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REVIEW ON NEW ADVANCEMENT IN CHEMOTHERAPY OF CANCER TREATMENT

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Abstract:

Cancer is caused by mutations to the DNA within cells.A disease in which abnormal cells divide uncontrollably and destroy body tissue.
Chemotherapy is an aggressive form of chemical drug therapy meant to destroy rapidly growing cells in the body. It's usually used to treat cancer, as cancer cells grow and divide faster than other cells.
Chemotherapy is most often used to treat cancer, since cancer cells grow and multiply much more quickly than most cells in the body.
Various cancer treatment options such as Surgery, Chemotherapy, Radiation therapy, Bone marrow transplant, Immunotherapy, Hormone therapy, Targeted drug therapy, Cryoablation etc.
Chemotherapy is often used in combination with other therapies, such as surgery, radiation, or hormone therapy.
Adjuvant chemotherapy given after surgery or irradiation to destroy micrometastasis and prevent development of secondary neoplasm. and Neo-adjuvant chemotherapy given before surgery or radiotherapy in order to diminish the volume of large primary neoplasm.
By primary site of origin, cancers may be of specific types like breast cancer, lung cancer, prostate cancer, liver cancer renal cell carcinoma (kidney cancer), oral cancer, brain cancer etc.
Leukemia is a cancer of white blood cells. There are four common types of leukemia namely Acute lymphoblastic leukemia (ALL), Acute myeloblastic leukemia (AML), Chronic lymphocytic leukemia (CLL), and Chronic myeloid/myclocytic leukemia (CML).
Result-Chemotherapy destroys cells with the aim of killing cancer cells and preventing their growth. It can be very stressful for the body and cause various side effects. some alternatives to chemotherapy, including surgery, immunotherapy,
targeted therapies, active surveillance, supportive measures such as massage therapy, or psychotherapy to manage stress and pain generated in patients.
Keywords- Chemotherapy, Cancer, Leukemia, Adjuvant chemotherapy, Neoadjuvant chemotherapy, carcinogenesis, AML, CML, CLL,ALL.

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INTRODUCTION:

1.1 Chemotherapy

Chemotherapy is a drug treatment that uses powerful chemicals to kill fast-growing cells in your body. Chemotherapy is a treatment that uses drugs that kill rapidly dividing cancer cells to prevent them from growing and making more cells. Chemotherapy drugs interfere with a cancer cell's ability to divide and reproduce. Drugs vary in how they work. Different drugs attack cancer cells at different phases in the cell life cycle. Many chemotherapy drugs have adverse effects that can be severe. However, if a doctor recommends a person have chemotherapy, this usually means that the benefits are likely to outweigh any adverse effects.[1]

• Short-term side effects

- Diarrhea
- Nausea
- Vomiting
- Hair loss
- Loss of appetite
- Fatigue
- Mouth sores
- Numbness
- Bleeding
- Headache
- Constipation
- Easy bruising.[2]

- **Long-term side effects**

These effects could include damage to the:

- Damage to lung tissue
- Heart Problems
- Nerve damage (peripheral neuropathy)
- Kidney Problems
- Infertility
- Risk of second cancer.[2]

The Cell Cycle

G0 phase (resting stage): the cell is at rest and has not started to divide. This can last for a few hours to a few years, depending on the circumstances (reproductive cells have a very short resting phase whereas plant seeds have been known to germinate many years after they have been deposited). The cell becomes activated.

G1 phase: the cell starts to make more proteins and is ready to divide. This usually lasts 18–30 hours.
S phase: the deoxyribonucleic acid (DNA) chains are copied so that the new cell has the same DNA. This usually lasts 18–20 hours.
G2 phase: this is just before the cell starts splitting into two cells. This phase usually lasts from 2–10 hours.
M phase: the cell splits into two new cells. This phase usually lasts 30–60 minutes.[3]

Basic principles of chemotherapy:

The cancer cell metabolic mechanisms functionally overlap with the host cells, so cancer treatment is very challenging.76,77 Designing drugs or therapeutics mainly focuses on selectivity, which can specifically kill the cancerous cells without affecting the non-cancerous cells.[4]

1.2 History of Chemotherapy

Chemotherapy was first developed at the beginning of the 20th century, although it was not originally intended as a cancer treatment.
During World War II, it was discovered that people exposed to nitrogen mustard developed significantly reduced white blood cell counts. This finding led researchers to investigate whether mustard agents could be used to halt the growth of rapidly dividing cells such as cancer cells.

In the 1940s, two prominent Yale pharmacologists, Alfred Gilman and Louis Goodman examined the therapeutic effects of mustard agents in treating lymphoma. First, they established lymphomas in mice and showed that the tumors could be treated with mustard agents. Then, together with a thoracic surgeon called Gustav Linskog, they injected a less volatile form of mustard gas called mustine (nitrogen mustard) into a patient who had non Hodgkin's lymphoma.

The scientists found that the patients tumour masses were significantly reduced for a few weeks after treatment and although the patient had to return to receive more chemotherapy, this marked the beginning of the use of cytotoxic agents for the treatment of cancer. The initial study was done in 1943 and the results were published in 1946.

The use of nitrogen mustard for lymphomas gained popularity in the United States after the publication of the article in 1946. Nitrogen mustard and other derivatives of mustard gas are called alkylating agent due to their ability to alkylate molecules including protein, DNA and RNA. Other examples of alkylating agents include the tetrazines and the cisplatin's.

After World War II, another chemotherapeutic approach was investigated. A pathologist from Harvard Medical School called Sidney Farber studied the anticancer effects of folic acid - an essential vitamin in DNA metabolism.

Faber and colleagues developed folate analogues (such as methotrexate) which they found were antagonistic to folic acid and prevented the action of enzymes that required folate. In 1948, these agents became the first to lead to remission in children with acute lymphoblastic leukemia, showing that antifolates had the potential to restore normal bone marrow.

In the 1950s, Eli Lilly and company announced that plant alkaloids such as those extracted from Vinca rosea were beneficial to leukemia patients. This led to the introduction of vinca alkaloids as anticancer agents in the 1960s. Examples include vinblastine used to treat Hodgkin's disease and vincristine used to treat pediatric leukemia.
Over the next two decades, combination chemotherapy regimens started to gain popularity. The concurrent use of drugs with different mechanisms of action led to further improvements in patient survival and to a decline in mortality rates, which have declined each year from 1990 until now. This fall in death rates is due to both early detection and treatment with chemotherapy agents [5]

1.3 Cancer

What is Cancer:

Our body is composed of many millions of tiny cells, each a self-contained living unit. Normally, each cell coordinates with the others that compose tissues and organs of your body. One way that this coordination occurs is reflected in how your cells reproduce themselves. Normal cells in the body grow and divide for a period of time and then stop growing and dividing. Thereafter, they only reproduce themselves as necessary to replace defective or dying cells. Cancer occurs when this cellular reproduction process goes out of control. In other words, cancer is a disease characterized by uncontrolled, uncoordinated and undesirable cell division. Unlike normal cells, cancer cells continue to grow and divide for their whole lives, replicating into more and more harmful cells.[6]

Scientists have identified different stage of cancers, indicating that several gene mutations are involved in cancer pathogenesis. These gene mutations lead to abnormal cell proliferation. Genetic disorders caused by heritance or inheritance factors have a pivotal role in the increase of cell growth. With the assistance of technological advances in bioinformatics and molecular techniques, additional information has been obtained that can be useful for early diagnosis and proper treatment. The effects of drugs on patients with cancer can predict and even manage some aspects of side effects.[7]

Classification of Cancer :

Classification by tissue types :

Based on tissue types cancers may be classified into six major categories:

•Carcinomas : cancers of the epithelial tissue.
•Adenocarcinomas : cancers of glandular epithelial cells.
•Sarcomas : cancers of muscles and connective tissue.
•Leukaemias : cancers of blood.
•Lymphomas : cancers of lymphatic tissues.
•Choriocarcinoma : Malignant tumors derived from the placenta.

Classification by site of Origin :

By primary site of origin, cancers may be of specific types like breast cancer, lung cancer, prostate cancer, liver cancer renal cell carcinoma (kidney cancer), oral cancer, brain cancer etc.

Classification by grade

- Grade 1 – well differentiated cells with slight abnormality
- Grade 2 – cells are moderately differentiated and slightly more abnormal
- Grade 3 – cells are poorly differentiated and very abnormal
- Grade 4 – cells are immature and primitive and undifferentiated. [8]

1.4 Treatments

Cancer treatment options include:

- Surgery : The goal of surgery is to remove the cancer or as much of the cancer as possible.
- Chemotherapy uses drugs to kill cancer cells.
- Radiation therapy
- Bone marrow transplant
- Immunotherapy
- Hormone therapy
- Targeted drug therapy
- Cryoablation

Fig.2 : Radiation Therapy [11]

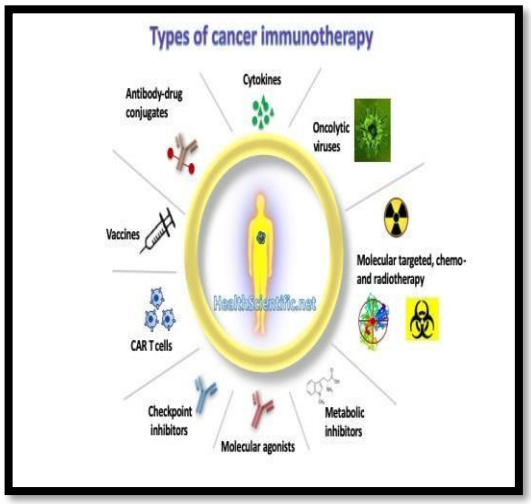

Fig.3 : Immunotherapy [12]

Fig. 4 : Chemotherapy[13]

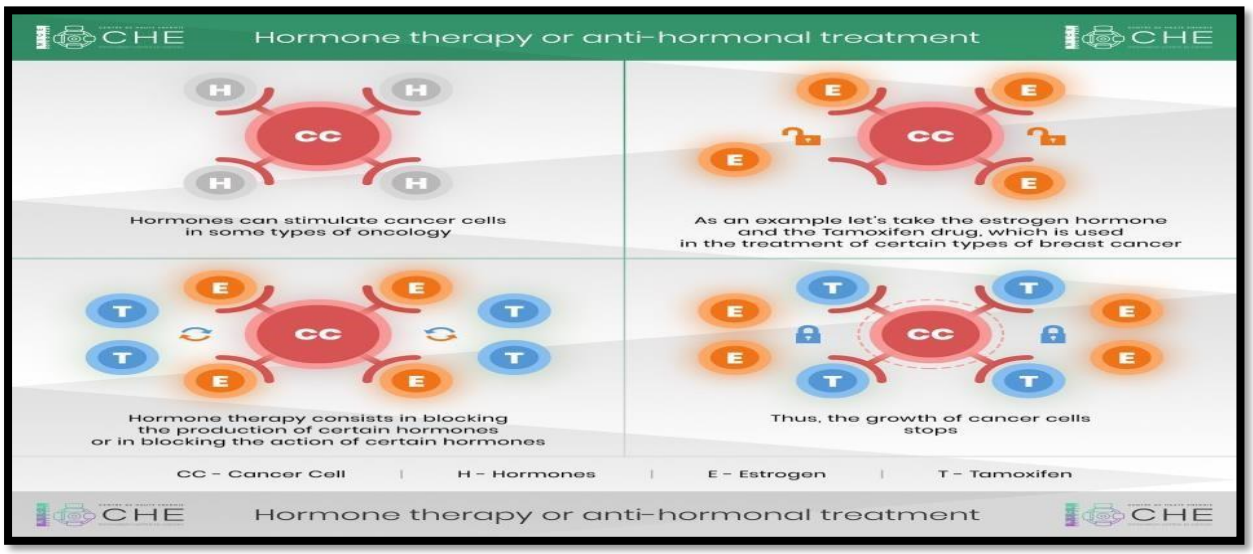

Fig. 5 : Hormone Therapy [14]

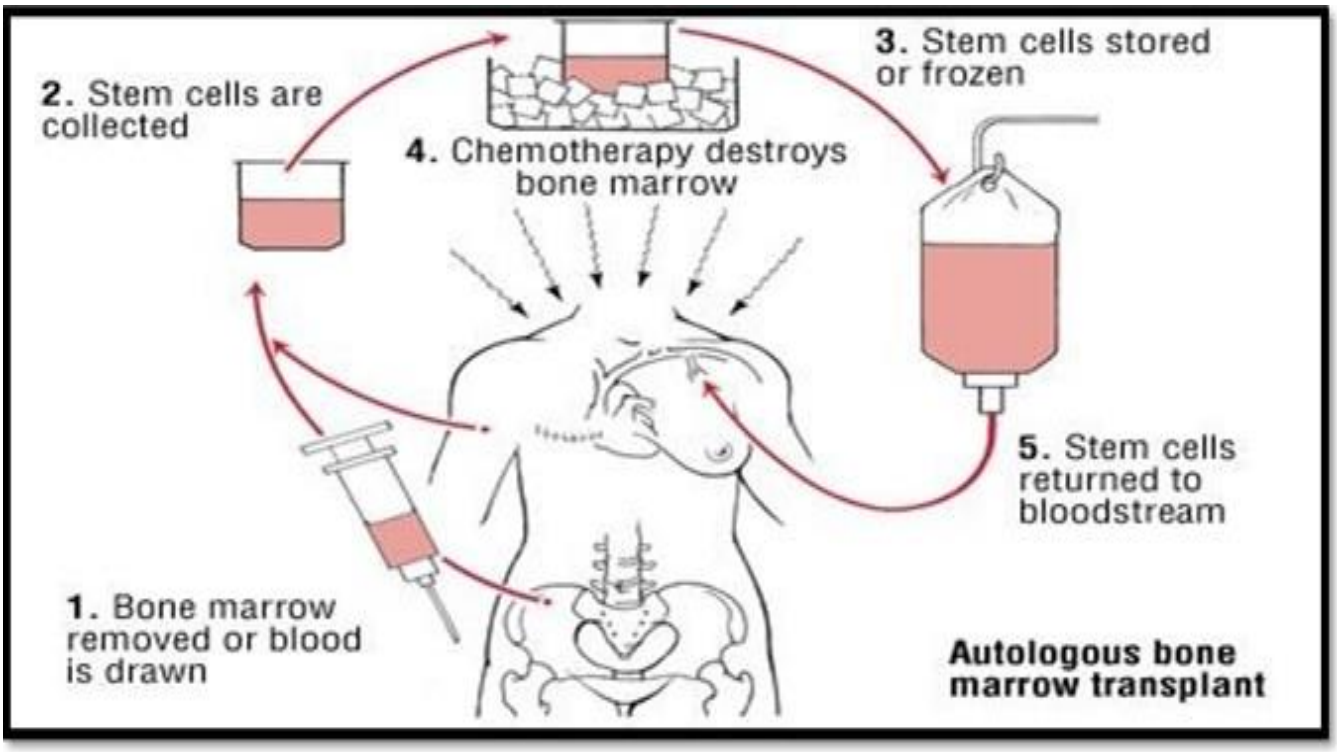

Fig. 6: Bone Marrow Transplant[15]

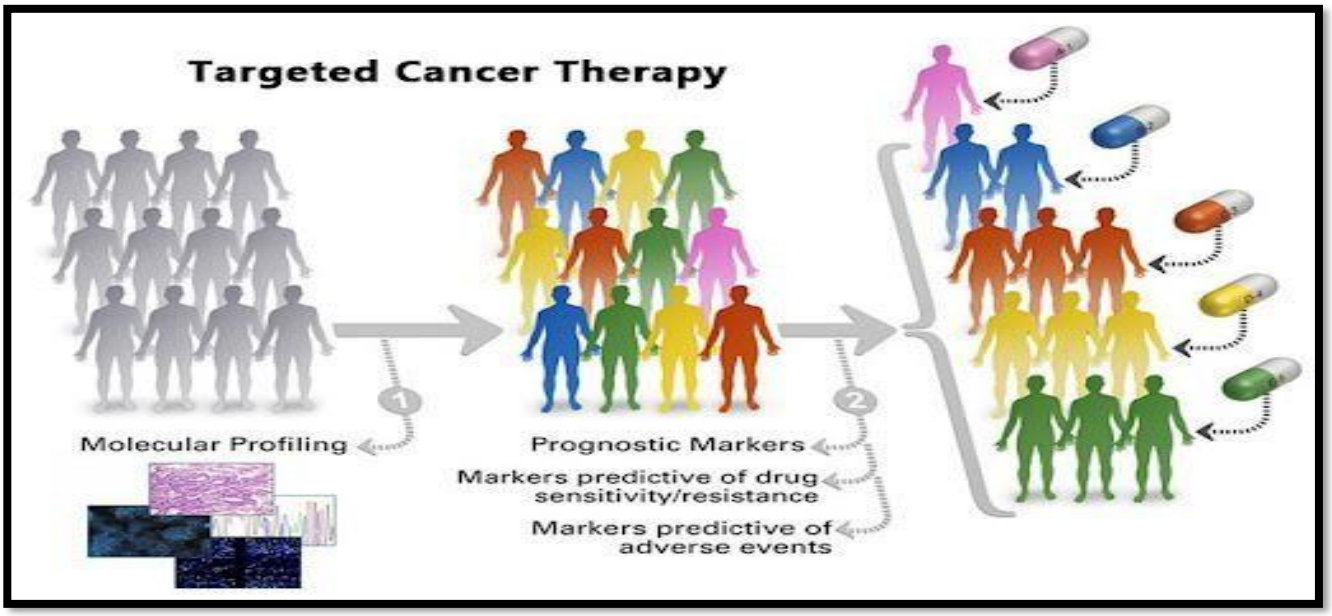

Fig.7 : Targeted drug therapy [16]

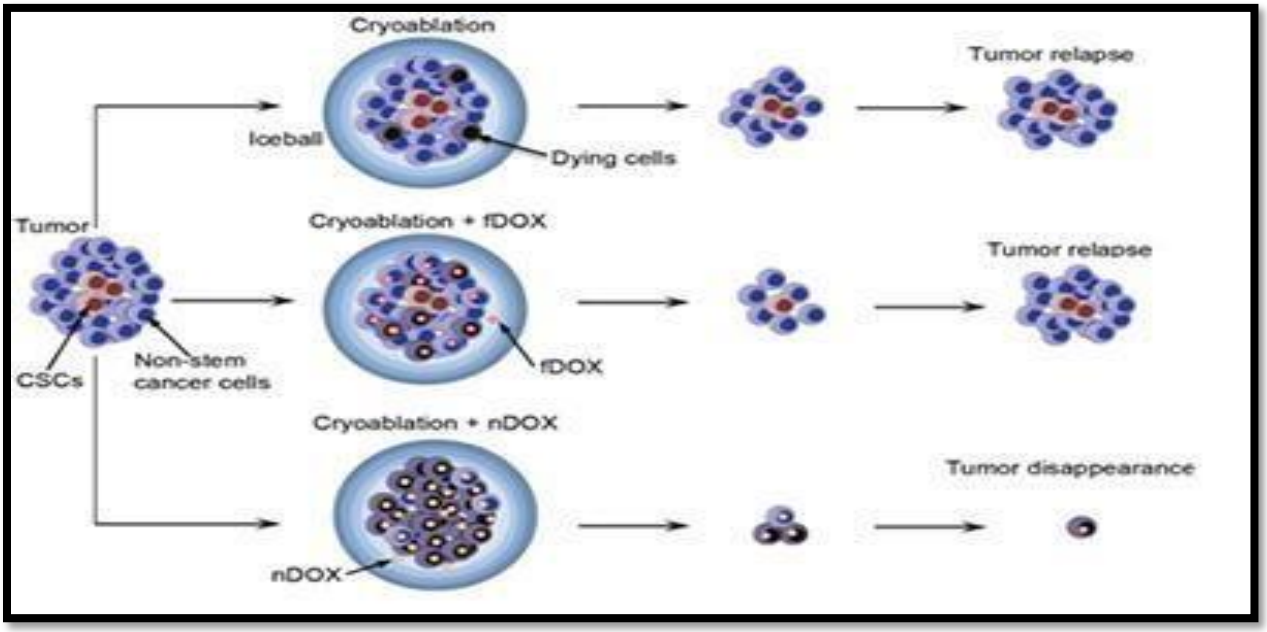

Fig. 8 : Cryoablation [17]

The combination of chemotherapeutic agents is delivered cyclically based on the three basic principles.

Fraction kill hypothesis: A uniform drug dose kills a constant fraction of tumor cells rather than a constant number regardless of tumor burden.
Neoplastic tumor cells have a linear response between the dose administered and the efficacy.
Goldie-Coldman hypothesis: Cancer cells acquire spontaneous mutations that cause drug resistance.[18]

Chemotherapy can have only palliative effect in:

- Breast Cancer
- Ovarian Cancer
- Endometrial Cancer
- Prostatic cancer

Guiding principles in cancer chemotherapy

- To achieve cure a TOTAL CELL must be tried
- Early diagnosis and early institution of treatment
- Combination chemotherapy
- Intermittent regimens
- Adjuvant and neoadjuvant chemotherapy occasionally.[19]

A] Total cell kill

- Aimed at destroying all the malignant cells, leaving none
- This approach ensures
- Early recovery

Cancer chemotherapy can be curative in:

- Acute Leukemia
- Wilm'sTumour
- Ewing's Sarcoma
- Choriocarcinoma
- Hodgkin's Disease
- lymphosarcoma
- Burkitt's lymphoma
- Testicular Teratomas
- Seminomas [19]

- Chronic lymphatic leukemia
- Chronic Myeloid leukemia
- Head and Neck Cancer
- Lung cancer [19]

- Prevents relapse
- Pharmacological sancturies [19]

B] Adjuvant and Neoadjuvant chemotherapy

- Adjuvant chemotherapy:- Chemotherapy given after surgery or irradiation to destroy micrometastasis and prevent development of secondary neoplasm.
- Neo-adjuvant chemotherapy:- Chemotherapy given before surgery or radiotherapy in order to diminish the volume of large primary neoplasm
- Oncologists typically use neoadjuvant chemotherapy to maximize the chance of the primary treatment, such as surgery, working

effectively. They can also use it to test a person's response to different drugs. Adjuvant chemotherapy kills cancerous cells that may remain after the primary treatment. [19]

C] Combination chemotherapy

- Hetrogenicity of cells, remaining in different phase of growth cycle, showing different level of sensitivity
- Nature of drug
- Avoid emergence of drug resistance
- Monotherapy adequate in Burkitts lymphoma and choriocarcinoma. [19]

D] Why intermittent regimen?

- Favours risk-benefit ratio.
- Allows time for damaged normal host cells yo recover
- Pulse therapy

- Type of intermittent chemotherapeutic regime employing highest tolerated dose within a short administration period
- Based on principles of drug conc.(C) × duration of exposure (T) = Constant. [19]

1.5 Etiology

Cancer is caused by **changes (mutations) to the DNA within cells**. The DNA inside a cell is packaged into a large number of individual genes, each of which contains a set of instructions telling the cell what functions to perform, as well as how to grow and divide. Errors in the instructions can cause the cell to stop its normal function and may allow a cell to become cancerous.

1.Age. Cancer can take decades to develop. That's why most people diagnosed with cancer are 65 or older. While it's more common in older adults, cancer isn't exclusively an adult disease — cancer can be diagnosed at any age.

2.Habits. Certain lifestyle choices are known to increase our risk of cancer. Smoking, drinking more than one drink a day for women and up to two drinks a day for men, excessive exposure to the sun or frequent blistering sunburns, being obese, and having unsafe sex can contribute to cancer.

3. Family history. Only a small portion of cancers are due to an inherited condition. If cancer is common in our family, it's possible that mutations are being passed from one generation to the next. we might be a candidate for genetic testing to see whether we have inherited mutations that might increase your risk of certain cancers. Keep in mind that having an inherited genetic mutation doesn't necessarily mean we'll get cancer

4. Health conditions. Some chronic health conditions, such as ulcerative colitis, can markedly increase our risk of developing certain cancers.

5. Environment. The environment around you may contain harmful chemicals that can increase your risk of cancer. Even if you don't smoke, you might inhale secondhand smoke if you go where people are smoking or if you live with someone who smokes. Chemicals in your home or workplace, such as asbestos and benzene, also are associated with an increased risk of cancer. [20]

1.6 Symptoms :

Some general signs and symptoms associated with, but not specific to cancer, includes:

• Fatigue	• Changes in bowel or bladder habits
• Cough	• Persistent cough or trouble breathing
• Weight changes, including unintended loss or gain	• Difficulty swallowing
• Hoarseness	• Abnormal Mole
• Lower abdominal pain	• Diarrhoea
• Haematuria	• Blood in Stool
• Chest infection	• Breast lump
• Back pain	• Neck lump
• Rectal bleeding	• Chest pain.[21]

1.7 Pathophysiology of Cancer

Pathophysiology is a combination of two medical terms; pathology and physiology. Pathology involves the study of structural and functional changes in cells, tissue, or organs that are caused by a particular disease. On the other hand, physiology explores the functions of the human body. Therefore, pathophysiology can be defined as the study of fundamental changes in the body's physiology, resulting from a disease.

For instance, the pathophysiology of the tumor explores the underlying changes in the body that results from the tumor or metastasis of cancer cells. Therefore, the **pathophysiology of cancer** includes the physical and hormonal changes associated with cancer and paraneoplastic syndrome. In general, cancer occurs in four main stages. The pathological stage of cancer is determined through biopsy (removal of small body tissue for laboratory examination) where the cancerous cells are compared to normal cells.

The four main stages of cancer are:

- Stage 1 — Cancer is normally localized in a small area
- Stage 2 — The size of the cancer increases
- Stage 3 — The size of cancer becomes larger and starts spreading to some parts of the body including lymph nodes
- Stage 4 — Cancer has grown and has spread to most parts of the body. [22]

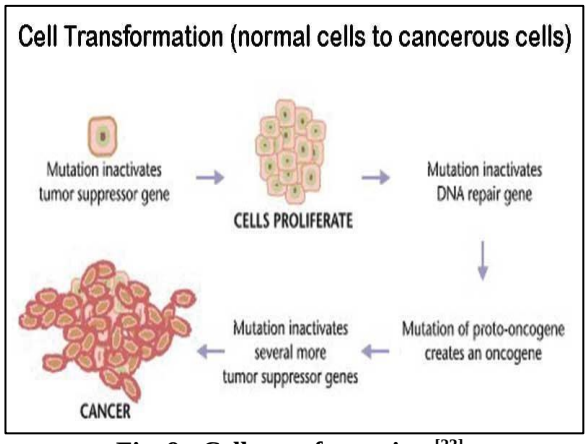

Fig. 9 : Cell transformation [23]

1.8 Phases of carcinogenesis

Phase - I (Initiation): Initiation, the first stage, is when initial cell mutation occurs. It may involve one or more cellular changes that are either spontaneous or started by exposure to a carcinogen. These changes create a potential for the affected cell and its daughter cells to develop into a cancer cell. A disruption in the cell development cycle can be caused by a response to the activation of cellular genes known as oncogenes, the portion of deoxyribonucleic acid (DNA) that regulates normal cell growth and repair. Inactivation, on the other hand, is the process whereby cellular genes known as tumor suppressor genes alter the normal cell cycle. Tumor suppressor genes are the components of DNA that stop, inhibit, or suppress cell division

Phase - II (Promotion): Promotion is the second stage where the transformed (or initiated) cells are stimulated to divide. The environment within (intracellular) and outside (extracellular) the cell influences cancer development. Malignant transformation may involve more than one step and requires repeated exposures to promoting agents. For example, one tumor promoter is estrogen, a naturally occurring hormone that by itself will not "initiate" cancer. However, estrogen can drive the growth of a mutated breast cell.

Phase – III (Progression) : Progression is the third stage in the three-stage theory of cancer causation. During progression, tumor cells compete with one another to survive, leading to more mutations that make the cells more aggressive. [24]

1.9 New Advancement in Cancer Chemotherapy

Gastric cancer:-By systematic review and meta-analysis were performed to assess the efficacy and tolerability of chemotherapy in patients with advanced gastric cancer.

Analysis of chemotherapy versus best supportive care and combination versus single agent, mainly fluorouracil (FU) -based chemotherapy showed significant overall survival benefits in favor of chemotherapy and combination chemotherapy, respectively. In addition, comparisons of FU/cisplatin containing regimens with versus without anthracyclines and FU/anthracycline-containing combinations with versus without cisplatin both demonstrated a significant survival benefit for the three-drug combination. Comparing irinotecan-containing versus nonirinotecan-containing combinations (mainly FU/cisplatin) resulted in a nonsignificant survival benefit in favor of the irinotecan-containing regimens, but they have never been compared against a three-drug combination. [25]

Breast cancer:-If breast cancer has spread to other parts of your body and surgery isn't an option,

chemotherapy can be used as the primary treatment. It may be used in combination with targeted therapy. The main goal of chemotherapy for advanced breast cancer is generally to improve quality and length of life rather than to cure the disease. Chemotherapy for breast cancer may be given in the following situations:

- Chemotherapy after surgery for breast cancer (Adjuvant Chemotherapy)
- Chemotherapy before surgery for breast cancer (Neoadjuvant Chemotherapy).

Neoadjuvant therapy is often used for:

- Inflammatory breast cancer
- HER2-positive breast cancer
- Triple-negative breast cancer
- High-grade breast cancers
- Cancers that have spread to the lymph nodes
- Larger breast cancers[26]

For breast cancer, a variety of chemotherapy drugs may be necessary, including:

- anthracyclines, such as doxorubicin
- methotrexate
- cyclophosphamide
- taxanes, such as paclitaxel
- epirubicin
- docetaxel. [27]
- fluorouracil

Colon cancer:-

Doctors may use chemotherapy for about 6 months after the surgery to destroy any remaining cancer cells.

For stage 3 and 4 colon cancer, cancer may have spread to other areas, and doctors may use a combination of surgery, chemotherapy, and radiation therapy.

Doctors may deliver chemotherapy in five ways :

- Systemic chemotherapy :- The individual receives the chemotherapy drugs orally or directly through a vein. The medication then enters their bloodstream and travels throughout their body.
- Regional chemotherapy :- Doctors administer the chemotherapy drugs via a person's artery that leads directly to the cancer's location. The advantage of this delivery is that lower amounts of the drug circulate throughout their body, reducing side effects.
- Adjuvant and neoadjuvant :- Doctors use neoadjuvant chemotherapy to shrink the tumor before surgery and adjuvant chemotherapy after surgery to kill any remaining cells. Adjuvant or neoadjuvant chemotherapy dosing schedules last for 3–6 months, depending on the medication.
- Immunotheray :- Immune checkpoint inhibitors that doctors may use for individuals with specific gene changes pembrolizumab (Keytruda) and nivolumab (Opdivo), PD-1 inhibitors that boost the immune response against cancer cells ipilimumab (Yervoy), an immune checkpoint inhibitor that also increases the immune response by blocking a specific protein on the immune cells.
- Radiation Therapy :- Radiation therapy uses high doses of radiation to kill cancer cells and reduce the size of tumors. Doctors may use external beam therapy (EBT) to deliver high-energy X-rays or proton beams to a tumor or place a radioactive source in the individual's body. Doctors may use radiation in combination with surgery.[26]

Doctors may use the following chemotherapy drugs for colon cancer:

5-fluorouracil(5-FU) irinotecan (Camptosar)
oxaliplatin (Eloxatin)
trifluridine and tipiracil (Lonsurf)
capecitabine (Xeloda)[27]

Non-Hodgkin lymphoma

Chemotherapy is the main course of treatment for non-Hodgkin lymphoma.

Doctors typically combine several drugs, including :

- cyclophosphamide
- chlorambucil
- bendamustine
- ifosfamide
- prednisone
- dexamethasone
- cisplatin
- carboplatin
- oxaliplatin
- fludarabine
- pentostatin
- cladribine (2-CdA)
- cytarabine (ara-C)
- gemcitabine
- methotrexate
- pralatrexate.[27]

Bladder cancer

Doctors may administer chemotherapy for bladder cancer indirectly through a vein or muscle or directly into the bladder. They typically opt for direct administration when the cancer is only present in the bladder's lining.

People with bladder cancer might receive a combination of radiation therapy and chemotherapy drugs that include:

- cisplatin
- cisplatin plus fluorouracil
- mitomycin plus fluorouracil

When using chemotherapy without radiation therapy, the options include:

- gemcitabine and cisplatin
- dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin
- cisplatin, methotrexate, and vinblastine
- gemcitabine and paclitaxel[27]

Melanoma

The two most common chemotherapy drugs for treating melanoma are dacarbazine and temozolomide.

Colorectal cancer

Chemotherapy drugs for colorectal cancer might include:

- 5-fluorouracil
- capecitabine
- irinotecan
- oxaliplatin
- trifluridine and tipiracil [27]

Doctors may use combinations of two or three drugs at a time for treating colorectal cancer.

Prostate cancer

Some chemotherapy drugs for prostate cancer include:

- docetaxel
- cabazitaxel
- mitoxantrone
- estramustine[27]

Lung cancer

Chemotherapy drugs for non-small cell lung cancer include:

- cisplatin
- carboplatin
- paclitaxel
- albumin-bound paclitaxel
- docetaxel[27]
- gemcitabine
- vinorelbine
- etoposide
- pemetrexed

Leukemia (Blood Cancer) :

Advances in the treatment of Acute lymphoblastic leukemia

Chemo for ALL uses a combination of anti-cancer drugs. The most commonly used chemo drugs include:

Vincristine or liposomal vincristine (Marqibo)
Daunorubicin (daunomycin) or doxorubicin (Adriamycin)
Cytarabine (cytosine arabinoside, ara-C)
L-asparaginase or PEG-L-asparaginase (pegaspargase or Oncaspar)
6-mercaptopurine (6-MP)
Methotrexate
Cyclophosphamide
Prednisone
Dexamethasone
Nelarabine (Arranon) [28]

Advances in the Treatment of Acute Myeloid Leukemia:

The chemo drugs used most often to treat AML are a combination of:

Cytarabine (cytosine arabinoside or ara-C)
An anthracycline drug, such as daunorubicin (daunomycin) or idarubicin Other chemo drugs that may be used to treat AML include:
Cladribine (2-CdA)
Fludarabine
Mitoxantrone
Etoposide (VP-16)
6-thioguanine (6-TG)
Hydroxyurea
Corticosteroid drugs, such as prednisone or dexamethasone
Methotrexate (MTX)
6-mercaptopurine (6-MP)
Azacitidine
Decitabine [29]

Advances in the treatment of chronic lymphocytic leukemia :

- BTK Inhibitors
- BCL2 Inhibitor
- Prognostic Markers
- MRD Tracking [30]

Advances in the treatment of chronic myelogenous leukemia (CML) :

Most people with CML have a specific chromosome alteration called the Philadelphia chromosome, which results in the production of an abnormal protein that drives the growth of leukemia cells. Drugs that target this abnormal protein—imatinib (Gleevec), nilotinib (Tasigna), dasatinib (Sprycel), and ponatinib (Iclusig)—have radically changed the outlook for

people with CML, who now have close to a normal life expectancy.

Frontline Therapy

Four tyrosine kinase inhibitors (TKIs), imatinib, dasatinib, bosutinib, and nilotinib are approved by the United States Food and Drug Administration for first-line treatment of newly diagnosed CML in chronic phase (CML-CP). Clinical trials with second generation TKIs reported significantly deeper and faster responses but had no impact on survival prolongation, likely because of the availability of effective TKIs salvage therapies for patients who have a cytogenetic relapse with frontline TKI therapy.

Salvage Therapy

For CML post failure on frontline therapy, second-line options include second and third generation TKIs. Although potent and selective, these TKIs exhibit unique pharmacological profiles and response patterns relative to different patient and disease characteristics, such as patients' comorbidities, disease stage, and BCR:: ABL1 mutational status. Patients who develop the T315I "gatekeeper" mutation display resistance to all currently available TKIs except ponatinib, asciminib, and olverembatinib. Allogeneic stem cell transplantation remains an important therapeutic option for patients with CML-CP and failure (due to resistance) of at least two TKIs, and for all patients in advanced phase disease. Older patients who have a cytogenetic relapse post failure on all TKIs can maintain long-term survival if they continue a daily most effective/least toxic TKI, with or without the addition of non-TKI anti-CML agents (hydroxyurea, omacetaxine, azacitidine, decitabine, cytarabine, busulfan and others). [31]

RESULT:

Chemotherapy destroys cells with the aim of killing cancer cells and preventing their growth. It can be very stressful for the body and cause various side effects. Side effects of chemotherapy drugs include hair loss, nausea, mouth sores, weight changes or loss of appetite, vomiting, diarrhoea, constipation, pain, fever.

In chemotherapy cycles of treatment usually last for 2-3 weeks and may be repeated for 3-6 months and drug recived as an injection.

Above study reviewed on the pathophysiology, mechanism of cancer and advance chemotherapy of cancer; it is clear there is no single therapy will serve as a treatment and it is most likely that in the near future, agents directed against the molecular events will have to be combined with the existing standard chemotherapy for the desired outcome.

Also concluded that there are some alternatives to chemotherapy, including surgery, immunotherapy, targeted therapies, active surveillance, supportive measures such as massage therapy, or psychotherapy tomanage stress and pain generated in patients.

ABBREVIATION

ALL- Acute lymphoblastic leukemia
AML-Acute myeloblastic leukemia
CLL- Chronic lymphocytic leukemia
CML -Chronic myeloid/myclocytic leukemia

REFERENCES:

1. Rachel Ann Tee Melegrito,What you need to know about chemotherapy,MedicalNews Today,2022.
2. Sidra Naveed,Aftab Ahmad,Zaigham Abbas, Muhammad Amin Athar,Side Effects of Chemotherapy in Cancer Patients and Evaluation of Patients Opinion about Starvation Based Differential Chemotherapy,Journal of Cancer Thetapy,817-822,Jan 2014
3. Elaine M Aldred BSc (Hons), DC, Lic Ac, Dip Herb Med, Dip CHM, Kenneth Vall, Chemotherapy, in Pharmacology, 2009
4. UttpalAnand,Abhijit Dey,Arvind K. Singh Chandel, RupaSanyal, Amarnath Mishra,Cancer chemotherapy and beyond: Current status, drug candidates, associated risks and progress in targeted therapeutics,Genes and diseases,18 March 2022.
5. Dr. Ananya Mandal,History of Chemotherapy, Medical life Sciences.
6. https://www.mentalhelp.net/cancer/
7. Seyed Hossein Hassanpour,Review of cancer from perspective of molecular,Journel of cancer research and practices,Volume 4,issue 4, December 2017,Pages 127-129.
8. Dr.Ananya Mandal,Cancer Classification,Medical life Sciences.
9. Maurie Markman,Expert cancer treatment,Cancer Treatment Centre of America, 29 April 2022.
10. https://images.app.goo.gl/k4wh8uBpz3u9juYw9
11. https://images.app.goo.gl/BZPc3Y8iRAjVzyDa6
12. https://images.app.goo.gl/EFYbV7cVRUwgN73U8
13. https://images.app.goo.gl/dMvg6mMKsibeXwfe8
14. https://images.app.goo.gl/km9iaDutWtoUbcbb7

15. https://images.app.goo.gl/viBpx4Ni3gtAiTia9
16. https://images.app.goo.gl/365wD94pY6LpXmsT7
17. https://images.app.goo.gl/KfNePBAJxkXfRv1i7
18. Amjad MT, Chidharla A, Kasi A,Cancer Chemotherapy,3 March 2022.
19. Naser Tadvi, Anti Cancer Chemotherapy,Nov 2022.
20. Mayoclinic Staff. Foundation for medical and Research (MFMER), Cancer Causes.
21. Minjoung Monica Koo, PhD, Ruth Swann, PhD, and Georgios Lyratzopoulos, Prof, MD,Presenting symptoms of cancer and stage at diagnosis: evidence from a cross-sectional, population based study,The Lancet. Oncolgy. Rachel Ann Tee Melegrito,What you need to know about chemotherapy,MedicalNews Today,2022.
22. An Overview of Cancer Pathophysiology, Study.com,25 August 2022.
23. https://www.researchgate.net/figure/Carcinogenesis-Transformation-of-normal-cells-into-cancer-Adapted-from-11_fig2_44227364
24. Marlon G. Saria,PhD,RN,AOCNS,FAAN, Overview of Cancer,Oncology nursing society.
25. Anna D. Wagner, Wilfried Grothe, Johannes Haerting, Gerhard Kleber,Axel Grothey,Wolfgang E.Fleig,Chemotherapy in Advanced Gastric Cancer: A Systematic Review and Meta-Analysis Based on Aggregate Data,Journal of Clinical Oncology,Vol. 24, No. 18, June 20, 2006.
26. Mayo Clinic Staff, Chemotherapy for breast Cancer, Mayoclinic Staff,August 13, 2019.
27. Christina Chun, Survival and chemotherapy success rates for various cancers, Medical News Today,August 13, 2019.
28. Hind Rafei et al,Recent advances in the treatment of acute lymphoblastic leukemia,2019 Nov.
29. Jifeng Yu, Peter Y. Z. Jiang,and Yongping Song,etal,Advances in targeted therapy for acute myeloid leukemia,BMC.
30. Stephanie Jackson,Recent Advances in Leukemia Treatment Continue to Improve Patient Outcomes,Oncology Nursing News Co-Editor in Chief, shares her opinion on recent developments in leukemia treatment options,September 30, 2021.
31. Elias Jabbour, Hagop Kantarjian,Chronic myeloid leukemia: 2020 update on diagnosis, therapy and monitoring, American Journal of Hematology,95 (6): 691-709,2020.