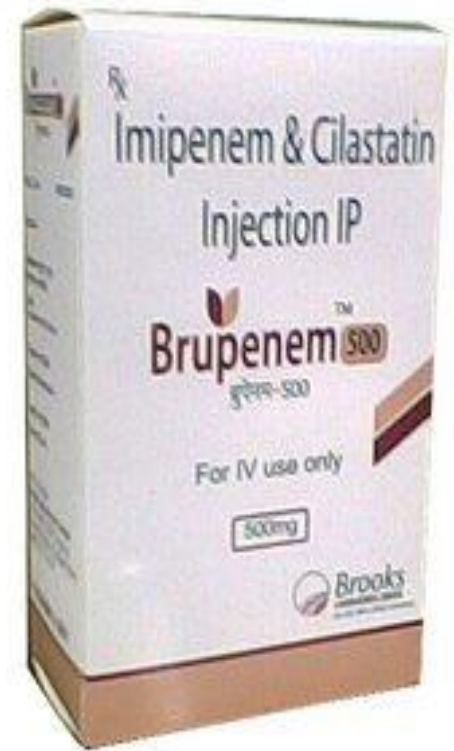


Imipenem

By enzyme dehydropeptidase give Inactive metabolite → this metabolite is nephrotoxic.

-it should combine with cilastatin

Cilastatin: renal dehydropeptidase inhibitor



Why combined with cilastatin???

1. To Prevents the formation of the toxic metabolite.
2. To prolonging its duration of action.





**Other cell wall
inhibitor
vancomycin**

Vancomycin

Administered Oral , IV

Narrow spectrum

Bactericidal /not B-lactam

Orally:- every 6 hrs for refractory pseudomembranous colitis due to C. difficile.

Slow IV infusion (1-2 hrs) for treatment of systemic infections or prophylaxis.

✓ is effective against MRSA. (**DOC**)

✓ Vancomycin in combination with A.G alternative regimen to treatment of enterococcal endocarditis.

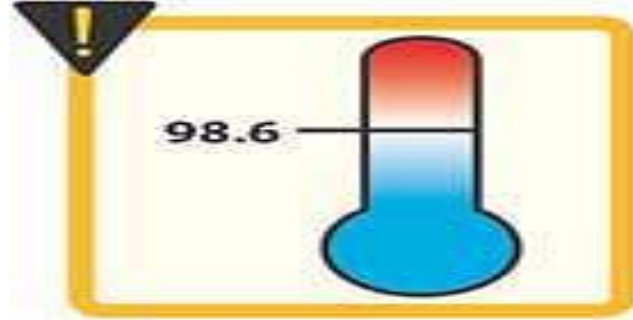
S.E:-

1-Flushing (**red man syndrome**) with a **rapid** infusion. (**More common**)

2- phlebitis (inflammation of vein) at site of injection.

3- ototoxicity & nephrotoxicity (rare) but increased risk when administered with A.G.

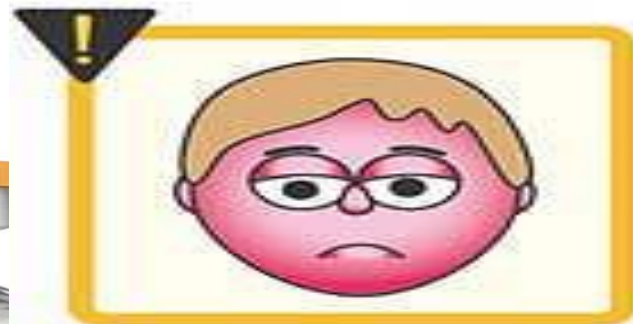




Fever



Chills



Flushing



Phlebitis

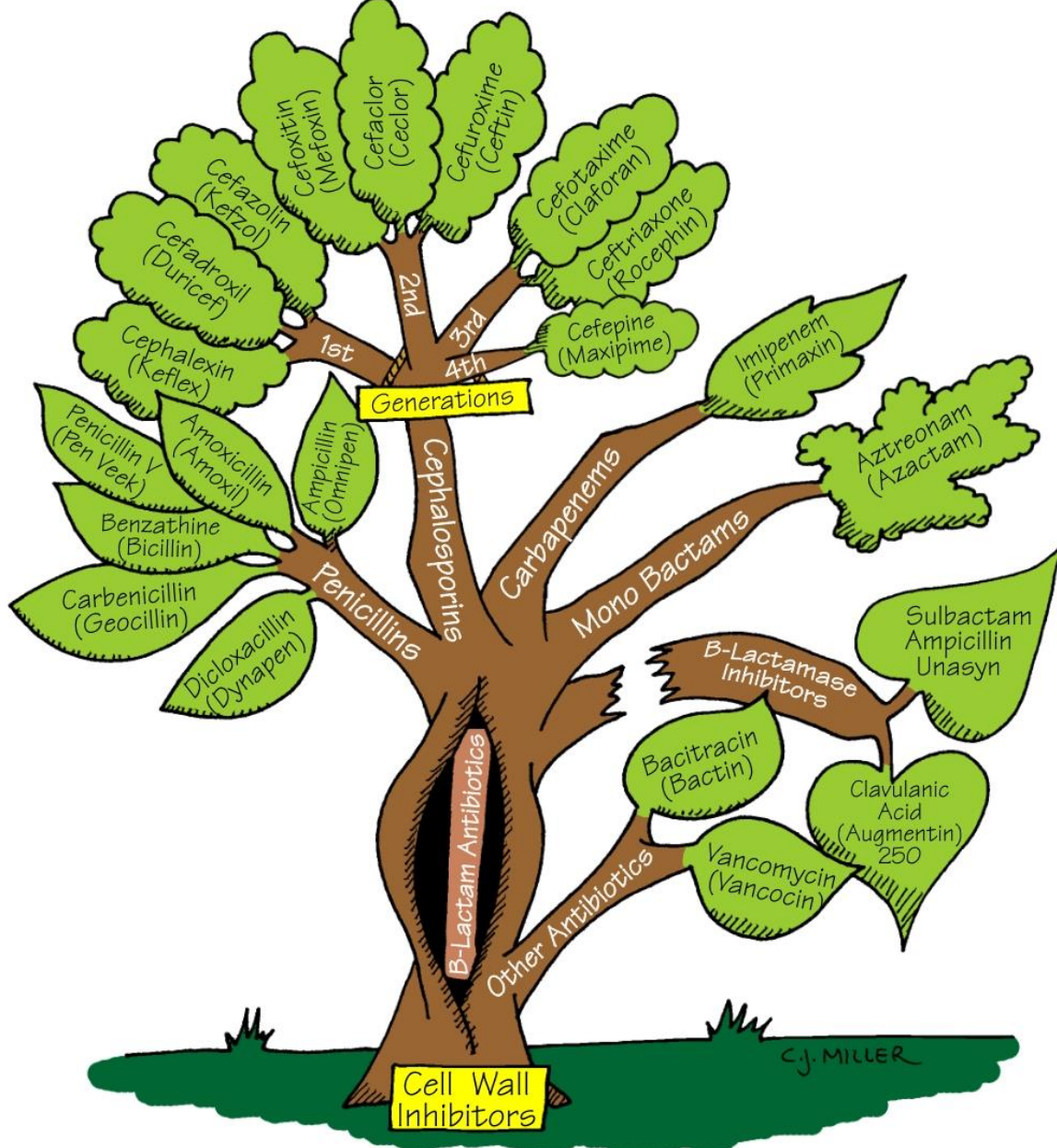


What about penicillin allergies?

cephalosporin /penicillins :

cross-reactivity of 1 – 10%

- The cross-reactivity of carbapenems/penicillins is also around 10% (similar to that of ceph/pen)
- The cross-reactivity of aztreonam/pen or ceph is essentially 0% ?????



THE ANTIBIOTIC TREE

Classification of Antimicrobial Agents

1) Inhibitors of cell wall synthesis

- B-lactams - Vancomycin

2) Inhibitors of Protein Synthesis

- Macrolides- Clindamycin -Tetracycline –
Aminoglycosides - Chloramphenicol.

3) Inhibitors of Metabolism

- Sulfonamides- Trimethoprim

4) Inhibitors of Nucleic Acid function or synthesis

- Fluoroquinolones- Rifampin

2. INHIBITORS OF PROTEIN SYNTHESIS

- I. Macrolides.
- II. Clindamycin.
- III. Tetracyclines.
- IV. Aminoglycosides
- V. Chloramphenicol.

**All of these drugs are bacteriostatic except
Aminoglycoside....**

Classification

Protein synthesis inhibitors

Aminoglycosides

- Gentamicin
- Tobramycin
- Streptomycin
- Neomycin
- Kanamycin
- Amikacin

Tetracyclines

- Tetracycline
- Doxytetracycline
- Minocycline
- Doxycycline

Macrolides

- Erythromycin
- Azithromycin
- Clarithromycin

Macrolides



MACROLIDE

I. Macrolides

Comprise in three drugs

1- Erythromycin.

2- Clarithromycin.

3- Azithromycin.



Macrolides

- a drug of first choice and as an **alternative to penicillin** in individuals who are allergic to B-lactam antibiotics.
- Diffuse into **prostatic fluid**.

Can be given to pregnant women.

- Erythromycin was the first of these drugs to find clinical application, The newer members of this family, **clarithromycin, azithromycin**.

- The macrolides bind reversibly to a site on the 50S subunit of the bacterial ribosome, thus inhibiting protein synthesis .
- They are considered to be **bacteriostatic**, they may be bactericidal at higher doses

Therapeutic applications

- **Whooping cough (pertussis).**
- *Atypical* Pneumonia (mycoplasma). (in children and pregnancy)
DOC: **Erythromycin**
- **Prostatitis. Why???**
- **Acne (erythromycin with zinc)**
- Eradication of H.pylori: **clarithromycin.**
- Syphilis ,tonsillitis.
Erythromycin as alternative).
- **Respiratory infection .**

Adverse effects

- **Epigastric distress:** it is common (esp. With erythromycin)
- **Cholestatic hepatitis**
 - Use > 1 to 2 weeks of erythromycin or EXP.date

- Legionella, C .diphtheriae, mycoplasma, bordetella.

Antibiotics: Macrolides

Azithromycin:

- It is a newer macrolide
- It is very effective against staph. aureus
- Better patient compliance
- It is very expensive
- Dose: 250 mg b.i.d. for first day;
Then 250 mg / day for 4 days
- AVOID in patients with hepatitis / cirrhosis

- Cholestatic hepatitis:
- In [medicine](#), **cholestasis** is a condition where [bile](#) cannot flow from the [liver](#) to the [duodenum](#). The two basic distinctions are an obstructive type of cholestasis where there is a mechanical blockage in the duct system that can occur from a [gallstone](#) or [malignancy](#), and metabolic types of cholestasis which are disturbances in bile formation that can occur because of [genetic defects](#) or acquired as a side effect of many medications. fever, nausea , vomiting, abdominal cramps then fever and jaundice with leukocytosis, elevated transaminases

<http://vanityfair-uk.blogspot.com>

Zineryt®

Erythromycin-zinc complex containing
the equivalent of 40 mg/ml erythromycin
and 12 mg/ml zinc acetate
(as the complex) on constitution

**Powder and solvent
for cutaneous solution**

30 ml



II. Clindamycin

Clinical use

-Infection of the bones and joint (osteomyelitis).

- Used by dentists.

The penetration of this drug inside bone is excellent.

intra **abdominal infection** used in bowel surgery.

(anaerobic bacteria:bacteroid fragilis)

3. Used in **sever acne vulgaris** treatment (gel ~ topically).

adverse effect

❖ **Diarrhea** is common.

pseudomembranous colitis

Super-infection with a strain of *Clostridium difficile*

Because : it's a broad spectrum

Treatment ?????

❖ Available as cap, lotion ,gel.



60 mL

NDC 0409-4197-01

Rx only

Clindamycin
Injection, USP
150 mg/mL

**PHARMACY BULK PACKAGE –
NOT FOR DIRECT INFUSION**

* This Pharmacy Bulk Package is intended for the preparation of I.V. admixtures only. Usual dosage: See insert.

For I.M. or I.V. use.*

Warning: Dilute Before I.V. use.

CA 2329



Clindamycin Therapeutics

Routes:

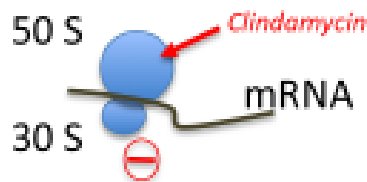


Pharmacokinetics:

- $t_{1/2} = 2.5$ hrs
- penetrates most tissues including abscesses
- does NOT penetrate into CNS or intracellular
- hepatic metabolism, no dosage adjustment with renal failure

Mechanism:

Binds to 50S (same site as erythromycin) & inhibits peptidyl transferase & translocation



bacteriostatic

Oral infections

Combined w/ pyrimethamine for toxoplasmic encephalitis in sulfa allergy

Lung abscess & aspiration pneumonia:

Rx: Necrotizing fasciitis & Streptococcal toxic shock

MRSA soft tissue infections

Gyn/Pelvic infections:
Pelvic Inflammatory Dx (PID)

Adverse Effects:

- nausea, vomiting, diarrhea
- fever, rash
- *Clostridium difficile* enterocolitis (~6%)



TETRACYCLINES

III. Tetracyclines

- **Tetracycline**



Short duration ,given 4 times daily

- **Doxycycline (PO,IV)**



Long duration ,given once daily

- They are **broad-spectrum**.
- Bacteriostatic antibiotics.
- Given Orally / parentrally.

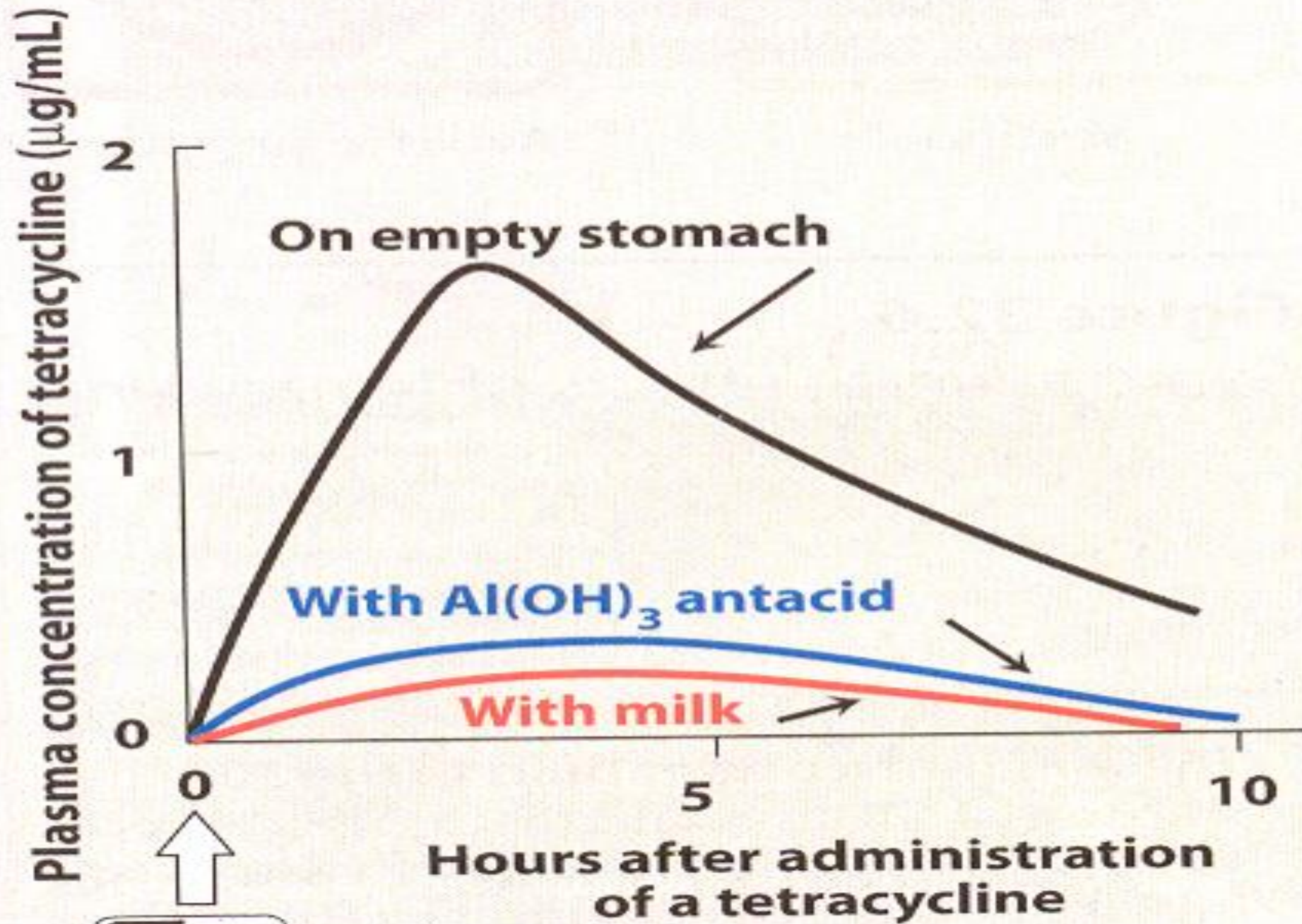
- Doxycycline slowly excreted , **why???**
Due to Enterohepatic circulation.

- **Pts with renal failure** give doxycycline (excreted via bile into feces).

Contra in pregnancy & children < 8 -12 yrs.

Food and milk decrease absorption by about
50%

Administer at least 1-2 hours prior to or 4 hours
after antacid or vitamins or various salts due to
the formation of non-absorbable chelates of the
tetracyclines with calcium ,zinc ,Al ,iron and Mg.



Therapeutic applications

- *Mycoplasma pneumonia* (atypical)
- Cholera (+ fluid replacement)
- Malt fever (combined with gentamicin).
- *Acne vulgaris* (doxycycline cap).
- Eradication of *H.pylori*.(Tetracyclin)

Adverse Effects

- *Gastric* : N/V/D; non compliance
- *Superinfection* .
- *Bone and teeth* : Deposition in the bone & teeth → discoloration (brownish to yellowish) & hypoplasia of teeth & temporary stunting of growth. ~ chelate Ca
Retardation in their growth (children).
- *Hepatotoxicity*: Fatal during pregnancy (2 g)
- *Photosensitivity* : (skin become dark brown skin)
- *Fanconi syndrome*.

- Cholera is an infection of the intestine by the bacterium *Vibrio cholerae*. Symptoms may range from none, to mild, to severe. The classic symptom is large amounts of watery diarrhea that lasts a few days.
- recent Cochrane Review found evidence of effectiveness for antibiotics in improving outcomes in those who are both severely and not severely dehydrated. Azithromycin and tetracycline may work better than doxycycline or ciprofloxacin.
- Zinc supplementation
- In Bangladesh zinc supplementation reduced the duration and severity of diarrhea in children with cholera when given with antibiotics and rehydration therapy as needed. It reduced the length of disease by eight hours and the amount of diarrhea stool by 10%.

- Brucellosis, Bang's disease, Crimean fever, Gibraltar fever, Malta fever, Maltese fever, Mediterranean fever, rock fever, or undulant fever: caused by ingestion of unpasteurized milk or undercooked meat from infected animals or close contact with their secretion.
- The GOLD standard treatment for adults is :daily IM streptomycin 1 g for 14 days and oral doxycycline 100 mg twice daily for 45 days (concurrently). Gentamicin 5 mg/kg by IM once daily for 7 days is an acceptable substitute when streptomycin is not available or contraindicated. Another widely used regimen is doxycycline plus rifampin twice daily for at least six weeks. This regimen has the advantage of oral administration. A triple therapy of doxycycline, with rifampin and co-trimoxazole, has been used successfully to treat neurobrucellosis. Co-trimoxazole and rifampin are both safe drugs to use in treatment of pregnant women who have brucellosis

Doxycycline is able to cross the BBB, but requires the addition of two other drugs to prevent relapse. Ciprofloxacin and co-trimoxazole therapy is associated with an unacceptably high rate of relapse. In brucellic endocarditis, surgery is required for an optimal outcome. Even with

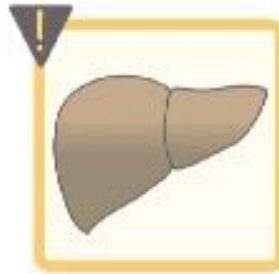
- Prophylaxis of malaria.(Doxycylin)
- Treatment of amebiasis(Doxycyclin)
- ADH-secreting tumor(Demeclocyclin)

It inhibits its renal effect

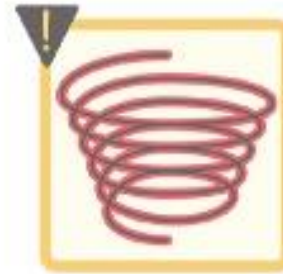
Tetracycline - Adverse Effects



GI disturbance



Liver failure



Vertigo



Deposition of
drug in bones
and teeth



Phototoxicity



Avoid in pregnancy

Adverse effects have restricted their usefulness

Hepatic Toxicity

● **Microscopic study of the liver reveals fine vacuoles, cytoplasmic changes and an increase in fat. Pregnant women are particularly sensitive to Tetracyclines - induced hepatic damage. Jaundice (increased UREA) azotemia, acidosis, shock. (in pregnant women experiencing pyelonephritis can be fatal)**



- A similar term is "pyelitis" which means inflammation of the pelvis and calyces.^{[3][4]} In other words, pyelitis together with nephritis is collectively known as pyelonephritis. Severe cases of pyelonephritis can lead to pyonephrosis (pus accumulation around the kidney), urosepsis (a systemic inflammatory response of the body to infection), kidney failure and even death.



Figure 1. Patient with black hairy tongue.



Q1) Why tetracyclin contra in pregnancy and children <12 yrs old????

Q2) Pregnant women suffering from mycoplasma Pneumoniae what do u think is the DOC ??????

Tetracycline or macrolides ???????

- For **acne vulgaris** Give the patient :

1- Doxycycline (oral)

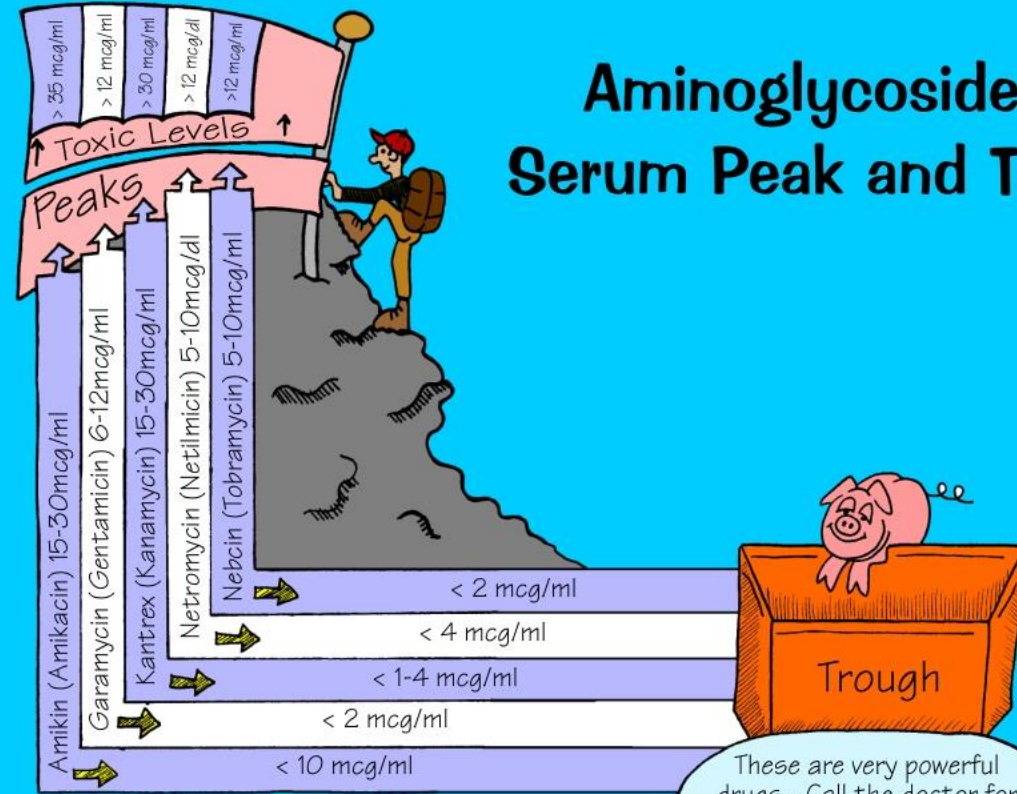
2- Clindamycin (topical)



3- erythromycin with zinc

Aminoglycosides

- **Streptomycin, Neomycin**, Framycetin, **Tobramycin**, Kanamycin, Spectinomycin,
- **Gentamicin**, **Amikacin**, Netilmicin
- **They resemble each other in their**
 - Mode of action
 - Pharmacokinetics
 - Therapeutic & Toxic effects
- ☐ They need TDM

Aminoglycosides - Serum Peak and Trough



- + Crosses Placenta
- Does not cross blood brain barrier
- May cause:
 -  RING-A-RING
 -  Ringing in ears & sick kidneys

These are very powerful drugs... Call the doctor for any abnormal lab values and watch for ototoxicity and nephrotoxicity



IV. Aminoglycosides

Ex. Neomycin, Gentamicin, Streptomycin .

- They are **bactericidal**.
- **Parenteral** administration is required for systemic effect, **except neomycin(orally)**.
coz IV neomycin : cause severe nephrotoxicity.
- These are poorly lipid soluble (water soluble), so **not absorbed orally**

neomycin

Use is limited to:-

1. **topical** (local effect) application for skin infections like in burns, in ear and eye ointments..
2. **oral** administration to prepare(sterilize) the bowel prior to colonic surgery. Make area aspect during surgery.

gentamicin

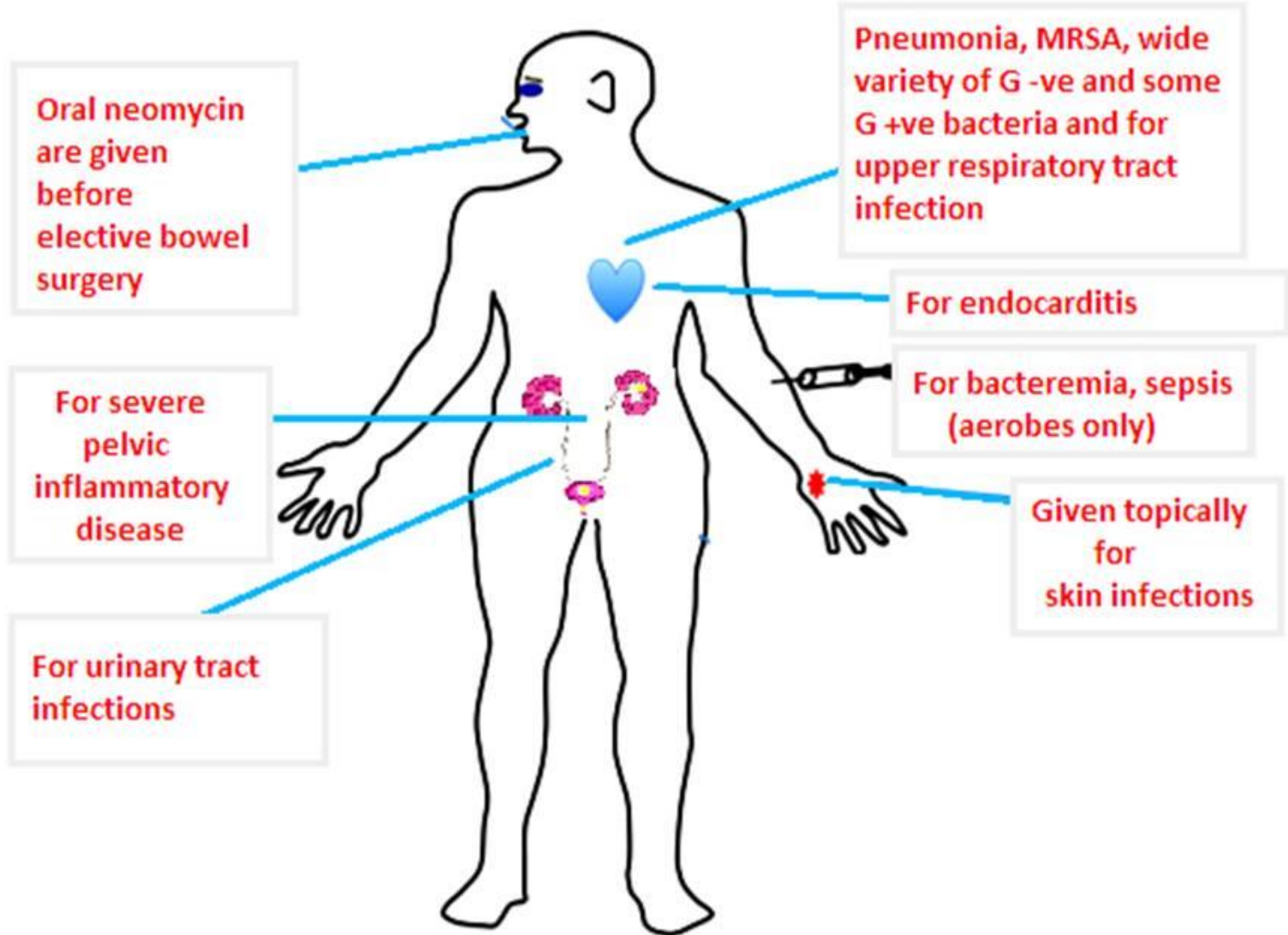
1. applied **topically** for local effect, ear and eye ointments.

e.g : conjunctivitis.

2. **For endocarditis (damage in Heart valve with bact.)**

gentamicin (IV/IM) are often **combined with a B-lactam antibiotic or vancomycin .**

Aminoglycoside Uses



Aminoglycoside Uses

Routes:



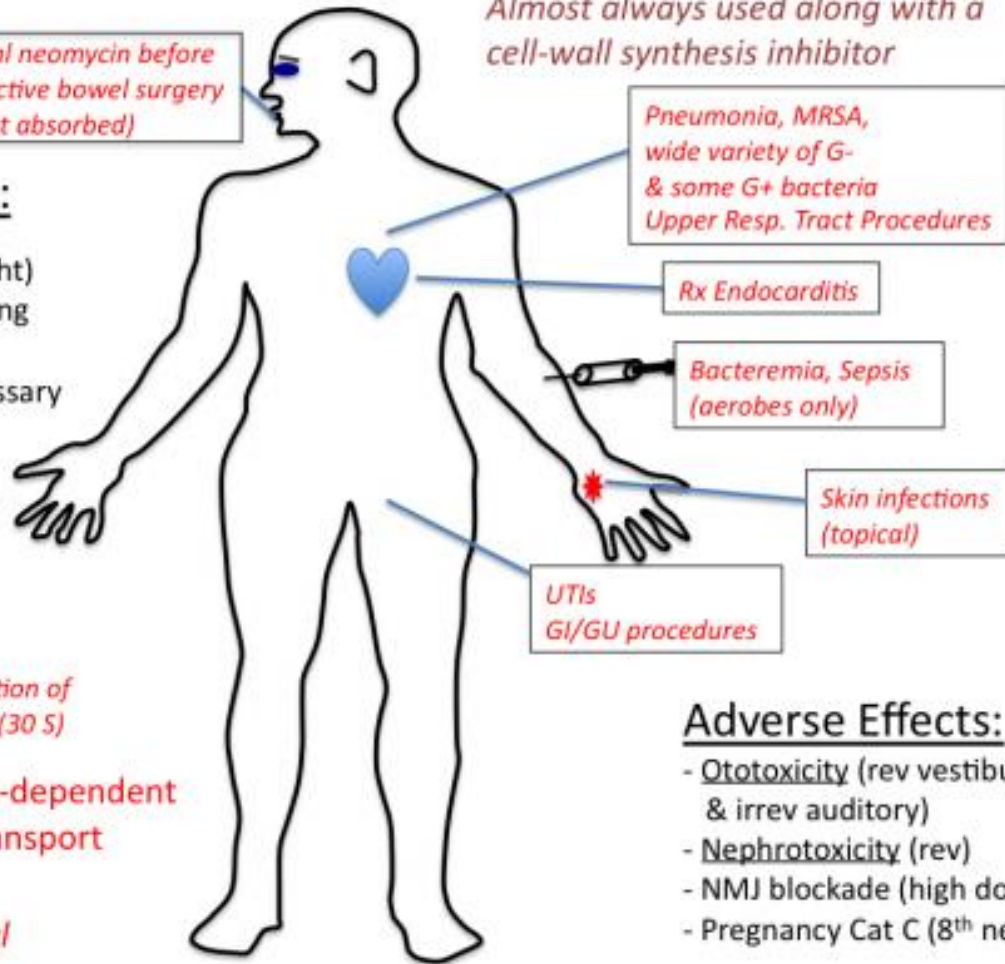
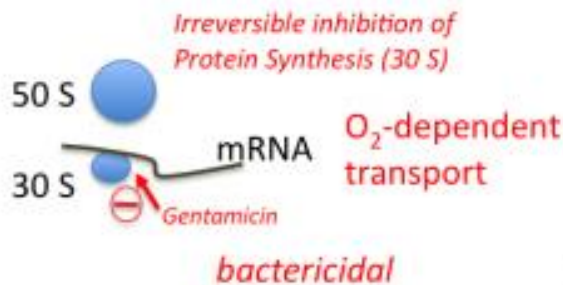
Oral neomycin before
elective bowel surgery
(not absorbed)

Almost always used along with a
cell-wall synthesis inhibitor

Pharmacokinetics:

- Vd = ECS (25% body weight)
- adjust maintenance dosing based upon [creatinine]
- plasma monitoring necessary

Mechanism:

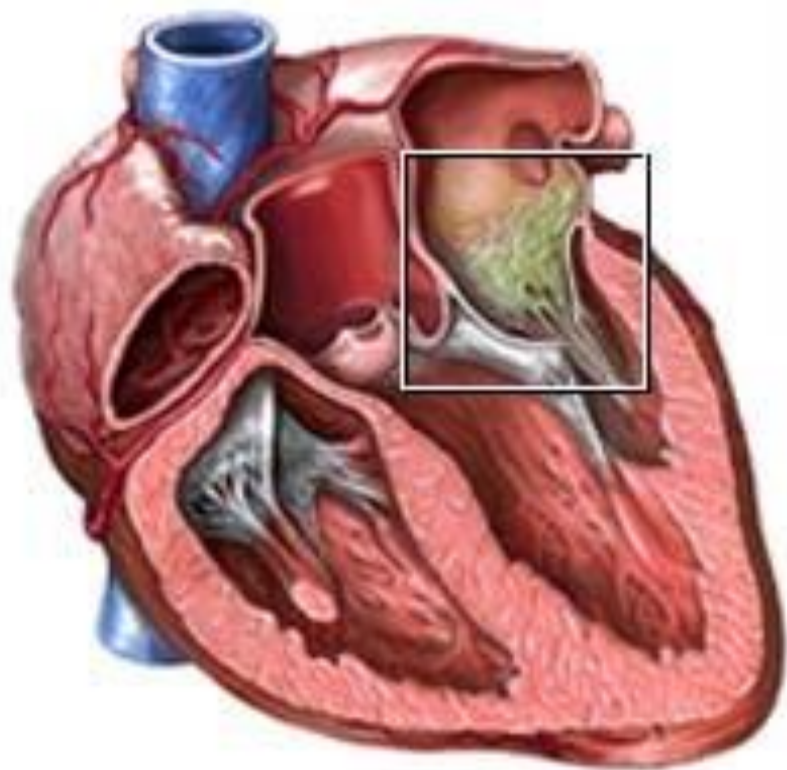


Adverse Effects:

- Ototoxicity (rev vestibular & irrev auditory)
- Nephrotoxicity (rev)
- NMJ blockade (high dose)
- Pregnancy Cat C (8th nerve)

- The antibacterial effects of all the B-lactam antibiotics are synergistic with the aminoglycosides.
- Because B-lactam facilitate the entry of aminoglycosides to gain access to intracellular target sites.
→ This can result in enhanced antimicrobial activity.
Are given together for 2 weeks

Endocarditis



Streptomycin

it is given in the treatment of TB.

IM for 2 months every week...

AminoGlycosides

- Clinical Uses

- Often combined with a β -lactam antibiotic for the treatment of serious infections or infective endocarditis caused by *enterococci* (e.g., with penicillin)

Synergistic effect

- Significant toxicity (> 5 days of use)

- Ototoxicity (irreversible)

- Nephrotoxicity (reversible)



*** Monitoring serum conc. is essential

Aminoglycosides (cont.)

Adverse effects

1. Nephrotoxicity.
2. Ototoxicity:
(tinnitus to deafness (irreversible)).
Drug monitoring is very imp
3. Neuromuscular blocking effect .

these are
dose and
time-related

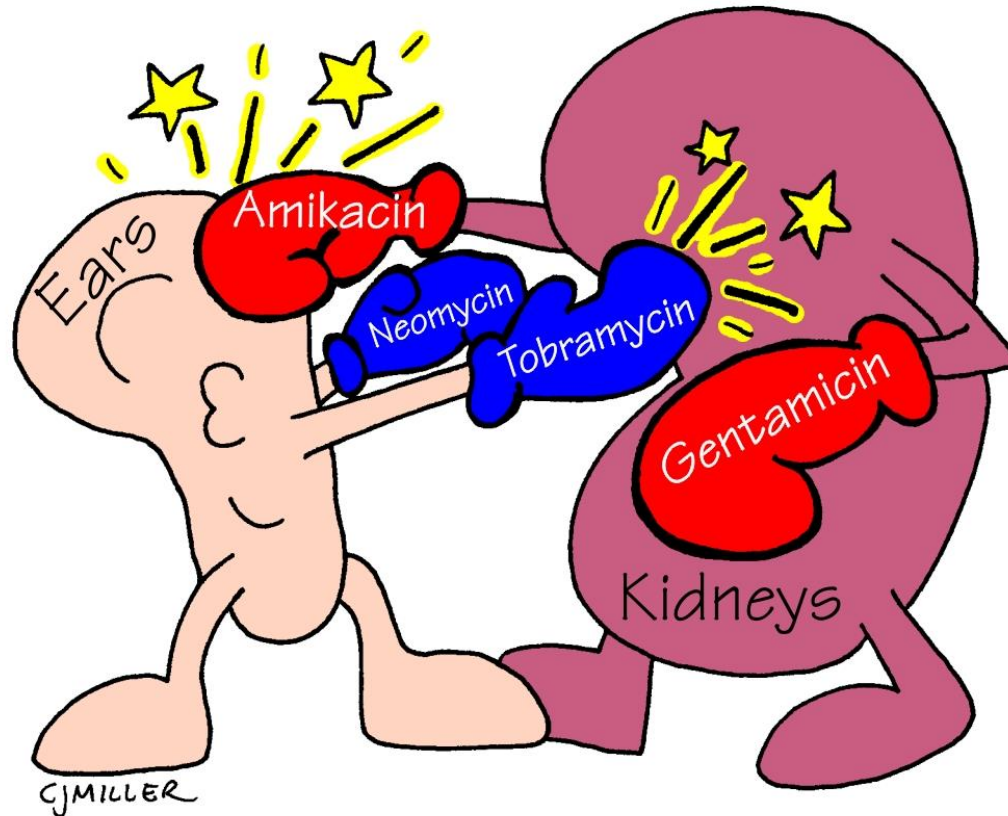
Adverse effects

□ Ototoxicity:

- Auditory: Deafness may be irreversible and has been known to affect fetuses in utero.
- Vestibular : Vertigo and loss of balance (especially in patients receiving streptomycin) may also occur, nausea vomiting because these drugs affect the vestibular apparatus.

- ❑ **Nephrotoxicity:** proteinuria. reduced GFR, increase in creatinine level
- ❑ **Neuromuscular paralysis:** curare- like effect. due to decrease in ACH release, it can be reversed by neostigmine. Thus C.I in myasthenia gravis.
- ❑ **Allergic reactions(not dose related):** topical neomycin.

AMINOGLYCOSIDE TOXICITY



Major toxic effects of Aminoglycosides
are Ototoxicity & Nephrotoxicity

V. Chloramphenicol (PO, IV)

- It has a **broad spectrum** of activity; primarily **bacteriostatic** but may be **bactericidal**.

DOSAGE FORM : orally, parenterally & drop.

- It is metabolized by **glucuronidation** in the liver, *be careful in neonates. ??????*
- Contra in pregnancy.

Chloramphenicol (cont.)

its use is restricted to **serious toxicity to life-threatening infections** for which no alternatives exist because of its toxicity

Indication :-

✓ Bacterial meningitis.(can cross BBB

✓ *Brain abscess(anaerobic inf.)*

But now 3rd generation of cephalosporin.

✓ Rickettsial infection(Typhus), (Typhoid fever.) **Alternative**
(ciprofloxacin & Co-trimoxazole)

✓ **Bact. conjunctivitis (topical as ED,EO)**



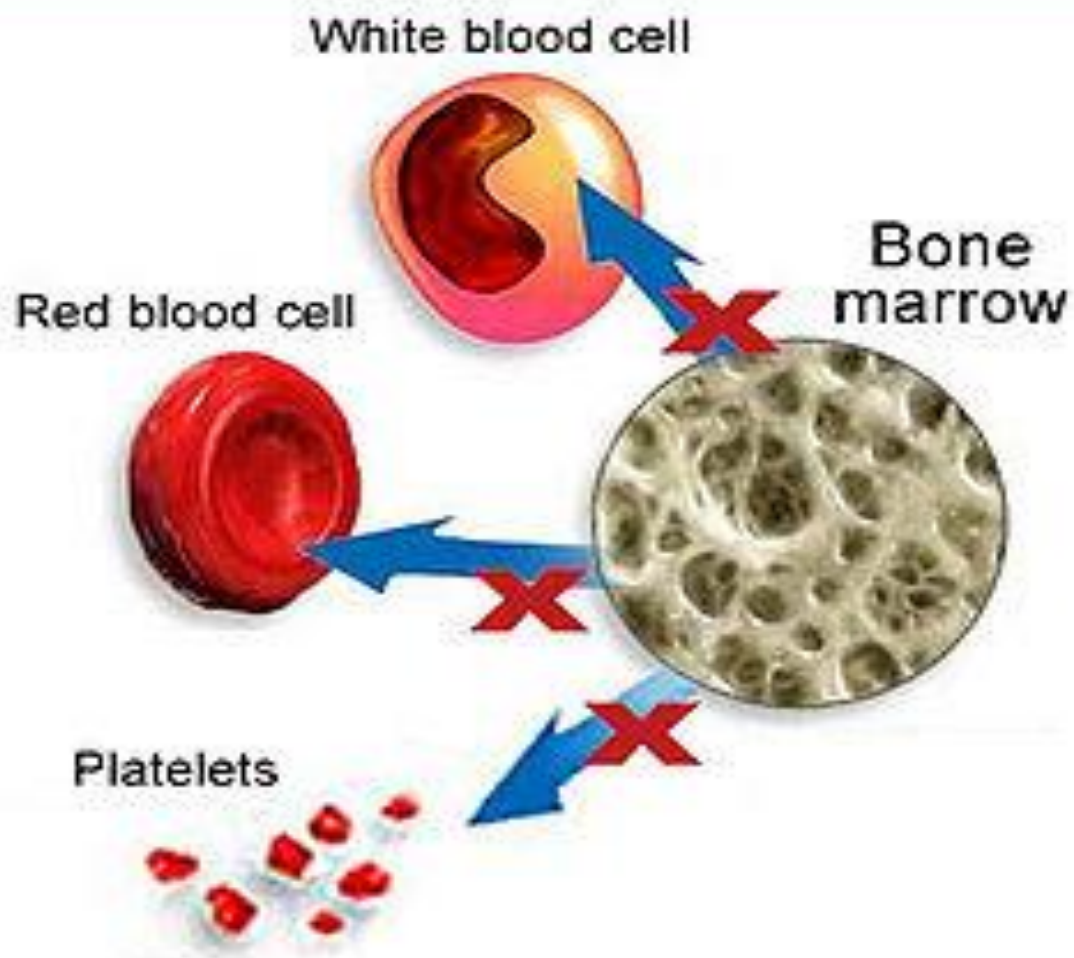
© Mayo Foundation for Medical Education and Research



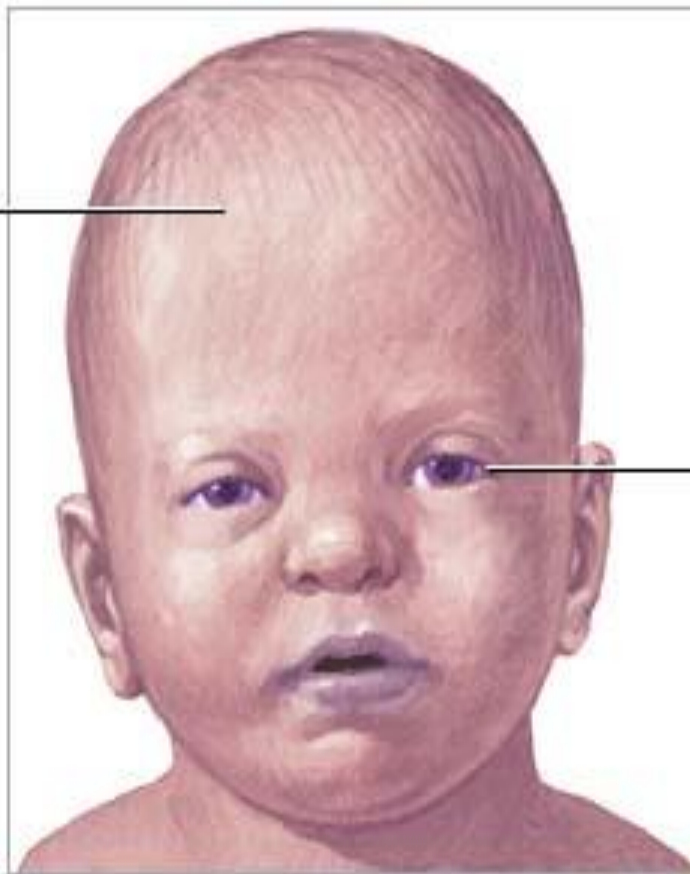
Adverse effects

1. A rare anemia ~ **fatal aplastic anemia** (non-dose-related)
2. **Reversible** bone marrow depression (dose related)
3. Hemolytic anemia in G6PD(**glucose 6 phosphate dehydrogenase enzyme**) deficient pts.
4. Liver enzyme inhibition.
5. **Gray Baby Syndrome (in premature baby)**' This leads to poor feeding, hypothermia, depressed breathing, cardiovascular collapse, **cyanosis** (hence the term gray baby), and death.

Aplastic Anemia



Pale or
blue skin



Lethargic
eyes

Classification of Antimicrobial Agents

1) Inhibitors of cell wall synthesis

- B-lactams - Vancomycin

2) Inhibitors of Protein Synthesis

- Tetracycline – Aminoglycosides - Macrolides-
Clindamycin - Chloramphenicol.

3) Inhibitors of Metabolism

-Sulfonamides- Trimethoprim

-Co-trimoxazole.

4) Inhibitors of Nucleic Acid function or synthesis

- Fluoroquinolones- Rifampin

3. INHIBITORS OF METABOLISM

I. Sulfonamides

- a. Sulfasalazine
- b. Silver sulfadiazine
- c. Sulfamethoxazole

II. Trimethoprim

- III. Co-trimoxazole (Balkatrin[®], Bactrim[®])
Combination of (**Sulfamethoxazole**
&**Trimethoprim**)

Sulfonamides and trimethoprim

- Both are rarely used alone today.
- Individually, these drugs (alone) are **bacteriostatic.....**
- Compounding the sulfonamide (**sulfamethoxazole**) with trimethoprim called (**co-trimoxazole**) provides a synergistic combination.

a combination is **bactericidal**



dihydropteroate diphosphate + p-aminobenzoic acid (PABA)

*dihydropteroate
synthetase*

sulfonamides

dihydropteroic acid

dihydrofolic acid =

Or folic acid

*dihydrofolate
reductase*

trimethoprim

tetrahydrofolic acid =

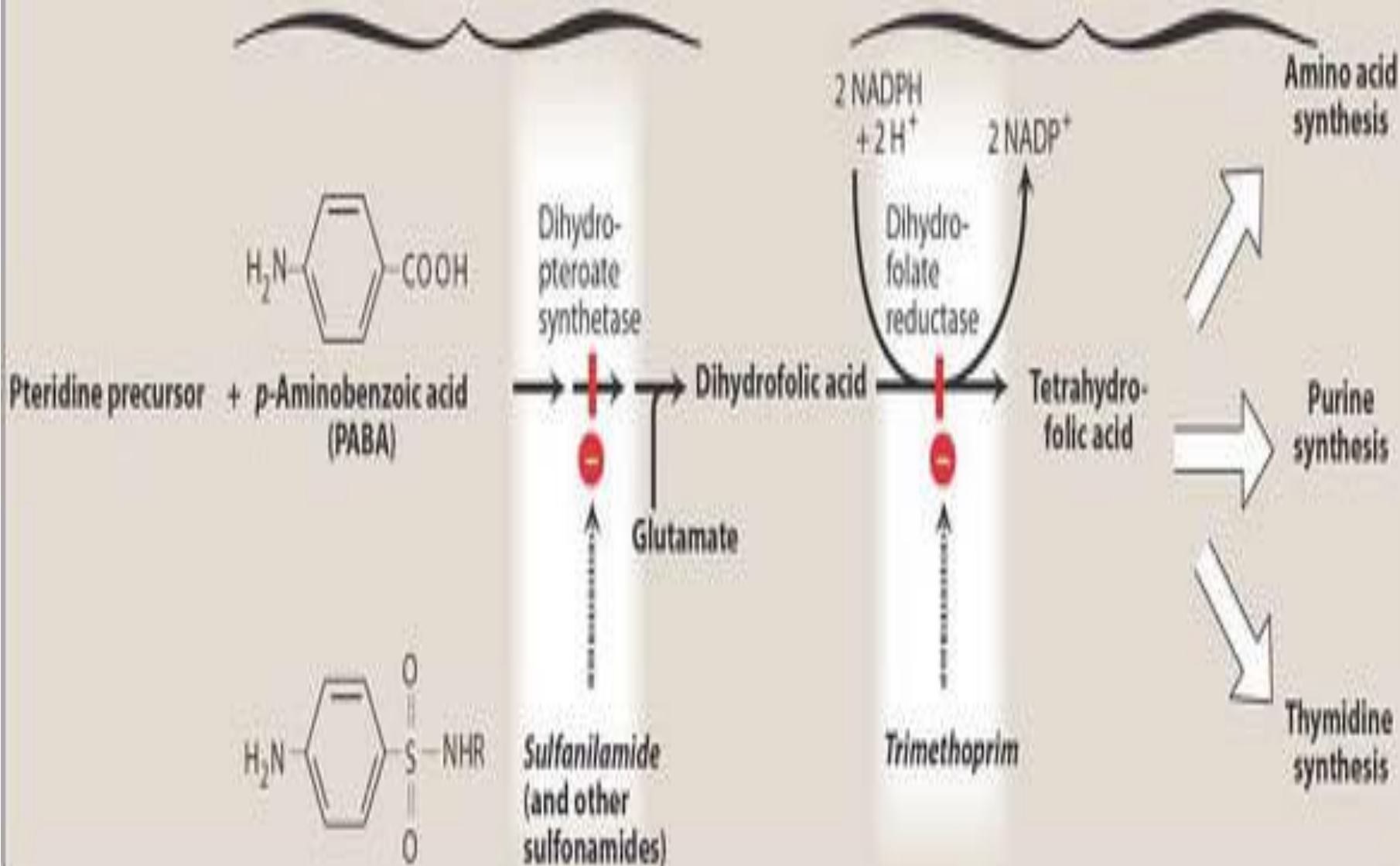
Or folinic acid

Occur in
bact.cell

Occur in both
mammalian &
bact. Cell

Microorganisms

Humans and microorganisms



- PABA : essential for synthesis of folic acid.

FIRST STEP:

By enzyme Dihydropteroic acid ,PABA converted to Dihydrofolic acid (FOLIC ACID or folate).

SECOND STEP:

By enzyme Dihydrofolate reductase , folic acid converted to Tetrahydrofolate (folinic acid)

❑ Sulfa drugs : inhibits synthesis of folate by inhibitor of dihydropteroate synthetase.

❑ Trimethoprim : also called **folate antagonist**.

A potent inhibitor of bacterial dihydrofolate reductase.

Folic acid ----x---- > folinic acid

Sulfonamides

- **Bacteriostatic.**

Dosage form: orally , IV & topically....



- **sulfasalazine** (coz it is not abs orally); **treatment of chronic inflammatory bowel disease IBD; ex: crohn's disease & ulcerative colitis (long term treatment)**
- **Silver sulfadiazine;** locally cream to prevent infection in sever burns, leg ulcer coz prevent colonization of bact.
- **Sulfacetamid:** ocular infection.



Adverse effects

- 1- Crystalluria (stone formation) → damage to the kidney.
- 2- Hypersensitivity (rash, angioedema)
- 3- Hemolytic anemia in (G6PD)....like???
- 4- **Kernicterus (yellowish in brain tissue) (in newborns)**
- 5- Photosensitivity. **LIKE??**

Contraindications

- ✓ In newborns and infants less than 2 months of age.
- ✓ Pregnant women at term.

Kernicterus:

This disorder may occur in **newborns**, because sulfa drugs displace bilirubin from binding sites on serum albumin. The bilirubin is then free to pass into the CNS, because the baby's blood-brain barrier is not fully developed .



Co-Trimoxazole

orally /IV

combination of : **Trimethoprim & sulfamethoxazole**

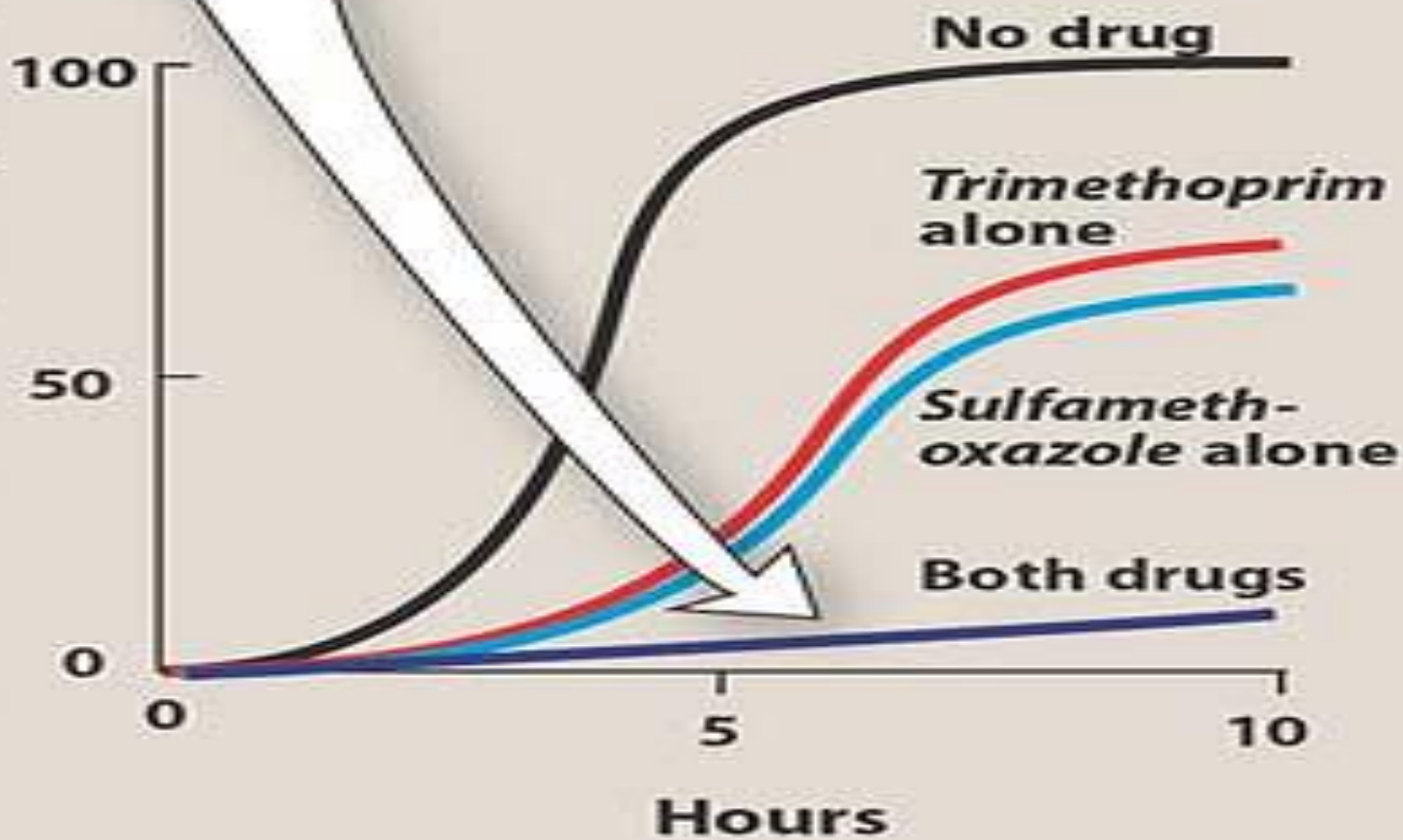
bactericidal. Greater anti-micro. activity than either alone.

Effective in:

1. Chronic UTI.
2. prophylactic in recurrent UTIs infection in women
3. Typhoid fever. (ALTERNATIVE TO CHLORAMPHENICOL)
but now the first choices is ciprofloxacin ,
2nd co-trimoxazole)
4. RTI .
5. **DOC: Pneumocystis carinii pneumonia → common in AIDs pts → IV High dose (coz life threatening disease).**

Trimethoprim and sulfamethoxazole together (cotrimoxazole) show greater inhibition of bacterial growth.

Number of bacteria (arbitrary units)





IV . INHIBITORS OF NEUCLEIC ACID FUNCTION OR SYNTHESIS

❖ Fluoroquinolones

- ✓ Wider range of activity or broad spectrum activity.
- ✓ All are **bactericidal**.

Generation	Drug Names	Spectrum
1st	nalidixic acid cinoxacin	Gram- but not Pseudomonas species
2nd	norfloxacin ciprofloxacin enoxacin ofloxacin	Gram- (including Pseudomonas species), some Gram+ (S. aureus) and some atypicals
3rd	levofloxacin sparfloxacin moxifloxacin gemifloxacin	Same as 2 nd generation with extended Gram+ and atypical coverage
4th	*trovafloxacin moxifloxacin	Same as 3 rd generation with broad anaerobic coverage

*withdrawn from the
market in 1999

Ciprofloxacin

Administration Very expensive.

IV infusion Orally 2x1

Indications:

❖ **UTI.**

❖ Used in genitourinary (ex. Gonorrhoea.)

❖ Traveler's diarrhea. (E.Coli)

❖ Typhoid. (DOC).

❖ TB second line.

❖ pseudomonas infections associated with cystic fibrosis

Fluoroquinolones

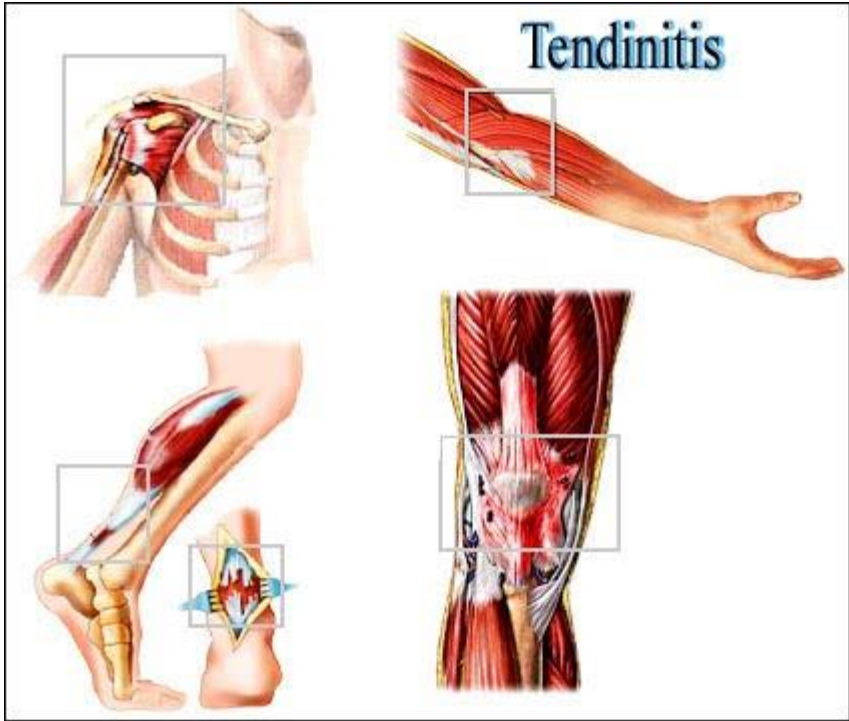
Adverse effects:

- GI distress : N,V,D
- Arthropathy thus Avoid in pregnancy & nursing mothers, child<18 yrs.
- Rupture of Achilles tendon(pain &inflammation) in adult
- **Photosensitivity** (avoid excessive sunlight)
like????

Notes

- ↓ absorption:
Al³⁺, Mg²⁺, and Ca²⁺ antacids & sucralfate.
- Like ?????
- **Enzyme inhibitor.**





Typhoid fever :-

1st choices ciprofloxacin.

2nd choices co-trimoxazole.

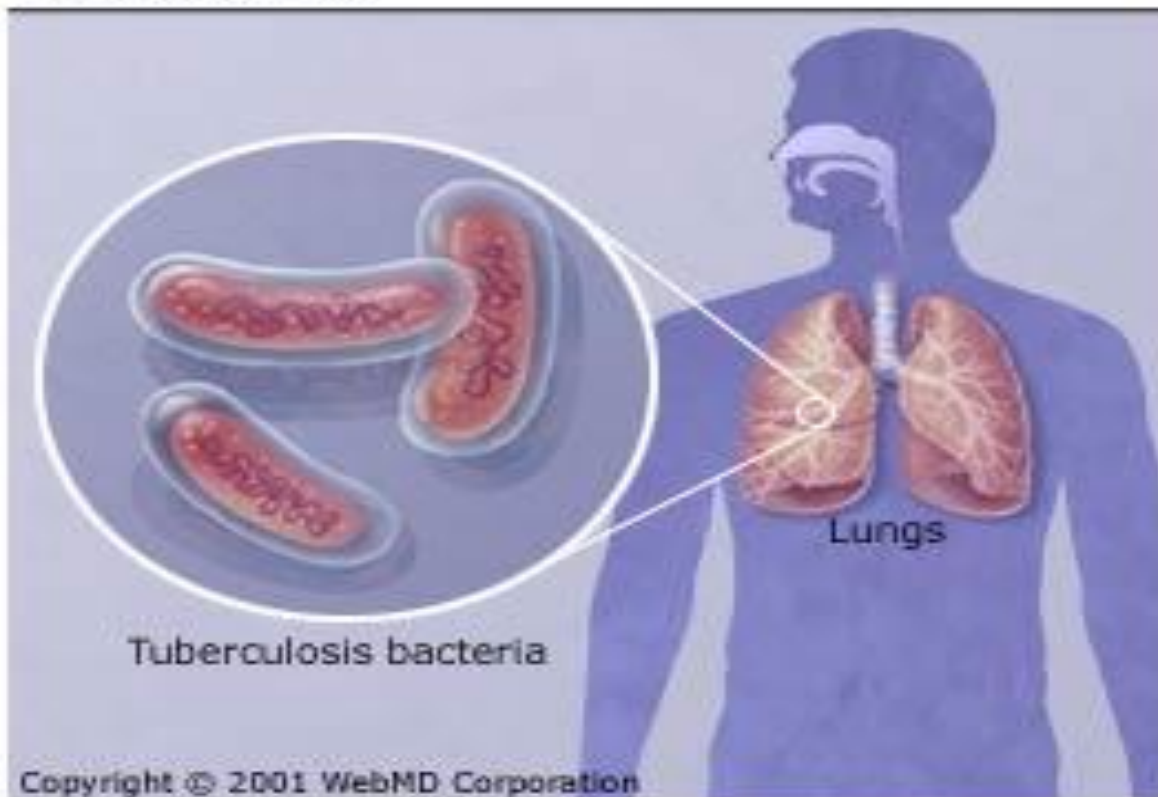
Ruptured
Achilles tendon



SCIENCEPHOTOLIBRARY

ANTI- MYCOBACTERIALS

Tuberculosis



TB

- It is a disease that caused by mycobacterium tuberculosis.
- Mycobacterium tuberculosis, one of a number of mycobacteria, can lead to serious infections of the lungs, genitourinary tract, skeleton, and meninges.

Main symptoms of Pulmonary tuberculosis



Central

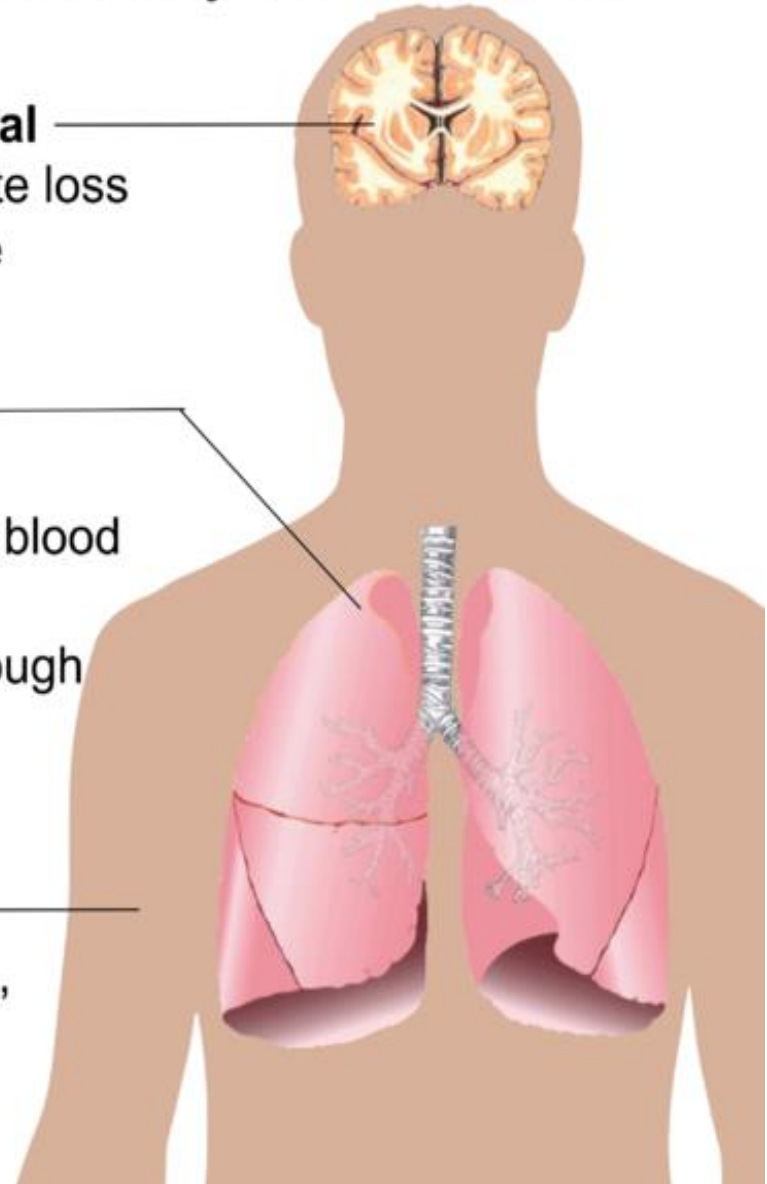
- appetite loss
- fatigue

Lungs

- chest pain
- coughing up blood
- productive, prolonged cough

Skin

- night sweats,
- pallor



- ❖ The organism grows slowly → Usually the treatment is long from 6 months to 2 years.
- ❖ In case of TB it is not useful to use only one drug, so combination of drugs should be used .

Why combination????

to delay or prevent the emergence of resistant strains.

❖ Drugs are divided into two groups:

- First line

- Second line

Second-line medications are either:

- less effective,

- more toxic

They are useful in patients:

- ✓ who cannot tolerate the first-line drugs

- ✓ who are infected with mycobacteria that are resistant to the first-line agents.

ANTIMYCOBACTERIAL AGENTS

DRUGS USED TO TREAT TUBERCULOSIS

Ethambutol
Isoniazid
Pyrazinamide
Rifamycins

First-
line
drugs

Aminoglycosides
Aminosalicyclic acid
Capreomycin
Cycloserine
Ethionamide
Fluoroquinolones
Macrolides

Second-
line
drugs

There are four currently recommended **first-line** agents utilized for antituberculosis therapy

The treatment of TB disease is divided into two stages :-

1- The initial phase :last for two months and usually 4 drugs are given in this stage.

isoniazid, rifampin, ethambutol, and pyrazinamide

2- The continuation phase :lasts from 4 to six months and sometimes to two years in this phase we use at least two drugs.

isoniazid and rifampin



Antimycobacterial drugs

First line of drugs:

- **Isoniazid (iso-nicotinic acid hydrazide INH). The most effective**
- **Rifampin.**
- **Ethambutol.**
- **Pyrazinamide.**

Isoniazid (INH)

Bacteriostatic at low conc. & bactericidal at high conc.

Orally /parentrally

Oral Absorption is impaired if *isoniazid* is taken with food (CHO), or with antacids (ALOH). LIKE ???

Adverse effect :

I. Peripheral neuritis

II. Hepatitis .

Make liver function test before/during treatment

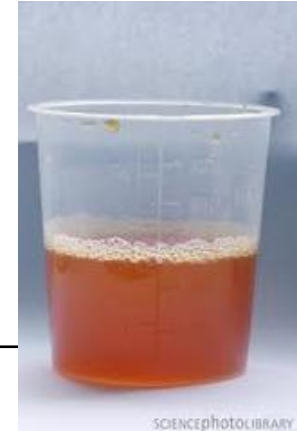
Enzyme inhibitor...

like???

Rifampin(Rifampicin)

It is bactericidal.

Orally



Adverse effect :

- it can cause red –orang discoloration of urine, sweat, tears , saliva , sputum.
- Cholestatic jaundice, hepatitis
- Flu-like syndrome (chills,fever)

Enzyme inducer .

Peripheral neuritis

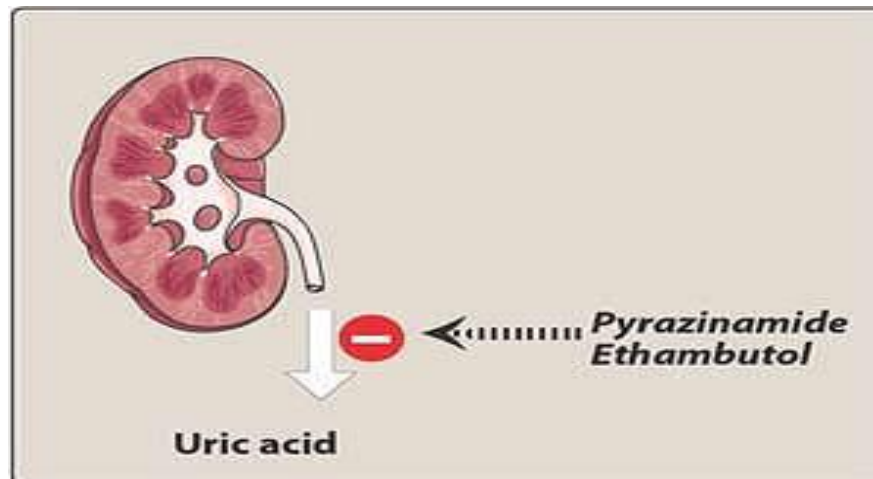
- Numbness of the hand and feet. inability to stand.
 - due to a relative **pyridoxine (vitamin B6)** deficiency.
- Most of the toxic reactions are corrected by supplementation of 25 to 50 mg per day of pyridoxine (vitamin B6)...
- Or given as injection along of treatment



- *Isoniazid* can achieve levels in breast milk that are high enough to cause a pyridoxine deficiency in the infant unless the mother is supplemented with the vitamin.



Pyrazinamide	Ethambutol
it is bactericidal.	<i>It</i> is bacteriostatic
Adverse effect : Hyperuricemia	Adverse effect : I. optic neuritis (inflammation of eye): causing loss of visual acuity and red-green color discrimination. II. Hyperuricemia





Antifungals

Systemic & Topical

*Some are fungistatic,
while others are fungicidal*

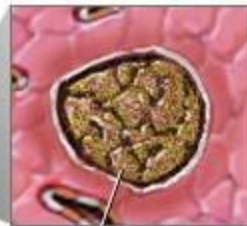
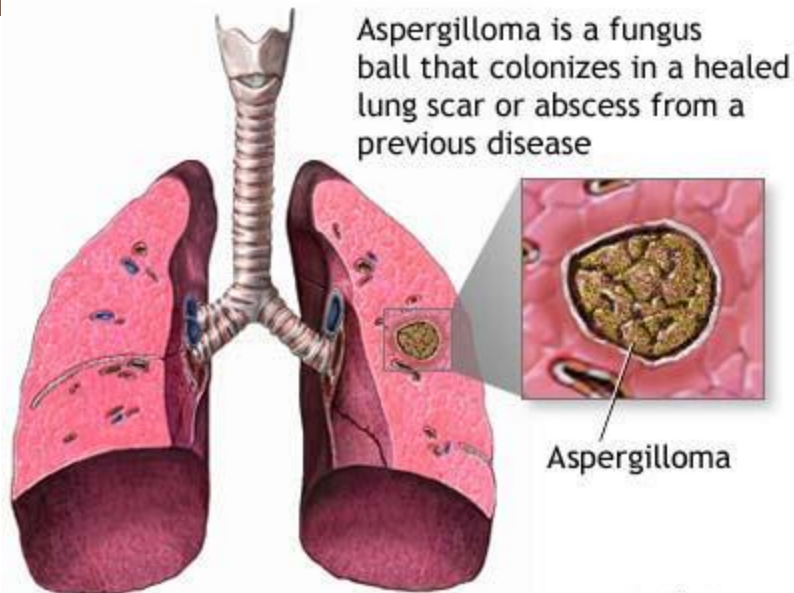
Fungal Infection in Humans = Mycoses

Mycoses : Infectious diseases caused by fungi , they are often chronic in nature.

**Candidiasis(thrush), dermatopytosis, aspergillosis
onchomycosis....ext..**

Major Types of Mycoses

1. Cutaneous: (superficial) infections of the skin. (ex. candidiasis, dermatophytosis).
2. Subcutaneous: fungi penetrate the skin.
3. Systemic : they are most difficult to treat , and often life-threatening. (systemic candidiasis, meningitis, or in aspergillosis infection in lung)



Aspergilloma



It is difficult to treat fungal infections more difficult than treatment of bacterial infections????????

Fungi has a cell wall which is quit rigid →
chitin + ergosterol

Ergosterol targeted by anti fungal drugs

incidence of fungal infections is increased in Individuals :

- On chronic immune suppression following organ transplant.
- Infected with the (HIV).
- Drugs (steroids, Chemotherapy)

DRUGS FOR SUBCUTANEOUS AND SYSTEMIC MYCOTIC INFECTIONS

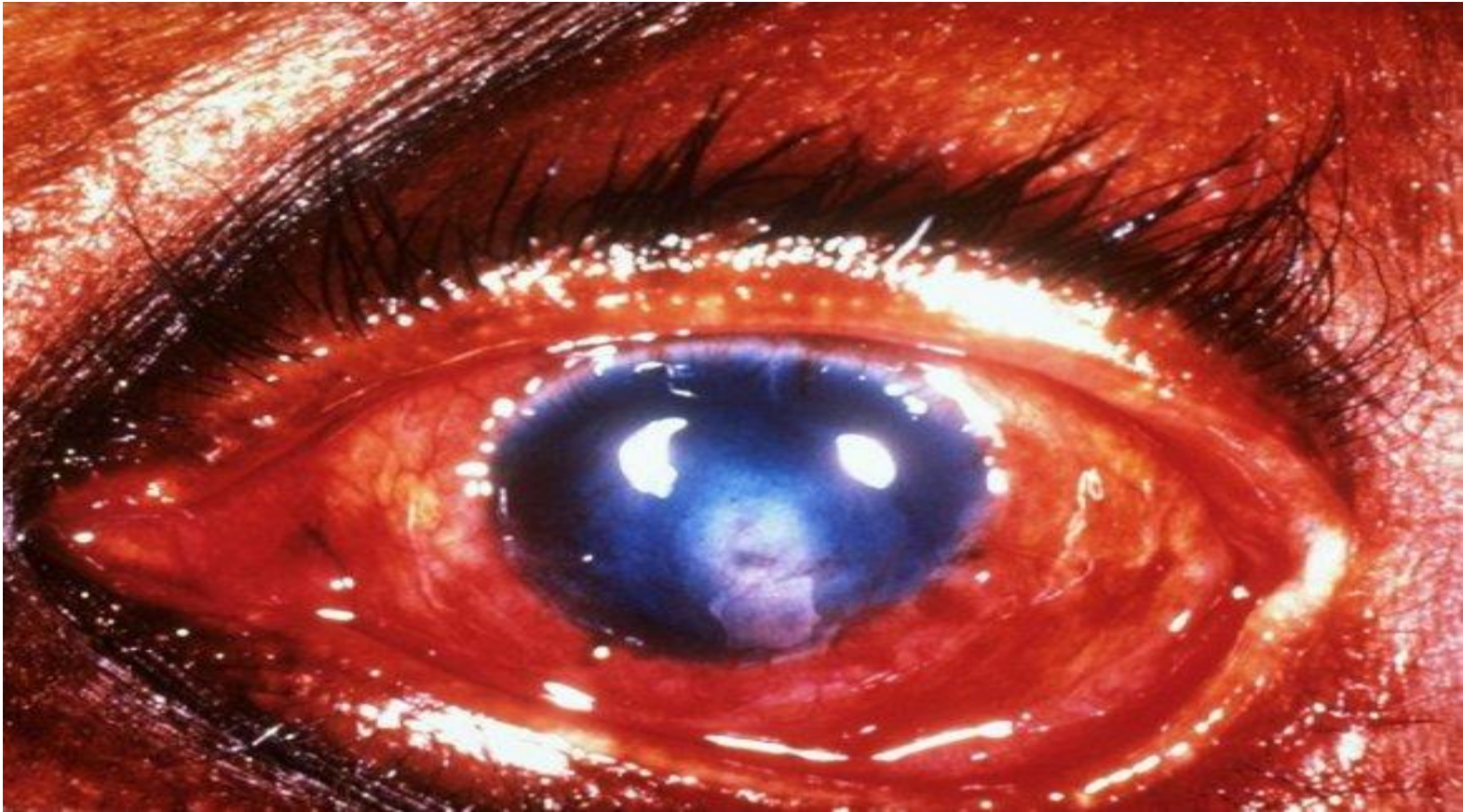
1. Amphotericin B → first discovered.
2. Fluconazole
3. Ketoconazole

Amphotericin B

- ❑ Poor absorption orally..
- ❑ has **a low therapeutic index.**

Indication

- ❑ **Orally only** for GI fungal infections.
- ❑ **Given parentally:**
 - **Slow IV infusion**- systemic FI.
 - **IT** – fungal meningitis.
 - **Intra articular** – fungal joint infections.
- ❑ **Eye drops** – fungal corneal ulcer.
- ❑ **Irrigation of bladder** – fungal cystitis(infection of urinary bladder).



Adverse effects

Fever and chills:

These occur most commonly 1 to 3 hours after starting the I.V administration.

Allergy(start with small dose)

Renal impairment:

a bolus infusion of normal saline before and after amphotericin B infusion may reduce the incidence of drug-induced nephrotoxicity.
rehydration with water

Hypotension:

shock-like fall in blood pressure accompanied by hypokalemia may occur.

Thrombophlebitis

Infusion related:

fever, chills, spasm, shock-like fall in BP

✓ Slow infusion

✓ Premedication with: antihistamine or glucocorticoids, antipyretics

Dose-related : nephrotoxicity

Ketoconazole

Flucanazole

- Available as tab, shampoo, cream.
- Ketoconazole **requires low PH for its absorption.**
- Wide spectrum.**
- ❖ ADRs:
 - Anti-androgenic effect (Gynecomastia in male & decreased libido in male).
 - ketoconazole inhibits cytochrome P450.

- Given Orally and IV.
- Highly effective in Candidiasis .
Ex, vaginal candidiasis
- Effective against FI (Cryptococcus neoformans) in pts. with AIDs.
(DOC)
- should not be given during pregnancy



DRUGS FOR CUTANEOUS MYCOTIC INFECTIONS

1. **Terbinafine.**
2. **Griseofulvin**
3. **Nystatin**
4. **Miconazole**

Terbinafine

- ❖ It is deposited in the skin, nails, and fat.
- ❖ So, it is the drug of choice for treating **onychomycosis** (fungal infections of nails).

Therapy usually:
Orally for up to 3 months.

Griseofulvin

- ❖ Has affinity to skin, nails and hair (bound to keratin)
- ❖ Effective in tinea infection (scalp, Hand & beard.
- ❖ Very effective in athlete's foot.

Therapy :
Orally for 6-12 months duration.

Until New hair and nail will be free from fungi.

onychomycosis





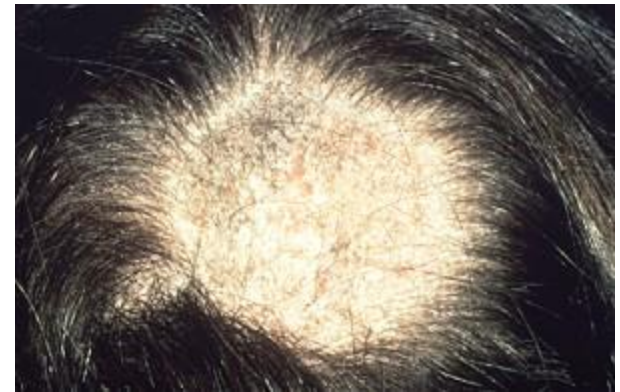
Figure 1. TOP. Patient 1 as she presented to my office in December 2009 with a clinical diagnosis and positive mycology of onychomycosis in all 10 toes. She received a single treatment on 14 December and a second treatment in October 2010. BOTTOM. Appearance of her nails at 13 months post-treatment. All 10 toes responded to treatment, most with 100% clear nail.

athlete's foot

Fungal infections
between toes



tinea infection





mercatorpharma.com



Nystatin

Too toxic for systemic use.

So, Used only topically or locally (incomplete absorption orally) .

In candida infections.

Vaginal, intestinal & mouth.

Oral gel or drops

Miconazole

• Too toxic for systemic use.

Used only topically or locally (incomplete absorption orally)

Oral gel:

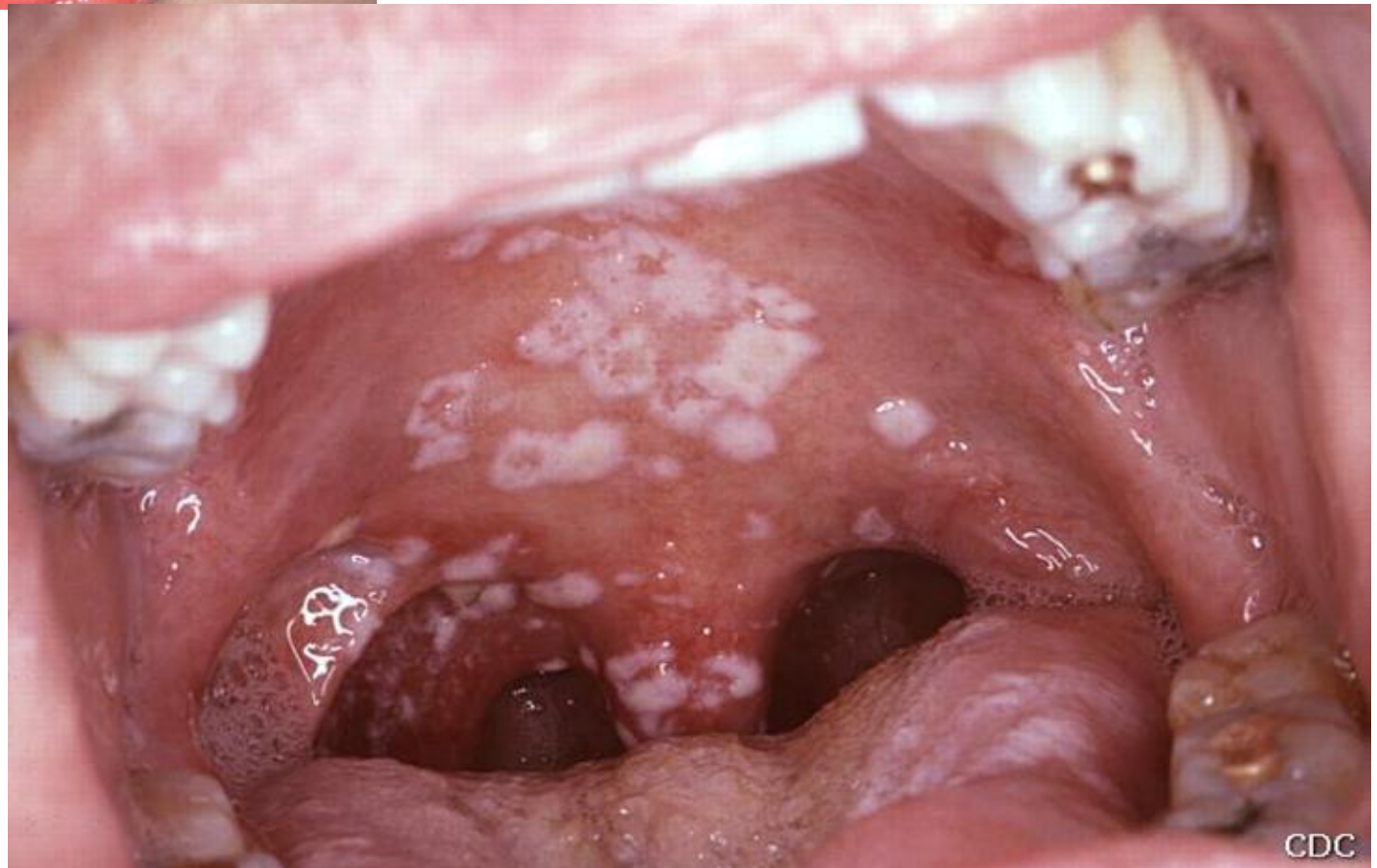
FI of the mouth (candidiasis : white spots on mouth) .very effective.

Taste is very well... DOC in children.

Topically: (locally)

Cream: for skin (dermatophytosis)

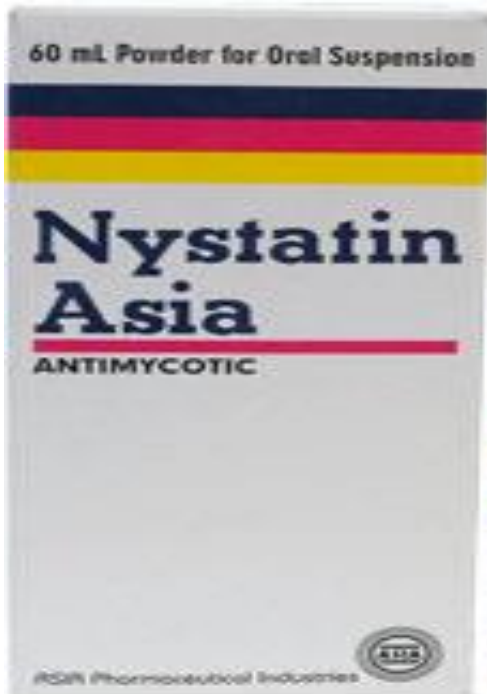
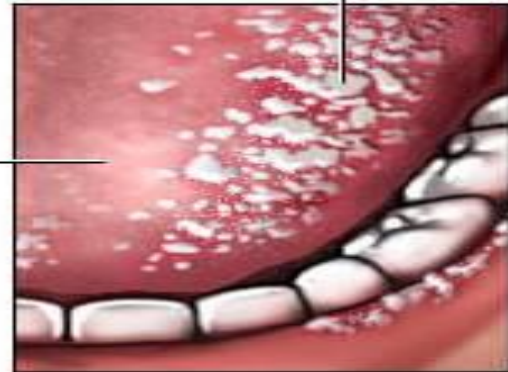
vaginal ovules: vaginal infection locally.





Thrush

Tongue






© 2002 GSM



© GoodLightscraps.com



Good Luck
4 ur
Exam