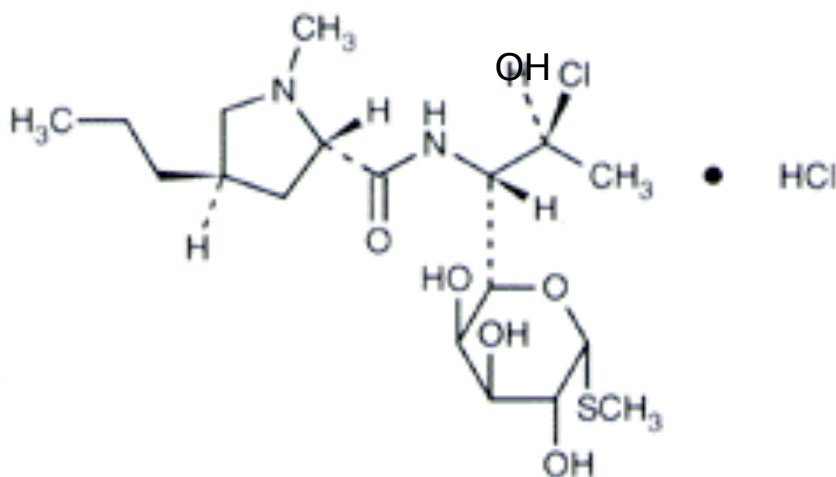
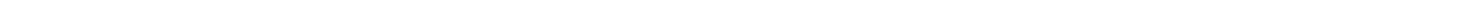




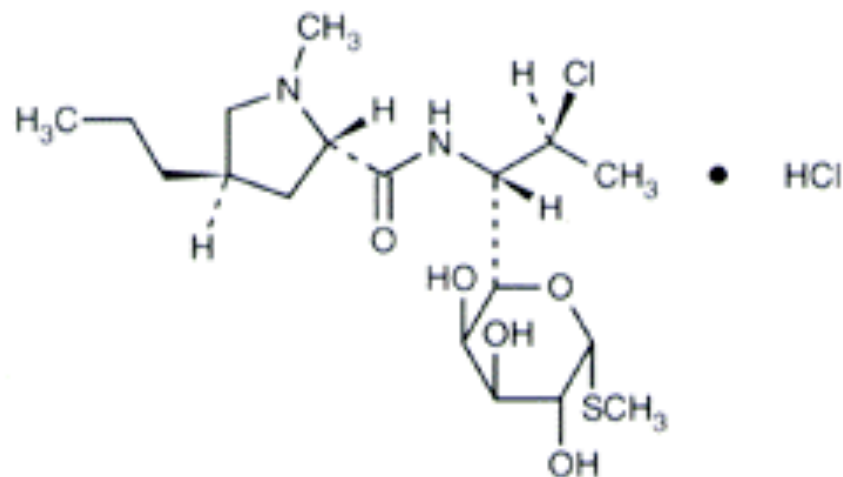
Clindamycin

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Lincomycin



Clindamycin

Clindamycin (Dalacin C)

Lincosamides

- lincomycin and clindamycin are lincosamides
- clindamycin much more active
- lincomycin seldom used

Mechanism of Action

- binds to 50 S ribosomal binding sites Same as erythromycin & chloramphenicol
- inhibits protein synthesis
(same as erythromycin and chloramphenicol
- may be cross - resistance)
- Bacteriostatic / Bactericidal



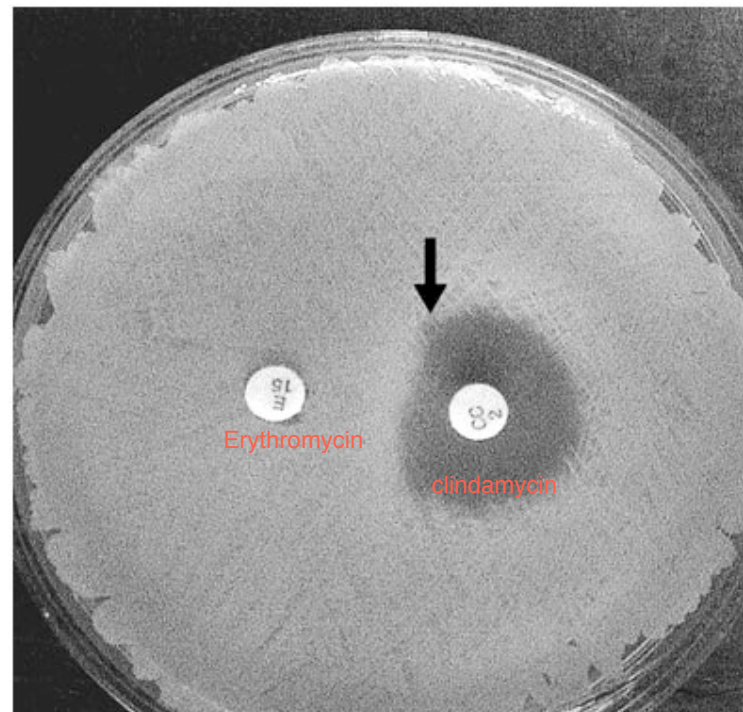
Resistance

- 1) *Alteration of 50S ribosomal receptor site
(cross resistance with macrolides)
- 2) * Alteration of 23S ribosomal RNA of 50S
ribosomal subunit
(Plasmid mediated MLS_B - *S. aureus*, *B. fragilis*)
Transposon Clindamycin's claim to fame was actually its activity against anaerobes.
- 3) Enzyme inactivation (adenylation of
lincosamide by staphylococci (more lincomycin)
(decreased activity of clindamycin)
- 4) Intrinsic resistance with enterobacteraciae and
Pseudomonas

D-test for Erythromycin Cross-Resistance

Looks for cross-resistance with erythromycin

NOT ON EXAM



Results: resistance to erythromycin and we also see that erythromycin also inhibits clindamycin activity

Spectrum of Activity

- Staphylococci (All) (77% 2011 Community). Main use
- (CA-MRSA 70%), (CNS 55%) ←
- **Streptococci**, *S. pneumoniae* (87% 2011), *S. pyogenes* (89%)
(not enterococci) However, not usually used here Not used primarily here-- just an alternative
- NO ACTIVITY AGAINST GM (-) RODS!!!!
- **most anaerobes** including
 - *B. fragilis* (some resistance)
 - Clostridia (but *C. difficile* resistant) C. diff is resistant to many drugs anyway
 - Actinomyces
- other - *Gardnerella vaginalis* First line treatment -- semi common cause of vaginitis
Toxoplasma, *Pneumocystis jirovecii*,
Plasmodia, unusual group of organisms
- all gram negative aerobic bacteria & enterococci are resistant

Activity

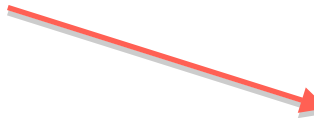
- ❑ Clindamycin is particularly noted for its activity in reducing toxin production in

Toxin-producing
strains



S. aureus

One of the drugs
used in necrotizing
fasciitis



S. pyogenes

Useful in the treatment of necrotizing fasciitis due to this effect.

Kinetics

- palmitate ester orally (rapidly hydrolyzed to active base)
- excellent absorption orally (**90%**)
 - slightly delayed but not reduced with food
 - excellent for '**step-down**' therapy
- phosphate for parenteral use
- well absorbed from I.M. site (little pain)

Kinetics

- ❑ good penetration into most tissues
 - ❑ (good levels brain not CSF)
 - ❑ (good levels in bone & abscesses)

- ❑ most metabolized in liver (85%)
 - ❑ some active metabolites
 - ❑ some excreted in urine

- ❑ $t_{1/2}$ 2.4 hr (6 hr in renal failure)

Adverse Effects

Nausea

- may limit oral dose
- 450 mg q6h better tolerated than 600 mg q8h

Diarrhea

- up to 20%
- more common with oral

Pseudomembranous Colitis

- 0.01-10% (not dose related)
- may occur more commonly after oral or parenteral therapy than other antibiotics

Adverse Effects - Other

Allergic Reactions

- ❑ Rashes (10% may develop maculopapular rash, fever)
- ❑ rarely anaphylaxis

Hepatotoxicity

- ❑ ↑ transaminases - reversible
- ❑ hepatocellular damage - rare

Neutropenia, Thrombocytopenia & Agranulocytosis
reversible rare, ? unrelated

Indications

Polymicrobial Infections

- intra-abdominal or pelvic infections

(as treatment or prophylaxis in combination for anaerobic coverage)

- Osteomyelitis, diabetic foot ulcers
- Aspiration pneumonia
- Dental Infections

Because of its
anaerobic
coverage

Necrotizing Fasciitis

- (toxin producing Grp A Streptococci)

Indications

- ❑ Alternative for *B. fragilis*
- ❑ Alternative for MSSA, MRSA, *S. pneumoniae* and *C. perfringens* , *Strep pyogenes*
- ❑ Topically in acne
- ❑ **Vaginally - bacterial vaginosis (Gardnerella)**
- ❑ Other- Alternative in treatment of *Y. pestis*
toxoplasmosis of CNS, alternative malaria,
alternative with primaquine for Pneumocystis

Dosing

Dose Normal Adults

Oral

- 150-300-450 mg q6-8h

Parenteral (give slowly)

- 600mg q8h
- Life threatening infection up to 4.8 g/day

Interactions

- ❑ antagonism between erythromycin and clindamycin
- ❑ may enhance the effects of neuromuscular blocking agents

ORAL ANAEROBES:

- bacteroides (forsythus)
- Prevotella
- Porphyromonas
- Fusobacterium

Found on mucosal surfaces, in tonsillar crypts, crypts of the tongue, dental plaque, gingival crevices