issue in girl and women
- Flu-like symptoms
- Hair loss (Alopecia)
- Infection and Neutropenia
- Lymphedema
- Memory or concentration problems
- Mouth and throat problems
- Nausea and vomiting
- Nerve problems (Peripheral Neuropathy)
- Organ related inflammation and immunotherapy
- Pain
- Sexual health issue in both men and women
- Skin and nail changes
- Sleep problems
- Urinary and bladder problems.

**Types of Cancer Treatments:** There are various types of cancer treatments, which depend upon the cancer type and how to advance it is. Some patients have only one cancer treatment but mainly have a combination of treatments like surgery with radiation therapy.

The various types of treatments are:<sup>27</sup>

❖ **Surgery:** To prevent or reduce the disease's spread and remove cancer from the body, surgeon may remove lymph nodes.

❖ **Radiation Therapy:** In this therapy high doses of radiation are used to treat cancer by shrinking tumors and to kill cancer cells.

❖ **Chemotherapy:** In this therapy, chemicals are used to treat cancer by killing cancer cells and also by shrink tumors but have severe side effects.

❖ **Immunotherapy:** In this therapy, the immune system is boost by medication or other treatments. Example, adoptive cell and checkpoint inhibitors treatment.

❖ **Targeted Therapy:** In this therapy, changes in a cancer cell that help them divide, spread and grow by targeting and immune system also boost. Example, monoclonal antibodies and small-molecule drugs.

❖ **Hormone Therapy:** In this therapy, hormones are used to treat cancer, such as prostate and breast by stop and slow growth.

❖ **Stem Cell Transplants:** In this therapy, the stem cells restore in cancer patients, which are destroyed by very high doses of radiation or chemotherapy.

❖ **Precision Medicine:** It is the newer approach, in which the best treatment for a patient is determined by genetic testing.

**Surgery:** To prevent or reduce the disease's spread and remove cancer from the body, the surgeon may remove lymph nodes. Small thin knives called scalpels are used by the surgeons and other sharp tools also used to cut through muscle, skin and sometimes bones during surgery. These cuts are painful after surgery before surgery anesthesia is given to the patient to relieve from pain<sup>29</sup>.

Surgeries are used for the solid tumor, which is the local treatment because it contained in one area. Surgery is not used for metastatic cancer or leukemia *i.e.*, blood cancer. The patient needs good nutrition before and after the surgery if he/she is underweight and weak.

Food intake of the patient will change after the surgery of the intestine, mouth, throat or stomach. The food is given in an IV or feeding tube. Other surgeries also present for treatment of cancer which does not involve any cuts are:

- i. **Cryosurgery / Cryotherapy:** This therapy is used to treat precancerous growth on the cervix and skin by argon gas and nitrogen gas to destroy abnormal cells from extreme cold.
- ii. **Lasers:** This treatment is used for more precise surgeries because it has an accurate focus on small areas and it is also used to shrink or destroy a tumor. This powerful beam of light is used for treatment on the skin or inside the lining of internal organs. For example, vaginal, cervical, basal cell carcinoma.
- iii. **Hyperthermia:** In this therapy, the small body part is exposed to a high temperature so this heat kills cancer cells and makes sense to radiation or chemotherapy drugs. High energy radio waves are used to provide heat.
- iv. **Photodynamic Therapy:** In this therapy, photodynamic drugs are used to treat cancer cells. These drugs are reacting with a particular light, and then tumors are exposed to that particular light, and this drug becomes active and kills cancer cells that are nearby it. Non-small cell lung cancer and skin cancer are treating by this therapy.

**How it Works:** Surgery conditions are depending on the cancer type and advancements of cancer. Surgery can be used to:

- Remove the entire tumor
- Remove some but not all tumor. De-bulking is used when removing an entire tumor might damage an organ or the body.
- Remove tumor that causing pressure or pain.

**Problems:** Common problems are:

- **Pain:** Pain at the part of the body where surgery has happened is a common problem regarding surgery.
- **Infection:** Infection can cause after surgery, it can be prevented by taking antibiotics.

**Radiation therapy/Radiotherapy:** In this therapy high doses of radiation are used to treat cancer by shrinking tumors, killing cancer cells, and slow the growth of cancer cells by damaging their DNA

because the damaged DNA does not repair and the cell die which is removed by the body. The treatment takes weeks or months and prevents from returning. Radiopharmaceuticals are the drugs of systemic radiation therapy, are used to treat pain that spread to bones, and the external beam is used to treat pain, loss of bowel, bladder control, and trouble breathing by the shrinking tumor. Systemic means the treatment travel through the blood to tissue throughout the body and treatment received by IV and by swallowing<sup>30-33</sup>.

Examples,

- Brachytherapy is used to treat breast, neck, cervix, and eye and head cancer with the help of external beam
- Thyroid cancer is treated by radioactive iodine or i-131.
- Radio nucleotide therapy is used to treat the gastro-entero-pancreatic neuroendocrine tumor and advance prostate cancer.

Radiation therapy is given with other cancer treatments for better results such as chemotherapy, surgery, and immunotherapy. For example, radiation therapy in combination with surgery:

- Before surgery, radiation therapy used to shrink the cancer
- During surgery, the radiation will go directly to cancer,
- After surgery, to kill cancer cells which remain?

**Side Effects:** Radiation therapy can cause many side effects, which are generally shown by the normal cells that are damaged by the radiation.

**Chemotherapy:** In this therapy, chemicals are used to treat cancer by stopping or slowing the growth of cancer cells or by killing cancer cells or also by shrink tumors that causing pain and other problems but have severe side effects. Chemotherapy is given only and also given with other cancer treatments that depend upon the cancer type<sup>34-36</sup>.

Example:

- Neo-adjuvant chemotherapy, in this tumor, is made smaller before surgery or radiation therapy.

- Adjuvant chemotherapy, in this the cancer cells are destroyed, which remains after the treatment.
- Help other treatments to work better.
- It also kills those cancer cells which are spread to other body parts.

Chemotherapy may give in various ways:

1. **Oral:** pills, liquids, and capsules.
2. **Intravenous (i.v):** Directly to the vein.
3. **Intramuscular (i.m):** Given in muscle of thigh, arm or hip.
4. **Intrathecal:** Injected space between the layers of tissues that cover the spinal cord and brain.
5. **Intraperitoneal (i.p):** Directly into peritoneal cavity, that area in the body which contains organs such as, stomach intestine and liver.
6. **Intra-Arterial (i.a):** Directly into an artery.
7. **Topical:** Creams that apply on the surface of the skin.

Mainly chemo is given as IV; a thin needle is placed in vein but it is given through ports or catheters and some time with pump.

- **Port:** During minor surgery, a small, round disc which is called port, is placed under the skin before treatment and remains until treatment ends.

A catheter connects the port to a large vein and nurses insert a needle into the port to give chemotherapy or draw blood.

- **Catheter:** It is a thin, soft tube, which has one end places in a large vein in the chest area, and another end is to stay outside of the body. It is also used to give drugs and draw blood.
- **Pump:** It controls the speed and quantity of drugs that are given from catheter or port. The pumps are of two types internal or external, internal pumps are placed under the skin during surgery, and external pumps are placed outside from the body.

Various tests and scans are used for checking the progress of chemotherapy, include blood tests, CT, Pet, and MRI scans.

**Side Effects:** Chemotherapy kills the cancer cells but it kills the healthy cells also. Side effects are caused by damaging healthy cells. The side effects are:

- Hair loss
- Mouth sores
- Nausea
- Fatigue, so child care is needed to a patient at least on the day of chemotherapy.

**TABLE 1: SIDE EFFECTS**

Part of the body being treated	Possible Side effects
Brain	Fatigue, Hair loss, Nausea and vomiting, Skin changes, Headache, Blurry vision
Breast	Fatigue, Hair loss, Skin changes Swelling (edema), Tenderness
Chest	Fatigue, Hair loss, Skin changes Throat changes, such as trouble swallowing, Cough, Shortness of breath
Head and neck	Fatigue, Hair loss, Mouth changes, Skin changes, Taste changes, Throat changes, such as trouble swallowing, Less active thyroid gland
Pelvis	Diarrhea, Fatigue, Hair loss, Nausea and vomiting, Sexual problems (men), Fertility problems (men), Sexual problems (women), Fertility problems (women), Skin changes, Urinary and bladder changes
Rectum	Diarrhea, Fatigue, Hair loss, Sexual problems (men), Fertility problems (men), Sexual problems (women), Fertility problems (women), Skin changes, Urinary and bladder changes
Stomach and abdomen	Diarrhea, Fatigue, Hair loss, Nausea and vomiting, Skin changes, Urinary and bladder changes

**Immunotherapy:** In this therapy, the immune system is boost by medication or other treatments. Example, adoptive cell and checkpoint inhibitors treatment, *etc.* The immune system is made up of WBC and tissues of lymph nodes help to provide the strength to the body to fight against the disease and infection. It is also called biological therapy, which means the substances used in the treatment made from living organisms to treat cancer. It is not yet widely used, but many immunotherapies are studied in clinical trials.

Some immunotherapies boost the body's immune system to work better or others make easier for the immune system to identify the cancer cells and then destroy it by marking on these cells.

Immunotherapies are given in different ways, include:<sup>37-41</sup>

- **Oral:** Pills or capsules.
- **Intravenous (i.v):** Directly into a vein.
- **Intravesical:** Directly into the bladder.
- **Topical:** Cream applies externally to the surface of the skin at an early stage of skin cancer.

### Types of Immunotherapy:

- **Checkpoint Inhibitors:** These are the drugs that are used to boost the immune system to treat cancer. These drugs do not target directly on tumor cells because these drugs interrupt the ability of cancer cells to avoid immune system attack. They release the brakes which keep t cells, which is a type of WBC and immune system<sup>42</sup>.
- **Adoptive Cell Transfer:** In this, the natural ability of T cell is boosted to fight against cancer and they are taken from the tumor. Then t cells are grown in large batches in the lab and take 2-8 weeks to grow, then given back to the body by a needle in a vein.
- **Monoclonal Antibodies:** These are proteins which are made up in the laboratory and have the ability to attach with specific targets on cancer cells. It is also called as therapeutic antibodies. Antibodies mark the cancer cells so that the immune system can easily find it and destroy it.

**Side Effects:** The most common side effects are at needle site like skin reactions. These side effects include:

- Pain
- Swelling
- Redness
- Soreness
- Rash
- Chills

- Fever
- Dizziness
- Nausea and vomiting
- Fatigue
- Weakness
- Muscle or joint aches
- Trouble breathing
- Headache
- Low and high blood pressure
- Diarrhea
- Risk of infection
- Organ inflammation
- Heart palpitations
- Sinus congestion

These therapies also cause allergic reactions which will be severe or fatal, but these reactions are rare.

**Targeted Therapy:** In this therapy, changes in a cancer cell that help them divide, spread and grow by targeting and immune system also boost. For example, monoclonal antibodies, and small-molecule drugs. This therapy is a foundation of precision medicine. In target therapy, specific proteins that help the tumor to grow and spread get interfere to treat cancer. This therapy can treat cancer in different ways, include:<sup>42-45</sup>

- It helps the immune system to destroy cancer cells by marking the cells by which the immune system can easily identify and destroy the cancer cells.
- It stops the growth of cancer cells, interfering with proteins that carry the signal on its surface and preventing them from telling the cells to divide. Cancer cells do changes in the proteins that carry the signals to divide, whether the signal is present or not, the cancer cells divide.
- It stops the signals which help to form blood vessels, by interfering with the signals to prevent blood supply, or if the tumor has a blood supply, then this therapy is used to shrink the tumor by the death of those blood supply.

For the growth of a tumor, it requires new blood vessels and form in response to the tumor. The therapy is called angiogenesis inhibitors.

- It delivers the cell-killing substance to cancer cells, by attaching the substance on the cell surface and cell take up these substances and can cause them to die. Like monoclonal antibodies, which are combined with chemotherapy drugs, toxins, and radiation.
- It can cause the death of cancer cells by the natural process of cell death.
- It can prevent the production of some hormones which are responsible for the growth of prostate and breast cancer. Hormone therapy is a type of target therapy.

#### Types of Target Therapy:

- **Monoclonal Antibody:** These antibodies are get attached to specific targets found on cancer cells and mark cancer cells and help the immune system to find and destroy it. Some antibodies also stop the growth of cancer cells and made self-destructed. These antibodies are proteins that are made in a laboratory.
- **Small Molecule Drugs:** By their small size these drugs can easily enter inside the cell and used for targets.

**Side Effects:** The common side effects are diarrhea, liver problems. Other side effects are:

- Fatigue
- Mouth sores
- Loss of hair color
- Nail changes
- High blood pressure
- Skin problems include dry skin and rash.
- Problem with wound healing and blood clotting

Rare side effects are: Might a whole form through the wall of the small intestine, esophagus, large bowel, or stomach

These side effects may prevent or treated by medicines.

**Note:** This therapy has some drawbacks, they are:

- Cancer cells become resistant to them so target therapy can use with other cancer therapies.

- Drugs are hard to develop for some specific targets like target structure and function.

**Hormone / Hormonal / Endocrine therapy:** In this therapy, hormones are used to treat cancer, such as prostate and breast by stop and slow growth of those hormones<sup>46-49</sup>.

If this therapy is taken for prostate cancer then regular PSA tests performed for checking the progress of the therapy. If the PSA level will stay the same or go down then the therapy is working, but if the PSA level goes up then are results that the therapy is not working.

If this therapy is taken for breast cancer then regular checkup of neck, chest, underarm and breast areas is performed. When this therapy is used with other cancer treatments:

- Neo-adjuvant therapy, in this tumor is made smaller before surgery or radiation therapy.
- Adjuvant therapy decrease the risk of coming back of cancer after therapy.
- Destroy cancer cells which are come back after treatment.

This therapy is given in many ways including:

- **Oral:** Pills to swallow
- **Surgery:** Remove organs which produce hormones, like ovaries in women and testicle in men are removed.
- **Injection:** Injection given in muscle in the arm, hip, or thigh.

**Side Effects:** The side effects are different in different persons. This therapy blocks the ability to produce hormones or interrupts with hormones leads to unwanted side effects. The side effects are different in different persons.

In men:

- Weakened bones
- Diarrhea
- Nausea
- Fatigue
- Loss of interest in or ability to have sex

- Hot flashes
- Tender and enlarged breast.

In women:

- Vaginal dryness
- Nausea
- Mood changes
- Loss of interest in sex
- Hot flashes
- Change in periods if not yet reached menopause
- Fatigue

**Stem Cell Transplant:** In this therapy, the blood-forming stem cells restore in a cancer patient, which is destroyed by very high doses of radiation or chemotherapy. The stem cells are grown in a different type of blood cells which are necessary to be healthy, the main type of blood cells are:<sup>50-52</sup>

- **RBC (Red Blood Cells):** Carry oxygen throughout the body.
- **WBC (White Blood Cells):** Part of the immune system and help the body to fight against infection.
- **Platelets:** Help in blood clotting.

This therapy usually does not work against cancer directly except for some type of leukemia and multiple myeloma, but it helps the patient to reproduce the stem cells after treatment with high doses of chemotherapy and radiation or both therapies. After the allogeneic transplant, the graft-versus-tumor effect happens, which means WBC from donor (graft) attack on the tumor that remains after the high dose treatments, and this effect improves the success of treatment<sup>53, 54</sup>. This therapy is very complicated and expensive.

The process starts with high doses of chemotherapy, radiation or both, and it goes on for a week or two after this treatment a few days are required to rest, it takes few months to complete. Then the stem cells are given through an IV catheter, this is like receiving a blood transfusion and it takes 1-5 h.

The recovery phase is started after receiving stem cells, in this phase the received stem cells start making new blood cells.

Even after the blood counts recover all blood cells, it takes several months for autologous and 1-2 years for allogeneic or syngeneic transplants.

**Types of Stem Cell Transplant:** Stem cells are injected through a needle in the vein, once they enter the bloodstream, and then they get a place of cells that get destroyed by treatments by traveling to bone marrow. The stem cells come from bloodstream, bone marrow, and umbilical cord<sup>55-57</sup>.

A transplant can be:

- **Allogeneic:** In this, the stem cells come from someone else like blood relations or other people.
- **Autologous:** In this, the stem cells come from the patient itself.
- **Syngeneic:** The stem cells come from identical twins if the patient has one.

**Side Effects:** Bleeding and increased risk of infection are the problems caused by cancer treatments before a stem cell transplant. If a patient has an allogeneic transplant, that might develop graft-versus-host disease, this means the WBC from a donor (graft) recognized cell in the body (host) as foreign and attacked them by this the skin, liver, intestine, and other organs are getting damaged. Steroids or other drugs are used to suppress the immune system and help to treat the graft-versus-host disease<sup>58-59</sup>.

**Precision/Personalized Medicine:** It is the newer approach, in which the best treatment for a patient is determined by genetic testing. Nowadays, cancer treatments are is same for patients who have same cancer and the same stage of cancer, but the responses are different in some patients. After a lot of research, scientists understand those tumors have genetic changes that cause cancer cells to grow and spread. The genetic changes in different cancer may be the same. Scientists see the future in precision medicine because it helps in receiving the best treatment for cancer. The research is going on, to test the treating patients with treatments that target the cancer-causing genetic changes in the tumor, many drugs are used as treatment known as target therapies<sup>60</sup>.

Precision medicine helps the doctors to decide the best treatment because it has all the information regarding the genetic changes in the tumor, size, type, and if spread. Nowadays, the patients receive a combination of treatment for cancers include chemo, radiation, immunotherapy, and surgery if the doctor has information, then the treatment is going to be easy.

**CONCLUSION:** In this review paper cancer and treatments of cancer were illustrated in detail like sign or symptoms, diagnosing tests and how the cancer cause, spread, *etc.* The cancer treatments include surgery, immunotherapy, chemotherapy, target therapy, hormone therapy, radiation therapy, stem cell transplant, precision medicine. These therapies include many drugs, like antibiotics, which are mainly used in chemotherapies, different targeted systems to treat cancer directly like nanotechnology, microspheres, *etc.* Different radiations are used to treat cancer in radiation therapies that directly attack cancer cells. In hormone therapy, different hormones are used to treat cancer, mainly breast and prostate cancer which are caused by hormones. In immunotherapy, the immune system is making stronger to fight against the cancer cells by different drugs.

Out of these therapies, commonly therapies and a combination of therapies are used to treat cancer such as radiation therapy with surgery, hormone therapy with surgery, chemotherapy with immunotherapy, *etc.* But these therapies have different problems/side effects because cancer cell which are made from certain genetic changes and genetic changes different in different patients and cancers. After a lot of research about these therapies, scientists prefer precision medicines for the betterment of cancer treatment because in this therapy doctor knows all about the genetic information of cancer cells, then it makes the treatment quite easy and with the help of this information problems/side effects can be decreased.

And after these therapies stem cell transplant is the best therapy to make the patient healthy by autologous, syngeneic transplant because it has lesser side effects, but allogeneic transplants have more side effects than these two because in this stem cells are taken from other person or blood relation.

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