Disclosure

• I have no financial disclosures pertinent to this presentation

• I will discuss off-label use of medications
5 THINGS TO KNOW

#1 Emerging therapies for SSTI
#2 Skin abscesses
#3 Recurrent lower extremity cellulitis
#4 MRSA coverage for cellulitis
#5 Seasonal soft tissue infection variability
Case

• 40 year old male presents with a 5 day history increasing erythema and purulent drainage from the dorsal aspect of the right 5th MCP joint following an abrasion of the hand on a door

• Took 2 days of cephalexin

• Past medical history significant for bipolar disorder, ongoing IV methamphetamine abuse
Case
Case

- He’s taken urgently to the OR, where abscess adjacent to the joint capsule is found. There is no evidence of septic arthritis.

- All operative cultures grow 4+ methicillin resistant Staphylococcus aureus.

- The patient admits to ongoing IV methamphetamine abuse and refuses to go to a skilled nursing facility for IV antimicrobials.

- There is concern for compliance with oral antimicrobials.
Case

What best describes the pharmacologic properties of dalbavancin and oritavancin that lead to a prolonged mechanism of action?

• A. Dissolving calcium sulfate depot implantation
• B. High protein binding and long terminal half-life
• C. Oral pills with extensive enterohepatic recirculation
• D. Slow release of medication from peripheral tissues
Case

- Treated with 4 weeks oral minocycline
#1 Emerging therapies for SSTI

New medications
- Telavancin (2009)
- Dalbavancin (2014)
- Oritavancin (2014)
- Ceftaroline (2010)

Related medications
- Vancomycin (glycopeptide)
- Ceftriaxone (cephalosporin, no MRSA activity)
- Linezolid (oxazolidinone)
Emerging therapies for SSTI
Telavancin (2009)

- Synthetic parenteral lipoglycopeptide: D-ala-D-ala binding, also affects membrane potential
- Dosing for SSTI: 10 mg/kg IV q 24 hrs
- Advantages over vancomycin:
  - Once daily dosing in normal renal function
- Caution:
  - Increased mortality in renal insufficiency (HCAP), QTc prolongation, increased AKI
- My opinion: no clear advantage over vancomycin
#1 Emerging therapies for SSTI

**Ceftaroline (2010)**

- 5\textsuperscript{th} generation parenteral cephalosporin: Binds PBP2a
- Dosing for SSTI: 600 mg IV every 12 hours
- Advantages over vancomycin:
  - Good safety profile
  - Gram negative coverage similar to ceftriaxone
- Caution:
  - Approved for CAP and SSTI caused by MRSA, but not MRSA pneumonia!
- **My opinion:** alternative to vancomycin, attractive in renal insufficiency, but still requires q12 hourly IV therapy
Emerging therapies for SSTI
Tedizolid (2014)

- Oxazolidinone prodrug - binds to ribosome, protein synthesis inhibition
- Dosing for SSTI: 200 mg IV or PO q 24 hrs
- Advantages over vancomycin/linezolid:
  - Oral, highly bioavailable
  - Less bone marrow toxicity
  - Less serotonergic drug interactions (theoretical)
- My opinion: an oral alternative, but no direct comparison to other generic oral agents (trimethoprim/sulfamethoxazole, minocycline)
Emerging therapies for SSTI
Dalbavancin and oritavancin (2014)

- Lipoglycopeptides- D-ala-D-ala binding, cell wall
  - Highly protein bound, half-life over 10 days

- Dosing for SSTI:
  - Dalba: 1,500 mg IV once; or 1,000 mg IV once, followed by 500 mg IV 1 week later
  - Orita: 1,200 mg IV once

- Cautions: what happens with serious adverse reactions?
  - No data on serious infection (bacteremia)

- My opinion: may be an attractive option in patients with limited compliance/IV access and serious SSTI
Emerging therapies for SSTI

Summary

- Telavancin: once daily IV alternative, caution in renal dysfunction
- Ceftaroline: good safety profile, twice daily IV
- Tedizolid: oral, less side effects/interactions than linezolid
- Dalbavancin and oritavancin: long-acting IV agents, may be a good choice for selected situations, serious infection data not there yet
5 THINGS TO KNOW

#1 Emerging therapies for SSTI
#2 Skin abscesses
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#4 MRSA coverage for cellulitis
#5 Seasonal soft tissue infection variability
Incision and drainage (I&D) is the primary treatment for uncomplicated (mild) skin abscesses

- Absence of systemic symptoms

The role of antibiotics for mild skin abscesses has long been unclear

- IDSA guidelines - no antibiotics if no systemic symptoms

# Management of skin abscesses

786 patients with small (<5cm) skin abscesses

I&D

10 days therapy

Oral clindamycin (n = 266)

83% cured after 10 days observation

Placebo (n = 257)

69% cured after 10 days observation

Oral trimethoprim/sulfamethoxazole (n = 263)

81% cured after 10 days observation

Notes:
- Decreased recurrence rate with clindamycin (7%) vs TMP/SMX (14%) or placebo (12%)
- Increased adverse effects with clindamycin (22%) vs TMP-SMX (11%) or placebo (13%)

5 THINGS TO KNOW

#1 Emerging therapies for SSTI

#2 Skin abscesses

A short course of oral antibiotics increases cure rate and may decrease recurrence, beyond I&D

#3 Recurrent lower extremity cellulitis

#4 MRSA coverage for cellulitis

#5 Seasonal soft tissue infection variability
#3 Recurrent lower extremity cellulitis

- **Common**
  - 16.7% recurrence within 2 years
  - Predominantly β-hemolytic Streptococci

- **Risk factors:**
  - Involvement of the tibial region
  - Malignancy
  - Ipsilateral limb dermatitis

- **Prevention:** treat risk factors
  - Lower extremity edema (compression, lose weight)
  - Skin breaks (tinea pedis, blisters, ulcerations, dermatitis)

- **What to do when treating risk factors isn’t enough??**

If all 3 present: 93% likelihood of recurrence at 2 years

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#3 Recurrent lower extremity cellulitis

Patients with ≥ 2 episodes of LE cellulitis (n = 274)

1 year of Penicillin 250mg p.o. b.i.d. vs placebo

45% reduction in infection with penicillin (22 vs 37%, p = 0.01)

5 patients needed to treat to prevent one recurrence
Found to be cost effective in additional analysis

#3 Recurrent lower extremity cellulitis
The nuts and bolts of prophylaxis

- Safety is paramount
  - Remember, most patients who receive the medication will not benefit!
  - Safety labs (CBC, ALT, Creat) periodically

- Use narrowest spectrum agent
  - Penicillin V K for most
  - Can consider cefadroxil

- Dose for the body weight/comorbidities
  - Would you really use PVK 250 mg b.i.d. (NEJM trial dose) for a 130 kg patient with peripheral arterial disease and edema??

- Correct the underlying conditions!
  - If the underlying condition (ie edema) has improved/resolved → stop and observe off prophylaxis
5 THINGS TO KNOW

#1 Emerging therapies for SSTI

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A short course of oral antibiotics increases cure rate and may decrease recurrence, beyond I&D alone

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Low dose oral penicillin prophylaxis is cost effective and decreases risk of recurrent cellulitis

#4 MRSA coverage for cellulitis

#5 Seasonal soft tissue infection variability
#4 MRSA coverage for cellulitis

- Knowledge of community-acquired MRSA (CA-MRSA)
  - Cluster of deaths investigated by MN Dept of Health in 1990s

- Concern for CA-MRSA has led to an increase in empiric MRSA therapy in patients with cellulitis

- When is MRSA coverage necessary for cellulitis?

Patients with non-purulent (n=369) or purulent cellulitis (n=96) hospitalized in Taiwan

- Excluded surgical site infection
- 83% of non-purulent cellulitis received β-lactam monotherapy

<table>
<thead>
<tr>
<th>Microbiologic diagnosis made</th>
<th>Non-purulent (n=131)</th>
<th>Purulent (n=80)</th>
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<tbody>
<tr>
<td>β-Hemolytic streptococci (%)</td>
<td>92 (70.2)</td>
<td>4 (5.0)</td>
</tr>
<tr>
<td>MSSA (%)</td>
<td>8 (6.1)</td>
<td>24 (30)</td>
</tr>
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On multivariate analysis, purulence was the only factor associated with MRSA infection
#4 MRSA coverage for cellulitis

500 patients with cellulitis (no wound, purulence, or abscess)

- Keflex + placebo
- Keflex + TMP/SMX

7 days therapy

- Modified intent to treat: Clinical cure (p = 0.07)
  - Keflex + placebo: 171/248 (69%)
  - Keflex + TMP/SMX: 189/248 (76%)

- Per protocol: Clinical cure (p = 0.50)
  - Keflex + placebo: 165/193 (85%)
  - Keflex + TMP/SMX: 182/218 (84%)

Took ≥1 dose of study medication

Took ≥75% of doses of study medication, not lost to f/u

Among patients who took medications, no difference in cure rate

Moran et al. JAMA. 2017;317(20):2088-2096
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Low dose oral penicillin prophylaxis is cost effective and decreases risk of recurrent cellulitis

#4 MRSA coverage for cellulitis

Empiric treatment for MRSA is not routinely needed for cellulitis, in the absence of purulence, fluctuance or a wound

#5 Seasonal soft tissue infection variability
# Seasonal soft tissue infection variability

- Soft tissue infections appear to be more common in the summer months.
- This may be due to exacerbation of risk factors for soft tissue infection during warm months:
  - Increased abrasions, cuts, scrapes
  - Increased foot perspiration → tinea pedis
  - Insect bites
- The impact of environmental temperature has not been well established.

#5 Seasonal SSTI variability

- National ICD-9 claims data; regional monthly temperature data

- Odds of admission to the hospital for cellulitis:
  - 5°F increase $\rightarrow$ 3.5% increase in cellulitis
  - Independent of month of year

- Odds of surgical site infection:
  - 5°F increase $\rightarrow$ 2.1% increase in SSI
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#5 Seasonal soft tissue infection variability
Cellulitis, surgical site infection and other SSTIs are more frequent in summer due to environmental temperature and risk factor exacerbation
Summary

#1 Emerging therapies for SSTI
Telavancin, ceftaroline, tedizolid, dalbavancin, oritavancin

#2 Skin abscesses
A short course of oral antibiotics increases cure rate and may decrease recurrence, beyond I&D alone

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Questions & Discussion

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