ANTI CANCER DRUGS

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Introduction

- Cancer occurs after normal cells have been transformed into neoplastic cells through alteration of their genetic material and the abnormal expression of certain genes.
- Neoplastic cells usually exhibit chromosomal abnormalities and the loss of their differentiated properties.
- These changes lead to uncontrolled cell division and many result in the invasion of previously unaffected organs, a process called metastasis.

Introduction

- Neoplasia is new growth. The terms benign and malignant correlate to the course of the neoplasm. Benign neoplasms stay localized in one place; malignant neoplasms invade surrounding tissue and, in most cases, can metastasize to distant organs
- Malignant disease accounts for a high proportion of deaths in industrialised countries.
- The treatment of anticancer drug is to give palliation, induce remission and, if possible, cure.
- Metastasis: is ability of tumor stem cells to migrate to distant sites in body to colonize various organs.

Categories of cancer

- Cancer is a term used for diseases in which abnormal cells divide without control and are able to invade other tissues.
- Categorized based on the functions/locations of the cells from which they originate:
- Categorized based on the functions/locations of the cells from which they originate:
- Carcinoma: skin or in tissues that line or cover internal organs. E.g., Epithelial cells

  % reported cancer cases are carcinomas.

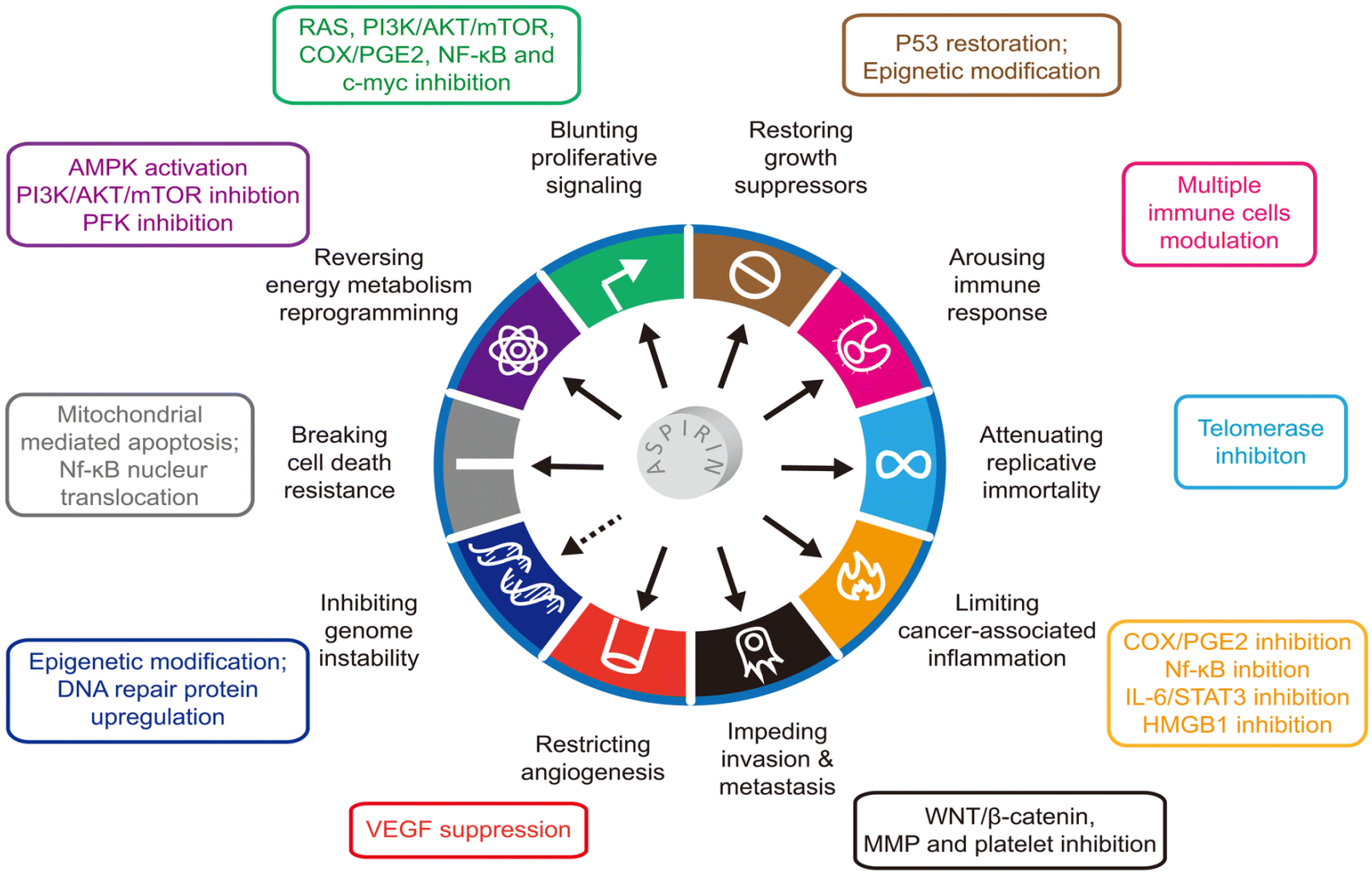
Categories of cancer

- Sarcoma : bone, cartilage, fat, muscle, blood vessels, or other connective or supportive tissue.
- Leukemia : White blood cells and their precursor cells such as the bon marrow cells, causes large numbers of abnormal blood cells to be produced and enter the blood.
- Lymphoma : cells of the immune system that affects lymphatic system.
- Myeloma: B-cells that produce antibodies- spreads through lymphatic system.
- Central nervous system cancers - cancers that begin in the tissues of the brain and spinal cord.

THE PATHOGENESIS OF CANCER

- Cancer cells manifest, to varying degrees, four characteristics that distinguish them from normal cells:
- uncontrolled proliferation
- dedifferentiation and loss of function
- invasiveness
- metastasis.

The hallmarks of cancer described by Hanahan and Weinberg have proved seminal in our understanding of cancer's common traits and in rational drug design



THE GENESIS OF A CANCER CELL

- A normal cell turns into a cancer cell because of one or more mutations in its DNA, which can be inherited or acquired.
- The development of cancer is a complex multistage process; involving not only more than one genetic change but usually also other,
- Epigenetic factors (hormonal action, co-carcinogen and tumour promoter effects, etc.) that are not in themselves cancer producing but which increase the likelihood that the genetic mutation(s) will result in cancer.
- There are two main categories of genetic change that lead to cancer:

I. the activation of proto-oncogenes to oncogenes

II. the inactivation of tumour suppressor genes.

Activation of proto-oncogenes to oncogenes

- These changes are a result of point mutations, gene amplification or chromosomal translocation, often due to the action of certain viruses or chemical carcinogens.
- Activation of proto-oncogenes to oncogenes
- Proto-oncogenes are genes that normally control cell division, apoptosis and differentiation but which can be converted to oncogenes by viral or carcinogen action.

Inactivation of tumour suppressor genes

- Normal cells contain genes that have the ability to suppress malignant change- termed tumour suppressor genes *(anti-oncogenes)*
- and there is now good evidence that mutations of these genes are involved in many different cancers.
- The loss of function of tumour suppressor genes can be the critical event in carcinogenesis.

Causes of Cancer

- The incidence, geographic distribution, and behavior of specific types of cancer are related to multiple factors, including sex, age, race, genetic predisposition, and exposure to environmental carcinogens.
- Environmental Exposure to ionizing radiation is a significant risk factor for a number of cancers, including acute leukemias, thyroid cancer, breast cancer, lung cancer, soft tissue sarcoma, and basal cell skin cancers.
- Chemical carcinogens (particularly those in tobacco smoke) as well as azo dyes, aflatoxins, asbestos, benzene, and radon have been clearly implicated in cancer induction in humans and animals

Causes of Cancer

- Viruses have been implicated as the etiologic agents of several human cancers. Expression of virus-induced neoplasia probably also depends on additional host and environmental factors that modulate the transformation process.
- Another class of genes, tumor suppressor genes, may be deleted or damaged, with resulting neoplastic change. The p53 gene has been shown to be mutated in up to 50% of all human solid tumors, including liver, breast, colon, lung, cervix, bladder, prostate, and skin.

Aims of treatment

- Give palliation, for example prompt relief of unpleasant symptoms such as superior vena cava obstruction from a mediastinal tumor
- Induce ‘remission’ so that all macroscopic and microscopic features of the cancer disappear, though disease is known to persist
- Cure, for which all the cells of the clone must be destroyed.

Aims of treatment

- neo adjuvant chemotherapy is given prior to surgery to shrink cancer.
- Chemotherapy is indicated when neoplasms are disseminated and are not amenable to surgery.
- Rapidly dividing cells are generally more sensitive to anticancer drugs whereas slowly proliferating cells are less sensitive

Common cancers

Disease Name	5 Years Survival Rate
• Childhood Acute Lymphoblastic Leukemia	50~80%
• Adult Acute Lymphoblastic Leukemia	20~60%
• Childhood Acute Myeloblastic Leukemia	20~60%
• Adult Acute Myeloblastic Leukemia	10~20%
• BreastCancer（Premenopausal）	10~20%
• BreastCancer（Postmenopausal）	0~15%
• Hodgkin’s lymphoma	*40~80%

Classification of Anti-cancer Drugs

1. According to chemical structure and resource of the drug;
2. According to biochemistry- mechanisms of anticancer action;
3. According to the cycle or phase - specificity of the drug
4. According to chemical structure and resource of the drug

Classification of Anti-cancer Drugs

1. According to chemical structure and resource of the drug:

I. Alkylating Agents,

II. Antimetabolite,

III. Antibiotics,

IV. Plant Extracts,

V. Hormones,

Classification of Anti-cancer Drugs

2. According to biochemistry mechanisms of anticancer action:

I. Block nucleic acid biosynthesis

II. Direct influence the structure and function of DNA

III. Interfere transcription and block RNA synthesis

IV. Interfere protein synthesis and function

V. Influence hormone homeostasis

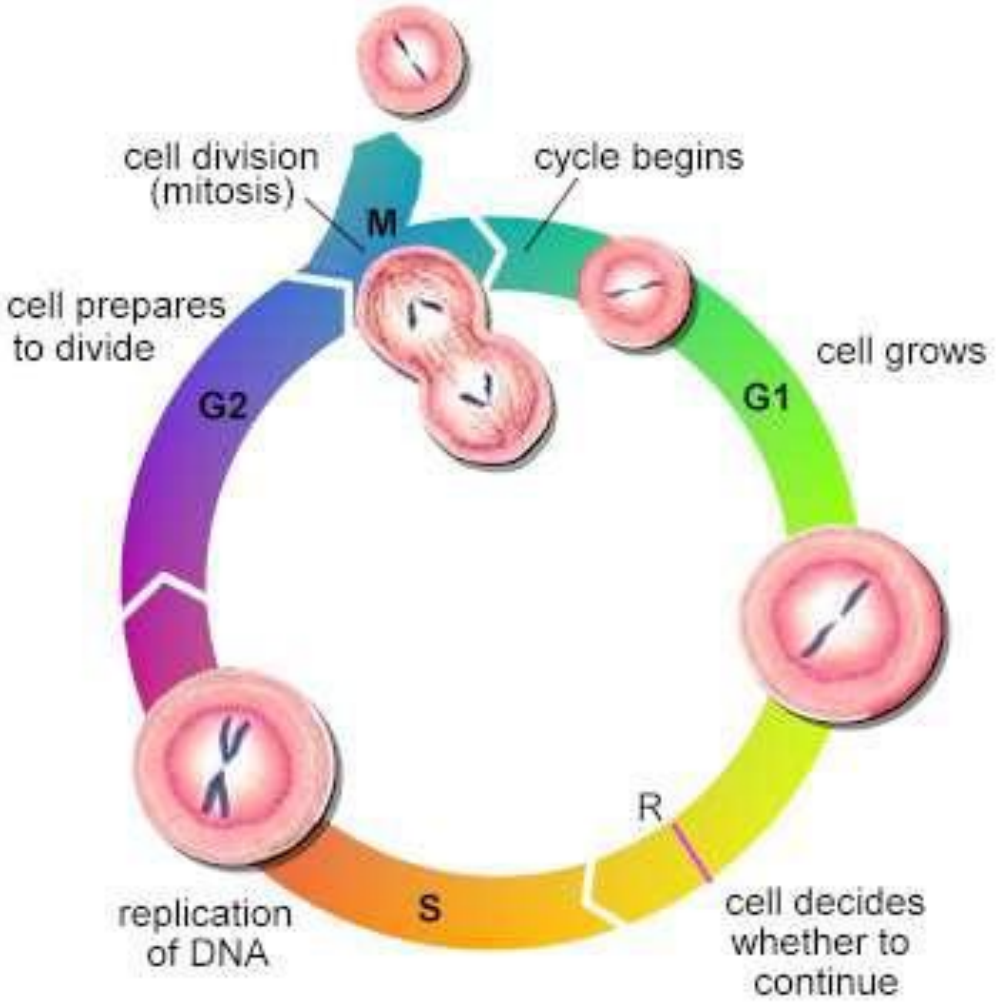
Classification of Anti-cancer Drugs

3. According to the cycle or phase specificity of the drug:

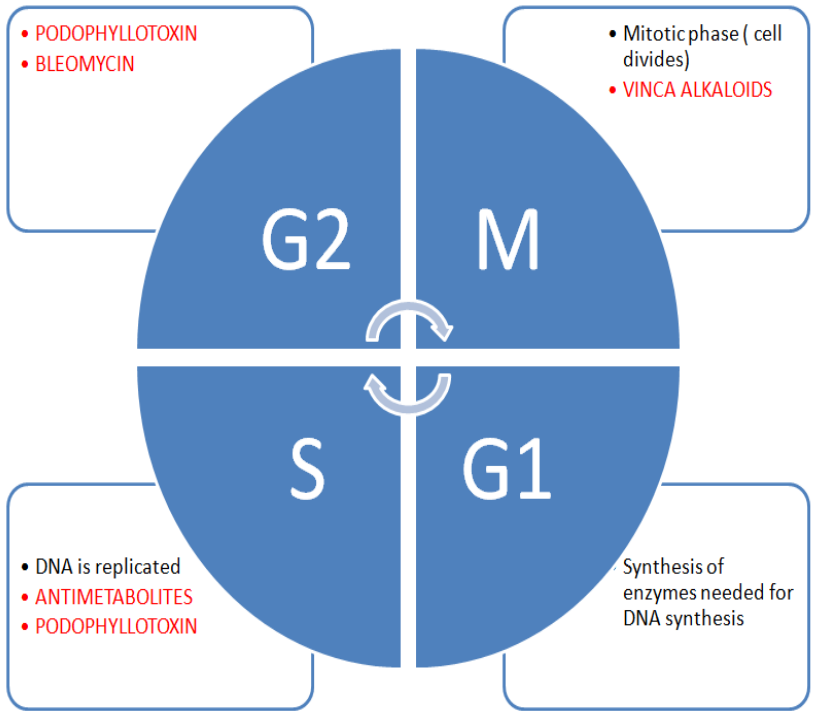
I. cell cycle nonspecific agents (CCNSA)

II. cell cycle specific agents (CCSA)

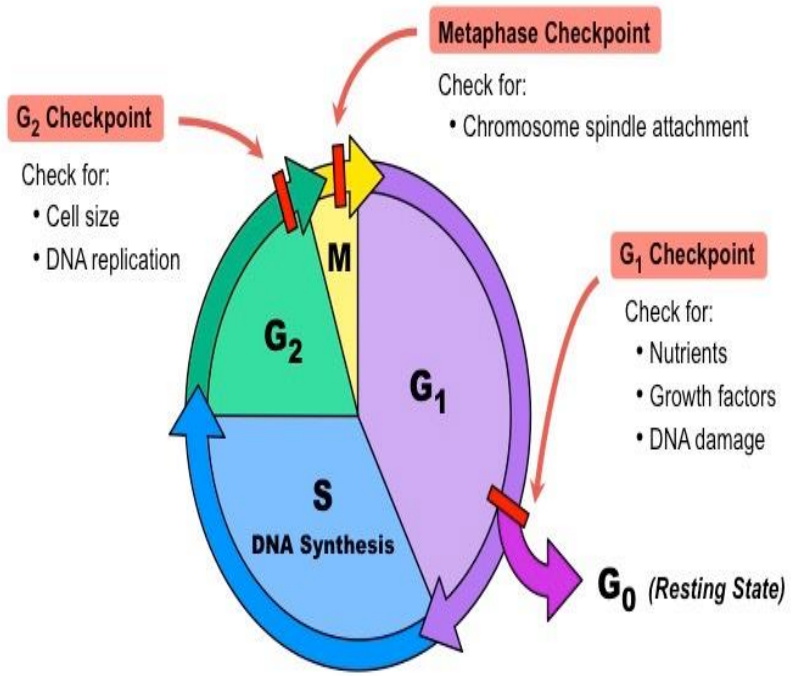
- The cycle of cell replication includes:
  - M（Mitosis）phase
  - G1（Gap1, period before S）phase
  - S（DNA synthesis）phase
  - G2（Gap2,period after S）phase

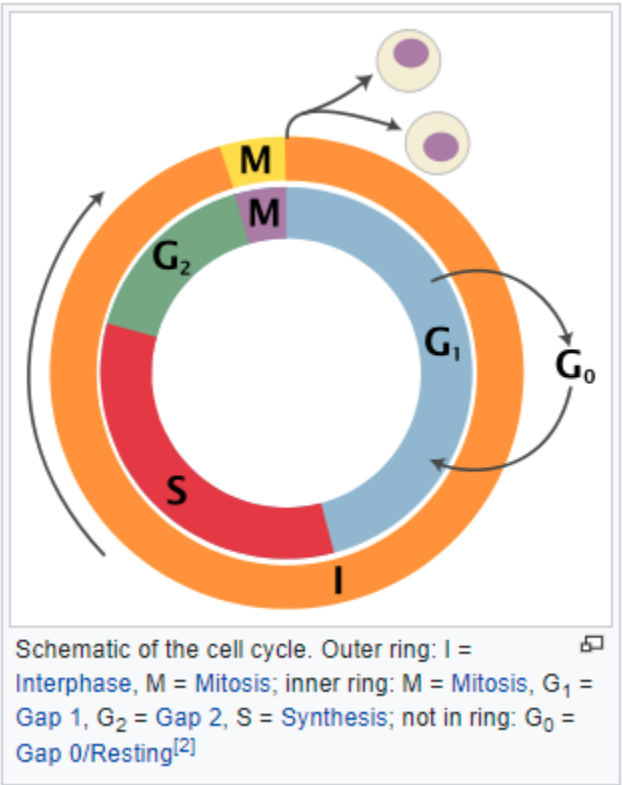


CELL CYCLE



State	Phase	Abbreviation	Description
Resting	Gap 0	G_0	A phase where the cell has left the cycle and has stopped dividing.
Interphase	Gap 1	G_1	Cells increase in size in Gap 1. The *G_1 checkpoint* control mechanism ensures that everything is ready for DNA synthesis.
	Synthesis	S	DNA replication occurs during this phase.
	Gap 2	G_2	During the gap between DNA synthesis and mitosis, the cell will continue to grow. The *G_2 checkpoint* control mechanism ensures that everything is ready to enter the M (mitosis) phase and divide.
Cell division	Mitosis	M	Cell growth stops at this stage and cellular energy is focused on the orderly division into two daughter cells. A checkpoint in the middle of mitosis (*Metaphase Checkpoint*) ensures that the cell is ready to complete cell division.





Schematic of the cell cycle. Outer ring: I = Interphase, M = Mitosis; inner ring: M = Mitosis, G_1 = Gap 1, G_2 = Gap 2, S = Synthesis; not in ring: G_0 = Gap 0/Resting[2]

Growth Fraction (GF)

GF＝Proliferating cell group/Total tumor cell group

- **CCNSA:** drugs that are active throughout the cell cycle.

I. Alkylating Agents

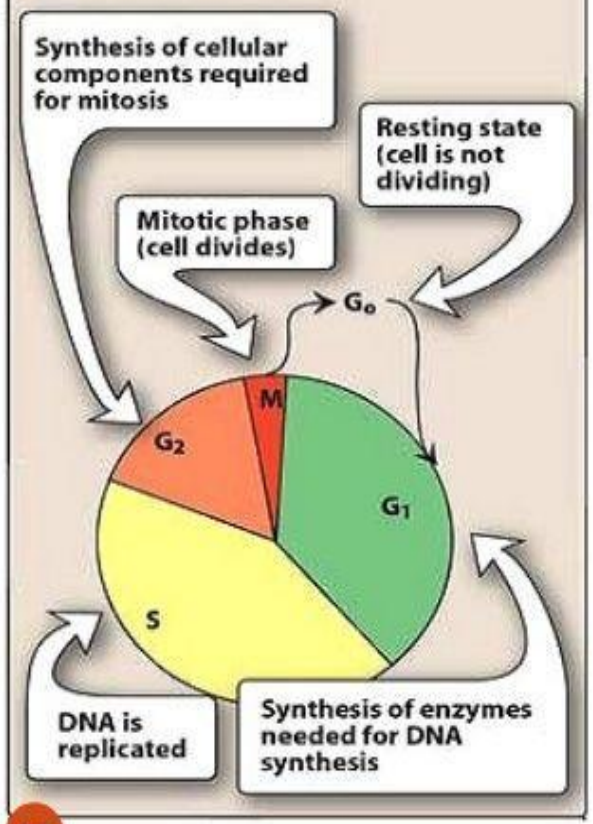
II. Platinum Compounds

III. Antibiotics

- **CCSA:** drugs that act during a specific phase of the cell cycle.
- S Phase Specific Drug: antimetabolites, Topoisomerase Inhibitors
- M Phase Specific Drug: Vinca Alkaloids,Taxanes
- G2 Phase Specific Drug: bleomycin

12.CELL CYCLE SPECIFIC /NON- SPECIFIC DUGS

A The cell cycle



B Cell-cycle specific drugs

Antimetabolites
Bleomycin peptide antibiotics
Vinca alkaloids
Etoposide

Effective for high-growth-fraction malignancies, such as hematologic cancers

C Cell-cycle non-specific drugs

Alkylating agents
Antibiotics
Cisplatin
Nitrosoureas

Effective for both low-growth-fraction malignancies, such as solid tumors, as well as high-growth-fraction malignancies

CON...

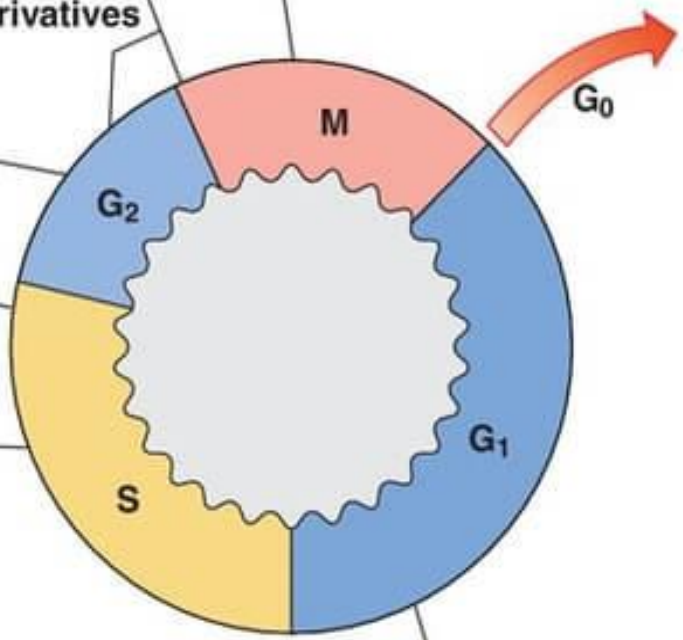
Taxanes
docetaxel
paclitaxel

Vinca Alkaloids
vinblastine
vincristine
vinorelbine

1. Epipodophyllotoxin Derivatives
etoposide
teniposide

2. Miscellaneous
bleomycin

Topoisomerase-1 inhibitors
topotecan
irinotecan



1. Antimetabolites

a. Folate Analogs
methotrexate

b. Purine Analogs
cladribine
fludarabine
mercaptopurine
pentostatin
thioguanine

c. Pyrimidine Analogs
capecitabine
cytarabine
gemcitabine
floxuridine
fluorouracil

2. Miscellaneous
hydroxyurea

1. Hormonal Drugs

2. Antineoplastic Enzymes
asparaginase
pegaspargase

ANTIMETABOLITES

Capecitabine XELODA
Cladribine LEUSTATIN
Cytarabine CYTOSINE ARABINOSIDE
Floxuridine FUDR
Fludarabine FLUDARA
5-Fluorouracil EFUDEX
Gemcitabine GEMZAR
6-Mercaptopurine PURINETHOL
Methotrexate (MTX) TREXALL
6-Thioguanine THIOGUANINE TABLOID

ANTIBIOTICS

Bleomycin BLENOXANE
Dactinomycin COSMEGEN
Daunorubicin CERUBIDINE
Doxorubicin ADRIAMYCIN
Epirubicin ELLENCE
Idarubicin IDAMYCIN

ALKYLATING AGENTS

Busulfan MYLERAN
Carmustine BICNU
Chlorambucil LEUKERAN
Cyclophosphamide CYTOXAN
Dacarbazine DTIC-DOME
Ifosfamide IFEX
Lomustine CEENU
Mechlorethamine MUSTARGEN
Melphalan ALKERAN
Streptozocin ZANOSAR
Temozolomide TEMODAR

MICROTUBULE INHIBITORS

Docetaxel TAXOTERE
Paclitaxel ONXOL
Vinblastine VELBAN
Vincristine VINCASAR PFS, ONCOVIN
Vinorelbine NAVELBINE

STEROID HORMONES AND THEIR ANTAGONISTS

Aminoglutethimide CYTADREN
Anastrozole ARIMIDEX
Bicalutamide CASODEX
Estrogens VARIOUS
Exemestane AROMASIN
Flutamide EULEXIN
Goserelin ZOLADEX
Letrozole FEMARA
Leuprolide LUPRON
Megestrol acetate MEGACE
Nilutamide NILANDRON
Prednisone DELTASONE
Tamoxifen NOVALDEX
Toremifene FARESTON

MONOCLONAL ANTIBODIES

Bevacizumab AVASTIN
Cetuximab ERBITUX
Rituximab RITUXAN
Trastuzumab HERCEPTIN

OTHERS

Asparaginase ELSPAR
Carboplatin PARAPLATIN
Cisplatin PLATINOL
Etoposide TOPOSAR, VEPESID
Gefitinib IRESSA
Imatinib GLEEVEC
Interferons PEG-INTRON
Irinotecan CAMPTOSAR
Oxaliplatin ELOXATIN
Procarbazine MATULANE
Topotecan HYCAMTIN

	CLASS OF DRUG	DRUGS
ALKYLATING AGENT	NITROGEN MUSTARDS	Cyclophosphamide Melphalan Mechlorethamine
	ALKYL SULFONES	Busulfan
	NITROSOUREAS	Carmustine Streptazocin
	TRIAZINES	Dacarbazine
	PLATINUM COORDINATION COMPOUNDS	Cisplatin Carboplatin Oxaliplatin
ANTI-METABOLITES	FOLIC ACID ANTAGONIST	Methotrexate
	PYRIMIDINE ANTAGONIST	5-fluorouracil Cytarabine Gemcitabine
	PURINE ANTAGONIST	6-mercaptopurine thioguanine

NATURAL PRODUCTS	VINCA ALKALOIDS	Vinblastine Vincristine
	TAXANES	Paclitaxel Docetaxel
	EPIPODOPHYLLOTOXINS	Paclitaxel Docitaxel
	ANTIBIOTICS	Dactinomycin Daunorubin Doxorubicin Bleomycin
	ENZYMES	L-asparginase
MISCELLANEOUS AGENTS	SUBSTITUTED UREA DERIVATIVES	Hydroxy urea
	PROTEIN TYROSINE KINASE INHIBITOR	imatinib
	INTERFERON'S AND CYTOKINE	Interferon α, IL 2

HORMONES	ADRENOCORTICOSTEROIDS	Prednisolone
	ANTIESTROGENS	Tamoxifen
	AROMATASE INHIBITORS	Anastrozole Letrozole
	ANTI ANDROGENS	Flutamide
	GONADOTROPHIN RELEASING HORMONE	leuprolide

Classification of Anti-cancer Drugs

2. According to biochemistry mechanisms of anticancer action:

I. Block nucleic acid (DNA, RNA) biosynthesis

II. Direct influence the structure and function of DNA

III. Interfere transcription and block RNA synthesis

IV. Interfere protein synthesis and function

V. Influence hormone homeostasis

I. Block nucleic acid (DNA, RNA) biosynthesis

Antimetabolites:

- Folic Acid Antagonist: inhibit dihydrofolate reductase (methotrexate)
- Pyrimidine Antagonist: inhibit thymidylate synthetase (fluorouracil); inhibit DNA polymerase (cytarabine)
- Purine Antagonist: inhibit interconversion of purine nucleotide (mercaptopurine)
- Ribonucleoside Diphosphate Reductase Antagonist:(hydroxyurea)

Antimetabolites

- General Characteristics：
- Antimetabolites are S phase-specific drugs that are structural analogues of essential metabolites and that interfere with DNA synthesis.
- Myelosuppression is the dose-limiting toxicity for all drugs in this class

Classification

- Folic acid Antagonists: MTX
- Purine Antagonists: 6MP, 6TG
- Pyrimidine Antagonists ： 5FU, araC, HU
- Mechanism of Action; Folic acid Antagonists: Methotrexate MTX
- The structures of MTX and folic acid are similar. MTX is actively transported into mammalian cells and inhibits dihydrofolate reductase, the enzyme that normally converts dietary folate to the tetrahydrofolate form required for thymidine and purine synthesis

Folic acid Antagonists: Methotrexate MTX

- Indications：
- The use of MTX in the treatment of chorio carinoma, a trophoblastic tumor, was the first demonstration of curative chemotherapy.
- It is especially effective for treating acute lymphocytic leukemia and for treating the meningeal metastases of a wide range of tumors

Methotrexate（MTX）

Adverse Effects：

- MTX is myelosuppressive, producing severe leukopenia, bone marrow aplasia, and thrombocytopenia.
- This agent may produce severe gastrointestinal disturbances.
- Renal toxicity may occur because of precipitation (crystalluria) of the 7-OH metabolite of MTX

Purine Antagonists:
6-Mercapapurine（6-MP）

- The drugs are believed to act similarly to inhibit purine base synthesis, although their exact mechanisms of action are still uncertain.
- Indications:
- Mercaptopurine is used primarily for the maintenance of remission in patients with acute lymphocytic leukemia and is given in combination with MTX for this purpose.
- Adverse Effects:
- Well tolerate.
- Myelosuppression is generally mild with thioguanine.Long-term mercaptopurine use may cause hepatotoxicity.

Pyrimidine Antagonists
5-Fluorouracil(5-FU)

- Mechanism of Action：
- Fluorouracil is an analogue of thymine in which the methyl group is replaced by a fluorine atom. It has two active metabolites: 5-FdUMP and 5-FdUTP.
- 5-FdUMP inhibits thymidylate synthetases and prevents the synthesis of thymidine, a major building block of DNA. 5-FdUTP is incorporated into RNA by RNA polymerase and interferes with RNA function

Pyrimidine Antagonists
5-Fluorouracil(5-FU)

Indications：

- Fluorouracil is exclusively used to treat solid tumors, especially breast, colorectal, and gastric tumors and squamous cell tumors of the head and neck. 5-Fluorouracil(5-FU)

Adverse Effects：

- Fluorouracil may cause nausea and vomiting, myelosuppression, and oral and gastrointestinal ulceration. Nausea and vomitting are usually mild.
- With fluorouracil, myelosuppression is more problematic after bolus injections, whereas mucosal damage is dose-limiting with continuous infusions.

Pyrimidine Antagonists
Cytarabine

Indications :

- Cytarabine has a narrow clinical spectrum and is primarily used in combination with daunorubicin or thioguanine for the treatment of acute non lymphocytic leukemia.

Adverse Effects:

- High doses of cytarabine can damage the liver, heart, and other organs.

II Direct influence the structure and function of DNA

- Alkylating Agent: mechlorethamine, cyclophosphamide and thiotepa
- Platinum : cisplatinium
- Antibiotic: bleomycin and mitomycin C
- Topoismerase inhibitor: camptothecine and podophyllotoxin

Alkylating Agent

- *One of the frightening developments of World War I was the introduction of chemical warfare. These compounds were known as the nitrogen mustard gases. The nitrogen mustards were observed to inhibit cell growth, especially of bone marrow. Shortly after the war, these compounds were investigated and shown to inhibit the growth of cancer cells.*

Mechanism of Action

- Nitrogen mustards inhibit cell reproduction by binding irreversibly with the nucleic acids (DNA).
- The specific type of chemical bonding involved is alkylation. After alkylation, DNA is unable to replicate and therefore can no longer synthesize proteins and other essential cell metabolites.
- Consequently, cell reproduction is inhibited and the cell eventually dies from the inability to maintain its metabolic functions.

Classification Alkylating Agent

- Cyclophosphamide, Chlormethine, Chlorambucil, Sarcolysine
- Alkysulfonates： Busulfan

Adverse Effects

- Myelosuppression is the dose-limiting adverse effect for alkylating agents.
- Nausea and vomiting are common as are teratogenesis and gonadal atrophy, although in the latter cases these are variable, according to the drug, its schedule, and route of administration.
- Treatment also carries a major risk of leukemogenesis and carcinogenesis.

Classification of Antibiotics:

I. Adriamycin (Anthracyaline Antibiotics)

II. Mitomycin C

III. Bleomycin

IV. Actinomycin D

Properties: Adriamycin and Daunorubicin

- Adriamycinand Daunorubicinare tetracycline rings with the sugar daunosamine. They are DNA intercalating agents that block the synthesis of DNA and RNA.
- These agents are primarily toxic during the S phase of cell cycle.
- These agents imparts a red tinge to the urine.
- Adramycin is used to treat acute leukemias, lymphoma, and a number of solid tumors.

MitomycinC:

- Mechanism:
- Mitomycin C is an antineoplastic antibiotic that alkylates DNA and thereby causes strand breakage and inhibition of DNA synthesis.

Indications:

- It is primarily used in combination with vinvristine as salvage therapy for breast cancer.

Adverse Effects:

- Mitomycinproducesdelaysandprolongedmyelosuppressionthatpreferentiallyaffect splateletsandleukocytes.

Actinomycin D:

- Actinomycin D intercalates DNA and thereby prevents DNA transcription and messenger RNA synthesis.
- The drug is given intravenously, and its clinical use is limited to the treatment of trophoblastic(gestational) tumors and the treatment of pediatric tumors, such as Wilms' tumor and Ewing's sarcoma.

Bleomycin:

Mechanism:

- The drug has its greatest effect on neoplastic cell in the G2 phase of the cell replication cycle.
- Although bleomycin intercalates DNA, the major cytotoxicity is believed to result from iron catalyzed free radical formation and DNA strand breakage.

Indications:

- It is useful in Hodgkin’s and non-Hodgkin’s lymphomas, testicular cancer, and several other solid tumors.
- Adverse Effects:
- Bleomycin produces very little myelosuppression. The most serious toxicities of Bleomycin are pulmonary and mucocutaneous reactions.

III. Interfere transcription and block RNA synthesis

- Bind with DNA to block RNA production .doxorubicin

IV. Interfere protein synthesis and function

- Antitubulin: *vinca alkaloids and taxanes;*
- Interfere the function of ribosome: harringtonines ;
- Influence amino acid supply: L-asparaginase
    - Bind tubulin, destroy spindle to produce mitotic arrest.

Tubulin-Binding Agents

- Vinca Alkaloids: The cellular mechanism of action of vincaal kaloids is the prevention of microtubule assembly, causing cells to arrest in the late G2 phase by preventing formation of mitotic filaments for nuclear and cell division.

Tubulin-Binding Agents Vinca alkaloids:

- Vinblastine, vincristin, vindesine and vinorelbine are all alkaloids derived from the periwinkle plant (Vinca rosea).

Indications:

- Vinblastine is used in combination with Bleomycin and Cisplatin for metastatic testicular tumors.
- Vincristine is used in combination with prednisone to induce remission in childhood leukemia.

Tubulin-Binding Agents

- Paclitaxel:
- Taxanes enhance all aspects of tubulin polymerization, an action that is the opposite to that of vinca alkaloids, but they are also cytotoxic, emphasizing the dynamic importance of tubulin polymerization as a target for cytotoxic drugs.
- Paclitaxel, Taxotere

Platinum Compound; Cisplatin:

- Mechanism of Action:
- Cisplatin binds to guanine in DNA and RNA, and the interaction is stabilized by hydrogen bonding. The molecular mechanism of action is unwinding and shortening of the DNA helix.

Indications:

- Cisplatin has efficacy against a wide range of neoplasms. It is given intravenously as a first-line drug for testicular, ovarian, and bladder cancer, and it is also useful in the treatment of melanoma and a number of other soild tumors.

Adverse Effect:

- Cisplatin produces relatively little myelosuppression but can cause severe nausea, vomiting, and nephrotoxicity

V. Influence hormone homeostasis

These drugs bind to hormone receptors to block the actions of the sex hormones which results in inhibition of tumor growth.

I. Estrogens and estrogen antagonistic drug

II. Androgens and androgen antagonistic drug

III. Progestogen drug

IV. Glucocorticoid drug

V. gonadotropin-releasing hormone inhibitor: leuprolide, goserelin

VI. aromatase inhibitor: amino glutethimide, anastrazole

Hormones

- Several types of hormone-dependent cancer (especially breast, prostate, and endometrial cancer) respond to treatment with their corresponding hormone antagonists.
- Estrogen antagonists are primarily used in the treatment of breast cancer, whereas androgen antagonists are used in the treatment of prostate cancer. Corticosteroids are particularly useful in treating lymphocytic leukemiasand lymphomas.

Estrogens:

- Estrogens inhibit the effects of endogenous androgens and androgen-dependent metastatic prostatic carcinoma.
- Diethylstilbestrol is usually the agent of choice.
- Cardiac and cerebrovascular complications and carcinoma of the male breast are potential adverse effects.

Progenstins:

- Progestins are useful in the management of endometrial carcinoma and back-up therapy for metastatic hormone-dependent breast cancer.

Antiestrogen: Tamoxifen

- Tamoxifen is the drug of choice in postmenopausal women with or recovering from metastatic breast cancer. It is most effective in patients who have estrogen receptor-positive tumors.
- Tamoxifen is also used as adjunvctive therapy to oophorectomy WITH leuprolide or goserelin in premenopausal women with estrogen receptor-positive tumors

Androgens:

- Androgen activity in breast cancer is similar to that of estrogens, perhaps for the same mechanistic reasons.
- Virilizing effects and hepatic toxicity make them unacceptable to most patients.
- Fluoxymesterone is the most widely used agent.
- Danazol has use in hematology in aplastic anemia and congenital anemias

Glucocorticoids:

- They are integral components of curative therapy for acute lymphoblastic leukemia, non-Hodgkin’s lymphoma, and Hodgkin’s disease.
- Glucocorticoids have essential roles in the prevention of allergic reaction, emesis control, relief of intracranial hypertension or spinal cord compression in neurologic complications, and pain relief.

Problem; Drug Resistance

- **De novo resistance** can be de novo genetic (i.e. the cells are initially inherently resistant), or can arise because drugs are unable to reach the target cells because of permeability barriers such as the blood-brain barrier.
- **Acquired Resistance**-Acquired drug resistance may result from genomic mutations, such as the induction or deletion of enzymes involved in drug inactivation or drug activation, respectively
- **Multidrug Resistance (MDR)-**P-glycoprotein transports many naturally occurring drugs out of neoplastic cells, and its induction may lead to multidrug resistance. As scientific understanding of the mechanisms of drug resistance increases, new treatments may be developed to counteract resistance.

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Drug Toxicity

- The most common toxicities of antineoplastic drugs result from inhibition of cell replication in the bone marrow, gastrointestinal epithelium, and hair follicles.
- Many antineoplastic drugs also stimulate the chemoreceptor trigger zone in the medulla and thereby elicit nausea and vomiting

Immunosuppressive Agents:

- Act to suppress immune mechanisms and are used to treat autoimmune diseases or to prevent graft rejection following tissue transplantation.
- Ciclosporin, Tacrolimus, adrenocortical hormones, antimetabolites, alkylating agent, antilymphocyte globulin, Mycophenolate Mofetil