



HEMATOPOIETIC & LYMPHATIC SYSTEM

-HAYAT BATCH-

SUBJECT : Pharmacology

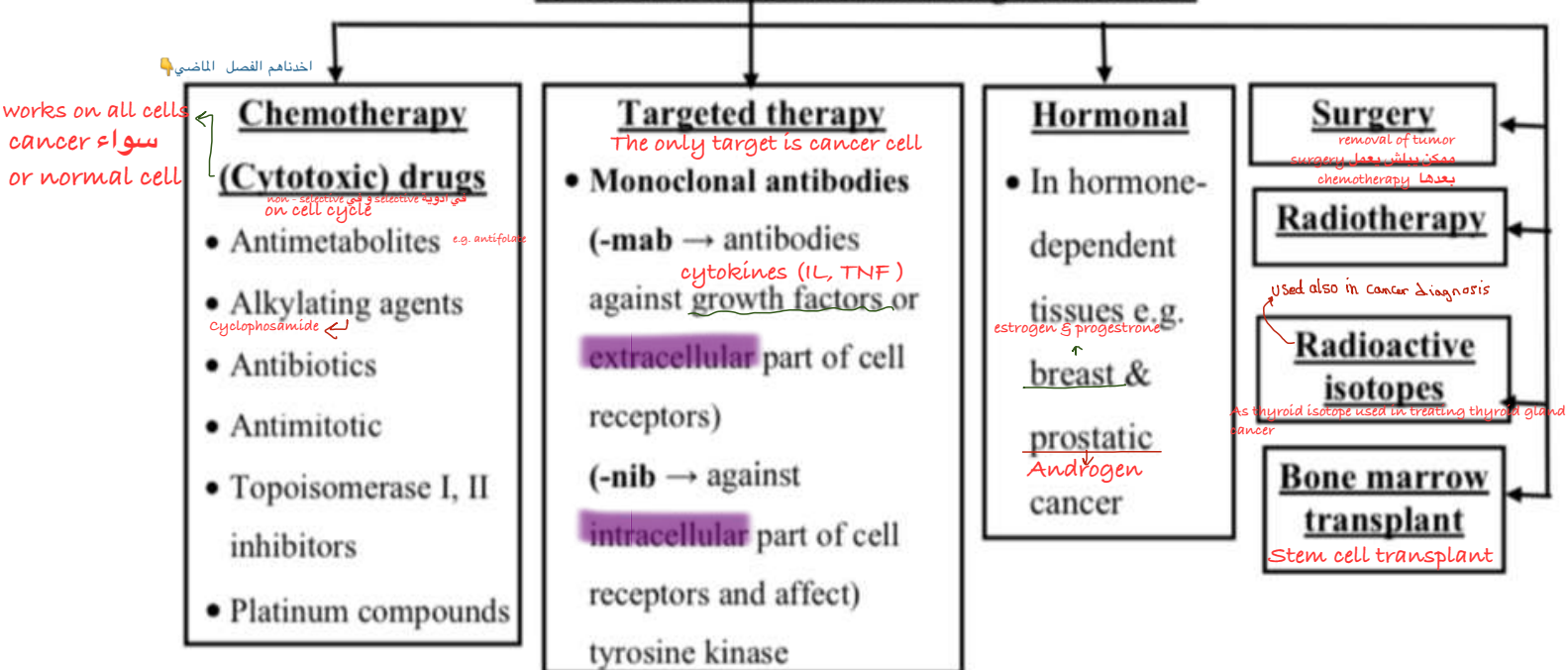
LEC NO. : 8

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TREATMENT OF LEUKEMIA

Lines of treatment of the malignant tumors



Types of treatment of the malignant tumors:

- 1. Iry therapy:** target the tumor itself e.g. surgical removal (solid tumor لو كان)
- 2. Adjuvant:** target the remnants of tumor i.e. after the Iry, use cytotoxic drugs, hormonal, or radiation therapy (Every tumor has its protocol of treatment)
- 3. Neoadjuvant:** target the tumor to decrease its size or vascularity i.e. before Iry, use cytotoxic drugs, hormonal, or radiation therapy (vascularity in thyroid gland causes bleeding)
- 4. Palliative (supportive) therapy:** target the complications occurred by tumor and therapy (e.g. bone marrow suppression which may cause aplastic anemia, neutropenia, or tumor itself causes pressure in certain place)

Cytotoxic drugs:

- In combination:

- Advantages:

- 1. Synergism:** Each drug attacks tumor cells at different phases of growth cycle (sequential effect) (حتى يشتغل بمراحل مختلفة)
- 2. Decrease incidence of resistance**
- 3. Decrease incidence of adverse effects due to use of small optimal doses.** (بدل ما ياخذ دوا واحد بجرعة كبيرة)

- Provided that drugs are None toxic to the same organ (For example using 2 or 3 drugs ,all of them is nephrotoxic)

- In cycles: act by % killing not absolute number killing
- Affect both cancer and normal cells:

بتأخذ على جلسات

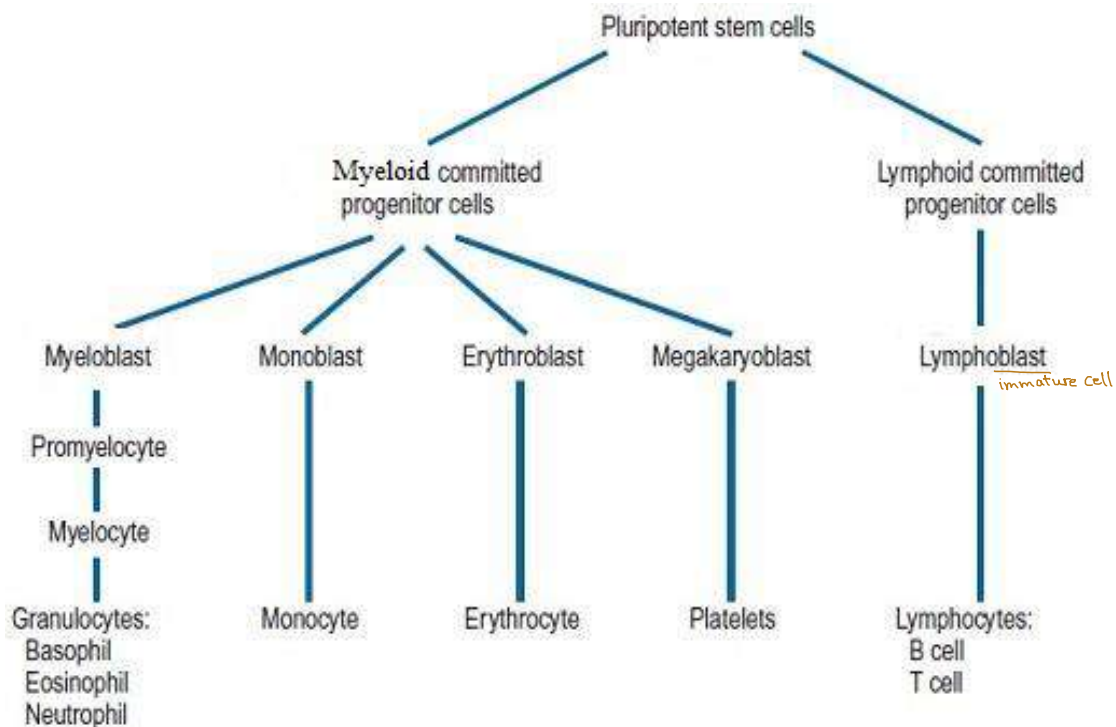
- Rapidly multiplying normal cells are more affected especially bone marrow cells → Neutropenia, thrombocytopenia and anemia

كلما كانت life span قصيرة كلما كان multiplication اسرع فرح تتأثر بالاول

Leukemias:

multiplication حسب ترتيب حسب WBC و platelet و RBC short life span 10 days و 120 days

- The normal process of haemopoiesis is altered → Accumulation of malignant cells → progressive impairment of the normal bone marrow function.



حسب lymphoid or myeloid و حسب cell اللي تكونت

Types of Leukemias

A- Acute leukemias: No maturation/rapid rate

- > 20% of the cellular elements of the bone marrow are replaced with blast cells
- ALL: derived from the lymphoid series. The blasts may infiltrate lymph nodes and other tissues such as liver, spleen, testis and the meninges. or
- AML: derived from the myeloid series. The blasts tend to infiltrate skin, gums, liver and spleen

B- Chronic leukemias *There is maturation of cells*

- The normal bone marrow is replaced by a malignant clone of morphologically maturing haemopoietic cells (functionally deficient). *خلل في تصنيع الخلايا*
- **CLL:** is characterised by a clonal expansion of mature lymphocytes of B-cell origin → accumulate in - the peripheral blood → lymphocytosis - lymph nodes, liver and spleen.
- **CML:** is characterised by the predominance of maturing myeloid cells in blood, bone marrow, liver, spleen and other organs.
- the Philadelphia chromosome translocation (Ph) seen in over 90% of cases (a translocation of genetic material between the long arms of chromosome 22 and chromosome 9 → the apposition of the BCR gene (chromosome 22) and the ABL gene (chromosome 9) → novel BCR-ABL gene → encodes a protein with tyrosine kinase activity → uncontrolled growth characteristic of leukemic cells).

Treatment of Leukemias *genetic abnormality بعالج tyrosine kinase because of abnormality بعالج leukemia, و في ابحاث بتحكي انو بعالج genetic abnormality في دوا بعالج*

I. Acute leukemia:

- **Induction of remission:** is the initial phase of treatment.
 - Remission is: 1- **Bone marrow:** *يمكن يعملوا division ثاني مرة* < 5% blasts with normal maturation of all cell lines
 - 2. **Peripheral blood:**
 - *القضاء على كل blast cell* Blasts 0%
 - Platelets $> 100,000/uL$ *→ normal*
 - Hgb ≥ 11 g/dL
 - Neutrophils $\geq 1500/uL$
 - Intensive combination **cytotoxic drugs** are given to achieve a complete remission (CR)
- **Consolidation (intensification) therapy:** *Maintenance for complete remission*
 - Aim: sustain **CR** (as minimal residual disease [MRD] will persist),
 - It comprises chemotherapy drugs and bone marrow transplantation.
- **CNS prophylaxis:** *لحتى يضمن ما يتكون blast cells ثاني*
 - *خاصة methotrexate* **Cytotoxic** (intrathecal).
 - **ALL:** for all patients – **AML:** for patients at risk. *in case of drugs that can't cross blood brain barrier*
 - Because it is common in CNS filtration*
- **Maintenance therapy** *الجرعات اقل*
 - to sustain CR. - Milder than induction or consolidation chemotherapy.

II. Chronic leukemia

1. CML:

- The main aim: keeping patients asymptomatic by normalising the WBC, so take care of occurrence of
 - Acceleration (\uparrow blast cells but not $> 20\%$)
 - Blastic crisis ($\uparrow\uparrow\uparrow$ blast cells)

- Include: - Chemotherapy

- Targeted therapy:

acute ←
chronic ← } - Palliative therapy e.g.

- Surgery: Splenectomy for splenomegaly In chronic (infiltration of cells in spleen)
- Radiotherapy for localised painful lymphadenopathy or splenic complications. Infiltration of lymph node (painful)

مثل خمير كثير

2. CLL:

Almost benign so we won't start the treatment if the case remains the same

- Currently, there is no cure for CLL. Just wait and see
- Indications of treatment:
 - Rapidly \uparrow WBC
 - \uparrow lymphadenopathy
 - Systemic symptoms
 - Bone marrow failure
 - Autoimmune complications.
- Include: - Cytotoxic drugs and targeted therapy
- Palliative therapy

تابع المريض خليه تحت ملاحظتك و لو احتاج تدخل بأي وقت نبدا نعطيها العلاج

Examples of drugs used for leukemia treatment: 7 اخذناهم بمحاضرة

- Chemotherapeutics: Corticosteroids, Cyclophosphamide, Methotrexate Alkylating agent
- Targeted therapy: Rituximab, imatinib (it inhibits the abnormal tyrosine kinase product of the BCR-ABL fusion gene) Antifolate
Monoclonal antibody
يعالج CML

Bone marrow transplantation: احد علاجات leukemia

- Steps: اما من جسم غريب (متبرع) او من الجسم نفسه
- Complications:

Infection is almost unavoidable after bone marrow transplant

Allogeneic stem cell transplant

Donor bone marrow or peripheral blood stem cells are harvested

Ablative therapy: chemotherapy +/- total body irradiation

Donor stem cells infused

+ Immunosuppressives حتى ما يصير rejection نفس فكرة autologous بين الفرق

All bone marrow cells died and these patients took immunosuppressive drug, so they should be in sterile tent to be not infected و هاي تعتبر اخطر بمرحلة العلاج

Autologous stem cell transplant

Homogenous

Patient's bone marrow or peripheral blood stem cells are harvested

Patient's own stem cells reinfused

اذا اخذت من جسم نفسه اللي عنده leukemia بالاول تعطيها chemotherapy بجرعة قليلة عشان بقدر الامكان تقلل من blast cells في bone marrow و بعدين تسحب عينة من نخاع العظم و تعمل filtration و تبلش تنتقي ال stem cells و هي اخذت اللي بدك ياه و تعطيها جرعات كبيرة من chemotherapy حتى تقتل كل الخلايا في bone marrow و بعدها تحقن ال stem cells اللي اخذتها و تبلش تنقسم لتنتج خلايا normal و اخطر مرحلة في bone marrow transplant لما يصير في اختفاء لجميع الخلايا في نخاع العظم

Common therapeutic problems in the leukemias:

bone marrow suppression هي

لازم تتعالج عشان ما يتاخر عن
جلسة chemotherapy الثانية

1. Neutropenia: treatment by ^{granulocyte}G-CSF or ^{megakaryocyte}GM-CSF →
- ↓ period of neutropenia → ↓ infection
 - Cycle of chemotherapy can be given on time
 - Risky in AML (need assessment of the case)

انت عم بتعالج و توقف انقسام خلايا cancer و بتعطي حاجة بتعمل stimulation
للاقسام .. بهاي الحالة بتعطي المريض حسب اذا رح يستفيد و لا لا

2. Thrombocytopenia: - treatment by platelets

- In female: ↓ bleeding of menstruation (give contraceptive pills)
- In expected bleeding ulcer: give ulcer protective drugs ↓bleeding

3. Anemia: - treatment by blood transfusion

- Erythropoietin Risky (need assessment of the case) تقييم الاستفادة

مهم جدًا

4. Tumour lysis syndrome especially in acute leukemia

- initiation of chemotherapy → lysis of cells → hyperuricaemia, hyperkalemia and hypocalcaemia → urate nephropathy

حتى يصير excretion لها
Since uric acid is salt, it
accumulates in kidney and
causes urate nephropathy

- treatment: high fluid intake

Allopurinol for hyperuricaemia

(K, Ca, uric acid)

Correct electrolytes disturbances

Close monitoring of renal function, serum urate levels

بال acute leukemia في خلايا كثير
بتعطيه chemotherapy عشان يقتل
الخلايا فيقضي عليها وكمان
nucleic acid, protein structure
تتبدل وتتكسر وتعطينا uric acid

gout يمكن uric acid يكون عالي و ما يعمل اشي و ممكن يؤذي الكلية او يعمل مرض ال