
# النادي الطبي MC

Done By :
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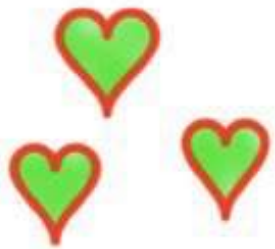
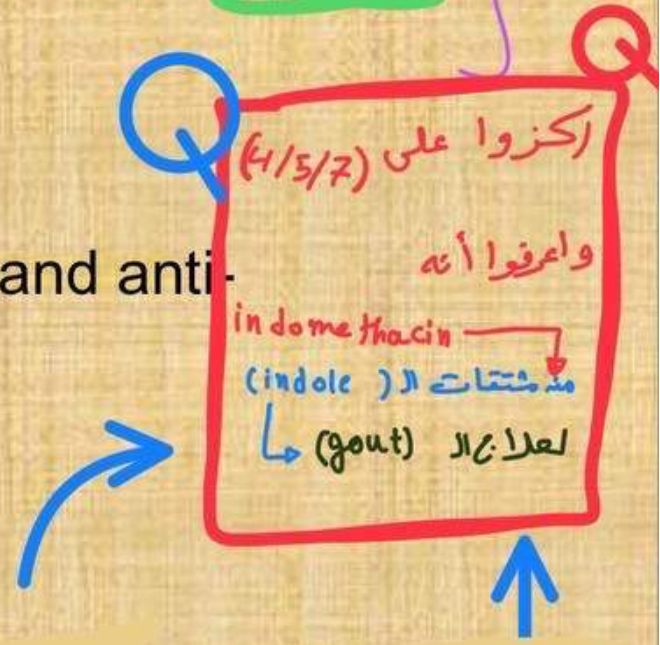


لا تنسونا من دعائكم بالتوفيق

# Common therapeutic uses of NSAIDs

- 1-Analgesic and antipyretic due to inhibition of PGE1 &2.
- 2-Antiinflamamtory due to inhibition of formation of inflammatory prostaglandins PGE1 &2 .
- 3-Antiplatelet due inhibition of thromboxane A2 in the platelet more that PGI2 in the vessel wall.
- 4-Treatment of dysmenorrheal: due inhibition of formation of PGF2α.
- 5-Treatment of precipitate labor due inhibition of formation of PGF2α in the uterine smooth muscles.
- 6-Treatment of patent ductus arteriosus
- 7-Treatment of gout
- In acute gout :indomethacin are used for its analgesic and anti-inflammatory effect.
- In chronic gout they are used for its uricosuric effect.



- Hypoprothrombinemia : (Large dose 5 g/day) silycylates, it competes with vit K. leading to decrease synthesis of prothrombin and factor VII IX and X ---> increase bleeding tendency.

- In patients with glucose 6 phosphatedehydrogenase enzyme deficiency ---> haemolysis of R.B.Cs. (idiosyncracy).

اعرف أنه ضاد لا (systemic action of silycylates) / واعرف أنه ممكن يتنافس مع vit(K) ويسبب (bleeding)
in the blood

اللي عنده (Bronchial asma) مابنفعهم يوخذ (NSAIDs)

Q

NSAIDs :

# 4. Acetic acid derivatives

- efficient drugs which differs in the incidence of AE

مهم Q

## a-diclophenac

- Antiinflamm., analgesic, weak antipyretic effect.
  - SE:mild: cephalgia, insomnia, irritation, GIT disorders, photosensitivity

Indications: muscle and postoperative pain (ألم بعد الجراحة), cephalgia, gynaecology (أمراض النساء)


Q


## b-indomethacin (مهمة)

- very strong nonselective COX inhibitor
- toxic ⇒ short-time treatment of acute states
- urikosuric effects (يزيد إفراز ال uric acid)
- used in gout attacks (كمضاد التهاب)

ويمكن يستخدم في ال (PDA) شرحناها قبل شوي

- overdose(10-15g)⇒ antidote: **N-acetylcysteine**

ترياقه

of paracetamol

لعلاج حالات التسمم من الباندول

مهم تعرفوا إنه جاي من AminoAcid

مهم

- Histamine is formed by the decarboxylation of the amino acid histidine by the enzyme L-histidine decarboxylase,

# The different Histamine receptors

منه تفاريغ اللجنة

رح تسألوا ليش ، الآلية مش مطلوبة منا بالتفصيل بس الموضوع برجع لوجود **sphincters** معينة على الأوعية الصغيرة (**arteriole**) وشغلة عليها هو عمل **V.D** وهاد الاشي مش موجود في الأوعية الكبيرة زي ال **artery**

| | Location | Effect | Treatment |
|---|---|---|---|
| H1 | 1 -smooth muscles<br>•2-vascular endothelia cells:Vasodilatation<br>•Of small BV<br>•-Smooth muscle of large vessels-vasoconstriction<br>3-CNS:+Ach (الأسيتيل كولين) (memory مهم جدًا ال Ach)<br>- +glutamat الغلوتاميت مهم للحفاظ على حالة اليقظة عنا وانه نقص مصحح<br>- 4-excocrine glands:<br>salivary,lacrymal, GIT (بزيد الإفرازات بتعوم) | Mediate an increase in vascular permeability at sites of inflammation induced by histamine (H1) المسؤولة عنه | Allergies<br>~~The effects of H1 receptor activation include increased vasodilation, vascular permeability, reduced smooth muscle contraction, and stimulation of glands. These effects lead to typical allergy symptoms such as skin redness, itching, and tissue swelling~~ |
| H2 | -gastric parietal cells (في المعدة)<br>-heart<br>-negative feedback release of histamine. | Increases the release of gastric acid (HCl) بتزيد إفراز ال | Stomach ulcers<br>~~as histamine binds to H2 receptors and promotes acid secretion, it simultaneously inhibits the release of additional histamine. This regulatory mechanism helps maintain a balance in histamine levels and prevents excessive stimulation of acid production.~~ |
| ~~H3~~ | Found mostly in the CNS:antagonise | Neural presynaptic | Unknown:sleep awake |

- **2nd Generation:** Fexofenadine, Loratidine

هدول مهمات

# H1-Receptor-Antagonists

# $H_2$ receptor antangnists

(GIT) اهمها في

١٥ فقط

(Cimetidine ,
Ranitidine,
Famotidine )

افهموا الفكرة

Q) we have two antibiotics (A/B)

(A) MIC is : 0.5

(B) MIC is : 0.7

what is the most potent drug : A

نفس الكلام لل (MBC)

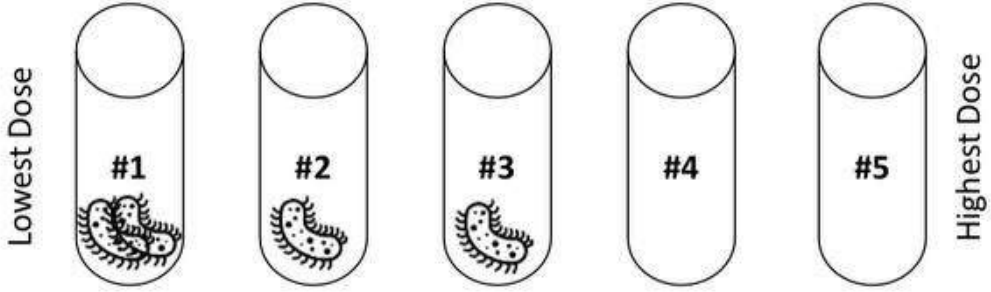
MIC : أقل (Dose) من اختفاء الـ(visible Bacteria) أول مايظهر بالأنبوب في (growth) ظاهر

MBC : أقل (Dose) من إلى اختفاء الكامل للبكتيريا سواء مرئية أو لا

في اسئلة الزراعة بنشوف أول اثنين بعد اختفاء البكتيريا (أول اثنين معدال (Non-growth) الأول بكونه (MIC) والثاني بكونه (MBC)

# Practice Question

- You have 5 tubes and want to do 5 dilutions of antibiotic X on the growth of E.coli. Tubes 4-5 do not have growth, but tubes 1-3 have visible growth, the tube with the MIC would be? 4



**Complications of Antibiotic Therapy** (Urticaria / Penicillin) / Red man syndrome / vancomycin — (Stevens johnson syn. / Penicillin / Sulfa drugs)

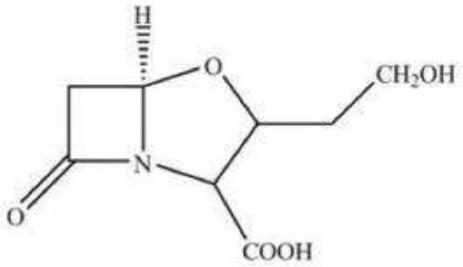
Hypersensitivity, direct toxicity, superinfections.

(broad-spectrum) يعني انه بعالج بسبب مرض تاني فقط

(Gastro intestinal infection) ويسبب (Normal flora) ال

# β-Lactamase Inhibitors

Dont have antibiotic effect



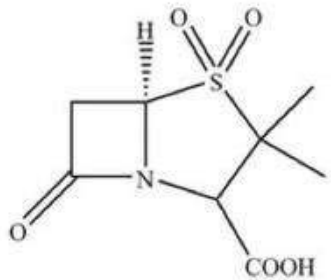
**Clavulanic acid**

+

amoxicillin

=

amoxiclav

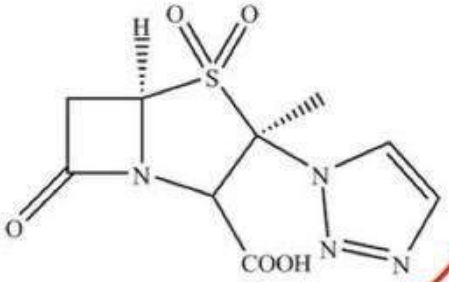


**Sulbactam**

+

Ampicillin

→ to treat Listeria monocytogenes



**Tazobactam**

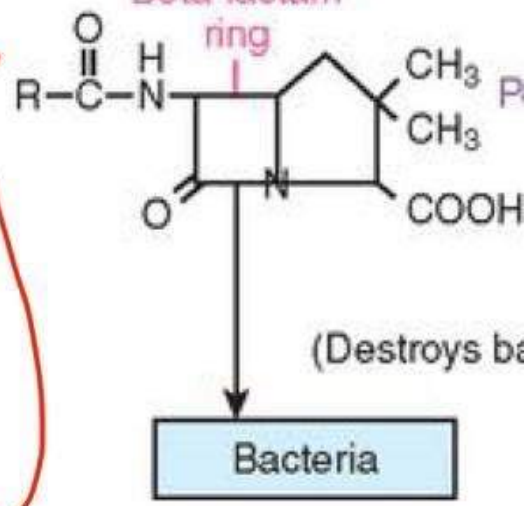
+ Piperacillin

+

Ticracillin

↓

to treat pseudomonos

# Penicillins

**Mechanisms of resistance**

- **Acquired Resistance:**

**2. Decreased permeability to the drug:**

- Reduced permeability e.g., *Pseudomonas aeruginosa* –ve
- Efflux pump e.g., *Klebsiella pneumoniae*.

**3. Altered PBPs:** → very difficult mechanisms to dail with unlike β-lactamase process

- Modified PBPs with lower affinity for β-lactams e.g., MRSA resistance to most β-lactams.

amoxiclav not affect MRSA, all the pencillins don't work against it.

- *Probenecid* is an inhibitor of renal tubular excretion of penicillin

treat Gout (نقرص) ⇒ interfuse with uric acid reabsorbtion + interfuse with the action of penicillin ⇒ half life ↑ ⇒ duration of action ? (we don't know if it increase or not)

(الدكتور ركز عليها وذكرها بأكثر من سلايد)

# Cephalosporins

Good luck

## Antibacterial spectrum

- **Third-generation cephalosporins:** (don't cover MRSA)
- Greater activity against gram-negative bacilli (broad-spectrum)
- Drugs of choice for the treatment of meningitis
- Must be used with caution "collateral damage"

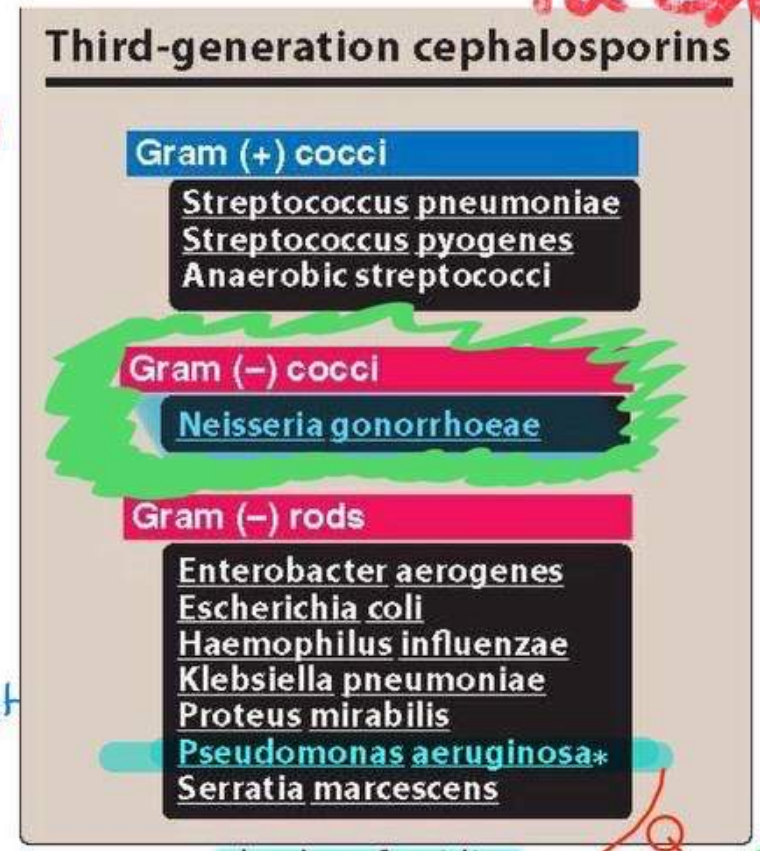
given parenterally

- Ceftriaxone
- Cefotaxime
- Ceftazidime

- Cefdinir

given orally

- very important because they are the first line for treatment
- ceftriaxone: first line for treat meningitis ⇒ it has good bacterial effect against streptococcus pneumonia (+ve) + Neisseria (−ve)



| | VANCOMYCIN | DAPTOMYCIN |
|---|---|---|
| **Mechanism of Action** | Inhibits bacterial cell wall synthesis | Causes rapid depolarization of the cell membrane, inhibits intracellular synthesis of DNA, RNA, and protein |
| **Pharmacodynamics** | Combination of time and concentration-dependent Bactericidal | Concentration dependent Bactericidal |
| **Common Antibacterial Spectrum** | Activity limited to gram-positive organisms: Staphylococcus aureus (including M S. agalactiae, penicillin-resistant S. pneumoniae, Corynebacterium jeikeium, *vanc* faecalis, and E. faecium | |
| **Unique Antibacterial Spectrum** | Clostridium difficile (oral only) | *Vancomycin*-resistant E. faecalis and E. faecium (VRE) |
| **Route** | IV/PO = per os = by mouth | IV |

That make it more potent than vancomycin

# Polymyxin B (Colistin)

(polymyxin E)

- Cation polypeptides
- **MOA**: bind phospholipids on the bacterial cell membrane of gram-negative bacteria (disrupt cell membrane not cell wall)
- Active against most gram-negative bacteria including P. aeruginosa + Acinetobacter
- Bactericidal
- Concentration-dependent
- Limited use because of nephrotoxicity/neurotoxicity → great toxicity, it must be the last choice
- **Spared for multi-drug resistant infections** (very poweful)

# Tetracyclines

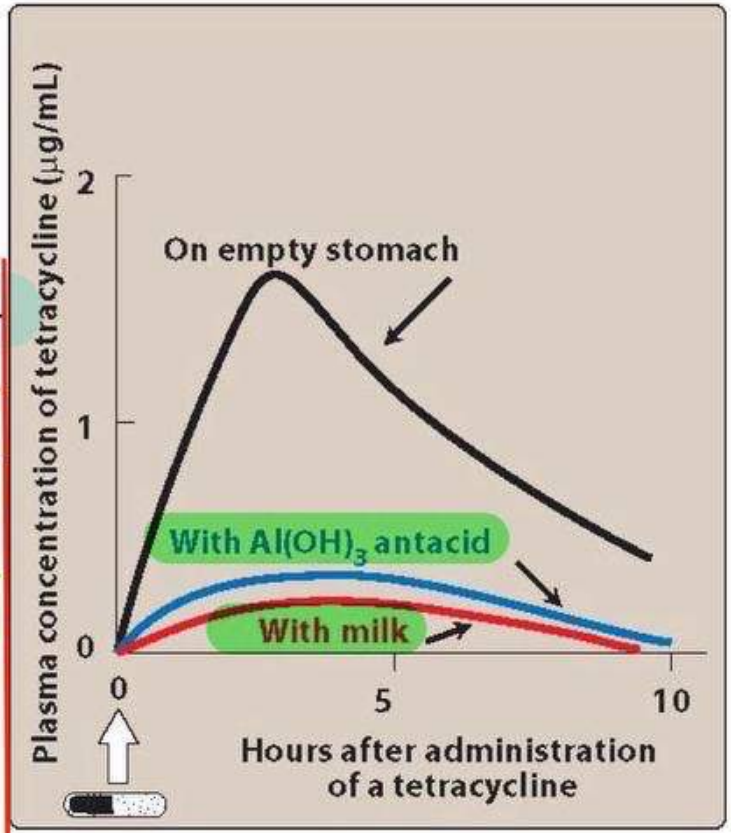
## Pharmacokinetics

### Absorption

- Oral → unlike β-lactams
- Adequately absorbed
- ↓ absorption when administered with dairy (high cations) → formation of nonabsorbable chelates

(chelates) لا يعطى مع مشتقات الحليب وتناولهما

- يعمل تكلس بالعظام و يخترقه الرحم
- لا يعطى للنساء الحوامل أو المرضعات أو أطفال تحت (8)
- إذا استخدم لفترات طويلة مثلا (٦ أشهر) سيؤثر على ما يؤدي إلى اضطرابات بالمعدة (Normal flora)
- يفرز (Tetra...) في (urin)
بينما (Doxy....) يفرز في (feces/bile)



# Tetracyclines

**Antibacterial spectrum**

- Bacteriostatic → Because of reversible binding
- Effective against gram-positive, gram-negative, protozoa, spirochetes, atypical, etc

**Commonly used for the treatment of:**

1. Acne (doxycycline) → Propionibacterium acnes (+ve)
2. Chlamydia (doxycycline)
3. Peptic ulcer disease (tetracycline)
4. Lyme Disease (doxycycline)
5. Mycoplasma Pneumonia (doxycycline)

Mycoplasma bacteria lack cell wall

most are available orally

# Aminoglycosides

**Mechanisms of resistance**

1) efflux pumps
2) decreased uptake → block the entry of drug from porins
3) modification and inactivation by plasmid-associated synthesis of enzymes that hydrolyze aminoglycosides

-Amikacin is less vulnerable to these enzymes

⊛ less cross resistance (because each drug have a specific enzymic bacteria to resist it)

**MACROLIDES/KETOLIDES**

*Azithromycin* ZITHROMAX (zomax)
*Clarithromycin* BIAXIN
*Erythromycin* VARIOUS
*Telithromycin* KETEK

# Macrolides and Ketolides

inhibit CYP 450 → so inhibit hepatic metabolism for some drugs. forexample :
✗ → metabolism warfarin → bleeding

may cause jaundice / ototoxicity

| Type of antibiotic | Mechanism of action |
| --- | --- |
| Tetracyclines | -bind ***reversibly*** to the **30S** subunit of bacterial ribosomes |
| Glycylcyclines (Tigecycline) | -bind ***reversibly*** to the **30S** subunit of bacterial ribosomes |
| Aminoglycosides | • Bind to 30S ribosomal subunit (1)<br>• Interfere with assembly of the functional ribosomal apparatus<br>(2) Cause the 30S subunit of the completed ribosome to misread the genetic code |
| Macrolides and Ketolides | bind *irreversibly* to a site on the 50S subunit of the bacterial ribosome<br>Inhibit translocation step |
| Fidaxomicin | **MOA**: acts on the σ subunit of RNA polymerase → disruption of bacterial transcription → protein synthesis قبل جيت مندوخ على الابيوسوم |
| Chloramphenicol | **MOA:** *reversibly* to the bacterial 50S ribosomal subunit and inhibits peptidyl transferase reaction |
| Clindamycin | bind *irreversibly* to a site on the 50S subunit of the bacterial ribosome<br>Inhibit translocation step |
| Oxazolidinones (LineZolid) | **MOA**: binds to the bacterial 23S ribosomal RNA of the 50S sub-unit, thereby inhibiting the formation of the 70S initiation complex |

orally

# Quinolones

Good Luck

(اللهم يرحلّه مهم)

**Antibacterial spectrum**

- **First-generation (nonfluorinated): nalidixic acid**

-narrow-spectrum

- **Second-generation: ciprofloxacin and norfloxacin** → since you know that -ve cause 95% of UIT ⇒ These drug is the first line in treatment UTI

-gram-negative (pseudomonas, H.influenzae) and atypical

- **Third-generation: levofloxacin** → treat RS infection / community acquired pneumonia *consider the first line to treat Pneumo

-gram-negative, atypical and gram-positive (including S. pneumoniae and MSSA)

- **Fourth-generation: moxifloxacin, Gemifloxacin, delafloxacin**

-enhanced gram-positive effects including staph and strep + coverage of gram-negative Enterobacteriaceae ,not affect against pseudomonas

-Homework: Which fourth-generation fluoroquinolone is effective against MRSA?

(→Delafloxacin)

# Fluoroquinolones

**Mechanisms of resistance**

-mainly chromosomal

1 • **Altered target:**

-mutations in *gyrA* or *parC*

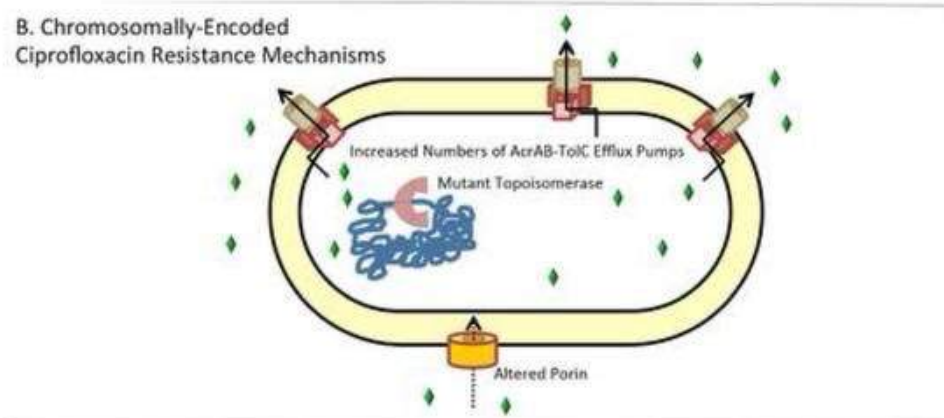
2 • **Decreased accumulation**

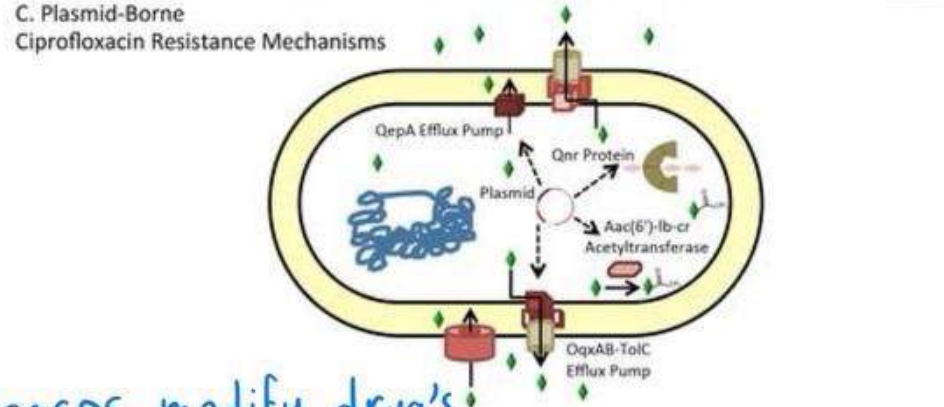
-porin channels

-efflux pumps

3 • **Fluoroquinolone degradation**

• Cross-resistance




4 • acetylation resistance → acetyltransferases modify dryg's structure

# Special Uses

**Pharmacokinetics**

- **Absorption**

-oral: well-absorbed (except sulfasalazine) → not absorbed

-how can you use sulfasalazine?

dont use as antibiotic

## TOXOPLASMOSIS RX

**First Line**

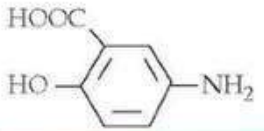
- Pyrimethamine (200mg-L/75C) + Sulfadiazine(6-8g/d -4d/d) till improve CD4 count
- Pyrimethamine + Clindamycine


as ointment for burns, ← act as antibiotic locally

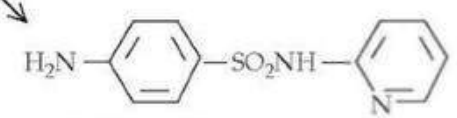
*Toxoplasmosis infection caused by Toxoplasma gondii parasite and affect immunosuppressive patient like HIV → treated by combination of Pyrimethamine + sulfa drugs ← sulfadiazine


Sulfasalazine

Colonic Bacteria




5-Aminosalicylic Acid (5-ASA)




Sulfapyridine

5-ASA → salicylic acid like aspirin → So this drug used as Anti-inflammatory rather than anti-biotic

Aspirine بذكرنا بال

# Urinary Tract Antiseptics/Antimicrobials

منتشر

- UTIs are more prevalent in women and elderly
- Most common cause: *E. coli* (80% of uncomplicated UTIs), other proteus, klebsiella
- Second most common cause: *Staphylococcus saprophyticus*

**Most frequently used agents:**

1. **Cotrimoxazole**
2. **Nitrofurantoin**
3. **Fluoroquinolones** → first line for complex UTI
4. **Methenamine**

→ for simple infections (first line for simple UTI)

- it is now the first line in treatment of uncomplicated cystitis.
- we can use it against E. coli

ال main lipid in lipid layer هو ال ergosterol وبشتغل عليه ال amphotericin B.

أما ال polysaccharide layer فيه B-glucans وبشتغل عليه اشي اسمه echinocandins

احنا حكينا انه ال Amphotericin الـ side effect صعبة جدا؛ طيب كيف ممكن اتغلب عليها or how to avoid toxicity ؟؟

معلم

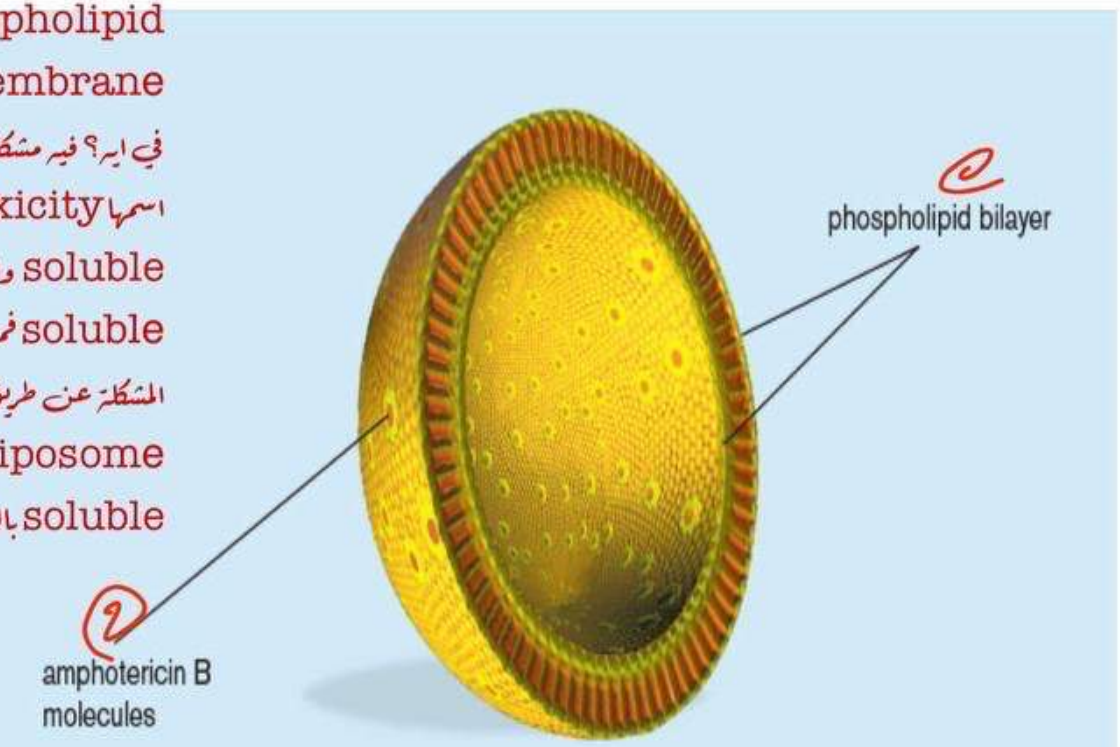
عندي طريقتين :١) بعمل منه اشي اسمه liposomal preparations

٢) بعطي معه دواء ثاني (synergism) بحيث إني أقلل ال dose of Amphotericin مثلا أعملله co-administration with flucytosine

# Amphotericin Liposome

## liposomal preparations

ال membrane يلي فيه عبارة عن phospholipid وال amphotericin embedded in cell membrane طيب وه بهمني في ايه؟ فيه مشكلة خطيرة جدا بتصير مع ال amphotericin اسمها nephrotoxicity؛ الكلية بتحب الاشي ال water soluble وال amphotericin is water soluble فمشان هيك هيأذي الكلية جامد فبروح بتجنب هاي المشكلة عن طريق عمل preparation منه يلي هو ال amphotericin liposome وبتكون lipid soluble بالتالي هيصير less nephrotoxic




co-administration with

منه اللجنة

الدكتورة ركزت هون مهم

ندمج ٥ مع ٦ ببطل S W بتحول الـ S L وما بأثر على الكلية

# PHARMACOLOGY OF FLUCYTOSINE

مهم انشرح أكثر من مرة

## Chemistry

-Flucytosine is a fluorinated pyrimidine

synthesis بحيث انه يدخل في ال bases of DNA يعني هو اشي شبه ال

cell division بالتالي ما يصير of DNA or mRNA

## Mechanism of action

-The drug is accumulated in fungal cells by the action of a ***membrane permease*** and is converted by a ***cytosine deaminase*** to 5-fluorouracil

5-fluorouracil is metabolized to 5-fluorouridylic acid

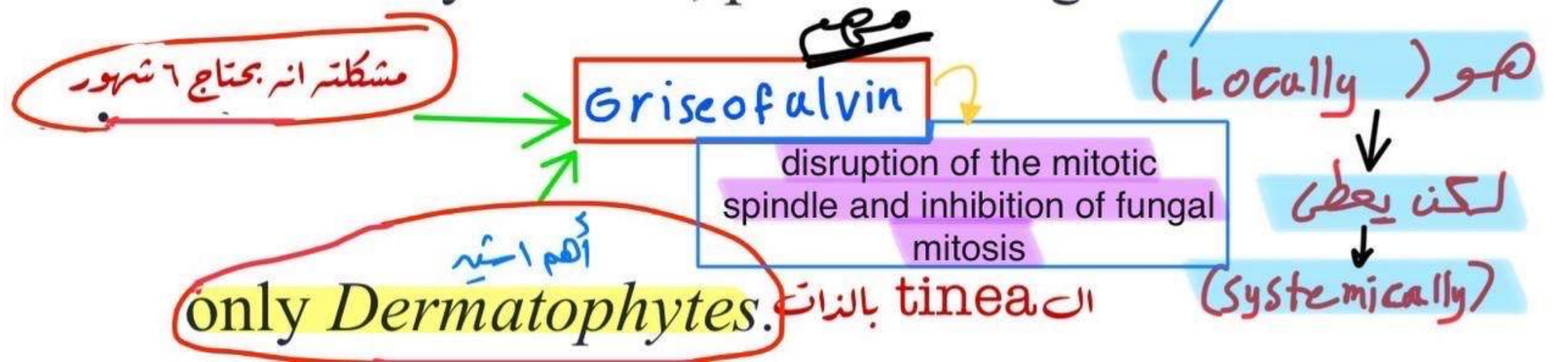
which can be

a) incorporated into the RNA (this leads to a ***misreading of the fungal genetic code***)

b) further metabolized to 5-deoxyfluorouridylic acid, a potent inhibitor of thymidylate synthase (this leads to a ***blockade of fungal DNA synthesis***)

* لما أعطي (Amphotericin B) بعطي معه (Flucytosin) عشانه أقلل الـ (dose) تلعت الـ (Amphotericin B) عشانه مايصيرلي (side effect)

مهم جدا

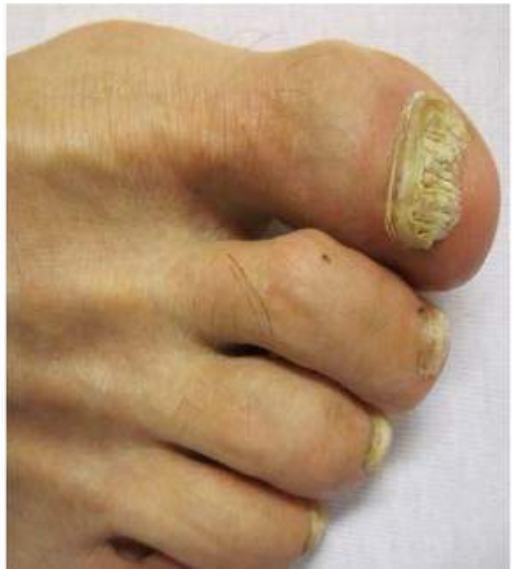

مشكلته انه بحتاج ٦ شهور
Griseofalvin
disruption of the mitotic spindle and inhibition of fungal mitosis
(Locally) هو
لكن يعطى
(systemically)
أهم اشيء
only Dermatophytes.
ال tinea بالذات

# Caspofungin

- First-line for patients with invasive candidiasis e.g., candidemia
- Second-line for invasive aspergillosis

# Terbinafine

- Drug of choice for treating dermatophyte onychomycoses
- More effective than itraconazole or griseofulvin for Trichophyton
- Useful in the treatment of tinea capitis



the deadliest type of cancer in both the males and females is the lung cancer.

* very aggresive.
* very malignant.
* very difficult to treat.

- لو بس حدد الذكور بكونه الجواب

Prostate

- ولو بس حدد الإناث بكونه الجواب

Breast

hydroxylation at 7th position to form 7- hydroxymethotrexate (less water soluble)

# How to overcome the adverse effects of methotrexate?

A. Always administer with folic acid and vitamin $B_{12}$ (to reduce GI/hematologic side effects)

B. Pretreatment with corticosteroids (to reduce cutaneous reactions)

C. Leucovorin folic acid IS tetrahyaro derivative of folic acid used to rescue

(folinic acid)

| DRUG | ROUTE | ADVERSE EFFECTS |
|---|---|---|
| **Cisplatin** it was a main drug in treating lung cancer with combination with paclitaxel | IV, IP, IA | Neurotoxicity, myelosuppression, ototoxicity, N, V, electrolyte wasting, infusion reaction, nephrotoxicity |
| **Carboplatin** only causes the normal and common side effects. | IV, IP, IA | Myelosuppression, N, V, infusion reaction |
| **Oxaliplatin** | IV | Neurotoxicity, N, V, infusion reaction, hepatotoxicity, myelosuppression |

- أعرف أنه الـ (carboplatin) تم العمل عليه عشانه ما يعطي (SE) إلّا الموجودة بكل دواء (cancer) عشانه هيك هو الأأمن بين الثلاث

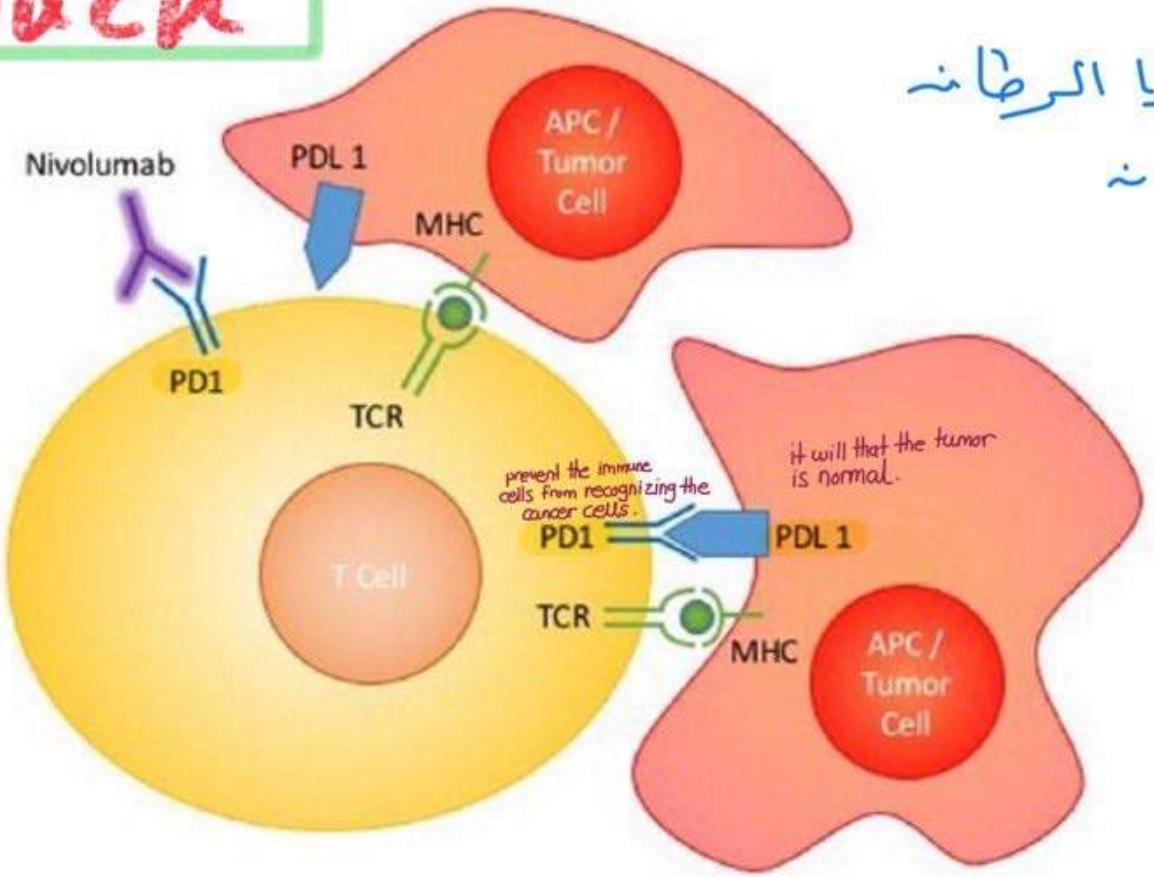
- الـ (٢) برتبطوا بالـ (Guanine) وبخلوا السلسلتين يلصقوا ببعض وما يفكوا وهاد اسمه (Alkylating Agents)

- أعرف أنه الـ (٢) (Non-Specific)

Good luck

# Nivolumab → يرتبط بـ PD1

يمنع ارتباط الخلايا المناعية بـ (PD1) في خلايا السرطانة
لحدوث استجابة مناعية ضد خلايا السرطانة




binds to the PD-1 receptor and blocks its interaction with PD-L1 and PD-L2, releasing PD-1 pathway-mediated inhibition of the immune response, including the anti-tumor immune response

- العلاج الوحيد اللي بستجيب فيه
خلايا المناعة لخلايا السرطانة

| | |
|---|---|
| Methotrexate | Cell cycle specific: S phase |
| Paclitaxel and Docetaxel | Cell cycle specific: M phase |
| Cisplatin, Carboplatin and Oxaliplatin | Non-cell cycle-specific |
| Camptothecin, irinotecan, topotecan<br>Topoisomerase I inhibitors | S-phase specific |
| Etoposide<br>Topoisomerase II inhibitor | |

# FDA Pregnancy Drug Risk Categories

| Pregnancy Category | Description |
|---|---|
| A | Appropriate human studies - no risk |
| B | Insufficient human studies, but animal research suggests safety<br>**or**: Animal studies show issues but human studies show safety |
| C | Insufficient human studies, but animal studies show problems<br>**or**: No animal studies, and insufficient human studies |
| D | Human studies, with/without animal research show fetal risks, but the drug is important to some women to treat their conditions |
| X | Fetal risks are evident; there are no situations where the risk/benefit justifies use |

متوقع سؤال

نادر ما نلاقي هيك دواء

متوقع

بهاي الحالة نقارن بين ال benefit و harm وبناءً عليهم بقرر أعطي الدواء أو لا.

متوقع سؤال

# Teratogenic Drugs

which of the following is/is not a teratogen drug?

الدكتورة قالت أنه كل الأسماء مطلوبة حفظ

Only drug name is required

**Table 1.** Drugs Identified With Known Risk of Teratogenicity

| Human teratogen | Identifiable or Related Outcome |
|---|---|
| Alcohol | Fetal alcohol syndrome: IUGR and FTT; decreased muscle tone and poor coordination; developmental delay; and craniofacial abnormalities |
| * Angiotensin converting enzyme inhibitors (ACEI) | Oligohydramnios; hypocalvaria; IUGR; renal effects (renal tubular dysplasia, anuria/oliguria, and hyperkalemia, end-stage renal failure); neonatal hypotension; cardiovascular abnormalities (e.g. patent ductus arteriosus, aortic arch obstructive); fetal death |
| Carbamazepine ضد التشنجات | 10 × increased risk of neural tube defects; fetal anticonvulsant syndrome (IUGR, developmental delay, craniofacial defects, fingernail hypoplasia) |
| Cocaine | Placental abruption, fetal loss, low birth weight, microcephaly, limb and urinary tract malformations, poor neurodevelopmental performance |
| Coumarin anticoagulants warfarin | Fetal warfarin syndrome (nasal hypoplasia, eye abnormalities [i.e. optic atrophy, microphthalmia, and blindness]); epiphyseal stippling, hypoplasia of the extremities and fingernails; low birth weight; developmental retardation; fetal hemorrhage |
| Diethylstilbestrol (DES) | Clear cell adenocarcinoma and benign adenosis in exposed offspring |
| * Methotrexate (Folic acid antagonists) Folic acid is needed for neural tube development | Central nervous system (i.e. anencephaly, neural tube defects); cardiovascular (tetralogy of Fallot); craniofacial (i.e. absence of lambdoid, coronal sutures, and frontal bone, low set ears, depressed/wide nasal bridge); long webbed fingers and absence of digits; growth and mental retardation |
| Phenytoin | Fetal anticonvulsant syndrome: IUGR, dysmorphic craniofacial features (i.e. microcephaly, low nasal bridge, cleft lip and cleft palate, maxillary hypoplasia); limb defects (i.e. hypoplastic nails and distal phalanges); cardiac defects |
| * Isotretinoin يستخدم لحب الشباب | Spontaneous abortion; craniofacial abnormalities (i.e. microcephalus, hydrocephalus, deformity of ears, face, limbs); thymic hypoplasia; cardiac defects |
| Lithium Li | Tricuspid valve malformation (Ebstein's anomaly) |
| Misoprostol → preterm | Association with limb and neural tube defects |
| Tetracyclines | Weakened fetal bones, tooth enamel dysplasia, permanent tooth discoloration |
| Thalidomide | Limb, ear, cardiovascular and gastrointestinal anomalies |
| Valproate | Neural tube defects; fetal valproate syndrome: dysmorphic facial anomalies including microcephaly, hypertelorism, prominent forehead, low flat nasal bridge, low-set or odd-shaped ears |

*FTT, failure to thrive; IUGR, intrauterine growth retardation*

الصفحة فهمها مهم

# Emergency treatment of poisoned patient

- Treat the patient not the poison:

I. Airway breathing circulation (ABC): give oxygen, IV access, heart monitoring

II. Life threatening toxic effects such as profound changes in blood pressure, heart rhythm , respiration and body temperature.

III. Correction acid/ base and electrolytes disturbance.

- If the patient have altered mental status, consider giving the " coma cocktail" (dextrose( for hypoglycemia), naloxone( possible opioid or clonidine toxicity, and thiamine ( for ethanol- induced Wernicke encephalopathy).

الصفحة والأسئلة مهمين

# Elimination enhancement

* بحكولنا كل طريقة بتتخلص من أي أدوية لو وصلت السمية للدم

1. **Hemodialysis** e.g., methanol, salicylate and lithium.
2. **Urinary alkalinization**( by administration of sodium bicarbonate): enhances urinary excretions of salicylate and phenobarbital.

❖**Serum pH shouldn't increase more than 7.55** ← monitor!

3. **Multiple dose activated charcoal**: e.g., phenobarbital, digoxin, and carbamazepine )

حفظ و مهم جدًا

# Antidotes:

عليه سؤال % 100

For a variety of chemicals and poisons, specific chemical antidotes have been developed.

| Poison | Antidote |
|---|---|
| Acetaminophen | N-acetylcysteine |
| Benzodiazepine | Flumazenil |
| Carbon monoxide | Oxygen(hyperbaric chamber) |
| Heparin | Protamine sulfate |
| Iron | Deferoxamine |
| Lead (ممكن يكونه بدطانه البيوت القديمه) | Succimer (DMSA), Dimercaprol, edetate (EDTA) |
| Methanol and ethylene glycol | Fomepizole |
| Opiates | Naloxone |
| Warfarin | Vitamin K |
| Organophosphates | Atropine, pralidoxime |
| Isopropanol (rubbing alcohol) | No antidote |

# 5 stages of drug Development


1. Target Selection
2. Lead discovery

(باللاب)

In-vitro and In-vivo Testing (1+2)

بدي أجرب على حيوانه

FDA Adverse Event Reporting System (FAERS)

احتمالية بتطلع للدواء اعراض جانبية بعد متعرضه بالأسواق

بعد نجاح كل اللي قبل صا يتم الموافقة عليه حسب شروط معينة

Once the new drug has been formulated for its best efficacy[3] and safety, and the results from clinical trials[2] are available, it's advanced forward for FDA review.

بجرب على انسانه

(a prospectively planned experiment)

(أول اشي ناس صحيحة مش مراضى/ثم عدد قليل من المرضى/ثم عدد كبير ودول كتيرة)

(Double-blind)

# Step 2: Preclinical Research

- Preclinical trials examine the new drug's efficacy, toxicity, and pharmacokinetic data in nonhuman subjects. Scientists undertake these trials in vitro and in vivo with unrestricted dosages
- **Researchers discover the following facts regarding the drug:**

1. Data on absorption, distribution, metabolization, and excretion
2. Potential advantages and action mechanisms
3. The best dosage and route of administration
4. Adverse events/side effects
5. Gender, racial, or ethnicity effects
6. Interaction with other medications
7. Efficacy in comparison to comparable medications

# Definitions

- **Single Blind Study**: A clinical trial where the participant does not know the identity of the treatment received
- **Double Blind Study**: A clinical trial in which neither the patient nor the treating investigators know the identity of the treatment being administered.
- **Placebo:**
  - Used as a control treatment
    1. An inert substance made up to physically resemble a treatment being investigated
    2. Best standard of care if "placebo" unethical
    3. "Sham control"
    4. Used in Randomized trials
- **Adverse event:**
  - An incident in which harm resulted to a person receiving health care.

# FDA Approval

- **Orphan Drug**
- An orphan drug is intended to treat disease so rare that financial sponsors are unwilling to develop it under standard marketing conditions.

- Recognizing the difficulty of clinical trials in rare patient populations, the US Congress passed the Orphan Drug Act to facilitate development of treatments for rare disorders

- **Accelerated Approval**
- New drugs may be granted accelerated approval if there is strong evidence of positive impact on a surrogate endpoint instead of evidence of impact on actual clinical benefits the drug provides. Expedition of approval means the medication can help treat severe or life-threatening conditions.