Antibiotics Update 2005
Jeffrey Buyten, MD
David Teller, MD
Francis B. Quinn, Jr., MD
The University of Texas Medical Branch
Department of Otolaryngology
Grand Rounds Presentation
December 2004
Overview of Antibiotics.
- Cell wall inhibitors.
- Protein synthesis inhibitors.
- Folate antagonists.
- Miscellaneous.

Treatment of Methicillin resistant *Staphylococcus aureus* (MRSA).

Fluoroquinolones in children.
Cell Wall Synthesis Inhibitors

Beta Lactams
  Penicillins (PCN)
  Cephalosporins
  Carbapenems
  Monobactams
Vancomycin
Bacitracin
Polymyxin
Beta Lactams

► B-lactams inhibit transpeptidase.
► Only effective against rapidly growing organisms that synthesize peptidoglycan. (Ineffective against mycobacteria.)
► The size, charge and hydrophobicity of the molecule determines the extent of its antibacterial activity.
Penicillins

- Derived from *Penicillium chrysogenum*.
- PCN G and PCN V are unaltered products of *Penicillium* fermentation.
- Semi-synthetic penicillins are formed by addition of R groups to the main 6-aminopenicillanic acid ring.
Adverse Reactions

- 5% of patients will develop a hypersensitivity reaction (penicilloic acid).
- Rashes - most common reaction. 50% do not have a recurrent rash.
- Ampicillin - rash in 50-100% of patients with mononucleosis.
Adverse reactions

- Anaphylaxis – 1/10000 patients
  - Hives, angioedema, rhinitis, asthma, and anaphylaxis.
  - 10% mortality rate.
  - Anaphylaxis possible after negative skin testing.
  - Desensitization is an option if penicillin must be given.
  - Avoid all other B-lactams.

![EpiPen and EpiPen Jr.]
Natural Penicillins

- PCN G (IV/IM; $12/day)
- PCN V (Oral; $0.52/day)
- Active against *Strep.*, *peptostreptococcus*, *B anthracis*, *Actinomycosis*, *Corynebacterium*, *Listeria*, *Neisseria* & *Treponema*.
- Used for common oral infections.
Anti-Staphylococcal Penicillins

- Methicillin, nafcillin, oxacillin, cloxacillin and dicloxacillin.
- Resist degradation by penicillinase.
- Useful for treating *S. aureus*.
  - No added benefit in treating *Strep*. species.
- Methicillin is rarely used due to toxicity.
- Dicloxacillin ($0.87/day) - highest serum levels orally.
- Nafcillin ($15/day) - preferred parenteral drug.
Aminopenicillins

- Ampicillin (IV; $1.95/day)
- Ampicillin/sulbactam (Unasyn; IV; $30.76/day)
- Amoxicillin (Oral; $0.32/day).
- Amoxicillin/clavulanate (Augmentin; $6.63/day)
- Sulbactam and clavulanic acid increase activity against B-lactamase producing organisms.
- Extended antimicrobial spectrum.
  - Gram negatives: *E. coli*, *Proteus*, *Salmonella*, *Haemophilus*, *M. catarrhalis*, *Klebsiella*, *Neisseria*, *Enterobacter*, *Bactoroides*.
- Used as first line therapy for acute otitis media and sinusitis.
Antipseudomonal Penicillins

- Ticarcillin, Piperacillin ($49.36/day), Mezlocillin.
- Piperacillin/tazobactam (Zosyn; IV; $53.24/day)
  - Tazobactam (β-lactamase inhibitor)
- Ticarcillin/clavulanate (Timentin; IV; $38.80/day)
- Active against *Pseudomonas, E. coli, klebsiella, enterobacter, serratia and B. fragilis*.
- Lower activity against gram positives
- Often used with aminoglycosides when treating pseudomonal infections.
Resistance Mechanisms

- **B-lactamase** – hydrolyze the B-lactam ring.
  - H. flu (7-24%)
  - M. cat (93-100%)
- **Penicillinase** – *Staph*
- **Alteration of penicillin-binding protein (PBP) affinity.** (*Strep. Pneumo.*, MRSA)
Alteration of PBP affinity.

- 6 PBP’s are found by PCN in susceptible pneumococci.

- Isolates with reduced susceptibility show decreased PCN affinity for one or more of the 6 PBP’s.
  - PBP-2b alteration is responsible for most PCN resistant strains.

- Increased concentration of PCN overcomes low binding affinity.
**Strep. pneumo resistance.**

- PCN resistance is increasing in the US.
  - Current national statistics:
    - Susceptibility 60%
    - Intermediate resistance 20%
    - Resistant 20%
  - Current UTMB statistics:
    - Susceptibility 46% (outpatient), 53% (inpatient)
    - Intermediate resistance 41% (outpatient), 40% (inpatient)
    - Resistant 13% (outpatient), 7% (inpatient)
  - Amoxicillin resistance < 5%.
Cephalosporins

- Semisynthetic B-lactams derived from chemical side chains added to 7-aminocephalosporanic acid.
- Generally more resistant to B-lactamases.
Cephalosporins

► Adverse reactions.

- 5-10% cross-sensitivity with pcn allergic pts.
- 1-2% hypersensitivity reactions in non-pcn allergic pts.
- Broader spectrum leads to opportunistic infections (candidiasis, C. difficile colitis).
First Generation

► Cefazolin (Ancef; IV; $9.60/day), Cephalexin (Keflex; Oral; $0.78/day)

► Spectrum: Most gram positive cocci (*Strep, S. aureus*), *E. coli, Proteus, Klebsiella*.

► Use: *S. aureus* infection, surgical prophylaxis.
Second Generation

- **Cefuroxime** (Ceftin; IV $\$7.84/\text{day}; \text{Oral } \$14.04/\text{day})

- Increased activity against *H. flu, enterobacter, Neisseria, proteus, E. coli, klebsiella, M. catarrhalis, anaerobes* and *B. fragilis*.

- Not as effective against *S. aureus* as the 1\text{st} generation.

- Cefpodoxime and Cefuroxime active against intermediate level resistant strep pneumo.
Third Generation

► Spectrum: gram negative > gram positive.

► Ceftriaxone (Rocephin; IM/IV; $25.79/day), Cefotaxime ($11.55/day).
  - Useful for meningitis.
  - Ceftriaxone used for highly resistant and multi drug resistant strep pneumo along with vancomycin.

► Ceftazidime active against pseudomonas.
Fourth Generation

► Cefepime (IV; $22.28/day)
► Active against *Strep, Staph* (mssa), aerobic gram negatives (*enterobacter, e. coli, klebsiella, proteus* and *pseudomonas*).
Carbapenems

► Imipenem-Cilastin (Primaxin; IV; $84.76/day; Requires ID approval @ UTMB).

► Cilastin - dehydropeptidase inhibitor that inhibits degradation into a nephrotoxic metabolite.

► Brodest spectrum B-lactam.
  - *Staph* (not MRSA), *Strep* (highly resistant), *Neisseria, Haemophilus, Proteus, Pseudomonas, Klebsiella, Bacteroides*, anaerobes (excluding *C. dif*).
  - Double coverage of *Pseudomonas* is recommended when using imipenem.

► Toxicities:
  - PCN allergy cross reactivity.
  - Seizures noted in Imipenem studies.
Monobactams

- Aztreonam (Azactam; IM/IV; $52.62/day)
- B-lactamase resistant.
- Narrow antibacterial spectrum.
  - Aerobic gram negative rods (*H. flu*, *N. gonorrhea* (penicillinase producers), *E. coli*, *Klebsiella*, *Proteus*, *Pseudomonas*).
  - Ineffective against gram positive and anaerobic organisms.
  - Antipseudomonal activity is greater than Timentin and Zosyn but less than the carbapenems.
Aztreonam

► Very little cross-allergenicity due to its low immunogenic potential. May be a safe alternative for pcn allergic patients.

► Adverse reactions;
  - Gram positive superinfection (20-30%)
Vancomycin

► Tricyclic glucopeptide - *Streptomyces orientalis*.

► Inhibits synthesis of cell wall phospholipids and prevents cross-linking of peptidoglycans at an earlier step than B-lactams.

► Active against gram positive bacteria, highly resistant *Strep. pneumo*, *Clostridia*, *Enterococcus*, *Staph. epi* and MRSA.

► Synergy with aminoglycosides.

► Used in treatment of MRSA and highly resistant *Strep.* species.
Vancomycin

► Resistance: changes in permeability and decreased binding affinity.

► Adverse effects.
  ▪ Fever, chills, phlebitis and red man syndrome.
    ► Slow injection and prophylactic antihistamines.
  ▪ Ototoxic – may potentiate known ototoxic agents.

► Renal excretion (90-100% glomerular filtration).
  ▪ Normal half-life 6-10 hours.
  ▪ Half life is over 200 hours in pts with ESRD.

► Cost - $8.39/day and $29.39/day with serum levels.
Bacitracin

► Polypeptide produced by *Bacillus subtilis*.
► Inhibits regeneration of phospholipids receptors involved in peptidoglycan synthesis.
► Originally isolated from debris in a pt’s wound.
► Active against gram positives and negatives.
► Topical use only (nephrotoxicity).
Bacitracin

► Adverse effects.
  ▪ Contact dermatitis – top 10 allergen.
  ▪ Reports of anaphylaxis.

► Dermatology study showed no increase in wound infection when clean surgical wounds were dressed with white petrolatum vs. bacitracin.

► Combinations
  ▪ Neosporin – neomycin, polymyxin B, bacitracin
  ▪ Polysporin – polymyxin B, bacitracin
Polymyxin

- *Bacillus polymyxa*
- Decapeptide that disrupts the phospholipid layer in cell membranes.
- Limited spectrum.
  - Decreased gram positive coverage.
  - Active against *Pseudomonas*, *Proteus*, *Serratia*, *E. coli*, *Klebsiella* and *Enterobacter*.
- Cross reaction with bacitracin.
Protein Synthesis Inhibitors

► Target the bacterial ribosome.
  ► Bacterial – 70S (50S/30S)
  ► Mammalian – 80S (60S/40S)
  ▪ High levels may interact with mammalian ribosomes.

► 50S binders - Macrolides, Clindamycin, Chloramphenicol, Streptogramins.

► 30S binders - Aminoglycosides, Tetracyclines

► Mupirocin
Macrolides

- Erythromycin (IV $13.64/day; Oral $0.59/day),
- Clarithromycin (Biaxin; IV $101.50/day; Oral $101.15/day)
- Azithromycin (Zithromax, Z-PAK; Oral $48.80/day, $20.30/day)
- Macrocyclic lactone structures - *Streptomyces erythreus*.
- Irreversibly bind the 50S subunit.
  - Binding site is in close proximity to the binding sites of lincomycin, clindamycin and chloramphenicol.
Macrolides

► Antibacterial spectrum:

- **Erythromycin:**
  - Gram positives: *Staph.* (MRSA is resistant), *Strep.*, *Bordetella*, *Treponema*, *Corynebacteria*.
  - Atypical: *Mycoplasma*, *Ureaplasma*, *Chlamydia*

- **Clarithromycin:**
  - Similar to erythromycin.
  - Increased activity against gram negatives (*H. flu*, *Moraxella*) and atypical.

- **Azithromycin:**
  - Decreased activity against gram positive cocci.
  - Increased activity against *H. flu* and *M. cat.*
Macrolides

► Adverse effects.
  ▪ 10-15% of pts do not finish the prescribed course of erythromycin because of GI distress.
  ▪ Jaundice
  ▪ Ototoxic (high doses)

► Drug interactions
  ▪ Oxidized by cytochrome p-450.
  ▪ Inhibits other substrates and increases their serum concentrations.
    ► Theophylline, warfarin, astemizole, carbemazepine, cyclosporine, digoxin, terfenadine.
Macrolides Resistance

► Efflux mechanism (msrA).
► Ribosomal alteration (ermA/ermC)
  ▪ MLS\textsubscript{B} (macrolide-lincosamide-streptogramin B) resistance.
  ▪ MLS\textsubscript{B} inducible strains are resistant to erythromycin and susceptible to clindamycin. Further exposure to clindamycin induces MLS\textsubscript{B} resistance.
Clindamycin

- Clindamycin (Cleocin; IV $24.45/day; Oral $13.71/day)
- Lincosamide
- Irreversibly binds the 50S subunit.
- Antibiotic spectrum:
  - *Strep* species, *Staph* (some MRSA), *B. fragilis*, anaerobes
  - Does not cover *Clostridium difficile*.
Clindamycin

- Used for deep neck space infections, chronic tonsillopharyngitis, odontogenic abscesses, and surgical prophylaxis in contaminated wounds.

- Concomitant use of macrolides or Chloramphenicol adds no benefit.

- Resistance: $\text{MLS}_B$ – ribosomal alteration.
Clindamycin Adverse Effects

- Pseudomembranous colitis
  - clindamycin > cephalosporins (Ceftin) > aminopenicillins.
  - Abdominal pain, fever, leukocytosis, bloody stool...
  - Diarrhea commonly develops on days 4-9 of treatment.
  - Typically resolves 14 days after stopping the antibiotic.
  - Treat with Flagyl (PO or IV).
  - Life threatening cases can be treated with oral Vancomycin.
Aminoglycosides

- Neomycin ($12.05/day), Gentamicin ($4.28/day), Tobramycin ($6.77/day), Amikacin ($7.81/day). (Additional $21.00/day with serum levels)
- Binds the 30S subunit.
- Only active against anaerobes because an oxygen dependent system is required to transport the molecules into the cell.
- Synergism with cell wall inhibitors is seen because they increase the permeability of the cell.
Aminoglycosides

► Antibacterial spectrum:
  - Gram negatives: *Pseudomonas, Proteus, Serratia, E. coli, Klebsiella*
  - Neomycin
    - *S. aureus and Proteus*
    - *Pseudomonas and Strep* are resistant

► Resistance – decreased uptake, decreased binding affinity, enzymes (plasmids).
Aminoglycosides

- Adverse effects:
  - Ototoxic – associated with high peak levels and prolonged therapy. Pts on loop diuretics, vancomycin and cisplatin are at higher risk.
    - Cochlear and vestibular.
    - Concentrates in endolymph and perilymph.
  - Nephrotoxic.
    - Proximal tubule damage.
Mupirocin

- Bactroban ($76.70)
- *Pseudomonas fluoroscens.*
  - (E)-(2S, 3R, 4R, 5S)-5-[(2S, 3S, 4S, 5S)]-2,3-Epoxy-5-hydroxy-4-methyl[hexyl]tetrahydro-3, 4-dihydroxy-B-methyl-2H-pyran-2-crotonic acid, ester with 9-hydroxynonanoic acid.
- Binds isoleucyl transfer-RNA synthetase.
- Active against *Staph aureus* (MRSA), *Staph epi, Strep pyogenes*.
- Used for Impetigo and elimination of *Staph* infections, including MRSA carriers.
  - Intranasal application qid can reduce carriage for up to one year.
Folate Antagonists

- Bacteria must synthesize folate in order to form cofactors for purine, pyrimidine and amino acid synthesis.

- $p$-aminobenzoic acid (PABA) agonists.
  - Substrates for dihydropteroate synthetase.
  - Sulfonamides
    - Sulfamethoxazole (SMP)
    - Sulfasoxazole

- Dihydrofolate Reductase Inhibitors.
  - Inhibits activation of folate to its active form, tetrahydrofolate.
  - Trimethoprim (TMP)
Clinical applications.

► Antibacterial spectrum.
  - *H. flu*, *Strep. pneumo*, *Neisseria* species, *S. aureus*, and *Pneumocystis carinii*

► Pediazole (erythromycin + sulfasoxazole)
  - Alternative to amoxicillin for first line treatment of acute otitis media.

► Co-trimoxazole (trimethoprim + sulfamethoxazole; IV $8.71/day; Oral $0.15/day)
  - MRSA, UTI’s, PCP prophylaxis.
  - 97% of UTMB outpt *Staph. aureus* isolates are susceptible to Bactrim.
Dermatologic: Rashes are common, ranging from photodermatitis to Stevens-Johnsons syndrome.

Hematologic: Hemolytic anemia (G6PDH deficient pts.), neutropenia and thrombocytopenia (up to 80% of HIV pts).

Drug interactions: Warfarin, phenytoin, methotrexate.
Miscellaneous

- Fluoroquinolones
- Rifampin
- Metronidazole
Fluoroquinolones

- **Ciprofloxacin** (Cipro; IV $103.75/day; PO/Topical; Restricted use @ UTMB), **Ofloxacin** (Floxin; Topical $60.90), **Levofloxacin** (Levaquin; IV 15.62/day; Oral $6.72/day).

- Synthetic derivatives of nalidixic acid.

- Inhibits DNA gyrase, causing permanent DNA cleavage.

- **Resistance:**
  - DNA Gyrase mutations
  - Cellular membrane efflux mechanisms.
  - Decreased number of porins in target cells.

- Wide distribution - CSF, saliva, bone, cartilage
Antibiotic Spectrum

► Effective vs. gram +, gram -, atypicals, and *Pseudomonas*.
► Decreased activity against anaerobes.
► Respiratory quinolones (levofloxacin).
  - Active against *Strep* (including penicillin-resistant forms), *S. aureus* (including MRSA), *H. flu, M. cat* (including penicillin-resistant strains), and atypicals.
  - Used in AOM, sinustiis, pharyngitis...
► Antipseudomonas quinolones (ciprofloxacin/ofloxacin)
  - Active against *Pseudomonas, H. flu, M. cat*.
  - *Strep pyogenes, Strep pneumoniae* and MRSA are resistant.
  - Used in children with Cystic Fibrosis.
  - Topicals used for otitis media.
► Levofloxacin and Moxifloxacin have increased *Staph* activity even against cipro-resistant strains.
Fluoroquinolones

► Adverse effects.

- Headache, dizziness, nausea, lightheadedness
- Limit use in pregnancy, nursing mothers, and children < 18.
- Drug interactions: may increase levels of theophylline, warfarin, caffeine and cyclosporine.
- Absorption decreased when taken with cations.
- Arthralgias - 1%.
Fluoroquinolones in children.

- Only one approved indication in children.
- Animal studies show joint/cartilage damage in wt bearing joints of young animals.
  - Dose and animal dependent.
- All fluoroquinolones have demonstrated this toxicity.
- Mechanism unclear.
Fluoroquinolones in children.

- Fluoroquinolones still given to children.
- Compassionate care cases have shed light on potential toxicity rates in children.
  - No significant differences have been found in children treated with long term Cipro and age matched controls.
  - CF pts - 1.3% incidence of arthralgia (self-limited).
  - Short term use – no acute arthritis or serious adverse effects (>1700 pts in general database review).
  - Bayer studies - 1% incidence of arthralgia (90% had CF). Control groups had similar side effect profile as study group.
  - No radiographic evidence of joint changes in any study.
Rifampin

- Interacts with the bacterial DNA-dependent RNA polymerase, inhibiting RNA synthesis.

- Antibacterial spectrum
  - *Mycobacteria*, gram positives, gram negatives.
  - Used to treat carriers of meningococci or *H. flu*.

- Resistance.
  - Develops rapidly during therapy. Should use in combination with other drugs to decrease resistance rates.
  - Decreased affinity of the polymerase.

- Metabolized in liver and may induce the cytochrome p-450 system.

- Cost: IV $106.90/day; PO $8.00/day
Metronidazole

- **Flagyl**: IV $17.00/day; PO $8.00/day
- Forms cytotoxic compounds by accepting electrons on its nitro group.
- Distribution: nearly all tissues, including CSF, saliva, bone, abscesses.
- Antibacterial spectrum: anaerobes and parasites.
- Used for *C. difficile* and other anaerobic infections (abscesses).
- Toxicity: disulfram reaction.
Treatment of MRSA

- Prevalence
- Mechanisms of resistance.
- Vancomycin intermediate susceptible strains (VISA).
- Vancomycin resistant strains (VRSA).
- Treatment approaches and new drugs.
First isolates of MRSA were reported in the early 1960’s after methicillin was introduced in 1959.

3 pandemic MRSA clones were traced back to the 1960’s isolates from Denmark and England.

5 major MRSA clones were identified by 2002.
Data through 2002 indicate that *S. aureus* isolates from ICU pts. were 51% MRSA and 41% from non-ICU pts.

A prospective study showed that MRSA prevalence rose sharply from 22% to 57% between 1995-2001.

Community acquired MRSA prevalence has been reported to be 21-29% in adults and 35-50% in children.

Current UTMB statistics.

- Modified from Antimicrobial Susceptibility Profile July 2003-June 2004

<table>
<thead>
<tr>
<th></th>
<th>Inpatient</th>
<th>Outpatient</th>
<th>TDC</th>
<th>PICU</th>
<th>Adult ICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA Prevalence</td>
<td>64%</td>
<td>59%</td>
<td>62%</td>
<td>47%</td>
<td>71%</td>
</tr>
</tbody>
</table>
MRSA – Resistance Mechanisms

- **Definition; Oxacillin MIC ≥ 4ug/ml... resistant to all B-lactams.**
- **mec gene – staphylococcal chromosomal cassette (SCCmec)**
  - Present in all MRSA isolates.
  - Five SCCmec types (I-V).
    - Types I-III – prevalent in healthcare associated isolates
    - Type IV – prevalent in community acquired isolates
- **mecA – encodes PBP2a (low affinity PBP)**
  - PBP2a is able to substitute for the activity of other inactivated PBP’s.
  - Resulting peptidoglycan is structurally different but functional.
- **mecR1-mecI – negative regulator if mecA transcription.**
- **B-lactamase genes – Can down regulate mecA transcription.**
MRSA – HA vs. CA

► Community acquired (CA) MRSA
  - Younger population.
  - High risk groups – athletes, prisoners, men who have sex with men, drug users and Native Americans.
  - More likely to produce skin and soft tissue infections.
  - Not multi-drug resistant.

► Healthcare associated (HA) MRSA
  - Multi-drug resistant.
  - Associated with foreign bodies.
MRSA antibiotic susceptibility.

- **UTMB Antibiotic Susceptibility Profile**
  - Percent Susceptible
  - Modified from Antimicrobial Susceptibility Profile July 2003-June 2004

<table>
<thead>
<tr>
<th>S. aureus</th>
<th>Cefazolin</th>
<th>Clindamycin</th>
<th>Erythromycin</th>
<th>Oxacillin</th>
<th>Tetracycline</th>
<th>Bactrim</th>
</tr>
</thead>
<tbody>
<tr>
<td>UTMB outpt.</td>
<td>41%</td>
<td>86%</td>
<td>24%</td>
<td>41%</td>
<td>88%</td>
<td>97%</td>
</tr>
<tr>
<td>UTMB inpt.</td>
<td>----</td>
<td>64%</td>
<td>24%</td>
<td>36%</td>
<td>84%</td>
<td>89%</td>
</tr>
<tr>
<td>PICU</td>
<td>----</td>
<td>88%</td>
<td>50%</td>
<td>53%</td>
<td>91%</td>
<td>100%</td>
</tr>
<tr>
<td>Adult ICU</td>
<td>----</td>
<td>43%</td>
<td>22%</td>
<td>29%</td>
<td>84%</td>
<td>85%</td>
</tr>
<tr>
<td>TDC</td>
<td>----</td>
<td>59%</td>
<td>25%</td>
<td>38%</td>
<td>75%</td>
<td>73%</td>
</tr>
</tbody>
</table>
VISA and VRSA

► Vancomycin intermediate susceptible strains.
  - Cases reported from Japan and NYC.
  - Likely due to altered peptidoglycan biosynthesis which causes thicker cell walls and decreased drug exposure to the cytoplasmic membrane.
  - Pts that respond poorly to vancomycin should be re-cultured and vancomycin susceptibility tested via broth dilution techniques.

► Vancomycin resistant strains – MIC > 32ug/ml
  - Possible cross resistance with VRE.
  - Vancomycin is unable to bind to its target site due to an altered terminal peptide.
Outpatient treatment

- **Bactrim**
- **Clindamycin**
  - Must check for erythromycin resistance as a marker for MLS\textsubscript{B} inducible resistance.
    - UTMB outpatients have a 8-10% prevalence of MLS\textsubscript{B} inducible resistance.
    - TDC pts have a 4-6% prevalence of MLS\textsubscript{B} inducible resistance.
- **Tetracycline**
- **Levaquin**
- **Combination therapy with Rifampin**
Inpatient treatment

- Vancomycin
- Clindamycin
- Bactrim
- Tetracycline
- Levaquin
- Combination therapy
New antibiotics for MRSA

- Linezolid
- Quinupristin-dalfopristin
- Daptomycin
- Lysostaphin
Linezolid

- Oxazolidinone – inhibits the initiation complex of bacterial protein synthesis.

- Zyvox; IV $116.85/day; PO $84.55/day.

- Antibiotic spectrum – gram positives.

- Oral = IV

- Similar cure rates when compared to vancomycin.
  - May be superior to vancomycin for MRSA pneumonia.

- Adverse effects.
  - Myelosuppression, thrombocytopenia.
Quinupristin-dalfopristin

- Quinupristin – streptogramin A
- Dalfopristin – streptogramin B
- Binds 50S ribosome.
- High activity against MRSA and VISA, and coag neg. staph.
- Synergy with B-lactams.
- Additive with vancomycin.
- Adverse effects:
  - Arthralgias, myalgias
  - Hyperbilirubinemia
Daptomycin

- Cyclic lipopeptide
- Disrupts cell membrane function.
- Similar efficacy when compared to vancomycin.
- Only approved for complicated skin and soft tissue infections.
- Not used for pneumonia due to low respiratory tract concentrations
- Adverse effects – reversible myopathy.
Lysostaphin

- *Staphylococcus simulans*
- Cleaves pentaglycine cross-links unique to *S. aureus* cell wall.
- Shown to reduce vegetations in rabbit endocarditis.
- Synergistic effect with B-lactams.
- Resistance – changes in the muropeptide crossbridge.
Bibliography

1) Boyce, John M. Epidemiology; prevention; and control of methicillin-resistant Staphlyococcus aureus in adults. Up To Date (12.3). 2004.
Bibliography


