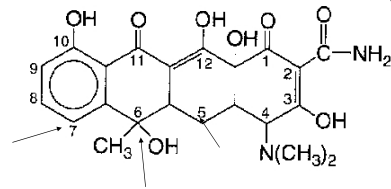


TETRACYCLINES AND CHLORAMPHENICOL

Bacteriostatic **NOT** bactericidal

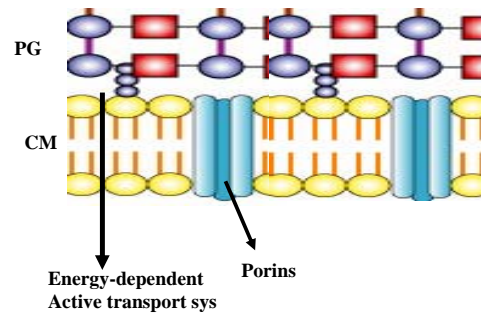
Tetracyclines



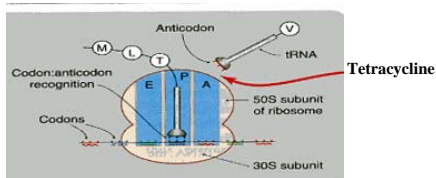
Sumycin®
Tetracyclin®
Panmycin® etc
Actisite® dental applications.

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)

Entry



I. Mechanism of antimicrobial activity:



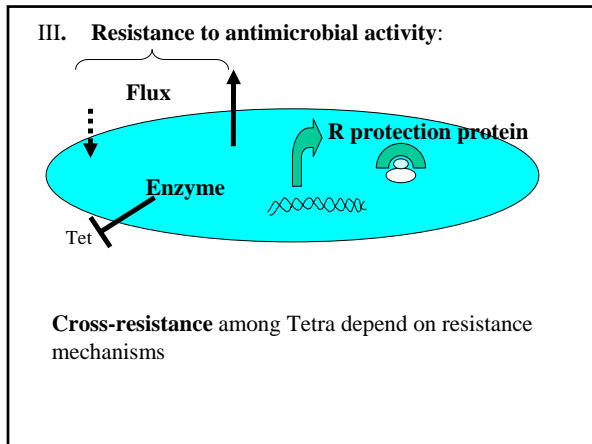
competes with tRNA for the **A site** on 30s ribosome

II. Bacterial Susceptibilities

More active against Gram (+) than Gram (-) i.e.
Haemophilus ducreyi, Brucella, Vibrio cholerae etc

Effective agnst Anerobic/ facultative bact
Actinomyces, Rickettsia, Chamydia spp., spirochaetes
and some protozoa (amoeba).

Minocycline is also effective against N.meningitidis



IV. Absorption, Distribution and Excretion

Incomplete oral absorptions
 Chlor < oxy/deme/tetra < doxy < **mino** (100%)
 absorbed in empty stomach from stomach and upper small intestine

Dairy products
 aluminum hydroxide gels,
 calcium and magnesium salts
 iron preparations

Chelate
 ↓
 Impairs absorption

ready accessible to most tissues
 cross placental barrier and enter fetal circulation and amniotic fluid
 high concentration can appear in milk
 significant concentrations found in CSF after I.V.

accumulate in:
 dentine and enamel of unerupted teeth
 reticuloendothelial cells of liver, spleen, bone marrow and bone

primary route of elimination is glomerular filtration except **doxycycline (fecal)**

doxycycline can be of value in treating patients with **impaired renal function**

Therapeutic Use

Rickettsial infections (i.e. Rocky Mountain spotted fever, typhus, Q fever)
 Mycoplasma infections
 Chlamydia infections
 Trachoma
 Anthrax
 Cholera
 Brucellosis (Tetra + rifampin/streptomycin)
 Acne (Tetra)

DOXYCYCLINE

Side Effects:

GI irritation lessen by concurrent food intake

Photosensitivity (Sun burn) more particularly with demeclocycline and doxycycline

Minocycline can produce dose-related **vestibular disturbances** such as dizziness and nausea

hepatic toxicity: Oxytetra and tetra
 (Pregnant woman more susceptible)

renal toxicity: All but less with **doxycycline**

High doses of tetracycline can decrease protein synthesis in the host cells- an **anti-anabolic effect**

discoloration of teeth in children;
can affect the baby of pregnant patients

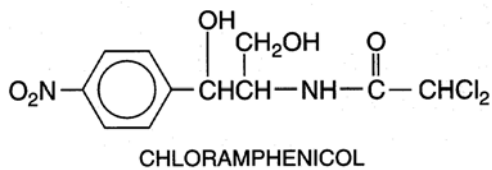
drug interaction with **penicillin's** (do not use concurrently)

Superinfection with yeast or resistant pathogenic bacteria may occur

Summary

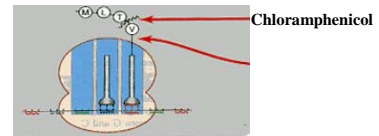
- Enter by porins/active transport sys in an energy-dependent Manner
 - Inhibit tRNA binding to A site
 - Bact develop resistance by generating ribosomal protection protein, altering fluxes, enzyme inactivation
 - Inactivation by Chelating agents
 - GI irritation, Discoloration of teeth, photosensitivity, hepatic and renal toxicity
 - Doxycycline**, most important member, broad spectrum
STDs, rickettsial infections, plague, brucellosis, RTI,
- Minocycline: Skin and soft tissue infections

Chloramphenicol (Chloromycetin)



Rapidly penetrates in bact cell (facilitative)

I. Mechanism:



Inhibits transferases

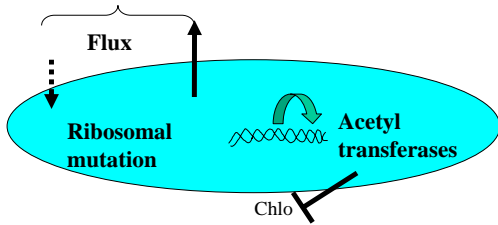
can also block **mitochondrial protein synthesis** in **mammalian** cells, especially in erythropoietic cells

II. Because of **potential toxicity**, only use in well defined and indicated conditions.

III. Antibacterial activity

- Broad; Gram (-) e.g., H. influenzae (bacteriocidal), N.meningitidis
- anaerobic bacteria
- Gram (+) cocci; clostridium
- Gram(-) rods: E. coli, V. cholerae, Shingella, Chlamydia and Mycoplasma
- **not effective** against pseudomonas, histolylica, Entamoeba

IV. Resistance:



V. Absorption, Distribution and Excretion

parent drug readily absorbed in GI tract

prodrug (chloramphenicol palmitate) hydrolyzed in duodenum

chloramphenicol succinate used for parenteral administration

readily accessible to tissues and bodily fluids

high concentration achieved in brain

enters CSF at therapeutic concentrations

Present in bile, milk, and placental fluid

metabolized in liver and inactive glucuronide metabolite excreted in urine

caution in treating patients with **hepatic cirrhosis**

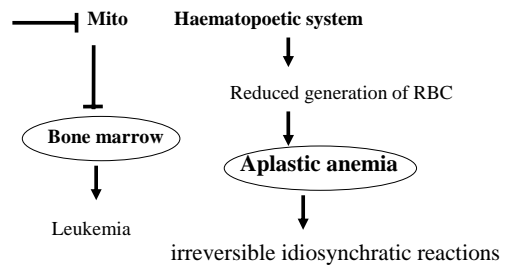
VI. Therapeutic use of Chloramphenicol

(ONLY WHEN OTHER REGIME FAILS)

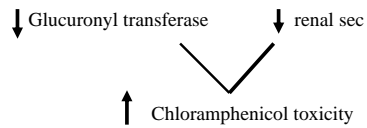
- i. Typhoid fever
- ii. Bacterial Meningitis
- iii. Certain anaerobic infections
- iv. Rickettsial diseases, e.g., epidemic, murine, scrub and recrudescent typhus, Rocky Mountain spotted fever and Q fever
- v. Brucellosis (tetracycline-sensitive patients)

VII. Untoward effects

Hematological toxicity: most important

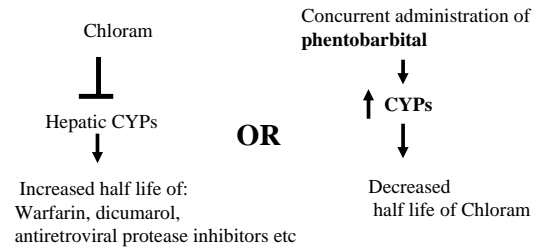


Neonatal toxicity: "**gray baby syndrome**"



interferes with iron metabolism

VIII. Drug Interactions



Summary

- Enters bact by facilitative transport
- Inhibits transferases
- Bact develops resistance by altering permeability of drug, ribosomal mutation, generation of acetyl transferases
- Induces hematological toxicity, gray baby syndrome
- rarely used in US, Europe due to toxicity
- Developing nations still use it: cheap and treat broad range of infections

alternative names in many different countries:

- Alficetyn®
- Amphicol®
- Biomycin®
- Chloromycetin® (U.S., intravenous preparation)
- Chlorsig® (U.S., eye drops)
- Fenicol®
- Kemicetine® (UK, intravenous preparation)
- Laevomycetin®
- Phenicol®
- Nevimycin®
- Tifomycine® (France, oily chloramphenicol)
- Vernacatin®
- Veticol®