



CHEMOTHERAPY

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Chemotherapy

- Cancer chemotherapy attempts to cause a **lethal cytotoxic** event or **apoptosis** in the cancer cell that can **arrest** a tumor's **progression**.
- Chemotherapy is used primarily to **treat systemic** disease **rather** than **localized** lesions that are amenable to surgery or radiation.
- **Ideally**, these **anticancer** drugs **should interfere only** with cellular processes that are **unique** to **malignant** cells
But, Unfortunately, most currently **available** anticancer drugs do **not specifically** recognize **neoplastic** cells but, rather, affect **all kinds** of proliferating cells, **both normal** and **abnormal**.

Work of Chemotherapy

- To understand how chemotherapy works , we should understand the normal **life cycle of a cell** in the body.
- All **living tissue** is composed of **cells**. Cells **grow** and **reproduce** to **replace** cells **lost** during **injury** or normal "wear and tear."
- The **cell cycle** is a series of steps that **both** normal cells and cancer cells **go through** in order **to form new cells**.

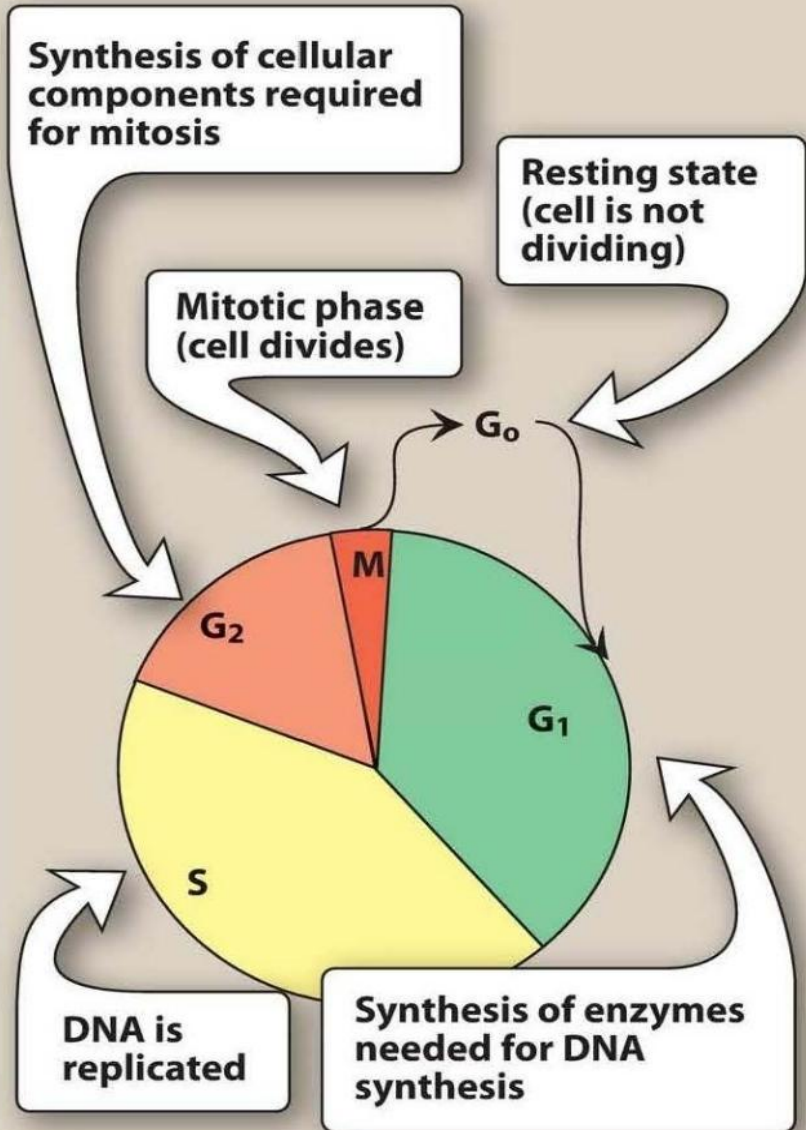
:Cell cycle phases

- The cell cycle phases are:
- G0 (resting G0; **nothing** is happening),
- G1 (or gap 1; a **growth** phase),
- S (**synthesis**; the **replication** of **DNA** occurs),
- G2 (gap 2; another **growth** phase)
- M (**mitosis**; the actual **division** from 1 cell into 2).

Note :

- * **cell cycle nonspecific drug**, means **kill** the cell in **various** and multiple **phases** of the **cell cycle**.
- * **cell-cycle specific drug**: means **kill** cancer cells **only** when they are **dividing**.

A The cell cycle



B

Cell cycle-specific drugs

Antimetabolites
Bleomycin
Etoposide
Vinca alkaloids



Effective for high-growth-fraction malignancies such as hematologic cancers

C

Cell cycle non-specific drugs

Alkylating agents
Antibiotics
Cisplatin
Nitrosoureas



Effective for both low-growth-fraction malignancies, such as solid tumors, as well as high-growth-fraction malignancies

The Cell Cycle

- **G0 phase (resting stage)**: The cell has **not** yet started to **divide**. Cells **spend much** of their lives in this phase. Depending on the type of cell, G0 can last for a **few hours to a few years**. **When** the cell is **signaled to reproduce**, it **moves** into the **G1 phase**.
- **G1 phase** : During this phase, the cell starts **making** more **proteins** and **growing** larger, so the new cells will be of normal size. This phase **lasts** about **18 to 30 hours**.

- **S phase:** In the S phase, the **chromosomes** containing the genetic code (DNA) are **copied** so that **both** of the new cells formed will have matching **strands of DNA**. This phase lasts about **18 to 20 hours**.
- **G2 phase:** In the G2 phase, the cell **checks** the **DNA** and **prepares** to start **splitting** into 2 cells. It lasts from **2 to 10 hours**.
- **M phase (mitosis):** In this phase, which lasts only **30 to 60 minutes**, the cell **actually splits** into **2** new cells.

: Anticancer Drugs

I. Cytotoxic drugs: they act **directly** on cells :

A. Alkylating agents

1-Nitrogen mustards: (Form **DNA cross-links**, resulting in **inhibition of DNA** synthesis and function)

E.X:

Cyclophosphamide (the **most commonly** used alkylating agent, **haemorrhagic cystitis** is its potential adverse effect).

Chlorambucil, Melphalan, Mechlorethamine.

2-Ethylenimide: thiotepa (an organophosphorus compound, **releases free radicals** which **disrupt the bonds** of cell **DNA**), used in **ovarian** tumour.

3-Alkyl sulfonate: Busulfan (has a selective effect on the **bone marrow** and used in chronic granulocytic **leukaemia**). Act by **slowing** or **stopping** the **growth** of cancer cells.

4-Nitrosoureas: Carmustine, Lomustine (both have **good penetration** to **CNS**), **streptozocin** (specifically **toxic to the β cells** of the islets of Langerhans, hence its use in the treatment of **insulinomas**).

5-Platinum analogs: cisplatin, carboplatin, and oxaliplatin (Form **intrastrand and inter strand DNA cross-links**; binding to nuclear and cytoplasmic proteins).

B. Anti metabolites

(1)Folate antagonist: Methotrexate, Pemetrexed

(2)Purine antagonist: 6-Mercaptopurine, 6-Thioguanine , Fludarabine, Cladribine.

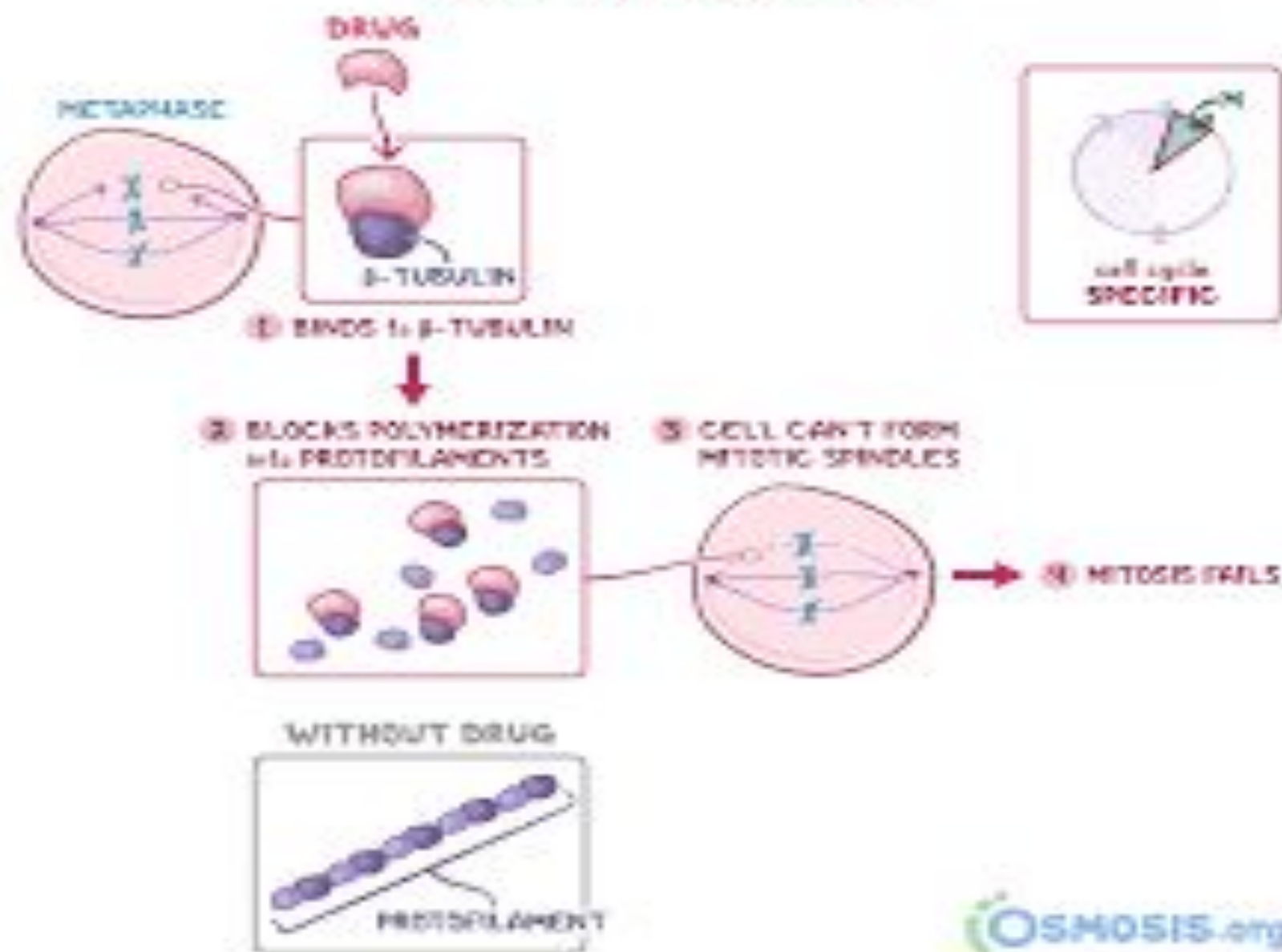
(3)Pyrimidine antagonists: 5-Fluorouracil, Cytarabine, Capecitabine, Gemcitabine.

C. Vinca alkaloids: Vincristine, Vinblastine and Vinorelbine (**inhibition** of **tubulin** polymerization)

D. Taxanes: Paclitaxel, Docetaxel (derived from the bark لحاء of the yew صنوبر tree, **mitotic spindle poison** results in **inhibition of mitosis** and cell division).

E. Epipodophyllotoxin: Etoposide and Teniposide (inhibition of topoisomerases II)

VINCA ALKALOIDS



F. Camptothecin: Topotecan and Irinotecan (**inhibit** the activity of **topoisomerase I**, the key enzyme responsible for **cutting** and **religating** single DNA strands).

G. Antibiotics: Anthracyclines (Doxorubicin, Daunorubicin, Idarubicin, Epirubicin, Mitoxantrone), Bleomycin, MitomycinC (**Oxygen free radicals** bind to **DNA** causing single- and **double strand DNA breaks**).

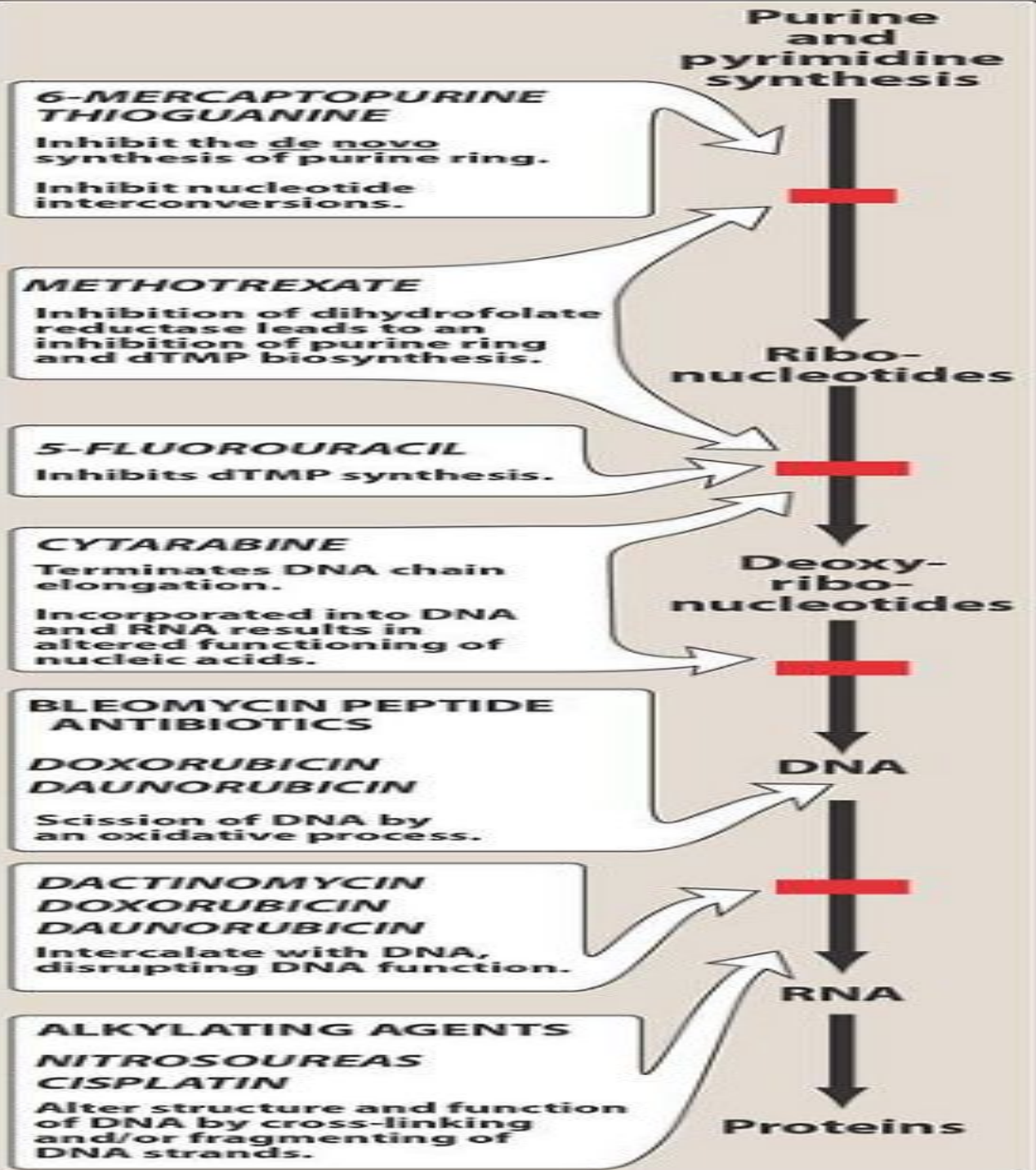
H. Miscellaneous:

1- Bendamustine (**bifunction** alkylating agent consisting of a **purine benzimidazole** ring and a nitrogen **mustard** moiety), Procarbazine, Dacarbazine (**Methylate DNA** and **inhibit DNA synthesis** and **function**).

2- Monoclonal antibodies (Trastuzumab, rituximab, bevacizumab, and cetuximab) .They are created from **B lymphocytes**.

Imatinib (acts as a **signal transduction inhibitor**, used specifically to **inhibit** tumor **tyrosine kinase** activity).

Gefitinib (**targets** the **epidermal growth factor receptor**. It is approved for the **treatment** of **non–small cell lung cancer** that has **failed** to respond to **other** therapy).



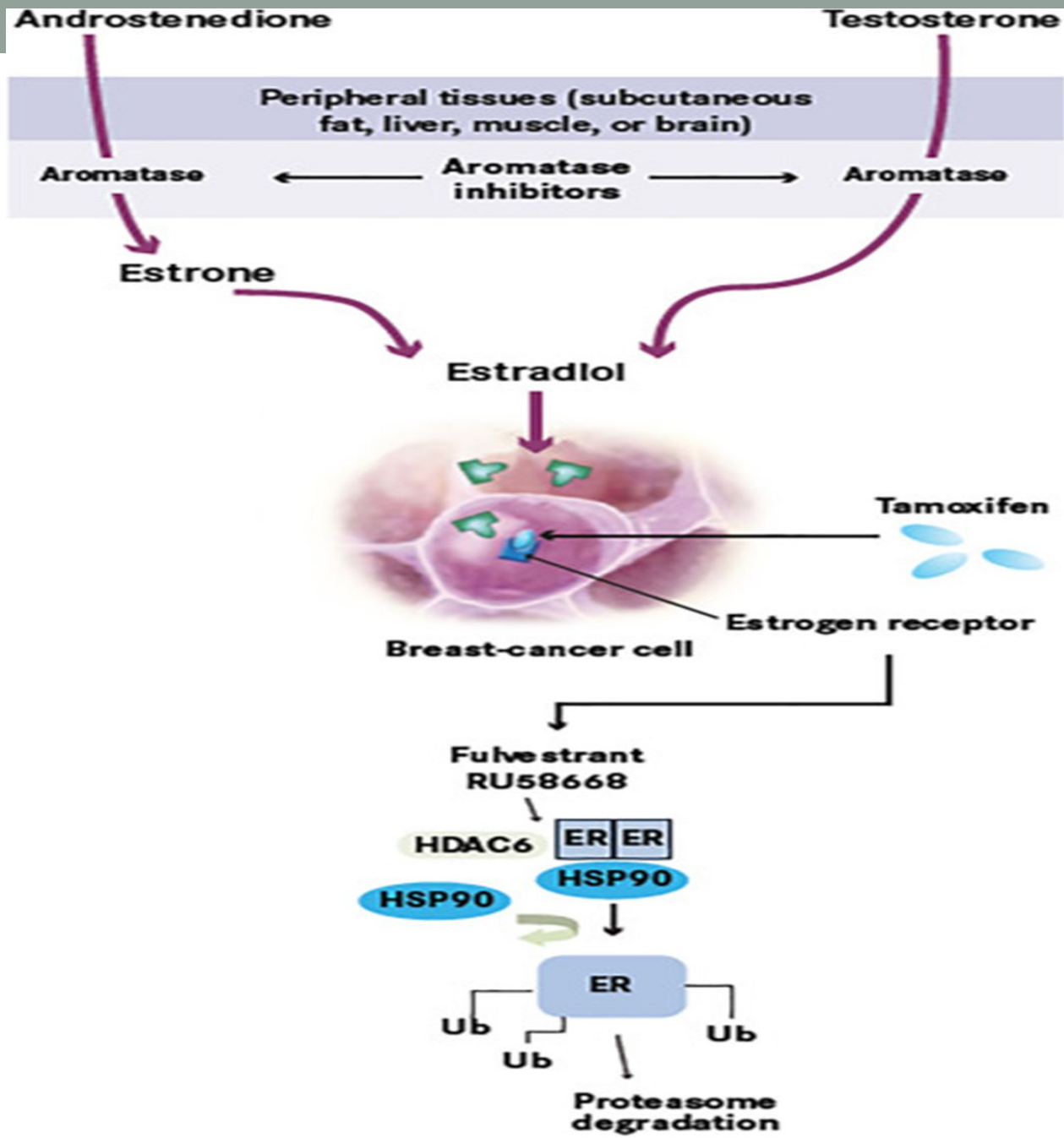
II. Hormones

A. SERMs: Tamoxifen, Tormifene.

B. Aromatase inhibitors: Letrozole, Anastrozole, Exemestane.

C. Anti androgens: Flutamide, Bicalutamide

D. GnRH analogues: Leuprolide and goserelin, Triptorelin, Naferelin (they act by **occupy the GnRH receptor** in the pituitary, which leads to its **desensitization** and, consequently, **inhibition** of **release** of FSH and LH. Thus, both androgen and estrogen syntheses are reduced)



Sequence of treatments:

- **Adjuvant therapy:** therapy given **after surgery** to **reduce** the likelihood of the **cancer returning**.
- **Neo-adjuvant therapy:** therapy given **before surgery** to **shrink** the **tumor**, allowing the **surgery** to be more **successful**.
- **Concurrent therapy:** when **2 or more therapies** are given together, such as **chemotherapy and radiation**.

:Chemotherapy can be given as

- **Orally** (by mouth, in pill form)
- **Intravenously** (IV, through a vein, either as a short infusion or continuously for one or more days)
- As an **injection** or needle
- **Directly** into a body **cavity** (i.e.: the bladder, abdominal cavity)
- **Intra-arterially** (in special cases, such as limb perfusion treatment for **melanoma**)

Side effects of chemotherapy

1- SKIN

- Alopecia

Hair loss occurs because chemotherapy can sometimes damage healthy cells.

It is so common because **hair follicle** cells **multiply very quickly** like cancer cells and chemotherapy drugs have **difficulty** in discerning the **difference**.

2- GASTROINTESTINAL SYSTEM SIDE EFFECTS

- **irritation** which can eventually lead to inflammation of the **mouth**, a condition known as **stomatitis**.
- **Mucositis** –inflammation of the **mucosal** lining (irritant)
- A **stinging sensation** in the throat may develop and lead to **dysphagia** (difficulty in swallowing).

Management: Good oral hygiene

- **Nausea & Vomiting**-most common side effects of chemotherapy and may **persist** for as long as **24-48 hrs.** after its administration.
- **Diarrhea**)Caused by the **destruction of normal** dividing cells of the gastrointestinal (GI) tract.

3- RENAL SYSTEM

Rapid tumor cell lysis -**increased** urinary excretion of **uric acid**, which can cause renal damage

4- HEMATOPOIETIC SYSTEM

- **Myelosuppression** -depression of **bone marrow** function, resulting in **decreased** production of **blood cells**.
- **Decreases** the number of **RBCs** (anemia), **WBCs** (leukopenia) and **platelets** (thrombocytopenia)

5- Growth factors:

- G-CSF (granulocyte-colony stimulating factor)
- GM-CSF (granulocyte macrophage colony-stimulating factor)
- EPO (erythropoietin)

Vinblastine
Nitrosoureas
Cyclophosphamide
Cytarabine
Doxorubicin



Carboplatin
Procarbazine
Etoposide
Methotrexate
5-Fluorouracil



Bleomycin
Vincristine
Methotrexate
(with leucovorin)



Mild **Strong**
Relative myelosuppression

6- PRODUCTIVE SYSTEM

- Take effective **contraceptive** precautions because the chemotherapy drugs might **harm the baby** if **pregnancy** occurs.
- In some women, **chemotherapy** brings on an **early menopause** may cause **dryness of the vagina** and a **decreased interest** in sex.

7- NEUROLOGIC SYSTEM

- Peripheral neuropathies
- Loss of deep tendon reflexes
- Paralytic ileus
- Fatigue

Problems with chemotherapy

Resistance

Multidrug resistance

toxicity

Nursing Management in Chemotherapy

- Assess **fluid** and **electrolyte** status

(**Anorexia**, nausea & vomiting, altered taste and diarrhea put patient at risk)

- Modifying risk for **infection** and **bleeding**

(suppression of the bone marrow and immune system)

- **Administering** Chemotherapy

-patient is observed for **extravasation** (particularly of vesicant agents, which may produce **necrosis** if deposited in subcutaneous tissues)

-Protect caregivers

Thank you!

