

Staph Cases



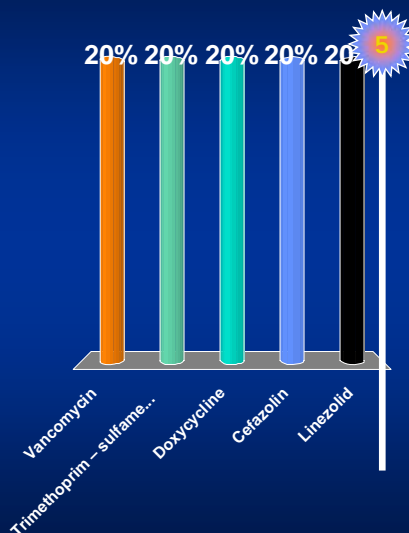
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Case #1

- A 60 y.o. man with well controlled HIV and DM presents to clinic with ten days of redness and swelling of his right LE. Otherwise, he appears well. He is noted to have tinea pedis. He is treated with cephalexin at home. He returns to clinic for scheduled follow up in 3 days, and the redness is only minimally improved. A decision is made to admit him to the hospital. Which antibiotic would you start?

Case #1: Choices

1. Vancomycin
2. Trimethoprim – sulfamethoxazole
3. Doxycycline
4. Cefazolin
5. Linezolid

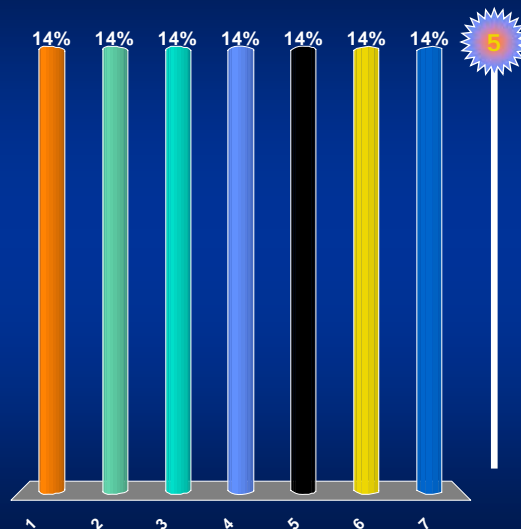


Case #2

- Your clinic patient comes for an urgent care visit for a 2.5 cm axillary abscess. CD4 count is ~ 700, and the patient is not taking ARVs. VS are normal. No previous h/o of abscesses or “boils.” No IDU. You I&D the abscess in clinic and express pus. What treatment is now appropriate?

Case #2

1. No antibiotics
2. Trimethoprim-sulfamethoxazole
3. Levofloxacin
4. Doxycycline
5. Clindamycin
6. Linezolid
7. Cephalexin



Case #2 cont.

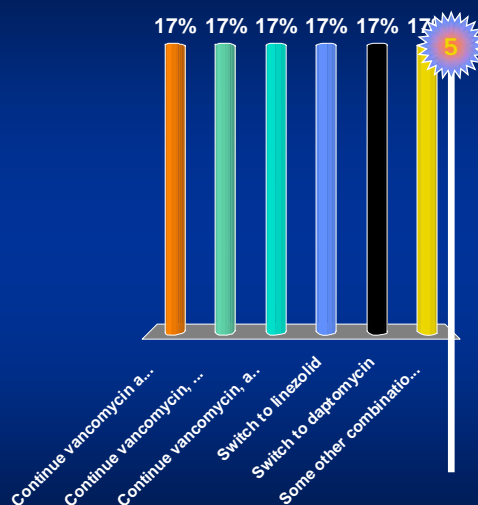
- What about decolonization???

Case #3

- A 28 y.o. woman with AIDS and active IDU is admitted to the hospital with fever. Blood cultures 2/2 are positive for MRSA. The patient is treated with vancomycin, trough level adjusted to 15. F/U blood cultures at 2, 4, and 6 days are still positive. TEE is negative for a vegetation. What would you do with her antibiotics?

Case #3

1. Continue vancomycin alone
2. Continue vancomycin, add gentamicin
3. Continue vancomycin, add rifampin
4. Switch to linezolid
5. Switch to daptomycin
6. Some other combination not listed above



Is Vancomycin Obsolete?

- Obsolescence predicted for a long time
 - Resurgence of use with MRSA – first healthcare associated, then community MRSA
- Rumors of its demise have been greatly exaggerated

Is Vancomycin Obsolete?

- New predictions of obsolescence
 - Clinically inferior to beta-lactams for MSSA
 - Poor tissue penetration (e.g. lung)
 - Frank resistance is rare but “MIC creep” is a real issue
 - ❖ Clinical and Laboratory Standards Institute (CLSI) revised standards in 2006
 - ≤ 2 susceptible; 4 – 8 intermediate; ≥ 16 resistant
 - Likely worse outcomes even with MIC = 2

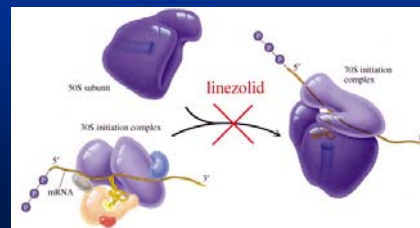
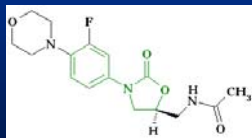
Novel Treatments for Serious MRSA Infections

- Antibiotics

- Quinupristin/dalfopristin
- Dalbavancin
- Linezolid*
- Telavancin
- Daptomycin*
- Oritavancin
- Tigecycline
- Ceftobiprole

Linezolid

- Trade name Zyvox®; FDA approved 2000
- Oxazolidinone class of antibiotic
 - Binds to 50S ribosomal subunit to prevent formation of 70S initiation complex



Linezolid

- FDA indications
 - Vancomycin resistant *Enterococcus faecium* infections (including bacteremia), healthcare-associated pneumonia, skin and skin structure infections, community-acquired pneumonia

Linezolid

- Oral and intravenous dosing equivalent
- Well tolerated for “short” courses
 - Adverse effects include
 - ❖ Hematologic, especially thrombocytopenia
 - ❖ Peripheral and optic neuropathy
 - ❖ Hyperlactatemia
 - ❖ Serotonin toxicity

Linezolid: better than vancomycin?

- Mixed data for skin and soft tissue infection
 - Not inferior (?? superior)
 - Associated with earlier transition to oral therapy, shorter length of stay, and lower total costs
- Retrospective analysis combining two studies suggests better outcome with linezolid for MRSA ventilator-associated pneumonia
 - Prospective, multi-center trial in progress

Linezolid: better than vancomycin?

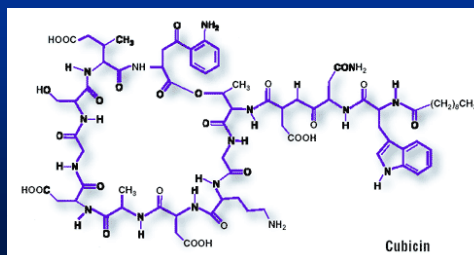
- Bacteremia: available data (limited) suggest equivalence
- Warning letter sent March 2007 regarding catheter-associated bloodstream infection study
 - Higher mortality in subjects receiving linezolid
 - ❖ Seen with Gram negative infections, not with Gram positive infections

Linezolid: better than vancomycin?

- Bottom line:
 - Appropriate drug for patients with MRSA pneumonia
 - ❖ May turn out to be drug of choice
 - A real alternative for vancomycin failure or intolerance
 - Caution with bacteremia
 - Much more expensive than other oral drugs and toxicity with long term use

Daptomycin

- Trade name Cubicin®; FDA approved 2003
- Cyclic lipopeptide; binds to and depolarizes bacterial cell membrane



Daptomycin

- FDA indications
 - Complicated skin and soft tissue infections caused by Gram positive organisms
 - *S. aureus* bacteremia, including right-sided endocarditis
- Cannot be used for pneumonia since binds to and inhibited by surfactant

Daptomycin

- Once daily dosing
- Generally well tolerated
 - Elevation of serum creatine phosphokinase (CPK) is chief concern
- May be more effective with a higher dose than currently approved

Daptomycin: better than vancomycin?

- Most important study published NEJM 2006
- 124 patients with *S. aureus* bacteremia received daptomycin, 122 received vancomycin or antistaphylococcal penicillin
- Overall outcomes were not statistically different
 - Trend toward better outcomes with daptomycin for MRSA (44% success vs. 32%)
- Microbiologic failure with daptomycin was associated with increase in daptomycin MIC

Daptomycin: better than vancomycin?

- Bottom line:
 - Likely equivalent to vancomycin for MRSA bacteremia (?? superior)
 - Development of resistance with microbiologic failure is a concern
 - Daptomycin MICs may be elevated in *S. aureus* with intermediate resistance to vancomycin or heterogeneous resistance to vancomycin