CHEMOTHERAPY

ANTIBACTERIAL DRUGS (in brief)

These are the drugs used for combating (ttt & prophylaxis) bacterial infections.

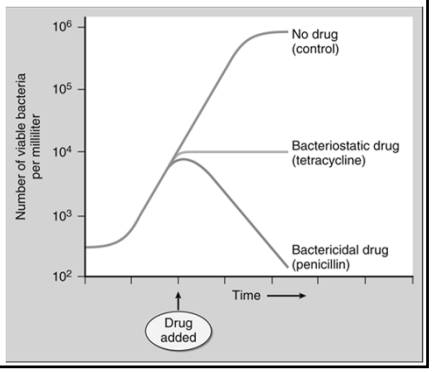
CLASSIFICATION

A. According to their antibacterial ACTION:

Bacteriostatic:

-They arrest the growth and replication of bacteria, thus limit the spread of infection while the body's immune system attacks and eliminates the pathogens.

-e.g., tetracyclines, chloramphenicol



Bactericidal:

-They kill bacteria and thus decrease the total number of viable organisms with less effort needed from the immune system.

-e.g., penicillins, streptomycin

CLASSIFICATION OF ANTIBACTERIALS

B. According to their SPECTRUM of action:

Narrow spectrum:

-They act only on a single or a limited group of microorganisms.

-e.g., isoniazid on T.B, Penicillin-G mainly on Gram +ve bacteria

Broad spectrum:

-They affect a wide variety of microbial species including large viruses & protozoa.

-e.g., tetracyclines, chloramphenicol

Extended spectrum:

-They have intermediate spectrum; for e.g., effective against Gram +ve organisms plus a few number of Gram -ve bacteria.

-e.g., carbenicillin acts against Gram +ve & some Gram -ve bacteria as *Pseudomanas & Proteus*.

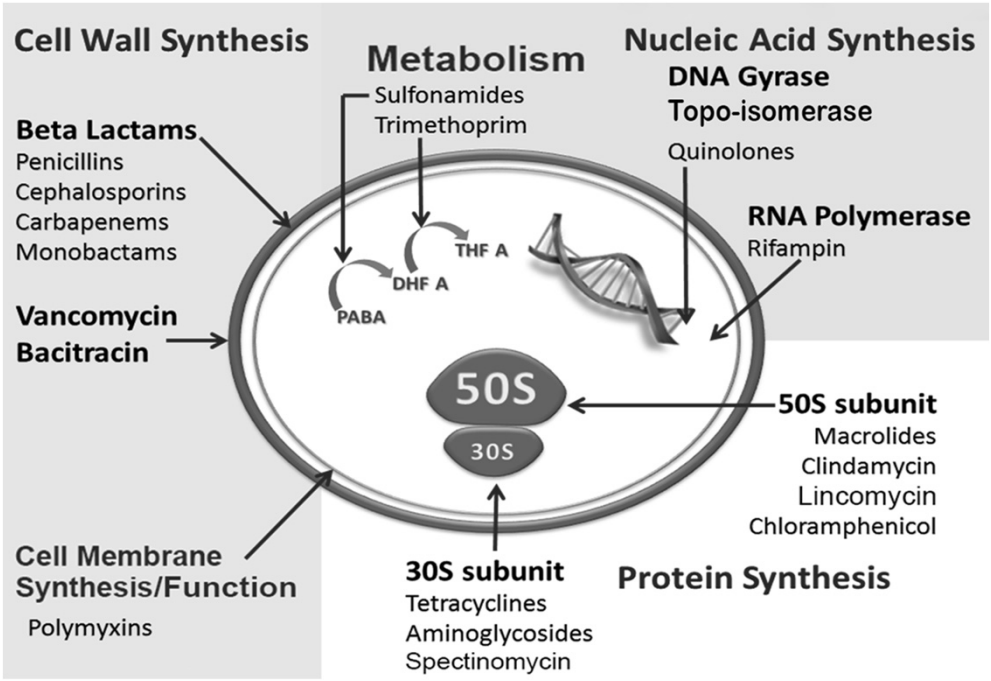
CLASSIFICATION OF ANTIBACTERIALS

C. According to their CHEMICAL STRUCTURE:

- **Para-amino benzene sulfonic acid (PABSA) derivatives:**
  -sulphonamides (sulphadiazine, -methoxazole, -doxine, …)
- **β-lactams:**
  -penicillins, cephalosporins, monobactams, carbapenems
- **Aminoglycosides:**
  -e.g., streptomycin, gentamicin, neomycin, kanamycin, …
- **Macrolides:**
  -e.g., erythromycin, clarithromycin, azithromycin, tylosin, …
- **Tetracyclines:**
  -e.g., oxytetracycline, chlortetracycline, doxycycline, …
- **Quinolones:**
  -e.g., ciprofloxacin, enrofloxacin, levofloxacin, moxifloxacin, …
- **Miscellaneous:**
  -e.g., chloramphenicol, lincomycin, novobiocin, polymyxins

CLASSIFICATION OF ANTIBACTERIALS

D. According to their MODE OF ACTION:



METABOLIC INHIBITORS
SULPHONAMIDES

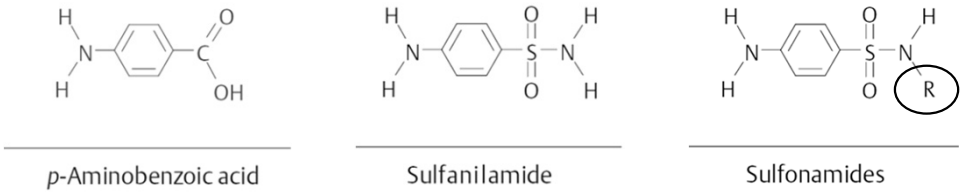
DEF.:

Sulpha drugs are synthetic organic chemicals with chemotherapeutic activity.

They have a common chemical nucleus (PABSA) which is essential for antibacterial activity.

This nucleus is very closely related to para-amino benzoic acid (PABA), a member of vit. B complex, which is essential for bacteria.

The first member was sulphanilamide; in 1935.



CLASSIFICATION OF SULPHONAMIDES

A. According to their SITE of action:

Systemic:

-They are reasonably absorbed from GIT; including:

- sulphanilamide
- sulphamerazine
- sulphadiazine
- sulphaquinoxaline
- sulphacetamide
- sulphamethazine (sulphadimidine)
- sulphathiazole
- sulphafurazole

Gut-active:

-They are poorly absorbed from GIT; and thus exert their effect ONLY on intestinal flora and mucosa; including:

- sulphaguanidine
- succinylsulphathiazole
- phthalylsulphathiazole
- phthalylsulphacetamide

Topical:

- sulphacetamide, eye drops for eye infection
- silver sulphadiazine, skin cream for burns

CLASSIFICATION OF SULPHONAMIDES

B. According to their DURATION of action:

SHORT acting (rapidly absorbed & rapidly excreted; ≈6 hs):

-sulphadiazine
-sulphathiazole
-sulphasomidine
sulphamerazine
sulphafurazole
sulphamethizole

MEDIUM acting (rapidly absorbed; 11~12 hs):

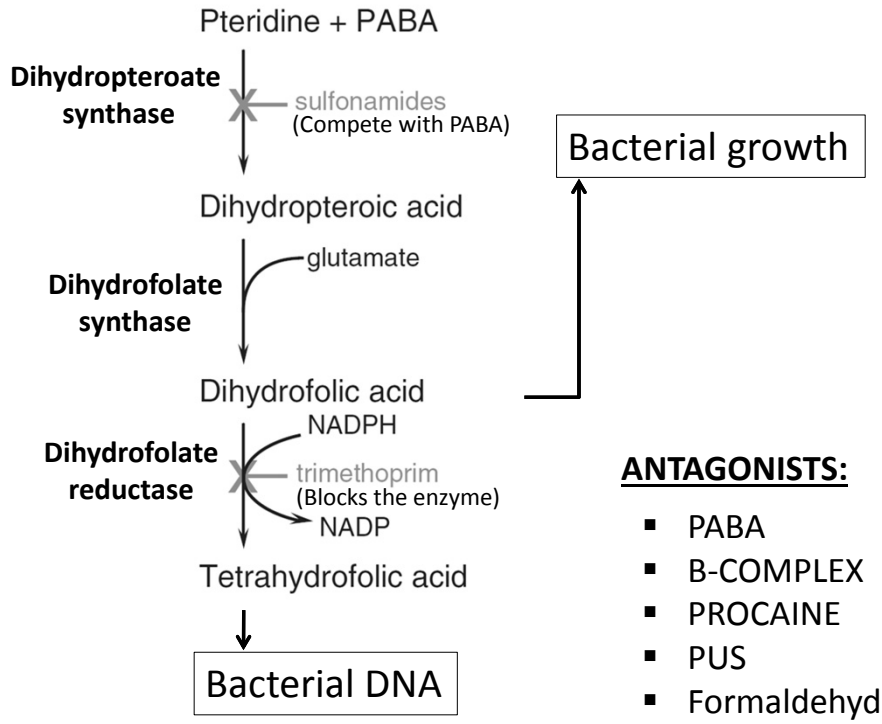
-sulphamethoxazole

LONG acting (rapidly absorbed & slowly excreted; <=>24 hs:

-sulphadimethoxine
-Sulphadoxine
-sulphamethazine

PHARMACODYNAMICS OF SULPHONAMIDES

M.O.A.



ANTAGONISTS:

- PABA
- B-COMPLEX
- PROCAINE
- PUS
- Formaldehyde

- **Action:**
  - **Bacteriostatic against Gram +ve & Gram –ve bacteria as:**
    Streptococci, *Pneumococci*, *Staphylococci*, *Meningococci*, *E-Coli, Salmonella, Chlamydia, Nocardia, Eimeria …*
  - **NOT effective against:**
    Pseudomonas, *Proteus, Rickettsia, Spirochetes, Viruses …*

- **Indications:**
  - Urinary tract infections: cystitis, urethritis
  - Respiratory tract infections: sinusitis, otitis media, bronchitis
  - Nocardiosis & chlamydiosis
  - Bacillary dysentery (gut active sulphonamides)
  - Salmonellosis & coccidiosis in poultry (sulphaquinoxaline)
  - Dephtheria, calf scour, strangles, mastitis (sulphadimidine)
  - Chronic infections (long acting sulphonamides)
  - Conjunctivitis (sulphacetamide) & Skin burns (silver sulphadiazine)

- **TOXICITY: Photosensitivity; Crystaluria; Flora suppression …**

TRIMETHOPRIM

- It is antibacterial agent that acts synergistically with sulphonamides.
- It acts by inhibiting dihydrofolate reductase enzyme.
- Its spectrum is similar to that of sulphonamides but more potent.
- It can be given by any route of administration.
- Its half life is about 11 hours as that of sulphamethoxazole
- Compared to sulpha drugs, it is more lipid soluble and distributes to a larger volume.
- Used for ttt of urinary and respiratory tract infections.
- Usually used as a combination with a sulpha drug, for e.g.:

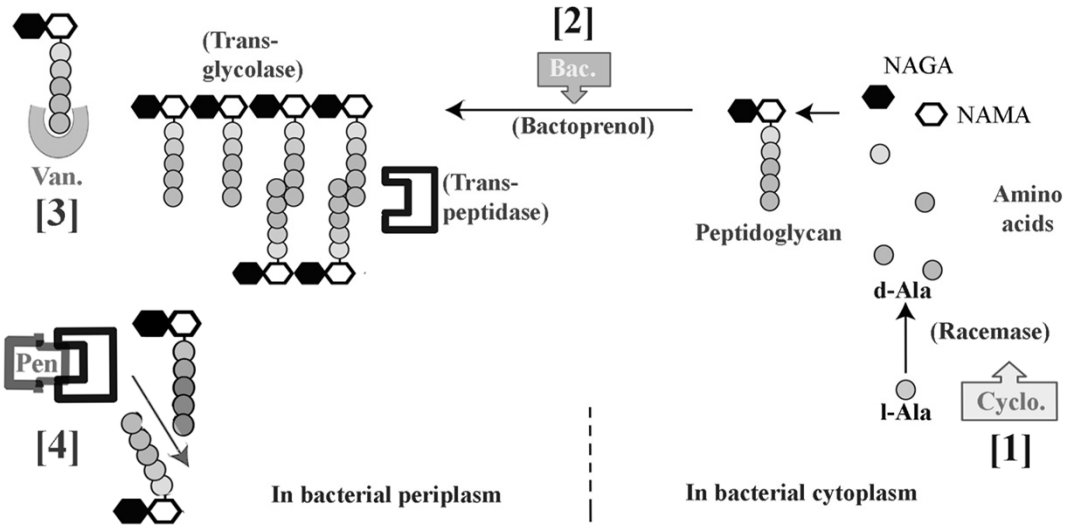
  Trimethoprim 80 mg + sulphamethoxazole 400 mg

  (Septazole®, Sutrim®, Chemotrim®, Septrin®).

CELL WALL SYNTHESIS INHIBITORS

General M.O.A:

-They interfere with synthesis of the bacterial cell wall—a structure that mammalian cells do NOT possess.



CELL WALL SYNTHESIS INHIBITORS

- The cell wall of a **Gram+ve** bacterium consists of multiple peptidoglycan strands. Each strand is a polymer of glycan units (NAGA & NAMA) joined to short peptide (alanine, lysine, glutamine, glycine, …).
- The building units of peptidoglycans (2 sugars and 5 amino acids) are formed within bacterial cytoplasm, and then transferred by a carrier named Bactoprenol to periplasmic space; where transglycolation and THEN transpeptidation occur.
- NAGA & NAMA are linked via glycosidic links mediated by Transglycolase.
- The strands are **cross-**linked via peptide links mediated by Transpeptidase.
- The cell wall of a **Gram-ve** bacterium has fewer number of peptidoglycan strands; that are surrounded by **lipopolysaccharide** layer containing channels called "**porins**".
- To be effective, inhibitors of cell wall synthesis require actively proliferating micro-organisms.
- Cell wall synthesis inhibitors include:
  - ✓ β-lactams as Penicillins (inhibit late step of peptidoglycan synthesis).
  - ✓ Others as Vancomycin, Bacitracin, Cycloserine (inhibit early steps).

CELL WALL SYNTHESIS INHIBITORS

-They include: Penicillins, Cephalosporins, & others…

PENICILLINS

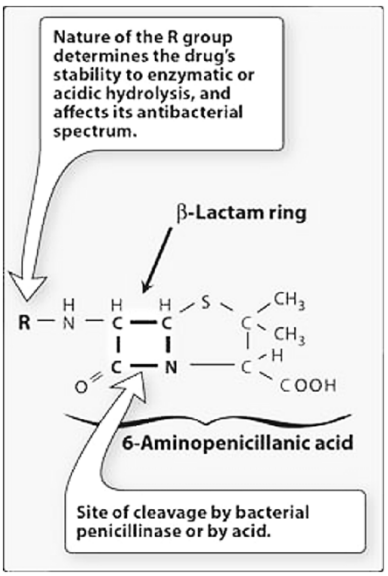
INTRO.:

-Penicillin-G was discovered by Fleming (1928) as a natural product from *Penicillium notatum* (a fungus).

-The antimicrobial activity of penicillin resides in the β-lactam ring.

-Splitting of the β-lactam ring by either acid hydrolysis or β-lactamases results in the formation of penicilloic acid, a product without antibiotic activity.

-Addition of various side chains (R) to the basic penicillin molecule creates **classes** of compounds with the same mechanism of action as penicillin but with different chemical and biological properties.



CLASSIFICATION OF PENICILLINS

A. Benzyl penicillin (Penicillin-G):

- It is a natural penicillin from *P. notatum.*
- it has the following shortage points:
  - -short duration (4-6 hours)
  - -acid-labile, destroyed by gastric acidity; NOT effective PO
  - -penicillinase- (β-lactamase-) labile; NOT effective against β-lactamase producing organisms as *Staph aureus.*
  - -narrow spectrum; NOT effective against Gram-ve bacilli
  - -low potency; dose 1 million IU/6 h, IM or IV

- **The coming derivatives or classes were derived to correct one or more of the undesired features of** Penicillin-G.

CLASSIFICATION OF PENICILLINS

B. Long acting penicillins:

- They are semisynthetic penicillins.
- They have the same shortage points of Penicillin-G except short duration.
-They include:
  -Procaine Penicillin-G; 600,000 U/12-24 h, IM
  -Fortified Procaine Penicillin-G:
    -(Penicillin-G 100,000 U + Procaine Penicillin-G 300,000 U)
    -Given IM/day
    -It has the advantages of quick onset + long duration
  -Benzathine Penicillin-G:
    -1.2 million U/month, IM
    -mainly for rheumatic fever

CLASSIFICATION OF PENICILLINS

C. Acid-resistant penicillins:

-They include Phenoxymethyl penicillin (Penicillin-V)
-It is a natural penicillin from *P. chrysogenum.*
-it has the same shortage points of Penicillin-G except acid sensitivity.
-250-500 mg/6 h, ORALLY.

D. Penicillinase-resistant penicillins:

-They include Methicillin
-It is a semisynthetic penicillin.
-It has the same shortage points of Penicillin-G except β-lactamase sensitivity.
-NOT used in therapeutics because of its nephrotoxicity.

CLASSIFICATION OF PENICILLINS

E. Acid & penicillinase-resistant penicillins:

-They are effective orally for ttt of *Staph* infections.

-They are semisynthetic penicillins.

-They have the same shortage points of Penicillin-G except acid & penicillinase sensitivity.

-They include:

-Oxacillin
-Cloxacillin
-Dicloxacillin
-Flucloxacillin

} 250-500 mg/6 h, ORALLY

-Nafcillin → 6g/day, IV, in severe *Staph* infections

CLASSIFICATION OF PENICILLINS

F. Broad spectrum penicillins (Aminopenicillins):

-They are effective against Gram+ve & Gram-ve bacteria as:

Salmonella, Shigella, Haemophilus, Helicobacter, Escherichia

-However, they are NOT effective against *Pseudomonas, Proteus, Klebsiella*

-They are semisynthetic penicillins.

-They are acid-resistant BUT penicillinase-sensitive

-They include:

Ampicillin	Amoxicillin
Incompletely absorbed from GIT	Better absorbed orally
Affected by food	Not affected by food
Useful in enteritis,	Less effective in enteritis
but affects intestinal flora	Less disturbing to intestinal flora
Of short duration (6 hours)	Relatively of longer duration (8 h.)

CLASSIFICATION OF PENICILLINS

G. Extended spectrum (Anti-Pseudomonal) penicillins:

-They are effective against Gram+ve & Gram-ve bacteria including:
Pseudomonas, Proteus, Klebsiella

-They are penicillinase-sensitive

-They are acid-sensitive except Carbenicillin indanyl

-They include:

-Carboxypenicillins:

-Carbenicillin, given IM, IV

-Carbenicillin indanyl, PO

-Ureidopenicillins:

-Piperacillin, IM, IV

H. Reversed spectrum penicillins:

-They are effective against Gram-ve bacteria *Salmonella, Shigella*
BUT NOT *Pseudomonas, Proteus, Klebsiella, Haemophilus*

-Useful in typhoid fever & urinary tract infections.

-They include:

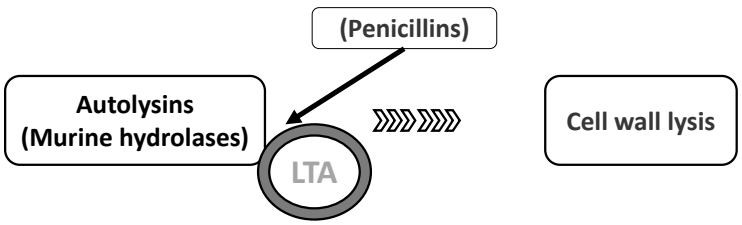
-Mecillinam, given IM, IV & Pivmecillinam, PO

PHARMACODYNAMICS OF PENICILLINS

❑ **MECHANISM OF ACTION:**

- Penicillins inhibit the synthesis of the bacterial cell wall.
- Penicillins interfere with the final step of bacterial cell wall synthesis (transpeptidation).

- Also, penicillins act as **Lipo-teichoic acid** (LTA) releaser:



❑ **ACTION:**

Bactericidal antibiotic against different bacterial spectra according to the class of penicillin described earlier.

Penicillin derivatives that can pass “porins” affect Gram-ve bacteria.

PHARMACOTHERAPEUTICS OF PENICILLINS

- **INDICATIONS:**
  - Streptococcal infections as pharyngitis, tonsillitis, …
  - Staphylococcal infections as abscesses (penicillinase-resistant)
  - Pneumococcal infections as pneumonia
  - Meningitis (penicillin-G in large doses)
  - Gonorrhea & Syphilis (Gram –ve)
  - Clostridial infections as anthrax, tetanus, gas gangrene
  - Actinomycosis
  - Bacilliary infections as cystitis, typhoid fever, *H. influenza & H. pylori* infections (broad spectrum)
  - Pseudomonal infection (extended spectrum + gentamicin)
  - Corynebacterial infections as diphtheria
- **CONTRA-INDICATIONS:**
  - Penicillin hypersensitivity

→ **PRECAUTION:**

- Sensitivity test

CEPHALOSPORINS

DEF.: β-lactam antibiotics firstly derived from the fungus *Ceph. acremonium*

CLASSIFICATION:

They are classified into **4 main** generations according to 3 bases:

-Spectrum: all broad with shifting from +ve >> to >> –ve along generations.

-Resistance: all resistant to β-lactamase but increases >> along generations.

-BBB: 1st and 2nd (except cefuroxime) do **NOT** pass;
while 3rd (except cefoperazone that is poor) and 4th **CAN** pass.

A. 1st generation:	as Cephadroxil; Cephapirin; Cefazolin; Cephradin; …
B. 2nd generation:	as Cefuroxime; Cefoxitin; Cefaclor; …
C. 3rd generation:	as Cefixime; Cefotaxime; Cefoperazone Ceftriaxone; Ceftiofur (Vet. use only)
D. 4th generation:	as Cefepime; Cefpirome; Cefquinome (Vet. Use only)
E. 5th generation:	as CeftoBiProl (*Pseudomonas);* Ceftaroline (MRSA)

ACTION & USES:

as Penicillins against susceptible bacteria.

Penicillinase (β-LACTAMASE) INHIBITORS

- **They include:**
  - **Clavulanic acid**
  - **Sulbactam**
  - **Tazobactam**
- They bind with the enzyme causing reversible inhibition
- They have weak/NO antibacterial activity
- They protect β-lactam ring from hydrolysis by β-lactamases secreted by some bacteria as *Staph aureus, Pseudomonas, Proteus, E-coli & H. influenza.*
- **Preparations such as:**
  - Clavulanic acid + Amoxicillin (Augmentin®)
  - Sulbactam + Ampicillin (Unasyn®)
  - Tazobactam + Piperacillin (Tazocin®)

CELL MEMBRANE INHIBITORS

General M.O.A:

-They interfere with synthesis and function of the bacterial cell membrane.

-They include the following:

POLYMIXINS

-They include **polymyxin B** and **polymyxin E (colistin)**.

-They are narrow spectrum active against Gram-ve bacteria.

-Owing to their significant toxicity with systemic administration, polymyxins have been largely restricted to topical use.

DAPTOMYCIN

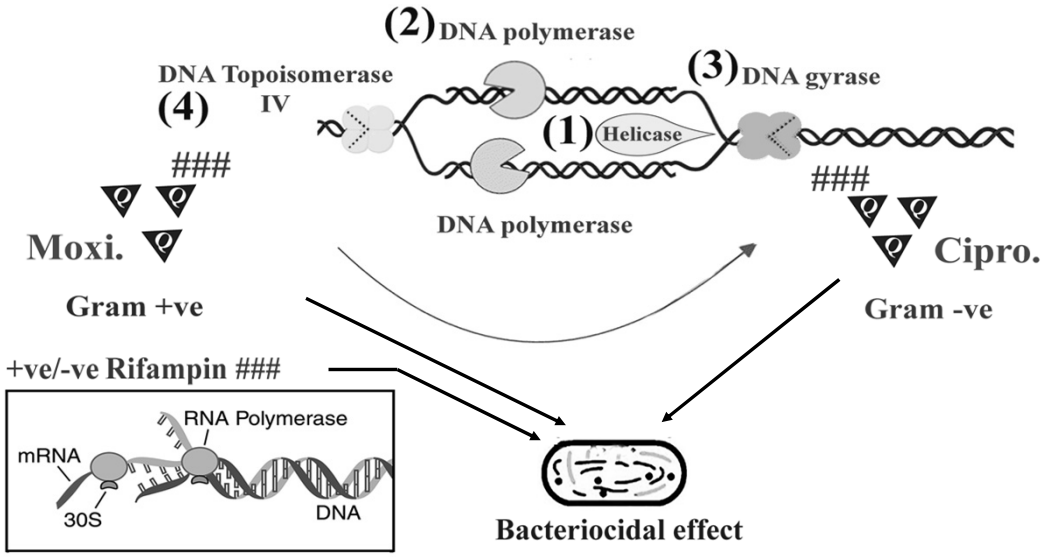
-It is a bactericidal antibiotic selectively active against aerobic and anaerobic Gram+ve bacteria.

-It binds to bacterial membranes resulting in depolarization, loss of membrane potential, and cell death. Given IV for *Staph* and *Strept.*

NUCLEIC ACID SYNTHESIS INHIBITORS

General M.O.A:

-They interfere with synthesis and function of the bacterial nucleic acids (DNA & RNA). Members are Quinolones and Rifamycins.



NUCLEIC ACID SYNTHESIS INHIBITORS

General M.O.A:

-DNA double helix is too long and thus supercoiled inside the nucleus.

-For replication, bacteria need to duplicate the DNA for the daughter cells.

-DNA helicase starts “replication fork” by separating the strands of the helix.

-DNA polymerase starts to synthesize the cDNA for each strand.

-As the replication force go forward, positive supercoils in the parent DNA are formed and accumulated impeding replication.

-To continue, DNA gyrase removes the accumulated supercoils by cuts and reversal negative twists.

-Finally, the interlink between the completed daughter DNA sets is removed by Topoisomerase-IV.

-The two new chromosome sets become apart, one for each daughter cell.

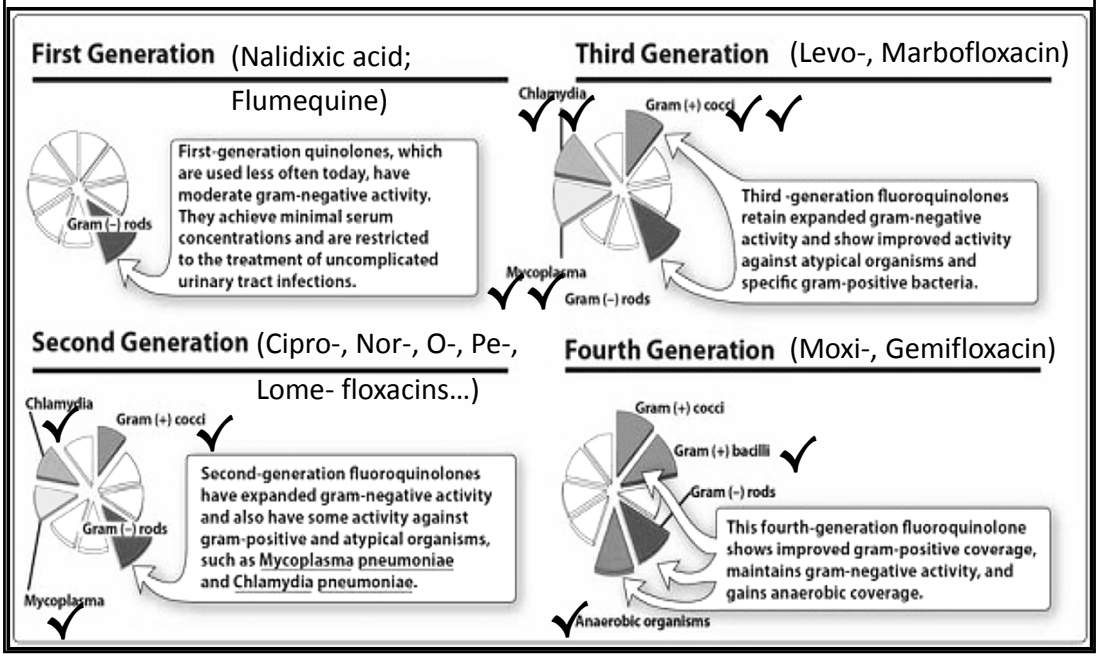
-The same process occurs partly for synthesis of mRNA by RNA polymerase in order to synthesize a needed protein.

-**These processes are inhibited by Quinolones and Rifamycins >>**

QUINOLONES

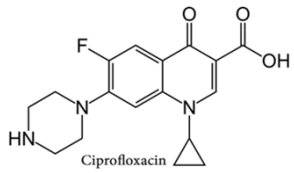
-Def.: They are synthetic antibacterials. Addition of "F" atom >> flouroquinolones.

-Classification: 4 generations acc. to spectrum & efficacy:



QUINOLONES, *contd.*

-M.O.A.: The quinolones enter bacterial cells by passive difusion & target bacterial DNA gyrase (Gram-ve bacteria as *E. coli*) & Topo-isomerase-IV (Gram+ve bacteria as *S. aureus*).



-Action: Bactericidal.

-**USES:**

-1st G: UTIs, BUT NOT *Pseudomonal*; NOW STOPPED.

-2nd & 3rd G:

-UTIs including *Pseudomonal*.

-Prostatitis -Typhoid & other GIT infections.

-URTIs & LRTIs caused by *H. influenzae, Moraxela, Mycoplasma*.

-Gonorrhea (BUT NOT syphilis).

-Chlamydiosis -Bone & soft tissue infections.

-4thG: as above + infections caused by Gram+ve bacilli & anerobes.

- Toxicity: -Disability due to tendonitis, cartilage dysplasia & neuropathy.
  -Central effects as insomnia & anxiety blockage of GABA-A receptor

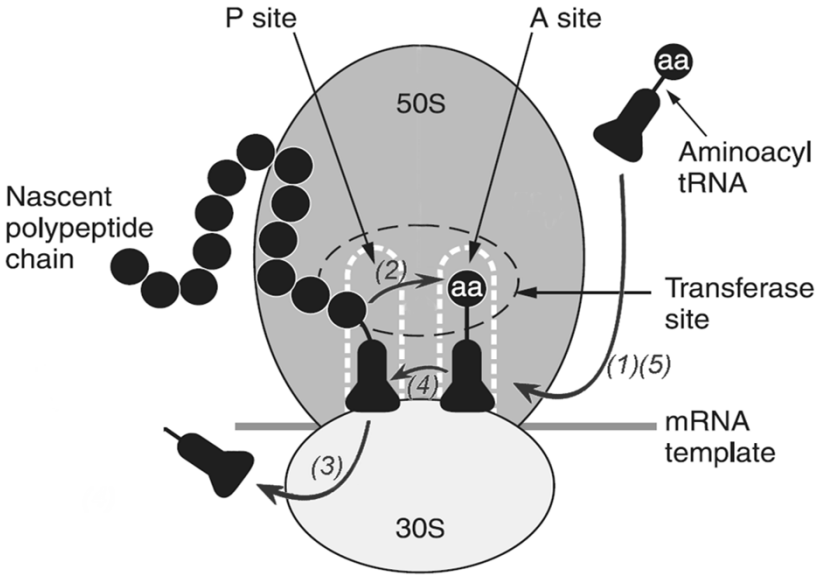
RIFAMYCINS

- Rifamycins are a group of complex macrocyclic antibiotics.
- **Rifamycin** is produced naturally from a Gram +ve bacterium known as *Amycolatopsis rifamycinica (mediterranei).*
- **Rifampicin & Rifabutin:** semisynthetic derivative; most commonly used.
- **Action:** bactericidal, against most Gram+ve & many Gram-ve microorganisms such as *E. coli, Pseudomonas, Proteus, Klebsiella, N. meningitidis, H. influenzae* & *M. tuberculosis.*
- **M.O.A.:** inhibits RNA polymerase by forming a stable drug-enzyme complex, leading to suppression of RNA synthesis.
- **Uses:** T.B (rifampin+ isoniazid) - Meningitis
- **Overdose:** - Hepatotoxicity, abdominal pains, skin rashes
  - Rifampin CYP inducer while Rifbutin not.
  - They stain all body fluids orange to red.

PROTEIN SYNTHESIS INHIBITORS

General M.O.A:

-They interfere with synthesis of protein by the bacterial cell:



(S): Svedberg unit, a measure of particle size based on sedimentation rate at high g-force.

1S = 10^{-13} seconds = 100 fs

General M.O.A:

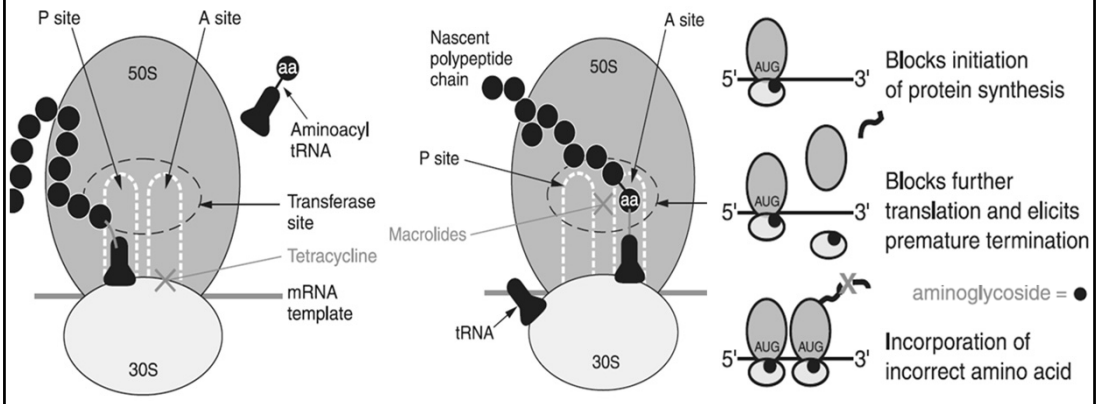
-They interfere with synthesis of protein by the bacterial cells:

- mRNA attaches to the **30S** subunit of bacterial ribosomal RNA.
- The **50S** subunit contains P (peptidyl) & A (acceptor) sites. …

- The aminoacyl tRNA charged with the next amino acid (aa) to be added to the chain moves into the A (acceptor) site (1).
- The peptidyl tRNA donates the growing peptide chain to the aa-tRNA at the A site (2).
- The tRNA, discharged of its peptide, is released from the P site (3) to make way for translocation of the newly formed peptidyl tRNA (4).
- The A site is then free to be occupied by the next "charged" aa-tRNA (5)…..

- Protein synthesis **inhibitors** bind to either 30S or 50S subunits interfering with the process. **They include the following:**
  - Aminoglycosides -Macrolides -Tetracyclines -Miscellaneous

Mechanism of action of protein synthesis INHIBITORS



Tetracyclines
bind to 30S subunit >> blocking aa-tRNA binding to the A site.

Macrolides
bind to 50S subunit >> at the peptidyl transferase site & thus inhibit transpeptidation and translocation steps.

Aminoglycosides
bind to the 30S subunit >> leading to any or all of the above outcomes.
The binding is strong and IRReversible unlike other groups.

AMINOGLYCOSIDES

- ✓ **Def:** They are antibiotics derived from *Streptomyces spp.* (with the suffix -mycin) & *Micromonospora spp.* (with the suffix -micin).
- ✓ Members: Streptomycin, gentamicin, tobramycin, kanamycin, amikacin, neomycin, ….
- ➢ They are strong bases therefore, poorly absorbed orally.

❑ **ACTION:**

- Bactericidal antibiotics against the following:

- MAINLY Gram-ve bacilli, including *Pseudomonas, Proteus & Klebsiella.*
- SOME Gram+ve cocci as β-lactamase producing *S. aureus* & *Enterococci*.
- *M. tuberculosis.*

- NOT effective against anaerobes.

❑ **PREPARATIONS & USES:**

STREPTOMYCIN:

- Used (IM) + isoniazid + rifampin for ttt of T.B.
- Used locally orally in ttt of Gram-ve enteritis.

GENTAMICIN , TOBRAMYCIN & AMIKACIN:

- Severe infections as Pneumonia, UT, Osteomyelitis, Septicemia Endocarditis, together with a penicillin.
- Topically (ointment, cream, solution) in wounds, burns,…

NEOMYCIN & KANAMYCIN :

- Used MAINLY for LOCAL use either orally or topically:
- Orally in:
  - intestinal antiseptic before operations.
  - hepatic coma with lactulose.
  - hyperlipidemia, combine with bile acids inhibiting their action and cholesterol absorption.
- Topically in: skin and mucous membrane infections.

❑ **TOXIC EFFECTS:** Nephrotoxicity, Ototoxicity, Neuromuscular blockade.

MACROLIDES

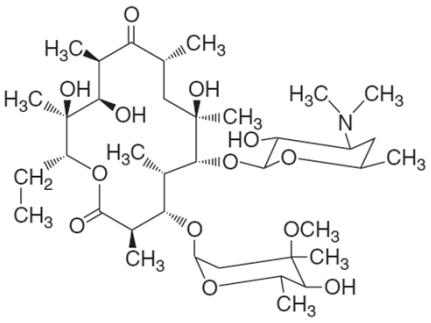
DEF.: Bacterial protein synthesis inhibitors, chemically contain a macrocyclic lactone ring, to which attached one or more deoxy sugars.

MEMBERS.:

-Erythromycin was discovered as product of *Streptomyces erythreus*.

-**Clarithromycin**, **azithromycin** & **roxithromycin** are semisynthetic derivatives of erythromycin of longer duration……

-**Tylosin, spiramycin ….** are also macrolides from different strains from *Streptomyces*.
-Tylosin>> Vet use
-Spiramycin>> Antiparasitic



ERYTHROMYCIN

-Absorbed orally; BUT acid-sensitive; so given as ENTERIC-COATED or formulated as ESTOLATE or STEARATE ESTER.

- **ACTION:**
  Bacteriostatic antibiotic against bacterial spectrum similar to penicillin including:
  - Gram+ve cocci; Gram+ve bacilli; Gram-ve cocci
  - Some Gram-ve bacilli: *H. pylori, H. flu, Bordetella pertussis.*
  - *Atypicals: Mycoplasma, Chlamydia, Treponema*

- **THERAPEUTIC USES:**
  - Infections in patients allergic to penicillin.
  - Drug of choice in *B. pertussis* (whooping cough).
  - Drug of choice in atypical pneumonia of *Mycoplasma & Legionella*.
  - Drug of choice in *Corynebacterial* infections as Diphtheria.
  - Drug of choice in *Chlamydial* infections either respiratory or genital or ocular.
  - Gonorrhea & syphilis
  - Topically in *Acne vulgaris*.

- **Adverse effects:**
  - Cholestatic jaundice (due to estolate ester).
  - Large doses cause REVERSIBLE ototoxicity.

TETRACYCLINES

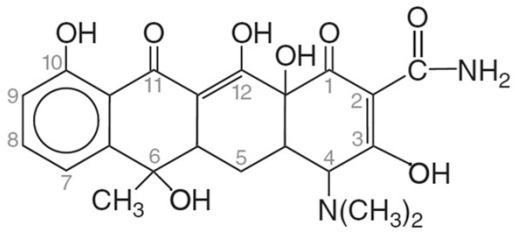
DEF.:

-Tetracycline antibiotics are inhibitors of bacterial protein synthesis; produced naturally from *Streptomyces rimosus.*

-Tetracycline consist of four fused rings conjugated with side chemical groups.

-Substitutions of these groups give different members of tetracyclines.

Tetracycline



Congener	Substituent(s)	Position(s)
Chlortetracycline	–Cl	7
Oxytetracycline	–OH,–H	5
Demeclocycline	–OH,–H; –Cl	6; 7
Methacycline	–OH,–H; CH_2	5; 6
Doxycycline	–OH,–H; $–CH_3$, –H	5; 6
Minocycline	–H,–H; $–N(CH_3)_2$	6; 7

CLASSIFICATION OF TETRACYCLINES

A. Short acting tetracyclines:

-tetracycline, chlortetracycline & oxytetracycline

-they have low lipid solubility

- serum half-life: 6–8 hours

B. Intermediate acting tetracyclines:

-demeclocycline & methacycline

-they have moderate lipid solubility

-serum half-life: 12 hours

C. Long acting tetracyclines:

-doxycycline, minocycline & tigecycline

-they have high lipid solubility

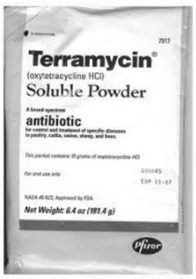
-serum half-life: 16-18 hours (doxy- & minocyclines)

36 hours (tigecycline), given IV.

- **ACTION:**

  Tetracyclines are **broad**-spectrum **bacteriostatic** antibiotics against:
  -many Gram+ve & Gram-ve bacteria, including anaerobes, *rickettsiae, chlamydiae, mycoplasmas*; (*Pseudomonas* & *Proteus* are **not** affected)
  -some protozoa, e.g, *amebas*; ….
  -some large viruses, e.g., *pox,*...

- **Absorption:**
  - Tetracyclines differ in their absorption after oral administration:
    - 30% for chlortetracycline;
    - 60–70% for tetracycline, oxytetracycline, demeclocycline and methacycline;
    - 95–100% for doxycycline and minocycline.



  - Absorption is impaired by:
    - food (except doxycycline and minocycline);
    - divalent (Ca^{2+}, Mg^{2+}, Fe^{2+}) or trivalents (Al^{3+}) cations;
    - dairy products and antacids, which contain such cations.

- **THERAPEUTIC USES:**
  - **A good** choice in infections with *Mycoplasma, Chlamydiae, Rickettsiae,…* (Infectious sinusitis in turkeys & CRD in chicken).
  - Good for gastric & duodenal ulcer disease caused by *H. pylori*.
  - Various Gram+ve & Gram-ve bacterial infections, including *vibriosis, leptospirosis, pasteurellosis, salmonellosis, mastitis, hepatitis, metritis, pneumonia, tonsillitis, bronchitis, cystitis, strangles, anthrax, ...*
  - A tetracycline (usually in combination with an aminoglycoside) is used for *plague, tularemia & brucellosis.*
  - Treatment of protozoal infections, e.g., *Entamoeba & Plasmodium. …*
  - Used topically for eye infections, *otitis externa*, burns, wounds, abscesses & other forms of pyogenic infections.

- **ADVERSE EFFECTS:**
  - Teeth discoloration, enamel dysplasia & bone deformity (in foetus).
  - Suppression of flora & overgrowth of *candida* & nonscusceptible m.o.
  - Photosensitivity (esp. demeclocycline).

MISCELLANEOUS

AMPHENICOLS

Examples: Chloramphenicol & Thiamphenicol.
Braod spectrum, Bacteriostatic.
Site: Ribosomal **50S** subunit at the peptidyltransferase site.

LINCOSAMIDES

-Examples: Lincomycin & Clindamycin.
-Similar to Erythromycin but more effective against anaerobes.
-Site: ribosomal **50S** subunit at peptidyltransferase site.
-This site is near to those of cloramphenicol & macrolide antibiotics. So, these agents interfere with each other if given concurrently.

SPECTINOMYCIN

-It binds to and acts on the **30S** ribosomal subunit.
-Its dynamics is similar to that of Aminoglycosides, but spectinomycin is NOT bactericidal and does NOT cause misreading of messenger RNA.

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