ANTI - NEOPLATIC 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 kinsase inhibitors
- Monoclonal antibodies
- Others

General Adverse Effects

- **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

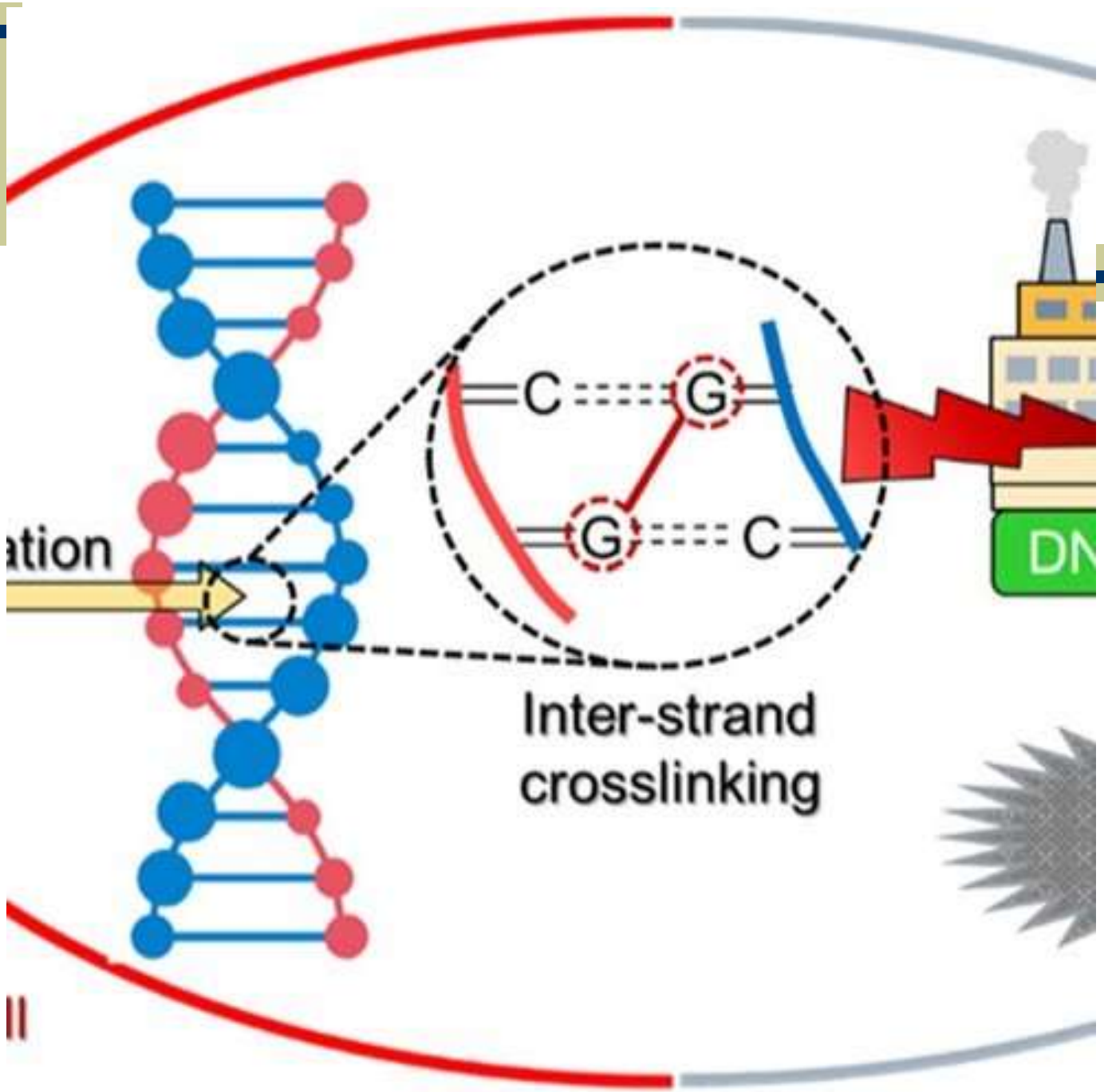
Alkylating Agents

- 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-spesific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Inter-strand
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Classification of Alkylating Agents

- Cyclophosphamide
- Carmustine
- Busulfan
- Cisplatin

Alkylating Agents—— Cyclophosphamide

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

Indications:

- 1- broad-spectrum anticancer: chronic lymphocyctic 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?

- SPESIFIC: Hemorrhagic cystitis?

Cisplatin

- **MOA**: 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-Mercapapurine（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 myelosuppresion: may be fatal

2- sever hepatotoxicity.

Mecahnism 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: cardiotoxixcity**
- **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 & vincristinare 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!