DEBUNKING ANTIBIOTIC MYTHS FOR THE INFECTIOUS DISEASES CLINICIAN

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DECLARATIONS

- EKM has served on advisory boards for: Abbvie, Merck, Basilea, Shionogi, Melinta, Ferring, Cidara, Entasis, LabSimply, Pfizer, and GSK, and received speaker honorarium from GSK, Shionogi, and Pfizer.
MYTH: CEFAZOLIN SHOULD BE AVOIDED FOR CNS INFECTIONS

Treatment of bacterial meningitis caused by specific pathogens in adults

**Staphylococcus aureus** — *Staphylococcus aureus* meningitis is typically associated with penetrating head trauma or neurosurgery [7]. Given substantial rates of methicillin-resistant *S. aureus* (MRSA), vancomycin (table 3) should be used as initial therapy when *S. aureus* is suspected or proven (table 4) [7,59]. If susceptibility testing reveals methicillin-susceptible *S. aureus* (MSSA), therapy should be changed to nafcillin (2 g IV every four hours) or oxacillin (2 g IV every four hours) (table 1B). **Cefazolin should not be used for MSSA meningitis because it does not adequately penetrate into the CNS.** If the organism is methicillin resistant, vancomycin should be continued. (See "Vancomycin: Parenteral dosing, monitoring, and adverse effects in adults".)
“unpredictable CSF levels”
- Cite studies with CSF concentrations ranging from 0 – 64.5 μg/mL
- 3 previously reported cases developing pneumococcal (1) or meningococcal (2) meningitis 18-60 hours into cephalothin therapy
- 5 additional cases (cephalothin dose)
  - Pneumococcus after 40h (1g q4h)
  - Neisseria meningitidis after 42h (500mg q6h)
  - Klebsiella spp after 24h (1g q4h)
  - Listeria monocytogenes after 96h (1g q4h)
  - Pneumococcus after 120h (1.5g q6h)
DOES ANY CEPHALOSPORIN “GET TO” THE CSF?

<table>
<thead>
<tr>
<th>Compound(s) for CSF penetration</th>
<th>AUC&lt;sub&gt;CSF&lt;/sub&gt;/AUC&lt;sub&gt;pl&lt;/sub&gt;</th>
<th>Relationship of CSF concn to MIC with usual doses</th>
<th>Compound(s) with broad clinical experience for CNS infections</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cefazolin (111)</td>
<td>0.007–0.1</td>
<td>Uninflamed or mildly inflamed meninges</td>
<td></td>
<td>Cefazolin, cefotaxime, ceftriaxone, ceftepime, cefpirome</td>
</tr>
<tr>
<td>Cefuroxime (112, 229)</td>
<td></td>
<td>Strong meningeal inflammation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefotaxime (96, 175, 194, 195, 230)</td>
<td>0.12</td>
<td>CSF concn with uninflamed meninges close to the MICs of moderately susceptible bacteria; because of binding to plasma proteins, AUC ratio for ceftriaxone is approx 1 order of magnitude lower than that of cefotaxime</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone (47, 118, 141, 162, 175, 195, 236)</td>
<td>0.007</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefazidime (24, 70, 83, 156, 160, 172, 265)</td>
<td>0.057</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefixime (165)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefepime (213)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefpirome (73, 181, 262)</td>
<td>0.103</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

7. Echinocandins

The CNS pharmacokinetics of each of the three available echinocandin compounds, caspofungin, micafungin and anidulafungin, has been studied in detail using a non-infected rabbit model [50-52]. In each instance, the investigators have reported **undetectable CSF concentrations** even using dose levels far exceeding those used in current clinical regimens. However, these same investigations found **brain parenchymal concentrations** in the range of 10 – 20% of those measured in serum. For example, Groll et al. performed extensive tissue distribution studies with anidulafungin in healthy rabbits [51]. Although a CSF assay for anidulafungin did not identify a measurable amount of drug, brain parenchymal concentrations ranged 0.24 – 3.9 μg/g over a dose range of 0.5 – 10 mg/kg [51]. These tissue concentrations exceed the MIC90 of fungal pathogens in the echinocandin spectrum and would be anticipated to be sufficient for treatment success. This same research group has undertaken similar
Penetration of Nafcillin, Methicillin, and Cefazolin into Human Brain Tissue

Peter T. Frame, M.D., Chatrchai Watunakunakorn, M.D., Robert L. McLaurin, M.D., and Ghahreman Khodadad, M.D.

Division of Infectious Diseases, Department of Internal Medicine (P.T.F.), and Division of Neurosurgery, Department of Surgery (R.L.M.), University of Cincinnati College of Medicine, Cincinnati; Division of Infectious Diseases, Department of Internal Medicine (C.W.), St. Elizabeth Hospital Medical Center, Youngstown; and Surgical Service (G.K.), Veterans Administration Hospital, Cincinnati, Ohio

- 27 patients getting a craniotomy
- Brain tissue + serum antibiotic concentrations obtained

<table>
<thead>
<tr>
<th>Drug</th>
<th>Tissue specimens with detectable drug</th>
<th>Tissue concentrations (μg/g, [mean])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nafcillin</td>
<td>11/13 (85%)</td>
<td>0.36-11.0 [2.7]</td>
</tr>
<tr>
<td>Methicillin</td>
<td>14/18 (78%)</td>
<td>0.56-5.0 [2]</td>
</tr>
<tr>
<td>Cefazolin</td>
<td>10/11 (91%)</td>
<td>2.0-40.0 [10.6]</td>
</tr>
</tbody>
</table>
SOME CLINICAL DATA

17 patients
- 8 cefazolin vs 9 cloxacillin
  - 4 cefazolin patients also received levofloxacin
- Median cefazolin dose = 8g continuous infusion
- Median CSF concentration = 2.8 mg/L [2.1, 5.2]
- All patient cured without recurrence

1 patient
- 10g continuous infusion → step down to 8g
  - Received levofloxacin too
- MSSA ventriculitis
- Median CSF concentration = 11.9 mg/L (10g), 6.1 mg/L (8g)
Effectiveness of antibiotic for treatment of bacterial meningitis is not just related to CSF penetration

Rapid bactericidal activity required for optimal therapy → increased rate of neurological complications if CSF isn’t rapidly cleared of bacteria

Ceftriaxone > cefuroxime for children with bacterial meningitis

Very limited clinical data on use of cefazolin for treatment of staphylococcal meningitis

Some patients received combination therapy in Le Turnier reference

Cefazolin is appropriate for spinal epidural abscess

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Effectiveness of antibiotic for treatment of bacterial meningitis is not just related to CSF penetration (agree)

Rapid bactericidal activity required for optimal therapy → increased rate of neurological complications if CSF isn’t rapidly cleared of bacteria (time to activity therapy critical, bactericidal vs static is more lab than clinical phenom)

Ceftriaxone > cefuroxime for children with bacterial meningitis\(^1\) (87% had gram-negative meningitis, no MSSA)

Very limited clinical data on use of cefazolin for treatment of staphylococcal meningitis (because we were taught we couldn’t use it 😊)

Some patients received combination therapy in Le Turnier reference (cloxacillin arm also received combo; some patients received cefazolin monotherapy with cure)

Cefazolin is appropriate for spinal epidural abscess (agree!)
Cefazolin is a reasonable treatment option for susceptible CNS infections.

Clinical data are limited and the most data is with MSSA.

I wouldn’t give cefazolin to my mom if she had a gram-negative CNS infection.

Studies describe higher brain tissue concentrations for cefazolin than nafcillin.

Many studies describe adequate CSF concentrations (if CSF concentrations matter).

High-dose, continuous infusion might be the answer, but optimal dose is to be determined.

2g IV q6h or 8-10g continuous infusion might be the way to go for now.

**MYTH: LINEZOLID MUST BE AVOIDED IN PATIENTS RECEIVING SSRIS**

*Monoamine Oxidase Inhibition:* Linezolid is a reversible, nonselective inhibitor of monoamine oxidase. Therefore, linezolid has the potential for interaction with adrenergic and serotonergic agents.

**Serotonin Syndrome**
*Spontaneous reports of serotonin syndrome associated with the co-administration of ZYVOX and serotonergic agents, including antidepressants such as selective serotonin reuptake inhibitors (SSRIs), have been reported (see PRECAUTIONS, Drug Interactions).*
• Retrospective, population-based cohort study using Canadian database
• 1134 adults 66 years or older from 2014-2021
  • 19% also taking an antidepressant
  • qSSRI, SNRI, TCA, MAOI, Bupropion, Trazodone, or others
  • Also collected data on other serotonergic meds
• Most overlap = 7 days (IQR 5-10 days)
• Primary outcome = SS requiring healthcare visit (outpatient or hospitalization) within 30 days of linezolid
• Less than 6 patients had SS (cannot report exact number due to privacy)
• Less cases in group with concomitant antidepressants
• Maybe more altered mental status (11.6% vs 6.9%, risk difference 4.8 (0.7 to 10.1))
FACT: LINEZOLID AND SSRI CO-ADMINISTRATION IS OKAY; COUNSEL AND MONITOR THE PATIENT

UPMC Health System Safe Practice Guideline Topic:
Linezolid Interaction Guideline
Date: 06/25/2023

LINEZOLID INTERACTIONS AND SIDE EFFECTS

1. Use of linezolid with concomitant serotonergic agents other than MAOI’s is not an absolute contraindication.
2. Patients on more than 1 serotonergic agent can also receive linezolid provided it is clinically appropriate and the patient is monitored for signs of serotonin syndrome
3. There are no food restrictions for inpatients receiving linezolid
4. Therapeutic drug monitoring for linezolid should be considered in patients requiring long term linezolid (greater than 2 weeks) or requiring greater than 1 week in the setting of renal failure.
“Renal Insufficiency: The pharmacokinetics of the parent drug, linezolid, are not altered in patients with any degree of renal insufficiency; however, the two primary metabolites of linezolid may accumulate in patients with renal insufficiency, with the amount of accumulation increasing with the severity of renal dysfunction. The clinical significance of accumulation of these two metabolites has not been determined in patients with severe renal insufficiency. Because similar plasma concentrations of linezolid are achieved regardless of renal function, no dose adjustment is recommended for patients with renal insufficiency. However, given the absence of information on the clinical significance of accumulation of the primary metabolites, use of linezolid in patients with renal insufficiency should be weighed against the potential risks of accumulation of these metabolites.”
# Accumulation in Renal Impairment

## Table 1
Concentrations of linezolid and its major metabolites stratified by renal impairment

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total (n = 39)</th>
<th>Study group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No renal impairment (n = 17)</td>
</tr>
<tr>
<td>No. of serum samples</td>
<td>138</td>
<td>41  (2–4)</td>
</tr>
<tr>
<td>No. of samples/patient</td>
<td>3 (2–4)</td>
<td>2 (2–3)</td>
</tr>
<tr>
<td>Concentration (mg/liter)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Linezolid</td>
<td>10.8 (6.3–17.4)</td>
<td>7.6 (4.4–14.3)</td>
</tr>
<tr>
<td>PNU-142300</td>
<td>4.4 (2.5–6.6)</td>
<td>1.6 (0.8–3.1)</td>
</tr>
<tr>
<td>PNU-142586</td>
<td>11.4 (6.2–19.4)</td>
<td>4.9 (2.7–7.0)</td>
</tr>
<tr>
<td>Time since last dose (h)</td>
<td>7.5 (3.6–9.7)</td>
<td>7.6 (3.6–9.8)</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data are presented as medians (IQR).

<sup>b</sup>Renal impairment defined as eGFR of <60 ml/min/1.73 m².

<table>
<thead>
<tr>
<th>PK/PD data</th>
<th>Cases* (n = 26)</th>
<th>Controls† (n = 26)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmin, ss (mg/L), median (IQR)</td>
<td>20.6 (17.4)</td>
<td>2.7 (11.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cmax, ss (mg/L), median (IQR)</td>
<td>34.1 (22.7)</td>
<td>16.5 (11.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cmin, ss &lt; 2 mg/L, n (%)</td>
<td>0 (0)</td>
<td>10 (38.5)</td>
<td>0.002</td>
</tr>
<tr>
<td>Cmin, ss &gt; 10 mg/L, n (%)</td>
<td>20 (76.9)</td>
<td>7 (26.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>100% time &gt; MIC, n (%)</td>
<td>26 (100)</td>
<td>16 (61.5)</td>
<td>0.002</td>
</tr>
<tr>
<td>Toxicity data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia‡, n (%)</td>
<td>7/25 (28.0)</td>
<td>6/25 (24)</td>
<td>0.747</td>
</tr>
<tr>
<td>Thrombocytopenia§, n (%)</td>
<td>13/25 (52.0)</td>
<td>8/24 (33.3)</td>
<td>0.187</td>
</tr>
<tr>
<td>Final platelet count, median (IQR)§</td>
<td>81 (87)</td>
<td>203 (14)</td>
<td>0.001</td>
</tr>
<tr>
<td>Final platelet count &lt;100.000/ mm³§, n (%)</td>
<td>17/25 (68.0)</td>
<td>4/24 (16.7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
## TDM Thresholds for Linezolid Efficacy and Toxicity

<table>
<thead>
<tr>
<th>Pharmacokinetic Measurement</th>
<th>Lower Threshold (Efficacy)</th>
<th>Upper Threshold (Toxicity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time spent above the MIC (T&gt;MIC)</td>
<td>&gt;82–98%&lt;sup&gt;40&lt;/sup&gt; or &gt;85%&lt;sup&gt;42&lt;/sup&gt;</td>
<td>N/A</td>
</tr>
<tr>
<td>Duration of therapy</td>
<td>N/A</td>
<td>Usually &gt;14–28 days&lt;sup&gt;42,83,91&lt;/sup&gt;</td>
</tr>
<tr>
<td>Area under the concentration versus time curve from 0 to 24 hours (AUC)</td>
<td>&gt;160–400 mg × h/L depending on the MIC of the infecting pathogen&lt;sup&gt;33,40,42&lt;/sup&gt;</td>
<td>&gt;280–300 mg × h/L&lt;sup&gt;33,42&lt;/sup&gt; or &gt;400–800 mg × h/L&lt;sup&gt;87&lt;/sup&gt; depending on the duration of therapy and severity of illness; the proposed higher end of this range may be tolerable for less than 2 weeks&lt;sup&gt;87&lt;/sup&gt;</td>
</tr>
<tr>
<td>AUC:MIC</td>
<td>&gt;100 (may vary with infection site)&lt;sup&gt;23,40,42,43&lt;/sup&gt;</td>
<td>Depends on duration of therapy and pathogen MIC</td>
</tr>
<tr>
<td>Trough concentration (C&lt;sub&gt;min&lt;/sub&gt;)</td>
<td>&gt;2 mg/L (may be higher depending on the MIC of the infecting pathogen)&lt;sup&gt;98&lt;/sup&gt;</td>
<td>&gt;7–8 mg/L&lt;sup&gt;46,48&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
FACTS

• 2-fold increase in risk of thrombocytopenia with eGFR < 60

• Linezolid myelosuppression is very likely exposure dependent

• PK/toxicodynamic model associates a Cmin of 8.06 mg/LL as the threshold for 50% decrease in platelet precursor cells

• Consider tdm in patients with renal dysfunction, dose adjustment may be necessary

Dosing Consult: Linezolid Therapeutic Drug Monitoring

Breakpoints

Health & Fitness

Listen on Apple Podcasts

In the second episode of Breakpoints' Dosing Consult series, Drs. Ryan Crass (@crasspofungin) and Amit Pai (@DosingMatters) join Dr. Jillian Hayes (@thejillianhayes) to break down the 5 Ws and 1 H of linezolid TDM.

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Bibliography
MYTH: CLINDAMYCIN IS A FIRST-LINE DRUG FOR PREVENTION OF SURGICAL SITE INFECTIONS IN PATIENTS WITH ALLERGIES
Implications of Penicillin / β-lactam Allergy

Use of second-line, non-β-lactam antibiotics

- Vancomycin
- Aztreonam
- Fluoroquinolones
- Clindamycin

Just 1 dose of clindamycin is associated with increased risk of *C. difficile* infection

14% Risk of death

> 3-fold Risk for adverse outcome

69% Risk of MRSA

26% Risk of Cdiff

50% Risk of Surgical Site Infection

+ $609 Drug costs during hospitalization

Penicillin allergy label is a key modifiable risk factor

I’m a big believer in finding the silver lining of drug shortages but this one is the holy grail: finally the date everyone realizes there is almost no role for clindamycin in the care of patients with infectious diseases.

(zosyn+linezolid for nec fasc don’t @ me)

Good afternoon,

Attached you will the drug shortage mitigation plan for
MYTH: ORAL FOSFOMYCIN IS AN EXCELLENT DRUG FOR UNCOMPLICATED CYSTITIS

- Oral
- Once dose
- Rapidly bactericidal?
- Not systemically absorbed (low collateral damage)
- Early RCT of 521 patients (female, cystitis, >80% E. coli) found no difference compared to 7-days nitrofurantoin

**Comparison of Single-Dose Fosfomycin and a 7-Day Course of Nitrofurantoin in Female Patients with Uncomplicated Urinary Tract Infection**

*Gary E. Stein, PharmD*

*Department of Medicine, Michigan State University, East Lansing, Michigan*
AND THEN, THE INFAMOUS ECCMID 2018 LATE BREAKERS

- 513 women with uncomplicated cystitis
- 5 days of nitrofurantoin at 28 days =
  - Greater clinical resolution (70% vs 58%, P = 0.004)
  - Greater microbiologic resolution (74% vs 63%, P = 0.04)
  - Same drug-related ADEs
WHAT CHANGED?

- Increasing resistance
- Improved AST showcasing issues with non-E. coli bugs
  - Requires G6P supplementation for agar dilution
  - Other methods have issues
- Glucose-6-phosphate (G6P) is not present in human urine
  - Antibacterial activity and pharmacodynamics of fosfomycin impaired \textit{in vivo}

FACT: ORAL FOSFOMYCIN IS THE BEST ASB DRUG IN THE WORLD

- Oral packets actually quite costly
- Same eGFR limitations as nitrofurantoin
- AST is a nightmare
- RCT evidence fairly convincing it’s not nitrofurantoin
- Does it work in the urine??
- Every now and then we’ll try to for an ESBL to avoid carbapenem outpatient
2. For patients who warrant MRSA coverage but do not need intravenous antibiotics, TMP-SMX, doxycycline, or linezolid can be initiated. Providers should note that while studies have demonstrated the activity of TMP-SMX against \( \beta \)-hemolytic streptococci, overall the activity of TMP-SMX and doxycycline against \( \beta \)-hemolytic streptococci is largely unknown (8,47).

a. If TMP-SMX or doxycycline is initiated, it is reasonable to consider combination therapy with a \( \beta \)-lactam antibiotic for the treatment of possible mixed MRSA/streptococcal infection (8).

**MYTH:** TRIMETHOPRIM-SULFAMETHOXAZOLE DOES NOT HAVE IN VITRO ACTIVITY AGAINST S. PYOGENES
Early studies did not control thymidine content of test media
- ↑thymidine ↓sulfa inhibitory effect
What if I told you...

TABLE 2 (Continued)

<table>
<thead>
<tr>
<th>Organism (no. of isolates) and drug $^g$</th>
<th>MIC$_{50}$ (µg/ml)</th>
<th>MIC$_{90}$ (µg/ml)</th>
<th>MIC range (µg/ml)</th>
<th>% of isolates with breakpoint according to $^c$:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>CLSI</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>S</td>
</tr>
<tr>
<td>Solithromycin</td>
<td>0.015</td>
<td>0.03</td>
<td>0.004–0.5</td>
<td>---</td>
</tr>
<tr>
<td>Telithromycin</td>
<td>0.015</td>
<td>0.12</td>
<td>0.008–32</td>
<td>---</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>0.12</td>
<td>&gt;32</td>
<td>0.03–32</td>
<td>75.2</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>≤0.25</td>
<td>&gt;2</td>
<td>≤0.25–&gt;2</td>
<td>84.9</td>
</tr>
<tr>
<td>Penicillin</td>
<td>≤0.06</td>
<td>≤0.06</td>
<td>≤0.06–0.12</td>
<td>100.0</td>
</tr>
<tr>
<td>Amoxicillin-clavulanate</td>
<td>≤1</td>
<td>≤1</td>
<td>≤1–2</td>
<td>---</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>≤0.06</td>
<td>0.12</td>
<td>≤0.06–0.5</td>
<td>100.0</td>
</tr>
<tr>
<td>Linezolid</td>
<td>1</td>
<td>1</td>
<td>≤0.12–1</td>
<td>100.0</td>
</tr>
<tr>
<td>Moxifloxacin</td>
<td>≤0.12</td>
<td>0.25</td>
<td>≤0.12–4</td>
<td>53.5</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>≤0.5</td>
<td>&gt;8</td>
<td>≤0.5–&gt;8</td>
<td>---</td>
</tr>
<tr>
<td><strong>TMP-SMX</strong></td>
<td>≤0.5</td>
<td>≤0.5</td>
<td>≤0.5–&gt;4</td>
<td>---</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>0.25</td>
<td>0.5</td>
<td>≤0.12–1</td>
<td>100.0</td>
</tr>
</tbody>
</table>

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$^g$ TMP-SMX, trimethoprim-sulfamethoxazole.

$^h$ Organisms include *Streptococcus pyogenes* (689 isolates), *Streptococcus agalactiae* (579), and *Streptococcus dysgalactiae* (225).

Early studies did not control thymidine content of test media
  – ↑thymidine ↓sulfa inhibitory effect
Nonpurulent cellulitis → β-lactam monotherapy
Impetigo, purulent cellulitis, abscess, wound → TMP/SMX monotherapy
  – >20% of patients had area erythema >75 cm²
  – Talan 2016
    • 2 DS TMP/SMX PO BID x 7 days = 80% cure of drained abscess
  – Miller 2015
    • 2 SS TMP/SMX PO BID x 10 days = 76.4% cure (abscess, cellulitis, & mixed)
Myth: Doxycycline is contraindicated in pregnancy and pediatric patients less than 8 years old.
FACT: PLEASE TREAT RICKETTSIAL DISEASES WITH DOXY

- Doxycycline has structural modifications that improve antibacterial activity, decrease calcium binding, and diminish ADRs compared to tetracycline
- AAP says ≤ 21 days of doxy is acceptable
- Pregnancy teams at FDA, WHO reviewing

The current label allows for the use of doxycycline in pediatric rickettsial patients because other antibiotics are not likely to be effective for treatment. However, clearer language on the drug label may help avoid hesitation in prescribing life-saving doxycycline to children, and reinforce CDC and AAP RMSF treatment recommendations. Despite the current label warning, it is important for healthcare providers to know that doxycycline has not been shown to cause tooth staining in the dose and duration used to treat rickettsial diseases. Early administration of doxycycline in adults and children can prevent severe illness and save lives.

CDC.gov: Research on doxycycline and tooth staining
MYTH: RIFAMPIN AND GENTAMICIN ARE ESSENTIAL FOR TREATMENT OF STAPHYLOCOCCUS SPP. PROSTHETIC VALVE ENDOCARDITIS

Fact: I direct you to a beautiful review on this topic in OFID

*Deconstructing the Dogma: Systematic Literature Review and Meta-analysis of Adjunctive Gentamicin and Rifampin in Staphylococcal Prosthetic Valve Endocarditis*

Jonathan H. Ryder, Steven Y. C. Tong, Jason C. Gallagher, Emily G. McDonald, Irani Thevarajan, Todd C. Lee, and Nicolás W. Cortés-Penfield
ID consult recommended

MRSA

Vancomycin (IV)
Dosing per pharmacy

OR

Daptomycin
8-10mg/kg IV q24h

Additional Information

For persistently positive blood cultures (i.e., ≥72 hours), consider escalation to daptomycin 8-10mg/kg IV every 24h plus ceftaroline 600mg IV every 12h to facilitate blood culture clearance. Cardiac surgery consult is strongly recommended in cases of persistent bacteremia.

*Prosthetic valve management in patients receiving oxacillin, cefazolin, or vancomycin:

- If blood cultures are negative (i.e., have cleared) and patient has plan for surgery, addition of gentamicin and rifampin is not recommended
- If blood cultures are negative and there is no surgical plan OR if blood cultures have not cleared, addition of gentamicin 3mg/kg IV every 24h for 2 weeks plus rifampin 300mg PO three times daily for 6 weeks is recommended
- Recent data suggests no benefit of rifampin therapy, so risk of antibiotic-related toxicities and drug interactions should be weighed when considering use (Le Bot, Clin Infect Dis. 2020 Jul 24;ciaa1040)

In patients receiving daptomycin, do NOT add rifampin and gentamicin as no synergy exists (LaPlante, Antimicrob Agents Chemother. 2009 Sep;53(9):3880-6).
DEBUNKING ANTIBIOTIC MYTHS FOR THE INFECTIOUS DISEASES CLINICIAN

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