***\*\*patients on chemotherapy :-***

-Patient receiving chemotheraptic agents should be diagnosed as having some type of malignancy…

-Of course the aim of chemotheraptic agents is to prevent cancer cells from multiplying, invading, metastasizing, and ultimately killing the host (patient).

- Most chemotherapeutic agents currently in use appear to exert their effect primarily on cell proliferation…so we have to have some kind of proliferation for the chemotheraptic agent to exert their effect..

-Cell multiplication is characteristic of many normal cells as well as cancer cells, so that’s why chemotherapeutic agents will have toxic effects on normal cells, particularly those with a rapid rate of turnover, such as ***bone marrow and mucous membrane…***

**First concept** :-so the effect of CT is generalized on all cells that are dividing ….more cell proliferation more effect of CT agents ..

**Second concept** :-The goal in selecting an effective drug is to find an agent that has marked growth inhibitory or controlling effect on the cancer cells and a minimal toxic effect on the host..also **another** concept is the delivery of this agent to the tissues ,,cancer cells are differ from vascularization..so this pointmust be considered ..

-Cancer, is a malignant neoplasm. It is a term for a large group of different diseases, all involving unregulated cell growth. In cancer, cells divide and grow uncontrollably, forming malignant tumors, and invade nearby parts of the body. The cancer may also spread to more distant parts of the body through the lymphatic system or bloodstream…..

\*\* in this graph we see the **burden of malignant** cells in the host through the time …

-In this example, **3 logs of cancer cells are killed with each treatment cycle**, and there is a one log growth between each cycle of treatment. The **net reduction is 2 logs** with each treatment. Such a model is liable for some changes when it comes to clinical practice for the following reasons:

1. All cells in the tumor are not equally sensitive to chemotherapy…
2. Drug accessibilty to tumour cells varies according to the site of the tumour within the host and local factors such as blood supply and regional fibrosis…(depend on vascularization )
3. Cell sensitivity may change during the course of therapy…
* --In an ideal system, each time the dose is repeated, the same proportion of cells-not the same absolute number- is killed **(fractional cell kill).** ****
* ***Main lines of cancer treatment includes***:
* *Medical (chemotherapy and molecular targeted therapy).*
* *Surgical (complete resection and palliative surgery)*
* *Radiotherapy*

--**Combination chemotherapy** is usually used with a number of drugs with different mechanisms of actions simultaneously administered, the main aim is to decrease tumor resistance and enhance response…

* --A careful review of the patient status should be undertaken to assess tolerability chemotherapeutic drugs and should include: cardiac, renal, hepatic assessment as well as performance status and other medical co-morbidities…
* Chemotherapy maybe given aiming for cure or for palliation of symptoms.
* **Curative Intent:**for curing of symptoms
* 1) **Neoadjuvant** :initial chemotherapy is designed to shrink the primary tumour, thereby rendering local therapy (surgery or radiotherapy) less destructive or more effective.
* 2) **Adjuvant**: chemotherapy is given post surgical resection to eradicate any potential remaining malignant cells.
* **Palliative intent:**for palliation of symptoms
* Chemotherapy is given to palliate symptoms of the malignancy, improving quality of life, and prolong life expectant. Used usually when the disease is metastatic or the general condition of the patient doesn’t allow surgical procedure ..

--cell cycle :dr just read the table

|  |  |  |  |
| --- | --- | --- | --- |
| **Description**  | **Abbreviation**  | **Phase**  | **State**  |
| A resting phase where the cell has left the cycle and has stopped dividing.  | G0  | Gap 0  | Resting  |
| Cells increase in size in Gap 1.  | G1  | Gap 1  | Interphase  |
| DNA repilcation  | S  | Synthesis  |
| Cell continue to grow  | G2  | Gap 2  |
| Cell growth stops at this stage and cellular energy is focused on the orderly division into two daughter cells  | M  | Mitosis  | Celll division  |

\*\***Cellular factor affecting sensitivity to chemotherapy:**

1. **Cellular growth fraction(percentage of cells that are dividing )علاقه طرديه مع زيادة التأثير**

**2)Tumor differentiationعلاقه طرديه ايضا مع زيادة التأثير**

**---In relation to cell cycle, chemotherapeutic agents can be divided into three different categories:**

1. **Phase specific drugs: Agents that are most active against cells in a specific phase of the cell cycle.**
2. **Cell cycle specific drugs: Agents that are effective while cells are actively in cycle but that are not dependent on the cell being in a particular phase.**
3. **Cell cycle nonspecific drugs: A third group of drugs that appear to be effective whether cancer cells are in cycle or are resting.**

**--- v.imp table**

|  |  |  |
| --- | --- | --- |
| **Type**  | **Agent**  | **Class**  |
| **Antimetabolite, Pyrimidine analog****Topoisomerase II inhibitor****Vinca Alkaloid**  | **Cytarabine (S phase)****Etoposide (G2 phase)****Vinblastine (M phase)**  | **Phase specific**  |
| **Alkylating agents**  | **Cyclophosphamide** **Melphalan**  | **Cell cycle specific**  |
| **Nitrogen Mustard**  | **Mechlorethamine**  | **Cell cycle non specific**  |

--classification of most ct agents :-

|  |  |
| --- | --- |
| **EXAMPLES**  | **CLASS**  |
| Cyclophosphamide Ifosfamide Melphalan Platinum analogues (Alkylating like)  | **Alkylating agents**  |
| Purine analogue (Fludarabine)Pyrimidine analogue (Cytarabine)Antifolates (Methotrexate)  | **Antimetabolites**  |
| Vinblastine Vincristine Paclitaxel  | **Plant alkaloids and taxanes**  |
| Irinotecan Etoposide  | **Topoisomerase inhibitors**  |
| Doxorubicin  | **Cytotoxic antibiotics**  |

\*\*\*\*\***Chemotherapeutic drugs have a range of side effects that depend on the type of medications used. The most common medications mainly affect the fast-dividing cells of the body, such as blood cells and the cells lining the mouth, stomach, and intestines…**

* Some common examples:
1. Myelosuppression and immune suppression”related to aeffect on bone marrow mainly ,,so myelosuppression means decreased bone marrow production and of course this will be followed by immune suppression”
2. Gastrointestinal side effects affect mucous membrane of GI system”diarrhaea ..ulcer ..”
3. Cardiotoxicity
4. Hepatotoxicity
5. Nephrotoxicity
6. Encephalopathy may induce seizure disorders “impaired cognition “
7. Increased risk of secondary neoplasms most commonly alklating agents
8. Infertility
9. Teratogenicity affect fetus
10. Tumor lysis syndrome is an immediate side affect where large n. of malignant cells are killed immedialtely ..
* \*\*\*\*\*(mylosuppression and immune suppression )**Depends on the type of chemotherapy and dose given.**
* Le**ads to anemia, thrombocytopenia”increase tendency to bleeding “, and leukopenia (neutropenia)**
* Neutropenia increases the risk of infections and the patients should be isolated and treated with broad spectrum antibiotics if an infection is suspected”**patient should be isolated** “
* Careful dental assesment should be carried out in patients who are expected to go into severe myelosuppression post chemotherapy as bad oral hygiene is associated with increased risk of dental abscess.
* ---***GI side effects*** :-Chemotherapy induced nausea and vomiting, which can be acute or delayed. Nausea and vomiting occurrence depends on the drug used as some drugs are considered more emetogenic than others.
* Ematogenic “tendency to N&V”
* Xerostomia, mucositis.
* Mouth ulcers
* Loss of appetite
* Diarrhea

Also hepatotoxicity”part of GI manifestations “ ..

* Some chemotherapeutic drugs can lead **to cardiomyopathy and heart** failure. This depends on the cumulative dose of the drug. In addition, previous or concomitant radiation to left hemithorax, risk factors for cardiovascular disease, and anemia may cause more cardiac toxicity. Some common examples of drugs with cardiac toxicity are adriamycin (anthracyclines).
* Cardiac toxicity can be acute or chronic. Chronic toxicity can occur even after many years of chemotherapy

**(tumor lysis syndrome** )

* potentially lethal complication of anticancer treatment, it occurs when large numbers of neoplastic cells are killed rapidly, leading to release of intracellular ions and metabolic byproducts into the systemic circulation.
* It is typically associated with acute leukemias and high-grade non-Hodgkin lymphomas,[such as Burkitt lymphoma.
* Characterized by rapid development of **hyperuricemia,hyperkalemia”release K+”, hyperphosphatemia, hypocalcemia, and acute renal failure (ARF**)”deposition of urate crystals “….

\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*note :the dr mainly was explaining the lec from the slides with some more info “I add them “

GOOD LUCK ☺