

Unit-IV

SPECIFIC CHEMOTHERAPEUTIC AGENTS

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Key Contents

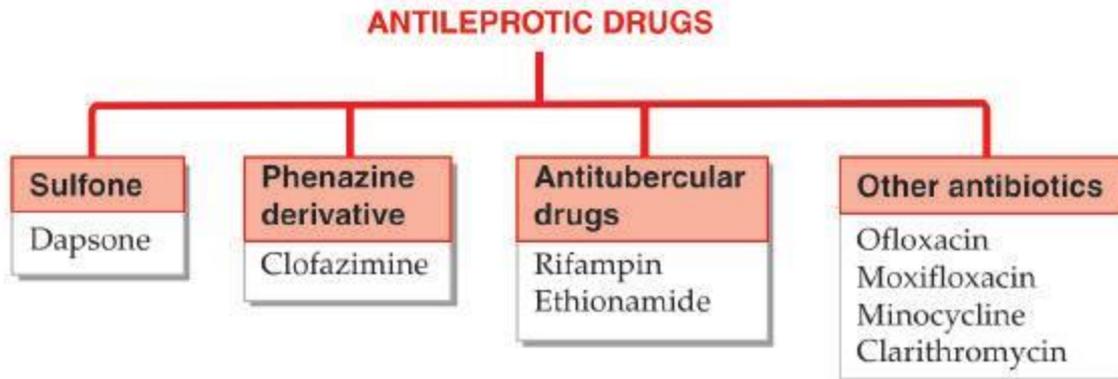
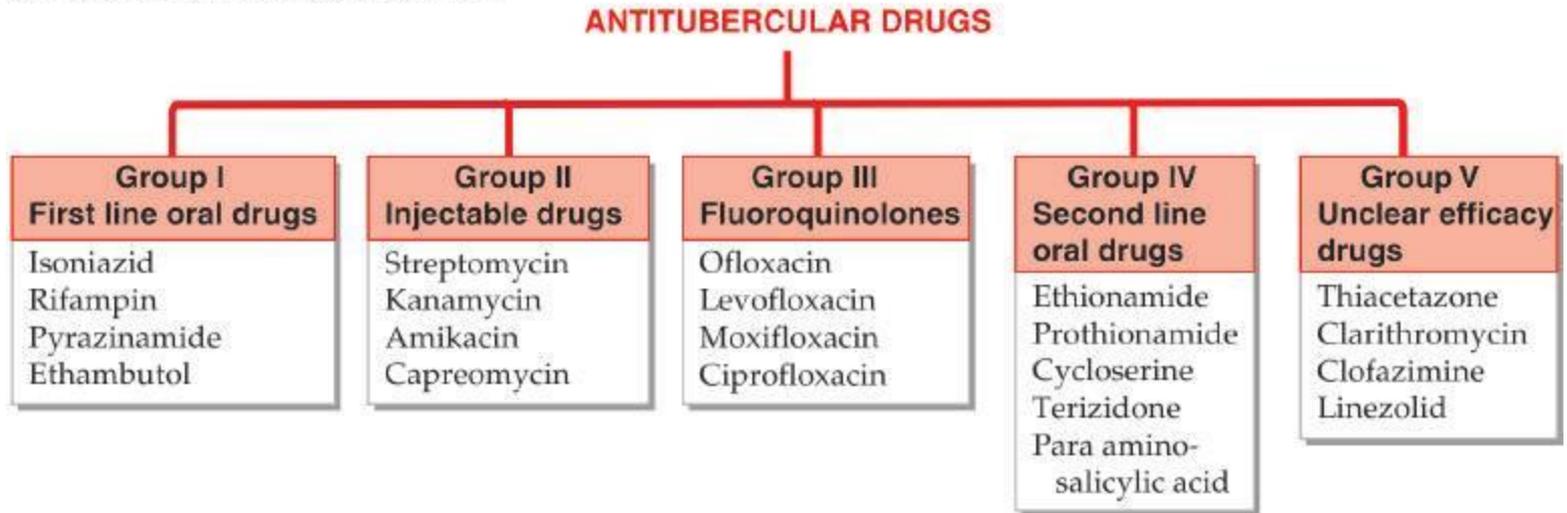
- General introduction
- Chemotherapy of T.B and Leprosy
- Chemotherapy of Malaria
- Chemotherapy of Protozoal infections
- Pharmacology of Antihelmintic drugs
- Cancer Chemotherapy

Chemotherapeutic Agents

- Chemotherapeutic agents, also referred to as antineoplastic agents, are used to directly or indirectly inhibit the proliferation of rapidly growing cells, typically in the context of malignancy.
- They are classified according to their mechanism of action and include-
 - Alkylating agents
 - Antimetabolites
 - Topoisomerase inhibitors
 - Mitotic inhibitors.
- Chemotherapy is associated with a range of adverse effects (e.g., nausea, vomiting, increased risk of infection, and impaired growth of healthy cells), and with some agents, an increased risk of secondary neoplasms.
- Symptomatic management of associated side effects is recommended to improve tolerance.

- **Chemotherapeutic agents (synthetic antibiotics):** antimicrobial agents of synthetic origin useful in the treatment of microbial or viral disease.
- Examples are sulfonilamides, isoniazid, ethambutol, AZT, nalidixic acid and chloramphenicol.
- Note that the microbiologist's definition of a chemotherapeutic agent requires that the agent be used for antimicrobial purpose and excludes synthetic agents used for therapy against diseases that are not of microbial origin.
- Hence, pharmacology distinguishes the microbiologist's chemotherapeutic agent as a "synthetic antibiotic".

ALTERNATIVE CLASSIFICATION



Reference: Textbook of K D Tripathi

Antimetabolites

- Antimetabolites replace natural substances as building blocks in DNA molecules, thereby altering the function of enzymes required for cell metabolism and protein synthesis.
- In other words, they mimic nutrients that the cell needs to grow, tricking the cell into consuming them, so it eventually starves to death.

Vinca alkaloids

Vinca alkaloids are antitumor agents derived from plants. These drugs act specifically by blocking the ability of a cancer cell to divide and become two cells. Although they act throughout the cell cycle, some are more effective during the S- and M- phases, making these drugs cell cycle specific.

Antibiotics

- Antitumor antibiotics are cell cycle nonspecific. They act by binding with DNA and preventing RNA (ribonucleic acid) synthesis, a key step in the creation of proteins, which are necessary for cell survival.
- They are not the same as antibiotics used to treat bacterial infections. Rather, these drugs cause the strands of genetic material that make up DNA to uncoil, thereby preventing the cell from reproducing.

Taxanes

- The principal mechanism of action of the taxane class of drugs is the disruption of microtubule function. Microtubules are essential to cell division, and taxanes stabilize GDP-bound tubulin in the microtubule, thereby inhibiting the process of cell division as depolymerization is prevented.

Camptothecin analogues

- **Camptothecin** binds to the topoisomerase I and DNA complex resulting in a ternary complex, stabilizing it and preventing DNA re-ligation and therefore causes DNA damage which results in apoptosis.

Some regimen of chemotherapeutic agents

1. CHOP
2. CHOP-R or R-CHOP
3. EPOCH
4. R-EPOCH or EPOCH-R
5. FLOT
6. VAC

CHOP

- An abbreviation for a chemotherapy combination that is used to treat non-Hodgkin lymphoma and is being studied in the treatment of other types of cancer.
- It includes the drugs cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin), vincristine sulfate (Oncovin), and prednisone.
- Also called CHOP.

R-CHOP or CHOP-R

- Most often, the treatment is chemotherapy (chemo), usually with a regimen of 4 drugs known as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), plus the monoclonal antibody rituximab (Rituxan).
- This regimen, known as R-CHOP, is most often given in cycles 3 weeks apart

EPOCH

- EPOCH regimen a chemotherapy regimen consisting of etoposide, prednisone, vincristine (Oncovin), cyclophosphamide and doxorubicin hydrochloride (hydroxydaunorubicin hydrochloride), which may be used in combination with rituximab (R-EPOCH) for the treatment of various aggressive B-cell and T-cell non-Hodgkin lymphomas.

R-EPOCH

Days	Drugs	Dose	Route
1-5	Prednisolone	60mg/m ² BD	PO
1	Rituximab	375mg/m ²	IV
1-4	Doxorubicin	10mg/m ² /day	IV
1-4	Vincristin	0.4mg/m ² /day	IV
1-4	Etoposide	50mg/m ² /day	IV
5	Cyclophosphamide	750mg/m ²	IV
6 onwards	GCSF (as per local policy)	Daily until neutrophils >1.0 x 10 ⁹ /L	SC

FLOT

- Docetaxel, oxaliplatin, leucovorin, and 5-fluorouracil (FLOT) may improve overall survival (OS) in patients with locally advanced gastric cancer (LAGC); however, evidence for its use as a standard treatment has not been established in China.
- The aim of this study was to investigate the effectiveness, safety, and feasibility of the FLOT regimen as neoadjuvant chemotherapy in Chinese patients with resectable LAGC.

VAC

- VAC is the name of a chemotherapy combination that includes:
- Vincristine, actinomycin D (also known as dactinomycin and Cosmegen) & cyclophosphamide.
- It is a treatment for a type of bone cancer called Ewing's sarcoma.
- These chemotherapy drugs destroy quickly dividing cells, such as cancer cells

Why chemotherapy causes side effects

- Cancer cells tend to grow fast, and chemo drugs kill fast-growing cells. But because these drugs travel throughout the body, they can affect normal, healthy cells that are fast-growing, too.
- Damage to healthy cells causes side effects.
- Side effects are not always as bad as you might expect, but it's normal to worry about this part of cancer treatment.

Common side effects caused by chemotherapy

- Fatigue.
- Hair loss.
- Easy bruising and bleeding.
- Infection.
- Anemia (low red blood cell counts)
- **Nausea and vomiting.**
- Appetite changes.
- Constipation.

- Most chemotherapy side effects go away shortly after you've finished chemotherapy.
- Still, some side effects may take several months or longer to go away completely. When you and your doctor are deciding on a chemotherapy regimen, weighing the benefits versus the side effects is part of the process.

Conclusion

- The latest advances in cancer treatment have created a whole new outlook on how to treat cancer.
- These advances have developed from a deeper understanding of the molecular basis of cancer.
- Some of the earlier treatments are still valuable however they have some drawbacks. For example, surgery and radiation are effective but they only treat one local area of the cancer. Chemotherapy can treat cancer cells that are spread all over the body but they have extremely toxic side effects.

Thank You...