

ANTI CANCER DRUGS

The medical term for cancer is **Neoplasm**, which means new growth and the process of cell proliferation is called **Neoplasia**. Cancer refers to a malignant neoplasm or new growth. Cancer disease is characterized by uncontrolled, irreversible, independent, autonomous, uncoordinated and relatively unlimited and abnormal over growth of tissues.

Cancer arises as a result of genetic changes in the cell, the main genetic changes being; inactivation of tumor suppressor genes and activation of oncogenes.

The branch of medicine which deals with the study of neoplasm and its development diagnosis and treatment is called **oncology**.

General principles of action of anticancer drugs

Anti-cancer drugs destroy a constant fraction, rather than a constant number of cells. Thus, if there are one lakh cancer cells and if dose which kills 99.99% of cells is given, then still one cell will remain viable and this cell will create problem, so a proper dosing schedule is required.

Use of combination of two or more cytotoxic agents at a time may help in getting total cell death.

Cell Cycle Phases

All cells must traverse the cell cycle phases before and during cell division.

Anticancer drugs may act on specific phase. Tumor cells are more responsive to specific drugs.

- **G0 phase** – Resting phase
- **G1 phase** – Synthesis of enzymes needed for DNA synthesis
- **S phase** – DNA replication (DNA synthesis)
- **G2 phase** – Synthesis of components needed for mitosis.
- **M phase**: Mitotic tubule formation.

There are three approaches for the management of cancer treatment:

1. Radiotherapy
2. Surgery
3. Chemotherapy

Most anticancer drugs are Antiproliferative, and hence affect rapidly growing dividing normal cells.

1. **Radiotherapy**

Radioisotopes: - radioiodine, radiogold, radiophosphorous.

2. **Surgery**

Antibiotics:- actinomycin-D, Daunorubicin, doxorubicin, mithramycin, mitomycin, blecomycin

3. **Chemotherapy**

Anticancer drugs are broadly classified into two: **cytotoxic drugs** and **hormones**.

Cytotoxic drugs are further classified into:

• **Alkylating agents and related compounds** (e.g. cyclophosphamide, lomustine, thiotepa, cisplatin): These groups of drugs act by forming covalent bonds with DNA and thus impeding DNA replication.

Alkylating agents

1. Nitrogen mustard :- mechlorethamine, cyclophosphamide, ifosfamide, uracil mustard, chlorambucil, melphalan
2. Ethylenimines:- triethylenemelamine, thiotepa, hexamethylmelamine.
3. Nitrosoureas:- streptozotocin, lomustine, carmustine, semustine,
4. Alkylsulfonates:- busulphan
5. Triazenes:- dacarbazine

Antimetabolites (e.g. methotrexate, fluorouracil, mercaptopurine): These drugs blocks or destabilize pathways in DNA synthesis.

1. Folic acid antagonist:- methotrexate
2. Pyrimidine analogues:- fluorouracil, cytarabine, azarabine, floxuridine

3. Purine analogues:- mercaptopurine, tioguanine, pentostatin, azathioprine

Cytotoxic antibiotics (e.g. Doxorubicin, bleomycin, dactinomycin): These drugs inhibit DNA or RNA synthesis or cause fragmentation to DNA chains or interfere with RNA polymerase and thus inhibit transcription.

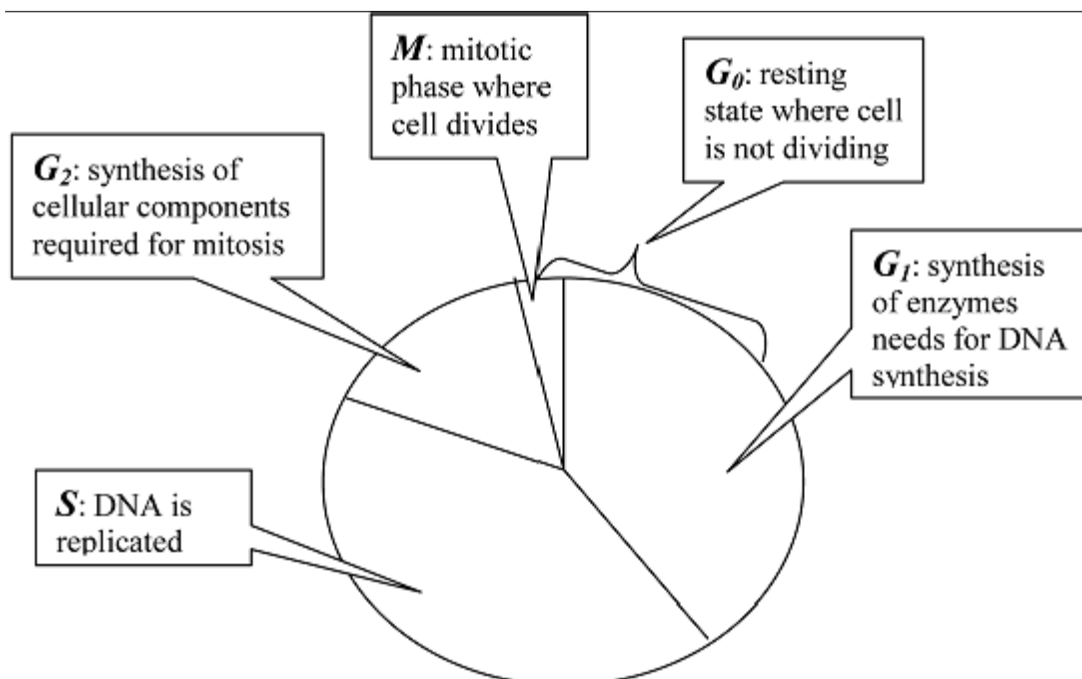
Plant derivatives (e.g. vincristine): Inhibits mitosis

Vinca alkaloids :- vincristine, vinblastine, vindesine, navelbine

Hormones and their antagonists are used in hormone sensitive tumors (eg. glucocorticoids for lymphomas, oestrogens for prostatic cancer, tamoxifen for breast tumors).

1. Enzymes:- L-asparaginase, Crisantaspase
2. Hormones :- estrogens, progestins, androgens, antiestrogens, corticosteroids
3. Biological response modifiers:- interferon alfa

Miscellaneous:- cisplatin, hydroxyurea, procarbazine, mitotane, cancer vaccine



Cell cycle phase specific drugs: More active against cells that are specific phase of cycle.

- **G1 phase:** L-asparagines and prednisone
- **S phase:** Methotrexate, 6-thioguanine, cytarabine
- **G2 specific.** Bleomycin and etoposide
- **M phase:** Vincristine vinblastine, and paclitaxol

Cell cycle specific drug (phase-nonspecific): Alkylating agents, antitumor antibiotic and cisplatin.

Cell cycle non-specific agents: Effective whether cancer cells are in cycle or resting phase, radiation, nitrosoureas, and mechlorethamine.

General toxic effects of anticancer drugs:

- Bone marrow toxicity.
- Impaired wound healing.
- Sterility.
- Loss of hair.
- Damage to gastrointestinal epithelium.