B. CEPHALOSPORINS

1. Development

2. Properties
   a) broad spectrum
   b) low toxicity
   c) Staph beta lactamase (penicillinase) resistant but not agent of choice for Staph.
   d) Generations
      1st - better Gm(+) than Gm(−) activity, susceptible to most Gm(−) beta lactamases; now are generic
      2nd - more resistant to Gm(−) beta lactamases some are generic now
      3rd - increased potency and penetration and resistance to Gm(−) beta lactamses; some have activity against Pseudomonas
      4th - even more than 3rd, active against Pseudomonas
   e) cleared renally (except cefoperazone)
   f) Probenecide ↓ elimination rate but rarely used
   g) distribution – similar to Pen G except that only cefuroxime and some 3rd and 4th generation penetrate CNS
   h) metabolism 5-30%
   i) toxicity – like the penicillins, is generally low
      i. renal – low but significant in patients with impaired renal function
      ii. GI overgrowth, colitis
      iii. bleeding – those cephalosporins with the methyl tetrazole ring (cefamandol, cefotetan, cefmetazole, cefoperazone) have some risk of bleeding.
         Mechanisms involve (1) decreasing gut flora and therefore vitamin K, (2) direct interaction with prothrombin, and (3) platelet dysfunction. The phenomenon is best associated with Moxalactam (2-3% with fatalities reported) (no longer on the market) but is possible for any cephalosporin with the methyl tetrazole ring.
      iv. disulfuram like reaction – cephalosporins with the methyl tetrazole ring have the potential to inhibit ADH resulting in a sick feeling when alcohol is taken with these drugs or up to 72 h after
      v. C. difficile overgrowth is possible → diarrhea, colitis, pseudomembranous colitis

3. Absorption – some orally absorbed; others IM or IV

4. Allergy – 5-10% cross reactivity with penicillin allergy

5. Cephalosporin spectrum
   a) Gram-positive – including penicillinase producers (older 1st generation better here)
      i. Staph – but penicillinase resistant penicillins are agents of choice
      ii. Strep but not Enterococcus faecalis or E. faecium
      iii. otherwise similar to Pen G except less potent
      iv. not MRS
b) Gram-negative (2\textsuperscript{nd}, 3\textsuperscript{rd}, 4\textsuperscript{th} generations are better)
   i.  \textit{E. coli} - usually sens.
   ii. \textit{Proteus}; 2\textsuperscript{nd} and 3\textsuperscript{rd} generation also active against \textit{Morganella, Providencia,} and \textit{Serratia}.
   iii. \textit{Salmonella}
   iv. \textit{Shigella} – usually sens.
   v. \textit{Neisseria meningitidis} – useful if ceph. will enter CSF
   vi. \textit{Neisseria gonorrhoeae} – OK, particularly ceftriaxone and cefixime which are agents of choice
   vii. \textit{H. influenza} – 2\textsuperscript{nd}, 3\textsuperscript{rd} and 4\textsuperscript{th} generations are better
   viii. \textit{Klebsiella} – \textit{K. pneumonia} – usually sens., and is important use of Ceph.
   ix. \textit{Enterobacter and Pseudomonas} – only 3\textsuperscript{rd} and 4\textsuperscript{th} generations; sensitivity varies
   x. \textit{Anaerobes} – Cefoxitin, cefmetazole, cefotetan and some 3\textsuperscript{rd} generation only

6. Use
   a) respiratory infections – gram-positive and gram-negative, Klebsiella
   b) sepsis – especially mixed infections using 3\textsuperscript{rd} or 4\textsuperscript{th} generations
   c) surgical prophylaxis – first or 2\textsuperscript{nd} generations
   d) meningitis – some will penetrate CSF and cover \textit{E. coli, Klebsiella pneumoneae, Serratia, and Neisseria meningitidis}
   e) UTI – very high renal conc.
   f) alternate drug for penicillin allergic patient, for penicillinase resistant penicillins, for staph infections

![Structure of Oral Cephalosporins](image)

<table>
<thead>
<tr>
<th>generation</th>
<th>name</th>
<th>brand name</th>
<th>structure</th>
<th>dose</th>
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<td>cephalexin</td>
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<td>R&lt;sub&gt;2&lt;/sub&gt;</td>
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<td>------------</td>
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<td>-CH&lt;sub&gt;2&lt;/sub&gt;-</td>
</tr>
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<td>Cefotan®</td>
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<td>-CH&lt;sub&gt;2&lt;/sub&gt;-</td>
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<td>-CH&lt;sub&gt;2&lt;/sub&gt;-</td>
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<td>-H</td>
</tr>
</tbody>
</table>
7. Formulary Oral Cephalosporins

   a) General comments: used for follow-up and ambulatory patient therapy, UTI (pen. Allergic), otitis media, staph. URI, LRI

   b) First Generation

   Cephalexin Keflex ® Distax and generics

   ![Chemical Structure]

   Indications:
   1) respiratory tract – *Strep. pneumoniae* and *Strep. pyogenes*
   2) otitis media – *Strep. pneumonia, H. flu, M. cat.* (the *H. flu* and *M. cat* may be resistant)
   3) skin – *Staph., Strep.*
   4) bone – *Staph., Proteus mirabilis*
   5) GU – *E. coli, Klebsiella, Proteus mirabilis*

   c) Second Generation – not on formulary in 2005

   Cefuroxime Axetil Ceftin® Glaxo Wellcome and generic

   Broad spectrum oral cephalosporin that gets into CNS

   Indications:
   1) pharyngitis and tonsillitis – *Strep. pyogenes*
   2) otitis media – *Strep. pneumoniae, M. cat., H. flu*, including β-lactamase producing
   3) sinusitis – *Strep. pneumoniae, H. flu*
   4) exacerbation of chronic bronchitis – *Strep. pneumoniae, H. flu, H. parainfluenzae*
5) UTI – *E. coli, Klebsiella, Proteus*
6) skin – *Staph., Strep.*
7) GU – *E. coli, Klebsiella, Proteus*
8) impetigo – *Staph., Strep.*

d) Third Generation

Cefpodoxime proxetil  Vantin® Pharmacia

Broad spectrum, beta lactamase resistant cephalosporin with an unusual structure
Indications:
1) acute CAP  Strep. pneumo, H. flu, M. cat
2) chronic bronchitis  Strep. pneumo., H. flu, M. cat
3) otitis media
4) pharyngitis
5) STD - N. gonorrhoeae, 200mg stat single dose
6) uncomplicated skin infections  Staph., Strep. pyogenes
7) UTI

e) cefdinir  Omnicef ® Abbott – suspension only is on formulary; good taste

8. Formulary parenteral Cephalosporins

a) First Generation

Cefazolin Ancef ® SKF  Kefzol ® Lilly and generic
T1/2 = 1.8 h.
0.5 – 1 g q. 8 h.
1M or IV

b) Second Generation

Cefotetan Cefotan ® Stuart
1) good anaerobic activity; this is its utility
2) q 12 h dosing
3) bleeding and antibuse effect possible although rare

Cefuroxime generic
1) introduced in 1984
2) T1/2 = 1.5 h. ∴ q. 8 h. dosing
3) penetrates CSF well and ∴ used successfully for meningitis

c) Third Generation

Cefotaxime Claforan ® Hoechst-Marion Roussel
1) desacetyl metabolite is active ∴ high urine levels
2) T1/2 - ~ 1 h. q. 4-6 h. doses
Ceftriaxone Rocephin ® Roche
1) very active against N. gonorrhea – 250 mg stat dose used
2) penetrates CSF
3) T1/2 6-8 h. . . once a day dose used
4) convenient, potent antibiotic; not the best for Pseudomonas infections

Ceftazidime Fortaz ® Glaxo
Tazidime ® Lilly
1) good Pseudomonas activity
2) penetrates CNS
3) BID – TID dose

d) Fourth Generation

Cefepime Maxipime ® Bristol-Myers Squibb
1) is more resistant to beta lactamases than others
2) relatively resistant to chromosomal beta lactamases and does not induce these enzymes like other cephalosporins
3) good Gm (+) activity as well
4) note: now has an FDA warning of neurotoxicity (encephalopathy, myoclonus, seizures). Mostly observed in patients with renal impairment.
C. CARBAPENEM ANTIBIOTICS

1. General Comments
   a) lack the sulfur in the 5-membered ring but still retain the beta lactam bond
   b) are similar in structure to penicillins but have a spectrum broader than penicillins and cephalosporins
   c) bind to PBP 1 & 2 of Staph aureus
   d) are very resistant to beta lactamases
   e) MRS and PRSP are resistant because of altered PBP’s
   f) some Pseudomonas are resistant due to altered porin channels
   g) E. faecalis is usually resistant and E. faecium is almost always resistant
   h) meropenem and ertapenem are the carbapenems on the UW formulary
   i) none are absorbed orally
   j) The drugs induce chromosomal beta lactamases though they are not hydrolyzed. Don’t switch to a cephalosporin after carbapenem therapy

2. Imipenem/Cilastatin Primaxin ® MSD

   a) the first carbapenem available
   b) Cilastatin inhibits renal dipeptidase which would otherwise inactivate the antibiotic in urine
   c) 0.5 g q. 6 h. is a common IV dose
   d) not approved for meningitis due to risk for seizures (~1.5%) but has 9 approved indications
   e) nausea if push IV dose too fast


   a) for now only indicated for intra-abdominal infections caused by Strep. viridans, E. coli, K. pneumoniae, P. aeruginosa, B. fragilis, B. thetaiotaomicron Peptostreptococcus, and bacterial meningitis caused by Strep. pneumonia, H. flu, N. meningitidis
   b) less seizures (0.4%) and less nausea than imipenem
   c) 1 g q 8h
   d) not MRS or PRSP
4. Ertapenem Invanz ® Merck, approved Nov 2001 - formulary

\[
\text{CH}_3 \quad \text{OH} \quad \text{H} \quad \text{CH}_3 \\
\text{N} \quad \text{C} \quad \text{N} \quad \text{C} \\
\text{S} \quad \text{N} \quad \text{C} \quad \text{O} \\
\text{Na}^+ \quad \text{H}_2 \quad \text{O} \\
\text{COO}^- \quad \text{COO}^- \\
\text{H}_3\text{C} \\
\]

a) 1 g q d dosing IV or IM
b) has Gram(+), Gram(-) and anti-anaerobic activity; not MRS or PRSP
c) FDA approved for
   1) complicated intraabdominal infections
   2) complicated skin infections
   3) complicated UTI
   4) pelvic infections
   5) community acquired pneumonia
D. MONOBACTAM ANTIBIOTICS

1. Aztreonam Azactam ® Squibb

   a) synthetic

   b) mostly gram-negative aerobic spectrum (similar to an aminoglycoside); has 8 approved indications for Gram Neg. infections

   c) defined, narrow, useful spectrum

   d) binds to PBP3

   e) highly resistant to β-lactamases and does not induce these enzymes

   f) dose 1-2 g q 8-12 h.

   g) no cross allergy with penicillins

   h) is on the UW formulary
E. **VANCOMYCIN (UW Formulary drug)**

1. Chemistry-History

Vancomycin is a glycopeptide antibiotic (MW=1450) isolated from Streptomyces orientalis. It was introduced in 1956 for use in penicillinase producing Staph. The spread of methicillin resistant Staph. (MRS) and Enterococcus has made Vancomycin an important drug. The original product was rather impure and associated with hypersensitivity, ototoxicity, and nephrotoxicity. In 1986 a new highly purified formulation was introduced that has fewer adverse effects.

2. MOA

Inhibits the attachment of the phospholipid pentapeptide to the cell wall acceptor (see earlier notes)

Binds to d-ala-d-ala of peptidoglycan monomer

Is bacteriocidal for growing cells

3. Spectrum

Has a rather narrow but useful spectrum against Gram-positive bacteria. No cross resistance with other cell wall inhibitors.

   a. Staph aureus and Staph epidermidis including MRS and beta lactamase producing strains. Synergistic with aminoglycosides.

   b. *Enterococcus faecalis* and *Enterococcus faecium*. Synergistic with aminoglycosides; vancomycin resistant Enterococcus (VRE) is a worry. *E. faecium* resistance is common but this is a less common infection.

   c. Anaerobes. Used for *Clostridium difficile* as alternative to metronidazole. Is a "stronger" treatment.

   d. Strep. - is alternative agent for serious infections resistant to other agents
4. Uses

   a. Agent of choice for methicillin res. Staph and Staph epidermidis. May be combined with an aminoglycoside or rifampin for MRS.

   b. As alternative drug for endocarditis caused by Strep or other serious Strep infections resistant to beta lactams (e.g. PRSP).

   c. As important drug for use against Enterococcus faecalis. Combine with an aminoglycoside.

   d. C. difficile. The dose is 500 mg QID x 10d or 125 mg QID x 10d Metronidazole is preferred for initial infections.

      C. difficile MIC for vanco is ~ 4 µg/ml. The concentration of vancomycin in stool with 500 mg QID is ~ 3.1 mg/ml.

5. Resistance

   Fortunately, resistance is rare at present but is increasing. "Van A" gene codes for decreased binding. "Van B" and "Van C" also. "Van A" codes for d-ala-d-lactate instead of d-ala-d-ala.

6. Disposition and Excretion

   Poor oral absorption. Rather poor CNS penetration. Renally cleared and dose must be adjusted in renal disease.

7. Adverse Effects

   a. Hypersensitivity reactions, rash, 3%

   b. Phlebitis, 13% (rarely used IM due to irritation)


   d. Ototoxicity. Rare now but be careful in older patients and when drug is used with aminoglycosides.

   e. Nephrotoxicity. Reversible and often associated with use of Vanco with aminoglycosides.

8. Products

   Vancocin ® (Lilly) and now generic products. As capsules (remember this is topical gut therapy only), powder for oral solution and powder for injection, the capsules are mainly used for C. difficile.

9. Teicoplanin Targocid ® Hoechst-Marion Roussel (not UW formulary drug)

   - Glycopeptide with structure similar to vancomycin
   - Similar antimicrobial spectrum although pathogens with "Van B" or "Van C" genes will be resistant to vancomycin but sensitive to teicoplanin. "Van A" gene codes for resistance to both.
   - Has longer T1/2 (can give qd), can be given IM, and is less irritating when given IV.
F. FOLIC ACID ANTIMETABOLITES

SULFONAMIDES AND TRIMETHOPRIM

1. MOA – competitive inhibitor for PABA in the biosynthesis of folic acid; bacteriostatic
2. Biosynthesis of folic acid in bacteria
Mammalian cells take up preformed folic acid or dietary folates by an active transport process. Bacteria do not have this transport and hence make their own folic acid.
2. Spectrum – have rather broad spectrum of antimicrobial activity, are bacteriostatic drugs and don’t work well in purulent infections due to the presence of thymine and purines. Because of their long history of use, resistance is a problem. They are commonly used to treat acute UTI. The combination with trimethoprim is more useful in therapy (see below).
   a) *E. Coli*
   b) *Proteus mirabilis*
   c) *H. influenza*
   d) *N. meningitidis* - now largely resistant and ideally you want a bacteriocidal drug
   e) *toxoplasma gondii*
   f) etc., but development of resistance has lessened the contribution these agents make to therapy; still useful in uncomplicated UTI and together with trimethoprim (see below) in a variety of infections. Have little activity against anaerobes and because of their bacteriostatic activity, are not used for strep infections.

3. Excretion - renal; metabolism is via hepatic acetylation - slow acetylators may experience increased toxicity

4. Distribution - penetrates into CNS and middle ear and prostate gland

5. Adverse Reactions - hypersensitivity reactions to sulfas → rash, eosinophilia, fever; crystalluria, kernicterus, hemolytic anemia in glucose-6-phosphate dehydrogenase def. patients, rare Stevens Johnson Syndrome; photosensitivity reactions may occur. Due to risk of kernicterus, not for infants < 2 mos. of age.

6. Products systemic
   a) sulfisoxazole - UTI drug
   b) sulfadiazine - chloroquin resistant Plasmodium falciparum (malaria)
   c) trimethoprim-sulfanethoxazle - see below
   d) sulfadoxine-pyrimethamine Fansidar® Roche - chloroquin resistant Plasmodium falciparum
   e) sulfadiazine-pyrimethamine - toxoplasmosis
   f) pyrimethamine - malaria (resistance ↑)
   g) trimethoprim - UTI
   h) Dapsone - leprosy
7. UW formulary sulfur drugs and combinations
   
a) Sulfisoxazole-Gantrisin ® Roche and generics: 2–4 g stat, then 1 g q. 4–6 h; 3% require discontinuation due to rash, fever, and GI upset; T1/2 = 5 h

```
\[
\begin{align*}
H_2N & \quad \text{H}_3C \\
\text{S} & \quad \text{H} \\
\text{N} & \quad \text{N} \\
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O}
\end{align*}
\]
```

b) Trimethoprim - Sulfamethoxazole (TMP-SMX)
   Co-Trimazoloe Bactrim ® Roche Septra ® BW generic

```
\[
\begin{align*}
H_2N & \quad \text{O} \\
\text{N} & \quad \text{O} \\
\text{NH}_2 & \quad \text{O} \\
\text{N} & \quad \text{O}
\end{align*}
\]
```

**Table 7–4. Binding of trimethoprim to bacterial and mammalian dihydrofolate reductases.** Folate reductase, purified from bacteria or from mammalian livers, was incubated with 50 μM dihydrofolate, NADPH, and varying concentrations of trimethoprim. Enzyme activity was recorded by the change in absorbance at 340 nm. The values in the table represent the concentrations of trimethoprim required for 50% inhibition of the enzyme activity. Thus, 60,000 times as much trimethoprim is required to inhibit the human enzyme as is required to inhibit that of *E. coli*.

<table>
<thead>
<tr>
<th>Source of enzyme</th>
<th>Trimethoprim concentration required for 50% inhibition (nM)</th>
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<tbody>
<tr>
<td><strong>BACTERIAL</strong></td>
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<tr>
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<tr>
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<td><em>Proteus vulgaris</em></td>
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</tr>
<tr>
<td>Rabbit</td>
<td>370,000</td>
</tr>
<tr>
<td>Human</td>
<td>300,000</td>
</tr>
</tbody>
</table>

*Source: Data from Burchall and Hitchings.*

1) A 1:4 ratio of TMP-SMX; double hit on bacterial folate coenzyme biosynthesis
2) T1/2 for both is 10-16 h. BID dosing
3) Spectrum
   - includes sulfur drug spectrum but has broader activity due to decreased resistance to this combination
   - *E. coli*, other Enterobacteriaceae, Klebsiella, Enterobacter, Morganella, Proteus vulgarus, Proteus mirabilis, *H. Influenzae*
   - Pneumocystis carinii
   - Strep. pneumoniae maybe
   - MRSA may be sensitive
   - Shigella
   - Salmonella
4) Uses
   - UTI
   - Salmonella
   - Pneumocystis carinii pneumonia - in HIV infected patients; used for prophylaxis treatment
   - otitis media
- bronchitis
- traveler’s diarrhea
- acute and chronic prostatitis

5) Adverse effects: No more than SMX alone; possible rash, pruritis, GI upset; if patient is low in folic acid, can cause megaloblastic anemia (folate dep.)

c) Trimethoprim alone (Proloprim ® BW, Trimnex ® Roche) for sulfa allergic patient; FDA allowed indications as "For initial episodes of acute, uncomplicated UTI due to susceptible strains"

d) Diaminodiphenylsulfone (dapone)

- has high affinity for PABA site in synthesis of folic acid in Mycobacterium leprae but low for other bacteria
- sometimes used alone or in combination with TMP-SMX for Pneumocystis carinii pneumonia.
- diminished use as a single agent for significant infections due to ↑ resistance

h) Pyrimethamine

- is a folic acid antagonist for Plasmodium sp.
- used with sulfadoxine (Fansidar®) for prophylaxis for malaria
G. METRONIDAZOLE, FLAGYL® SEARLE and generics; is UW Formulary drug

\[
\begin{align*}
\text{CH}_2-\text{CH}_2\text{OH} \\
\text{O}_2\text{N} - \text{N} - \text{CH}_3 \\
\end{align*}
\]

a) History - primarily developed for protozoal infections

b) Metabolism - "suicide substrate" for anaerobes

\[
\begin{align*}
\text{O}_2\text{N} - \text{N} - \text{CH}_3 & \quad \text{liver} \quad \text{P-450} \\
\text{CH}_2-\text{CH}_2\text{OH} & \quad + \\
\text{O}_2\text{N} - \text{N} - \text{CH}_3 & \quad \text{CH}_2-\text{CH}_2\text{OH}
\end{align*}
\]

\[
\frac{2 \text{e}^-}{2 \text{H}^+} \quad \text{nitroreductase (anaerobic bacteria and protozoa)} \\
\text{low redox potential}
\]

\[
\begin{align*}
\text{R} - \text{N} = \text{O} & \quad \text{reactive intermediates} \\
\text{R} - \text{NHOOH} & \quad \text{cell damage}
\end{align*}
\]

\[
\begin{align*}
\text{H}_2\text{N} & \quad \text{CH}_2-\text{CH}_2\text{OH} \\
\text{O}=\text{CH} & \quad + \\
\text{COOH} & \quad \text{CH}_3 \\
\text{NH} & \quad \text{C}=\text{O} \\
\end{align*}
\]

2-hydroxyethyl oxamic acid

acetamide

c) Spectrum

1) excellent activity against gram-negative anaerobic bacilli, e.g. Bacteroides, also gram-positive anaerobes

2) antiprotozoal

3) has bacteriocidal activity

d) Properties

1) well absorbed and good tissue levels and CSF levels
e) Uses

1) *Trichomonas vaginalis* "Tric"
   - 2 g stat dose or 4 tabs BID x 1d or 250 mg TID x 7d; treat male partner also
2) *Amebiasis (Entamoeba histolytica)* – 750 mg TID x 10d
3) Giardiasis - 250 mg TID x 7
4) anaerobic bacterial infections - IV use for serious infections
5) Bacterial vaginosis (BV) – associated with *Gardnerella vaginalis* and many anaerobes - 0.5 g BID x 7, also 2 g stat dose
6) *Helicobacter pylori* - used together with tetracycline and Bismuth, or amoxicillin or clarithromycin
7) *Clostridium difficile* - 1 g/d x 10d; is "first time" therapy
8) topical use in acne
9) CNS infections, often together with another antibiotic to cover aerobes

f) Adverse effects

1) metallic taste, nausea, disulfuram reaction, rare peripheral neuropathy
2) is CYP2C9 inhibitor therefore interactions with warfarin, tolbutamide, diclofenac, etc.
3) teratogenic  
4) carcinogenic  
   { CDC now considered safe but prudent use is warranted as long term, high dose feeding to rats and mice result in tumors}
H. Bacteriostatic Inhibitors of Bacterial Protein Synthesis

CLINDAMYCIN (Formulary Drug)

\[
\text{CH}_3 - \text{CH}_2 - \text{H}_2 \text{C} - \text{CH}_3
\]

1. Chemistry

Clindamycin is a derivative of Lincomycin, an antibiotic from a soil organism found near Lincoln, Nebraska by workers at Upjohn (then Pharmacia, then Pfizer).

2. Mechanism of Action

a) Binds to the 50S ribosomal subunit (a site shared by macrolides and chloramphenicol) to prevent translocation. It is bacteriostatic but is ‘cidal in high conc. Cross resistance to other drugs binding to 50S ribosomal subunit exists (macrolides & chloramphenicol).

b) Is metabolized in humans to a N-demethyl inactive metabolite and excreted in urine. Not for urinary tract infections. Sulfation of OH group also occurs.

3. Spectrum

a) Gram-positive cocci, especially Strep. Staph may be sensitive although resistance is important. Enterococcus faecalis is resistant.

b) Anaerobes. This is a big feature of this antibiotic. Good activity against Bacteriodes fragilis and other Bacteriodes sp. Active against other anaerobes and Propionibacterium acnes.

c) Parasites. Toxoplasma gondii and Pneumocystis carinii (alternative drug)

d) Others. Gardnerella vaginalis, Chlamydia trachomatis (alternative drug)

e) Gram (−). resistant (doesn’t get in)

f) Resistance can occur by production of methylated ribosomal binding sites for clindamycin. MRS is resistant to clindamycin.

4. Uses

a. As an alternative drug for treatment of serious Strep and Staph infections in the penicillin allergic patient. Not 1st or 2nd line drug

b. Use for nectrotizing faeciitis
c. An important drug for serious anaerobic infections particularly B. frag.; good penetration into bone

d. Topical treatment for acne

e. Alternate drug for Bacterial vaginitis

f. Alternative drug for Toxoplasmosis treatment

g. Alternative drug for Pneumocystis carinii pneumonia

h. Alternative agent for Chlamydia trachomatis pelvic inflammatory disease (PID)

5. Disposition, Metabolism, Excretion

Well absorbed but undergoes hepatic metabolism. Distributed very well into tissues and abscesses but not into CNS. Extensively excreted in bile and undergoes entero hepatic recycling. High gut levels even after IV admin.

6. Adverse Effects

a. diarrhea in 20-30%

b. risk for PMC but no worse than beta lactam antibiotics. "Boxed Warning" on PMC risk on package insert. Risk for topical products is very low as the drug is not absorbed.

c. hepatic toxicity - elevation of transaminases; reversible; rare jaundice

d. hypersensitivity reactions, hematopoietic abnormalities, renal toxicity have been reported.

7. Products

Cleocin ® (Pharmacia) and generic products

capsules, suspension, solution for injection and topical products for acne and for vaginal use

8. Summary

A useful drug for serious anaerobic infections. It is not an agent of choice but an alternative drug. Topical use has minimal risk.