Management of MRSA Infections in Adult Patients

2011 Clinical Practice Guidelines by the Infectious Diseases Society of America

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Objectives

To provide evidence-based guidance to adult and pediatric clinicians managing patients with MRSA infections

To discuss the management of different clinical syndromes caused by MRSA

The guidelines do not address:

- MRSA infection prevention strategies in healthcare settings (e.g. active surveillance testing, perioperative prophylaxis)
- Management of outbreaks in community settings
Background

Panel first convened in 2007

Literature review performed via PUBMED between 1961-2010: mostly clinical human studies, but also experimental animal models and in vitro studies

Reviewed and endorsed by the Pediatric Infectious Diseases Society, American Academy of Pediatrics, and American College of Emergency Physicians
Clinical Topics

1. Skin and soft tissue infections
2. Recurrent skin and soft tissue infections
3. MRSA bacteremia and endocarditis
4. MRSA pneumonia
5. MRSA bone and joint infections
6. MRSA central nervous system infections
7. Role of combination or adjunctive therapies
8. Vancomycin dosing and monitoring
9. Vancomycin susceptibility testing
10. Management of persistent bacteremia and vancomycin treatment failures
11. MRSA neonatal infections

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# Evidence Grading System

## Strength of recommendation
- **A** Good evidence to support a recommendation for or against use
- **B** Moderate evidence to support a recommendation for or against use
- **C** Poor evidence to support a recommendation

## Quality of evidence
- **I** Evidence from $\geq 1$ properly randomized, controlled trial
- **II** Evidence from $\geq 1$ well-designed clinical trial, without randomization; from cohort or case-controlled analytic studies (preferably from $> 1$ center); from multiple time-series; or from dramatic results from uncontrolled experiments
- **III** Evidence from opinions of respected authorities; based on clinical experience, descriptive studies, or reports of expert committees.


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Case 1

32 y/o M with 3 days of an enlarging, painful lesion on his L thigh that he attributes to a “spider bite”.

T 36.9 BP 118/70 P 82
What is the appropriate management of this patient?

A. Incision and drainage alone

B. Incision and drainage **plus** oral anti-MRSA antimicrobial agent

C. Oral anti-MRSA antimicrobial agent
Abscesses

Incision and drainage is the primary treatment (AII).
- For simple abscesses or boils, I&D alone likely adequate

Do antibiotics provide additional benefit?
- Multiple, observational studies: high cure rates with or without abx
- 3 RCTs of uncomplicated skin abscesses; 2 large NIH trials ongoing

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Is clinical cure the only important endpoint?

Development of recurrent lesions


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Antibiotic therapy is recommended for abscesses associated with:

- Severe, extensive disease, rapidly progressive with associated cellulitis or septic phlebitis
- Signs & sx of systemic illness
- Associated comorbidities, immunosuppressed
- Extremes of age
- Difficult to drain area (e.g. face, hand, genitalia)
- Failure of prior I&D

(AIII)
Microbiology of Purulent SSTIs

- MRSA: 59%
- MSSA: 17%
- B-hemolytic strep: 3%
- non-B hemolytic strep: 4%
- other: 8%
- unknown: 9%

Moran NEJM 2006; 355: 666-74

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Purulent Cellulitis: *S. aureus* >>> β-hemolytic strep

Cellulitis associated with purulent drainage or exudate **without** a drainable abscess

- Empiric Rx for CA-MRSA is recommended *(AII).*
- Empiric Rx for β-hemolytic strep unlikely needed *(AII).*
- Duration of therapy: 5-10 days, individualize based on clinical response *(AII).*
<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dose</th>
<th>Evidence Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMP-SMX</td>
<td>1-2 DS BID</td>
<td>All</td>
</tr>
<tr>
<td>Doxycycline, Minocycline</td>
<td>100 BID</td>
<td>All</td>
</tr>
<tr>
<td>Clindamycinin</td>
<td>300-450 TID</td>
<td>All</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600 BID</td>
<td>All</td>
</tr>
</tbody>
</table>
Case 2

28 year old woman presents with erythema of her right arm over past 48 hours. There is no purulent drainage, exudate or abscess. No evidence of joint or bursa involvement.

T 37.0 BP 132/70 P 78
What is the appropriate management of this patient?

A. Clindamycin 300 mg PO tid

B. Cephalexin 500 mg QID, monitor clinically with addition of TMP/SMX if no response

C. Cephalexin 500 mg QID and TMP/SMX 2 DS tab PO bid
Nonpurulent Cellulitis: β-hemolytic strep vs. S. aureus?

Empiric Rx for β-hemolytic strep recommended (AII)

- Prospective study\(^1\), 248 hospitalized pts
  - 73\% due to β-hemolytic strep (diagnosis by serologies for ASO and anti-DNAse-B, blood cultures); 27\% with no identified cause.
  - Overall 96\% response rate to β-lactam antibiotic.
- Retrospective study\(^2\)
  - ↑ treatment failures with TMP-SMX vs. β-lactam or clindamycin

The role of CA-MRSA is unknown.

- Empiric Rx for MRSA if fails to respond to β-lactam
- Consider in patients with systemic toxicity

\(^1\) Jeng et al Medicine 2010; 89:217-26  \(^2\) Elliott et al Pediatrics 2009; 123:e959-66

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Outpatient nonpurulent cellulitis: Empiric Rx for $\beta$-hemolytic streptococci +/- MRSA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Adult Dose</th>
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<tbody>
<tr>
<td>Cephalexin</td>
<td>500 QID</td>
</tr>
<tr>
<td>Dicloxacillin</td>
<td>500 QID</td>
</tr>
<tr>
<td>Clindamycin*</td>
<td>300-450 TID</td>
</tr>
<tr>
<td>Linezolid*</td>
<td>600 BID</td>
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</table>

*Also have activity against CA-MRSA

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Complicated SSTI

- Surgical debridement & empiric therapy for MRSA pending cultures

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<td>15-20 mg/kg IV Q8-12</td>
<td>AI</td>
</tr>
<tr>
<td>Linezolid</td>
<td>600 mg PO/IV BID</td>
<td>AI</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>4 mg/kg IV QD</td>
<td>AI</td>
</tr>
<tr>
<td>Telavancin</td>
<td>10 mg/kg IV QD</td>
<td>AI</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>600 mg PO/IV Q8</td>
<td>AIII</td>
</tr>
</tbody>
</table>

*Tigecycline associated with ↑ mortality; consider alternate agent for MRSA SSTI
*Ceftaroline: FDA approved after guidelines

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Case 3

The patient in case 1 returns 4 weeks later with another abscess on his opposite thigh. He notes that after I & D of his first abscess, he didn’t keep his wound covered and occasionally touched the site to “make sure it was healing.”

The site of his old abscess is clean with a well-healed scar. He undergoes I&D and receives 1 week of TMP-SMX.
What is the appropriate management of this patient?

A. Emphasize personal hygiene measures
B. Decolonize with mupirocin and chlorhexidine showers
C. Decolonize with TMP-SMX and rifampin
D. A and B
E. A, B, and C
What is the Management of Recurrent Skin and Soft Tissue Infections?
What is the Management of Recurrent Skin and Soft Tissue Infections?

**Personal Hygiene/Wound Care (AIII)**
- Cover draining wounds
- Hand hygiene after touching infected skin
- Avoid reusing/sharing personal items if active infection

**Environmental Hygiene (CIII)**
- Clean high-touch surfaces

**Pathogen**

**Host**

**Environment**

*Decolonization (CIII)*
- If above measures fail
- If ongoing household transmission

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Recurrent MRSA SSTI: Decolonization Regimens

Mupirocin twice daily x 5-10 days (CIII)
- ↓ recurrent MSSA SSTI in small RCT\(^1\)
- RCT military recruits: ↓ in CA-MRSA nasal colonization but not 1\(^{st}\) time SSTI\(^2\)

Mupirocin twice daily x 5-10 days AND topical skin antiseptic (e.g. chlorhexidine) x 5-14 days (CIII)
- RCT military recruits: CHG wipes alone not ↓ SSTI rates\(^3\), transient effect on colonization
- Consider dilute bleach baths: ¼ cup per ¼ tub (13 gallons) of water for 15 min, 2x/week for 3 mths

\(^1\)Raz Arch Intern Med 1996; 156:1109-12; \(^2\)Ellis MW AAC 2007; 51: 3591-8 \(^3\)Whitman ICHE 2010; 12: 1207-15

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Oral Antibiotics for Decolonization?

Not routinely recommended for decolonization (AIII). An oral agent in combination with rifampin (if susceptible) may be considered if infections recur despite other measures (CIII).

- Cochrane review¹: No benefit of oral abx in MRSA eradication among patients in healthcare settings

- Systematic review²: Rifampin + staph abx vs. staph abx alone
  - Rifampin combo superior in ↓ S. aureus colonization
  - No studies evaluated impact on infection rates

- Watch out for drug interactions, side effects, resistance

¹Cochrane Review 2003; 4CD003340 ²Falagas ME AJIC 2007; 35: 106-14

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Case 4

35 y/o F previously healthy with 4 days of fever, chills, myalgias, and cough. Now with increasing dyspnea and hemoptysis x 24 hrs

T38.7 P120 BP96/60 R24 89%RA

Moderate respiratory distress with coarse rhonchi

WBC 15, Hct 44, Plt 425

Rapid flu: + influenza A

Sputum gram stain/ cx: pending

Intubated, admitted to ICU
In addition to starting anti-influenza therapy, would you treat with antibiotics and if so which?

A. None

B. Ceftriaxone and azithromycin

C. Vancomycin and ceftriaxone and azithromycin

D. Linezolid and cefepime
## MRSA pneumonia

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</tr>
<tr>
<td>Clindamycin</td>
<td>600 mg PO/IV TID</td>
<td>BIII</td>
</tr>
</tbody>
</table>

*Jung Crit Care Med 2010*
MRSA pneumonia: Vancomycin vs. Linezolid?

- No difference in microbiologic success rates
- No difference in eradication rates of MRSA


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**MRSA pneumonia**

- Daptomycin should **not** be used for Rx of pneumonia, (inactivated by pulmonary surfactant)
  - Daptomycin may be used in patients with hematogenous septic pulmonary emboli

- Empiric Rx for MRSA recommended for severe CAP (ICU admission, necrotizing or cavitary infiltrates, or empyema)
  - Discontinue empiric Rx if cultures do not grow MRSA

- Duration of therapy: 7-21 days

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1Rehm JAC 2008;62:1413-21; Silverman JID 2005; 191:2149-52
Case 5

60 year old male prison inmate presents with 4 days of fevers and chills and decreased L eye vision.

T 38.5 BP 102/71 P 104 R 20 O2 sat 98% RA weight 100 kg

Eye: Bilateral creamy white-yellow discharge, vitreous strands/ infiltrates, L eye - intraretinal hemorrhage

Heart: 2/6 systolic murmur at apex

Chest: CTAB

Skin: no peripheral stigmata of endocarditis

Labs: 15.5> 39 > 350 Cr 0.8

Started on IV vancomycin 1 gram every 12 hours
Case continued

HD #1 blood cx: 3/4 MRSA (vanco MIC 1)
- Received intravitreal injection of vancomycin

HD # 5
- T 37.8 BP 138/70 P 113 R 16 O2 sat 96% RA
- Alert and interactive, no new physical exam findings
- Blood cx: 2/2 MRSA (vanco MIC 1)
- Vancomycin trough 7 μg/mL

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Echocardiogram

2 cm mitral valve vegetation
Brain MRI
What changes to the patient’s antibiotics should be made?

A. Add gentamicin to vancomycin

B. Add rifampin to vancomycin

C. Increase vancomycin dose to 1.5 gram IV Q12 hrs, target goal trough of 15-20 μg/mL

D. Discontinue vancomycin and start IV daptomycin 6 mg/kg Q24 hrs
MRSA bacteremia and endocarditis

IV vancomycin (AII) or IV daptomycin 6 mg/kg QD (AI).
236 pts randomized to IV daptomycin 6 mg/kg QD vs. (vancomycin or nafcillin) + gentamicin 1 mg/kg Q8 x 4 days

Some experts recommend IV daptomycin 8-10 mg/kg QD (BIII).

Fowler VG NEJM 2006; 355: 653-65
Is there a role for adjunctive gentamicin or rifampin? More is not always better...

Addition of gentamicin (AII) or rifampin (AI) to vancomycin is not recommended. No clear evidence of benefit.

- Vanco + rifampin: 1 RCT MRSA endocarditis

<table>
<thead>
<tr>
<th></th>
<th>Vancomycin</th>
<th>Vancomycin + rifampin</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment failures</td>
<td>4/ 22 (18%)</td>
<td>2/20 (10%)</td>
<td>&gt;.05</td>
</tr>
<tr>
<td>Median duration of bacteremia</td>
<td>7 days (5-11)</td>
<td>9 days (6-13)</td>
<td>&gt;.05</td>
</tr>
<tr>
<td>Median duration of fever</td>
<td>7 days (3-8)</td>
<td>7 days (3-10)</td>
<td>&gt;.05</td>
</tr>
</tbody>
</table>

- Vanco + gentamicin: in vitro data, but no clinical studies.

- Nafcillin + gent vs. nafcillin RCT MSSA bacteremia: ↓ duration of bacteremia x 1 day but no difference in morbidity/ mortality

Addition of gentamicin or rifampin to vancomycin is associated with ↑ toxicity

↑ risk of nephrotoxicity with initial low-dose gentamicin

↑ risk of elevated transaminases (≥ 5X baseline), drug interactions with rifampin, resistance concerns

*Gentamicin was an independent predictor of clinically significant ↓ in CrCl

1 Fowler NEJM 2006;355:653-65; Cosgrove S CID 2009;48:713-21; 2 Riedel D AAC 2008;52:2463-7

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MRSA bacteremia and endocarditis: Source control is critical

- Identify source and extent of infection; eliminate and debride other sites of infection (AII).

- Repeat blood cultures 2-4 days after initial positive cultures and as needed thereafter to document clearance of bacteremia (AII).

- Echocardiography recommended for all patients with bacteremia (AII). TEE is preferred over TTE.

- Evaluate for valve replacement surgery if:
  - vegetation > 10 mm, ≥ 1 embolic event, severe valvular insufficiency, valvular perforation, decompensated heart failure, perivalvular/myocardial abscess, new heart block
Duration of therapy

Lower success rates in pts receiving < 14 days of therapy have been observed

- Uncomplicated bacteremia: Minimum duration is 2 weeks if:
  - Exclude endocarditis
  - No implanted prostheses (e.g. prosthetic valves, cardiac devices, arthroplasties)
  - Negative follow-up blood cultures for MRSA at 2-4 days
  - Defervescence within 72 hours of therapy
  - No evidence of metastatic sites of infection

- Complicated bacteremia (if do not meet above criteria): 4-6 weeks

1Fowler NEJM 2006;355:653-65; Cosgrove CID 2008;46:S386-93
Vancomycin Dosing

IV vancomycin 15-20 mg/kg (actual body weight) every 8-12 hrs, not to exceed 2 g per dose (BIII).

In seriously ill patients with suspected MRSA infection, a loading dose of 25-30 mg/kg (actual body weight) may be considered (CIII).

- Given risk of red man syndrome and possible anaphylaxis associated with large doses, consider prolonging infusion time 2 h and pre-medication with antihistamine.

Continuous infusion vancomycin is unlikely to substantially improve patient outcome, compared with intermittent dosing (AII).

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Vancomycin Therapeutic Drug Monitoring

- Obtain serum troughs at steady state (b/f 4\(^{th}\) or 5\(^{th}\) dose) (BII).
- Monitoring of peak vancomycin concentrations is not recommended (BII).
- For serious infections (e.g. bacteremia, endocarditis, osteomyelitis, pneumonia, severe SSTI [nec fasc]), target vancomycin trough concentrations of 15-20 \(\mu g/mL\) (BII).
- For most patients with SSTI with normal renal function and not obese, traditional doses of 1 g Q12 are adequate and trough monitoring is not required (BII).


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Targeting Higher Vancomycin Troughs: What is the Evidence?

- **pK/pD:** Higher troughs ↑ likelihood of achieving target AUC/ MIC
  
  AUC/ MIC ≥ 400 vs. <400 associated with improved clinical/ microbiologic response\(^1\)

<table>
<thead>
<tr>
<th>Mean Trough</th>
<th>Mean AUC(^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9.4 µg/mL</td>
<td>318 ± 111 µg/h/mL</td>
</tr>
<tr>
<td>20.4 µg/mL</td>
<td>418 ± 152 µg/h/mL</td>
</tr>
</tbody>
</table>

- **Resistance:** Lower troughs may select for resistant subpopulations (e.g. hVISA)\(^3\).

- **Clinical outcomes:** Unclear correlation between ↑ troughs\(^4\)
  
  - Further clinical study is needed
  - Watch for potential ↑ nephrotoxicity

A few words on Vanco MICs....

- Probability of achieving target AUC/MIC is 0% if vancomycin MIC = 2 µg/mL with low or high-dose vancomycin
- Vanco MICs of 2 µg/mL associated with ↑ vanco Rx failures
- “MIC creep” observed in some centers but not others
  - Perhaps due to clonal dissemination or technical artifact


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Vancomycin Susceptibility Testing

There is considerable variability in MIC results depending on method used

- Certain methods (Etest, Microscan, BD-Phoenix) report higher MICs than reference methods while others (Sensititre and Vitek 2) tend to undercall resistance

Acceptable variability for MIC methods is +/- one doubling dilution (e.g. is MIC of 1 really 2 or vice versa?)

Swenson JCM 2009; 47:2013-7
Detection of Isolates with Vancomycin MIC of ≤ 2 µg/mL

- BMD: 97% (MIC≤1), 3% (MIC=1.5), 0% (MIC=2)
- Etest: 58% (MIC=1.5), 32% (MIC=2)

N=1800

Sader AAC 2009; 53:4127-32
How should Vancomycin MIC Results be used to Guide Therapy?

For isolates with a vanco MIC $\leq 2 \mu g/mL$, the patient’s clinical response should determine continued use of vancomycin, independent of the MIC (AIII).

- If clinical and microbiological response to vanco, continue with close follow-up
- If no clinical or microbiologic response despite adequate debridement and removal of other foci of infection, alternative to vancomycin is recommended regardless of MIC.

For isolates with a vancomycin MIC $> 2 \mu g/mL$ (VISA or VRSA), an alternative to vancomycin should be used (AIII).
Case continued...

- Vancomycin dose increased to 1.5g Q 12 hours
- HD #6 blood cx: 2/2 MRSA (vanco MIC 1), vanco trough 13 (drawn before 3rd dose)
- HD #8 blood cx: 2/2 MRSA (vanco MIC 1, dapto MIC ≤ 0.5)
- HD #9 blood cx: prelim 1/2 Staph spp
  - T37.2 BP132/84 HR94 R18 O295-100% RA
  - R eye – retinal detachment
  - No other significant changes to physical exam
  - Repeat Echo: ↑ vegetation size with longer mobile element and extension along the annulus
In addition to CT surgery eval, what changes to the patient’s antibiotics, if any, should be made?

A. No changes to his antibiotics should be made

B. Add gentamicin to vancomycin

C. Discontinue vancomycin and start IV daptomycin 8 mg/kg Q24 hrs

D. Discontinue vancomycin and start IV daptomycin 8 mg/kg Q24 hrs + linezolid 600 mg BID
Defining Vancomycin Treatment Failure: Approach to Persistent MRSA Bacteremia

Median time to clearance of bacteremia\(^1,2,3\):

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<table>
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<tr>
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<tbody>
<tr>
<td>MSSA with (\beta)-lactam abx</td>
<td>3-4 days</td>
</tr>
<tr>
<td>MRSA with vancomycin, daptomycin</td>
<td>7-9 days</td>
</tr>
</tbody>
</table>

Consideration factors when contemplating change in therapy:
- Patient’s overall clinical response
- Vancomycin trough concentrations
- Results of susceptibility testing (e.g. vanco MIC)
- Presence of and ability to remove other foci of infection


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Management of Persistent MRSA Bacteremia on Vancomycin Therapy

Consider change in therapy if:
1) Unsatisfactory clinical response, regardless of MIC
   or
2) Vanco MIC = 2

No change in therapy if:
1) Clinically responding and
2) Vanco MIC < 2

Day of vancomycin therapy

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Persistent MRSA Bacteremia/ Vancomycin Treatment Failures: Therapeutic Considerations

In general, recommend a change in therapy rather than addition of other agents (e.g. rifampin/ gentamicin) to vanco

High-dose daptomycin (10 mg/kg/day), if susceptible, in combination with another agent (BIII):

- Gentamicin 1 mg/kg IV Q8
- Rifampin 600 mg PO/ IV QD or 300-450 mg PO/ IV twice daily
- Linezolid 600 mg PO/ IV BID
- TMP-SMX 5 mg/kg IV BID
- β-lactam antibiotic

Note: prior vanco exposure and elevated vanco MICs associated with ↑ dapto MICs (> 1 µg/mL).


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How to manage reduced susceptibility to vancomycin and daptomycin?

- **Quinupristin-dalfopristin 7.5 mg/kg/dose IV Q8 (CIII)**
  - Used successfully in vanco Rx failures, but lower response rates for endocarditis and bacteremia of unknown source

- **TMP-SMX 5 mg/kg/dose IV BID (CIII)**
  - In vitro study: combo of dapto + TMP-SMX vs. dapto alone had more rapidly bactericidal activity for a dapto non-susceptible strain

- **Linezolid 600 mg PO/ IV BID (CIII)**
  - Case series suggest success when used alone or in combination with other abx; poor outcomes for left-sided endocarditis.

- **Telavancin 10 mg/kg/dose IV QD (CIII)**
  - 1 case report of persistent MRSA bacteremia successfully treated

**Case follow-up**

- **HD #9 blood cultures:** 1/2 MRSA
  - Daptomycin + linezolid started
  - R vitrectomy performed
- **HD #11 blood cultures:** negative
- **HD #15 OR for valve replacement surgery**
  - Intraoperative cultures mitral valve vegetation: + MRSA
- **Complicated course:** status epilepticus, ventilator-associated pneumonia, PEA arrest 2° to submassive PE, eventually recovered and discharged to SNF
- Received daptomycin 10 mg/kg QD + rifampin 300 mg TID for 6 weeks after MVR.
MRSA bone and joint infections

Surgical debridement is mainstay of therapy (AII).

Some experts recommend adding rifampin 300-450 BID:
- Animal models, small human trials of MSSA osteomyelitis
- Retrospective study: cure rate of 80%, no added benefit if debridement occurred

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<td>BII</td>
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<td>Linezolid</td>
<td>600 mg PO/ IV BID</td>
<td>BII</td>
</tr>
<tr>
<td>TMP-SMX + rifampin</td>
<td>4 mg/kg/dose (TMP) BID 600 mg QD (rifampin)</td>
<td>BII</td>
</tr>
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<td>600 mg PO/ IV Q8</td>
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Oral vs. IV vs. IV/PO therapy?

Optimal route of administration not established (**AII**).

**Chronic non-axial MSSA osteo, randomized trial**¹

<table>
<thead>
<tr>
<th></th>
<th>IV cloxacillin (6 wks IV/2 wks PO)</th>
<th>PO cotrimoxazole + rifampin X 8 wks</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cure rate</td>
<td>91%</td>
<td>89%</td>
<td>1.0</td>
</tr>
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**Retrospective cohort (MRSA subset)**²

<table>
<thead>
<tr>
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<th>IV (median 6 wks)*</th>
<th>IV (median 2 wks), then PO (median 42 days)</th>
<th>P-value</th>
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<tbody>
<tr>
<td>Cure rate</td>
<td>65%</td>
<td>65%</td>
<td>.99</td>
</tr>
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</table>

*61% also received oral therapy for median PO 21 days

** Median total duration of total therapy 60 and 56 days in both groups

¹Euba AAC 2009;53:4305-10; ²Daver J Infect 2007;54:539-44

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Duration of therapy?

Optimal duration is unknown; minimum 8 wks (AII).

Hematogenous MSSA vertebral osteo: 8 wks vs < 8 wks associated with improved outcomes \(^1,^2\)

<table>
<thead>
<tr>
<th>Duration of therapy</th>
<th>Recurrence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-6 weeks</td>
<td>~20-32%</td>
</tr>
<tr>
<td>8 weeks</td>
<td>~ 8%</td>
</tr>
<tr>
<td>≥ 10 weeks</td>
<td>10-14%</td>
</tr>
</tbody>
</table>

Some experts suggest an additional 1-3 months (and possibly longer for chronic infection or if no debridement) of oral rifampin-based combination therapy (CIII)

MRSA Infections of the Central Nervous System

Treatment difficult due to blood-brain barrier

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>CSF penetration</th>
<th>CSF concentration</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin (BII)</td>
<td>1-5%</td>
<td>2-6 µg/mL</td>
<td>Some experts recommend adding rifampin¹ (BIII)</td>
</tr>
<tr>
<td>Linezolid (BII)</td>
<td>66%</td>
<td>Peak 7-10 µg/mL</td>
<td>Successful use in few case reports, small case series²</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trough 2.5-6 µg/mL</td>
<td></td>
</tr>
<tr>
<td>TMP-SMX (CIII)</td>
<td>TMP 13-53% SMX 17-63%</td>
<td>TMP 1.9-5.7 µg/mL SMX 20-63 µg/mL</td>
<td>Few case reports, only MSSA³</td>
</tr>
</tbody>
</table>

Management of MRSA infections of the Central Nervous System

**CNS Shunt infections/ meningitis**
- Shunt removal is recommended; replace only when CSF cultures are repeatedly negative (AII).
- Intraventricular vancomycin or daptomycin may be considered if not responding to systemic therapy\(^1\).

**Brain abscess, subdural empyema, spinal epidural abscess**
- Neurosurgical evaluation for incision and drainage (AII).

**Septic cavernous or dural venous sinus thrombosis**
- Debride contiguous sites of infection or abscess (AII).
- Role of anticoagulation controversial due to risk of intracranial hemorrhage


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Adjunctive Therapies in Treatment of MRSA Infections

Protein synthesis inhibitors (e.g. clindamycin and linezolid) and IVIG are not routinely recommended as adjunctive therapy (AIII).

- Limited in vitro data, animal model data (some conflicting)
- Some experts may consider these agents in selected scenarios (e.g. necrotizing pneumonia or severe sepsis.) (CIII).
Performance Measures

- The management of all MRSA infections should include identification, elimination, and/or debridement of the primary source and other sites of infection when possible.
- In patients with MRSA bacteremia, document clearance of bacteremia (follow-up blood cultures 2-4 days after initial positive cx and as needed thereafter).
- Vancomycin should be dosed according to actual body weight (15-20 mg/kg/dose every 8-12h), not to exceed 2 gram per dose. Target trough of 15-20 µg/mL in patients with serious infections.
- Document in vitro susceptibility when an alternative to vancomycin is being considered.
- For MSSA infections, a β-lactam antibiotic is the drug of choice.
Conclusion

It is important to realize that guidelines cannot always account for individual variation among patients. They are not intended to supplant physician judgment with respect to particular patients or special clinical situation. IDSA considers adherence to its guidelines to be voluntary, with the ultimate determination regarding their application to be made by the physician in the light of each patient's individual circumstances.

The full text of the guideline can be found at:

http://www.idsociety.org/IDSA_Practice_Guidelines/