

* Lec 4 *

تنويه: حضور المحاضرة جدد!!!! مفيد

بعد ما تحمد الله - عز وجل - وتنتهي عليه وتصلّي على سيّد الخلق ﷺ تقول:
 "اللهم إني أسألك فهم النبيين وحفظ المرسلين والملائكة المقربين.. سبحانه لا علم لنا إلا ما علمتنا إنك أنت العليم.. اللهم إني أستودعك ما سأقرأ وأحفظ وما تقع عيني عليه، فردّه إلي وقت حاجتي إليه".

بعدين بلش دراسة..

وقبل ما تفتح ورقه الاسئلة في الامتحان قول:

"اللهم ردّ لي ما استودعتك إيّاه يا خير الحافظين، اللهم لا سهل إلا ما جعلته سهلاً، وإنك تجعل الصعب إذا شئت سهلاً"

Basic Cancer Concepts and Classification:

Cancer is introduced as a complex topic involving **solid tumors and hematologic malignancies** (leukemias, lymphomas).

Cancer definition: A **monoclonal origin disease**, meaning it arises from a single mutated cell.

The challenge in cancer treatment is to **eliminate all malignant cells**, because **even a single surviving cell can divide and cause tumor recurrence**

*** Cancer Initiation, Progression, and Immune Evasion**

Cancer starts from a single cell undergoing mutations:

Initiation → Promotion → Progression → Invasiveness stages detailed.

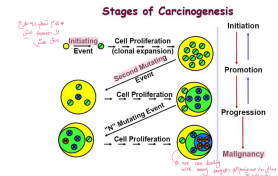
Cancer cells exhibit **heterogeneity**, meaning **within the tumor, cells differ genetically and phenotypically, complicating treatment.**

As cancer progresses, cells lose **immunogenicity**, enabling them to evade the immune system effectively.

The **bone marrow is often heavily infiltrated with cancer cells**, especially in leukemias and lymphomas, necessitating treatments like bone marrow transplantation.

The immune system in cancer patients is often severely compromised (**immunocompromised**).

Despite many therapeutic targets, eradication of all cancer cells is difficult without aggressive treatment, which risks severe side effects including death due to bone marrow suppression.



القدرة على إقناع جهاز المناعة

Differences Between Hematologic and Solid Tumors & Hypoxia in Solid Tumors
 Hematologic cancers (leukemias, lymphomas) are described as generally more responsive and easier to treat than solid tumors.

Solid tumors develop layers of cancer cells, with cells inside the tumor core experiencing hypoxia (low oxygen levels).

Hypoxic tumor cells enter a dormant state called **G0 phase** in the cell cycle, making them resistant to chemotherapy, which **targets proliferating cells.**

This explains cancer relapse after treatment because dormant cells evade therapy and later proliferate.

افهوها
بس ما
أهين إلكترو
يحب عليها

Chemotherapy drugs are generally cytotoxic agents ("burners") **targeting rapidly dividing cells, not just cancer cells but also normal proliferating cells** (e.g., hair follicles, GI tract lining, bone marrow).

Side effects include:

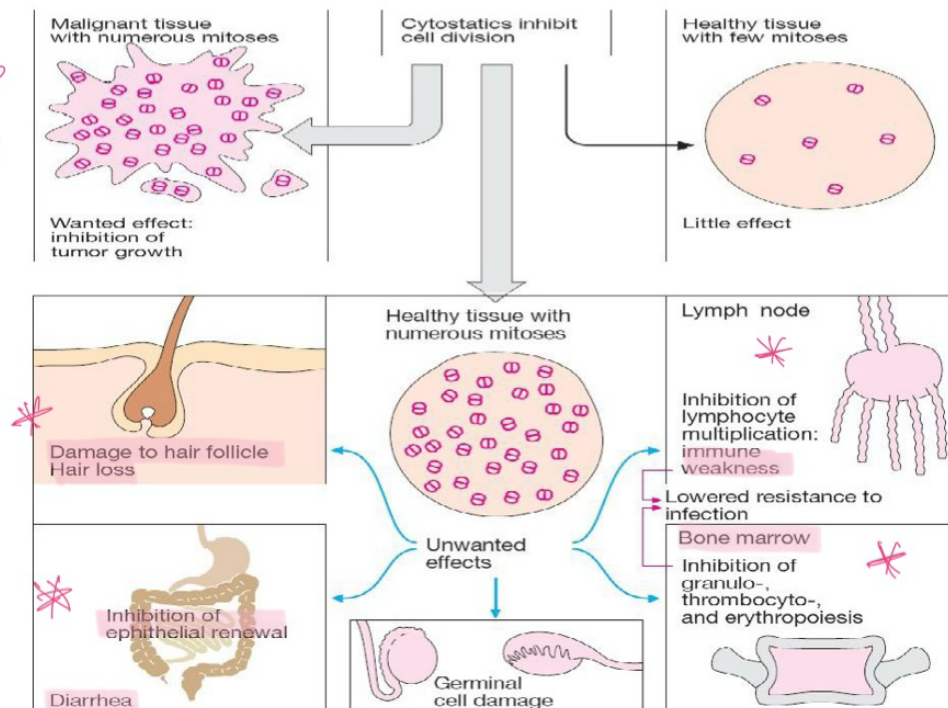
- 1) **Alopecia** (hair loss) due to hair follicle damage.
- 2) **Gastrointestinal toxicity** (nausea, vomiting, diarrhea) from GI mucosa damage.
- 3) **Bone marrow suppression**, leading to **thrombocytopenia, neutropenia, anemia**, and increased infection risk.
- 4) Chemotherapy causes **immunosuppression**, compounding cancer patients' vulnerability to infections.
- 5) Non-dividing cells are mostly unaffected by chemotherapy.
- 6) Cancer cells often harbor mutations in critical genes like p53, KRAS, BRAF, or overexpression of the epidermal growth factor receptor (EGFR) can make tumor cells resistant to treatment.
- 7) Cancer cells also have mutated DNA repair systems, allowing them to survive despite chemotherapy-induced damage.
- 8) Infertility: caused by the destruction of germinal

• الـ Cancer هاتين لـ immune
 • هتوف هتوف إداري مستخدمه
 • نقل خلايا المناعة

كل مكونات
الدم

من هادي
الطفرات
Cancer
cells
مقاومة للعلاج
فهي تاتر العلاج
نهاي وفالاية
خلايا حميا

عقار
السرطان



Ethical Considerations and Treatment Decisions in Cancer Management:

The doctor discusses the difficult decisions regarding treating cancer patients, especially for aggressive or late-stage cancers.

Some patients refuse chemotherapy due to severe side effects and reduced quality of life.

Ethical practice demands informing patients about prognosis, treatment benefits, and side effects to allow informed decision-making.

In some countries, palliative care and medical euthanasia (e.g., UK) are options for end-stage patients, but such practices are not common in Jordan and many Arab countries.

Financial constraints significantly affect access to advanced treatments like immunotherapy (e.g., cost of breast cancer immunotherapy at 36,000 Jordanian dinars for six injections).

Resource allocation challenges exist worldwide, leading to selective treatment based on cost-benefit evaluations.

مريض
معه
الطبيب
يسأل
الدكتور
شرحها
:

Cancer Treatment Types and Tumor Burden Concepts:

Upon diagnosis, tumor burden is often very high (e.g., 10^9 cancer cells).

Early detection tools like mammograms or PET scans only detect tumors above a certain size ($\sim 10^9$ cells).

المهزلة
يستوفى من
فقد الجسم فقط
عند (cancer)
موجود في ما
تقدر تشخصه
لما يكبر

Treatment classifications:

Two main treatment approaches:

1. Curative treatment

- Surgery: drastically reduces tumor size.
- Chemotherapy: eliminates microscopic metastases not visible during surgery.
- Used in cancers like Wilms tumor, skin cancer, testicular cancer, acute lymphoblastic leukemia, and sometimes melanoma.

2. Palliative chemotherapy

- Goal: relieve symptoms, shrink the tumor, and improve quality of life. → breast Cancer
- May slow disease progression but does not cure.

Treatment Outcomes in Acute Lymphoblastic Leukemia (ALL)

Adults:

- Complete Remission (CR): 80-85%
- Leukemia-Free Survival (LFS): 30-40%

Children:

- Complete Remission (CR): 95-99%
- Leukemia-Free Survival (LFS): 70-80%

} → better outcome ?

Adult cancers develop over a longer time, accumulate more mutations, and adapt well to their environment. Despite a mature immune system, cancer cells often evade immune detection, making treatment more difficult.

Key Definitions

1) Complete Remission (CR):

- ^{معنى} Blast cells in bone marrow reduced to <5%
- ^{فشل خلايا سرطانية} No clinical symptoms
- ^{بسرعة} Achieved shortly after treatment

2) Leukemia-Free Survival (LFS):

- Period without detectable leukemia cells
- Reflects long-term remission

Combination Chemotherapy

our target

• We use **combination chemotherapy** in order to :-

1. Obtain synergistic action
2. Minimize side effects.
3. Attack leukemic cells in different phases of mitosis.
4. Delay the onset of resistance of the malignant cells.

* Important: Never combine two drugs with the same mechanism of action, as the goal of combination therapy is to achieve a synergistic effect

Effective Drugs for ALL

1. Vincristine → Arrest cell mitosis
2. Prednisone → Lympholysis
3. 6-M.P. → Inhibit DNA synthesis
4. Methotrexate → Inhibit RNA and protein synthesis
5. Doxorubicin (Adriamycin) → Inhibit DNA synthesis
6. L-asparaginase

هذا العلاج يمتص كل ال Asn برميها

(تتوقع خلايا سرطان ال Asn)

ولأنه خلايا سرطان ما عندها القدرة على تصنيعه ففيل خلايا السرطان ما م تقدر تصنع بروتينها وهذا لدراسة

• We use this treatment for 3 years in males and 2 years in females because cancer is more aggressive in males.

مهم لأنه
يحل
targeting

رج نأخذهم المعاقرة الباقية

Use of L-asparaginase is critical because leukemic cells cannot produce asparagine, unlike normal cells, allowing selective killing. * مهم

Combination chemotherapy exploits synergistic mechanisms to maximize cancer cell kill.

Chemotherapy for ALL is multi-phased:

eliminating both normal and malignant cells.

1) Induction: Eradicates most leukemia cells; causes bone marrow suppression and neutropenia. ? هون يقضي على الخلايا بوج ما مانع بادن خطوة

2) Intensification (Consolidation): Further reduces residual disease. هون يقضي على الخلايا بوج ما مانع بادن خطوة

febrile neutropenia

3) Maintenance: Prolonged low-dose therapy to prevent relapse. هون يقضي على الخلايا بوج ما مانع بادن خطوة

4) CNS prophylaxis is essential since leukemia cells may hide in the brain, protected from systemic chemotherapy, causing CNS relapse (up to 70% without prophylaxis). Best Remission therapy

CNS prophylaxis involves intrathecal chemotherapy or high-dose systemic drugs that cross the blood-brain barrier. من الضغط خلايا السرطان بتهرب على الدماغ فبد اداة وقيل ما يسير هاد اليرش يكون محبذ لمرلن ؟