



# **ANTI - NEOPLASTIC DRUGS II**

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# Objectives

- 1- Alkylating Agent
- 2- Antimetabolites
- 3- Antibiotics
- 4- Microtubule inhibitors (mitotic inhibitors)



# Anticancer Drugs classification

- **Alkylating Agent**
- **Antimetabolites**
- **Antibiotics**
- **Microtubule inhibitors  
(mitotic inhibitors)**
- **Hormones**
- **Protein kinase inhibitors**
- **Monoclonal antibodies**
- **Others**



# General Adverse Effects of antineoplastic drugs

- **Anticancer drugs damage rapidly growing cells.**
- **1- Gastrointestinal mucosa:** Inflammation of the mucous membranes lining the digestive tract from the mouth to the anus.
- **2- Myelosuppression:**
- Granulocytopenia and lymphocytopenia (increased risk of infection)
- Thrombocytopenia (increased bleeding risk)
- Anemia (fatigue)
- **3- Hair follicles:** hair loss (alopecia)
- **4- Peripheral neuropathy**
- **5- Hepatotoxicity**
- **6- Gonadal hypofunction**
- **7- Teratogenic**
- **8- Carcinogenic**



# Alkylating Agents

- These compounds were known as **the nitrogen mustard gases**.
- One of war gases



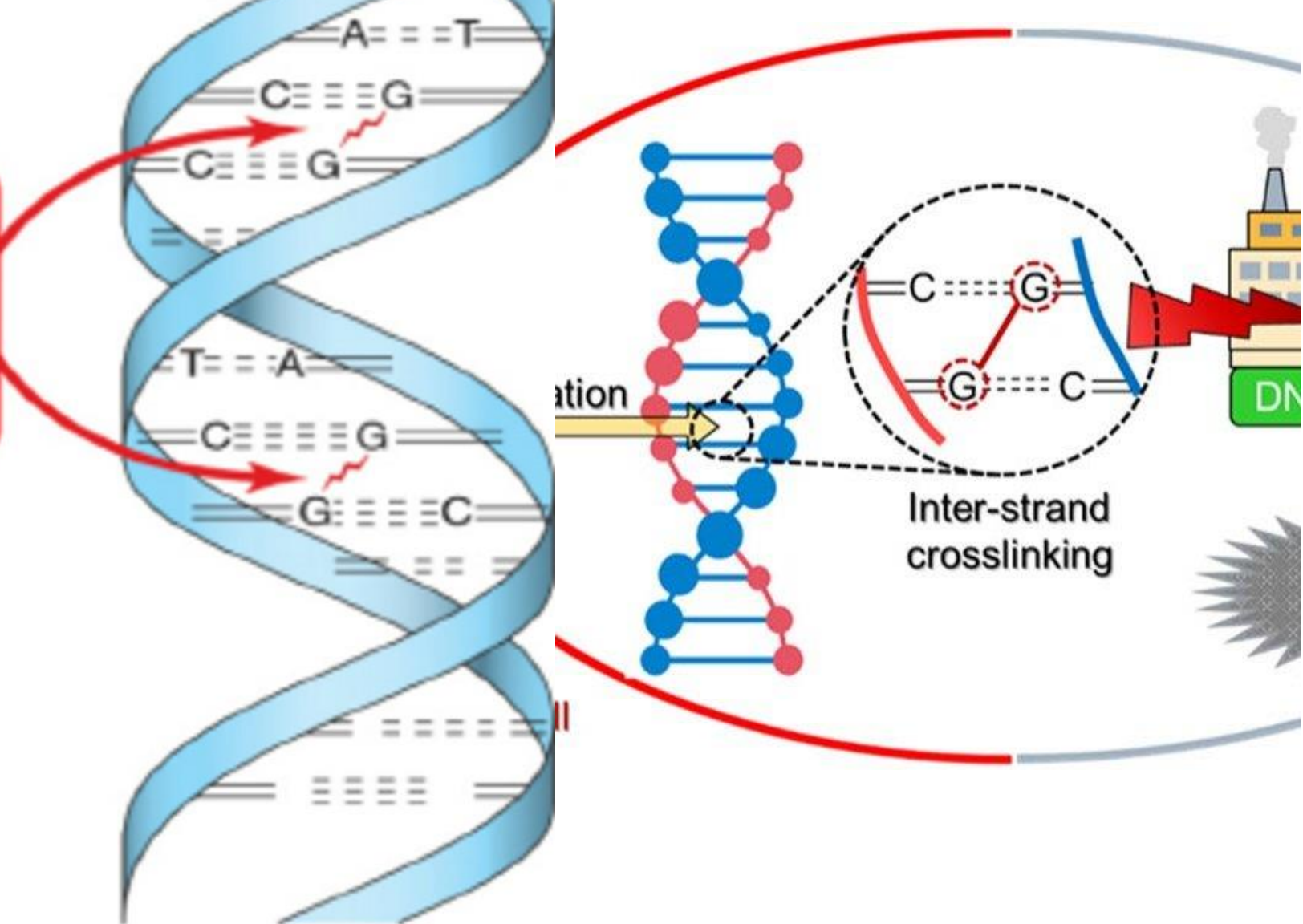
# 1-Alkylating Agents

## Mechanism of Action

- **Binding irreversibly with the nucleic acids (DNA). The specific type of chemical bonding involved is *alkylation*.**
- These agents act directly on DNA, resulting in its cross-linking and causing DNA strand breaks, leading to abnormal base pairing and inhibiting cell division, eventually resulting in cell death.
- Alkylating anticancer drugs are effective during all phases of cell cycle :
- **cell cycle non-specific**



**Bifunctional alkylating agents can cause intrastrand linking and cross-linking**



# Classification of Alkylating Agents

- **Cyclophosphamide**
- **Carmustine**
- **Busulfan**
- **Cisplatin**





# Alkylating Agents: Cyclophosphamide

*PRODRUG: inactive and activated VIA metabolism by hepatic cytochrome enzymes.*

## Indications:

- ◆ 1- Broad-spectrum anticancer: chronic lymphocytic leukemia, non-Hodgkin's lymphomas, breast and ovarian cancer, and a variety of other cancers.
- ◆ 2- Potent immunosuppressant, it is used in the management of rheumatoid disorders and autoimmune nephritis.

## Adverse Effects:

### General?

- ◆ **SPECIFIC:** Hemorrhagic cystitis?



# Cisplatin

- ◆ Mechanism of action

- ◆ as cyclophosphamide

- ◆ Concentrated in:

- ◆ genitourinary tissues

- ◆ Used in:

- ◆ ovarian and testicular tumors

- ◆ Side effects:

- ◆ 1- nephrotoxicity: 70%

- ◆ 2- sensory hearing loss: high-pitched sounds

- ◆ 3- peripheral neuropathy



## 2-Antimetabolites

### General Characteristics:

- Antimetabolites are specific drugs that are structural analogues of essential metabolites and that interfere with DNA synthesis.
- **Cell-cycle specific:** G1, S phases



# Classification of Antimetabolites

- ◆ **Folic acid Antagonists: MTX**
- ◆ **Purine Antagonists: 6MP**
- ◆ **Pyrimidine Antagonists: 5FU**



# Antimetabolites: Folic Acid Antagonist

## *Methotrexate (MTX)*

### Mechanism of Action:

- 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 DNA synthesis.



# Antimetabolites: Folic Acid Antagonist

*Methotrexate (MTX)*

## Indications:

- Different types of malignant tumors
- Immunosuppressant in rheumatoid arthritis

## Adverse Effects:

- 1- Hepatotoxicity: monitor liver function tests
- 2- Megaloblastic anemia: avoided by folic acid therapy



# Antimetabolites: Purine Antagonists

## *6-Mercaptopurine (6-MP)*

The drug act similarly to inhibit purine base synthesis.

### Indications:

- Maintenance of remission in patients with acute lymphocytic leukemia.

### Adverse Effects:

- 1- sever myelosuppression: may be fatal
- 2- sever hepatotoxicity.

**Mechanism of adverse effects:** lack of S-methyl transferase and xanthine oxidase enzymes



## 3- Cytotoxic Antibiotics

- Mechanism of action: inhibition of DNA synthesis

- Cell-cycle specific

Adverse effects:

- Doxorubicin: cardiotoxicity
- Mitomycin C : nephrotoxicity
- Bleomycin: pulmonary fibrosis

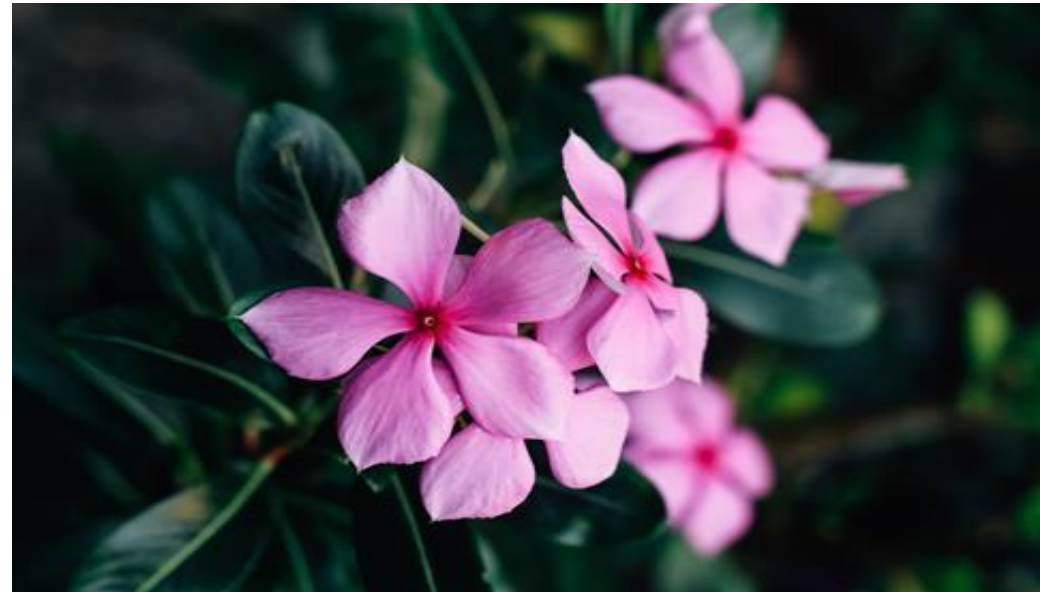




## 4- Microtubule inhibitors (cell-cycle specific)

### *Vinca Alkaloids*

- Interfere with microtubules (cellular structures that help move chromosomes during mitosis)
- A vinca alkaloid is a type of mitotic inhibitor and a type of antimicrotubule agent.



# VINCA ALKALOIDS

*Vinblastine & vincristine are alkaloids derived from the periwinkle plant (Vinca rosea).*

Adverse effects	Vinblastine	Vincristine
Bone marrow depression	++++ sever	+ marrow-sparing
Peripheral neuropathy	+	++++ sever



# Taxanes

- **Paclitaxel: breast cancer & ovarian cancer**



## **References**

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*Thanks!*

