MRSA Bacteremia in Adults: FAQs

Methicillin-resistant *Staphylococcus aureus* (MRSA) bacteremia is a serious bloodstream infection associated with a high mortality rate of about 30%. The chart below answers common questions about MRSA bacteremia, including diagnosis, initial treatment, and salvage therapies.

**Abbreviations**: AUC = area under the curve; BMI = body mass index; IV = intravenous; MIC = minimum inhibitory concentration; MRSA = methicillin-resistant *Staphylococcus aureus*; TEE = transesophageal echocardiography; TTE = transthoracic echocardiography.

<table>
<thead>
<tr>
<th>Clinical Question</th>
<th>Pertinent Information/Clinical Pearls</th>
</tr>
</thead>
<tbody>
<tr>
<td>How is MRSA diagnosed and classified?</td>
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</tbody>
</table>
  - Diagnose MRSA bacteremia using blood cultures. Follow hospital policies and procedures for drawing blood cultures including the required number of cultures to be drawn (usually two or three sets; each set includes one aerobic and one anaerobic bottle) and how many different sites to draw blood from.
  - Continue to recheck blood cultures about every two days to monitor for clearance of infection and to see if a change in therapy is needed.
  - Once MRSA bacteremia has been identified, consult the infectious disease (ID) team (ID consult may be associated with reduced mortality). Also, be sure to:
    - remove infectious sources (e.g., lines, catheters, prosthetic devices), if possible. Debride wounds and drain abscesses.
    - look for metastatic infections (e.g., endocarditis, osteomyelitis, abscesses) to further classify the type of MRSA.
      - Use echocardiography to look for endocarditis. TEE is preferred over TTE in most patients.
      - TEE is better at detecting vegetation, intracardiac abscesses, and valvular perforation compared to TTE.
      - TEE is more invasive and therefore has additional risks (e.g., rare esophageal perforation). Absolute contraindications to TEE include esophageal stricture, tumor, perforation, laceration, or an active upper gastrointestinal bleed.
      - Evaluate and use imaging (e.g., x-ray, CT scan) when the history and physical are positive for signs and symptoms associated with osteomyelitis (e.g., back pain) or abdominal abscesses (e.g., costovertebral angle tenderness), etc.
  - **Uncomplicated MRSA** bacteremia is defined with ALL of the following:
    - initial positive blood cultures.
    - exclusion of endocarditis (rule out with TEE, if possible) or other metastatic sites of infection (e.g., osteomyelitis).
    - no implanted prosthetic devices.
    - negative blood cultures and clinical improvement (e.g., resolution of fever) within about three days of starting treatment.
  - **Complicated MRSA** bacteremia is defined as:
    - initial positive blood cultures in patients who do not meet criteria for uncomplicated MRSA bacteremia.

More...
<table>
<thead>
<tr>
<th>Clinical Question</th>
<th>Pertinent Information/Clinical Pearls</th>
</tr>
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| **What initial therapy is appropriate for MRSA bacteremia?** | • First-line treatment options for MRSA bacteremia include vancomycin (generally preferred) and daptomycin.\(^1,5,6,8\)
Combination therapy is usually not indicated for initial therapy. Rifampin is added for MRSA bacteremia from prosthetic valve endocarditis.\(^1\)
• **Start with vancomycin** in most patients (following hospital protocols for initial dosing and dose adjustments based on pharmacokinetics).\(^1,5,6\) (NOTE: updated guidance from the Infectious Diseases Society of America [IDSA] regarding vancomycin dosing is expected to be released in the Fall of 2019.)
o Don’t jump to daptomycin (*Cubicin*), just for a vancomycin MIC of 2 mg/L. MICs vary depending on the dilution method used.\(^1\) In addition, data supporting improved outcomes with daptomycin in this scenario are mixed.
  ▪ Older studies suggest that high-vancomycin MICs increase the risk of vancomycin treatment failure for MRSA bacteremia compared to daptomycin.\(^1,10\) However, more recent data indicate that:
    • use of vancomycin in patients with high-vancomycin MICs (≥1.5 mg/L [upper limit not provided]) does not appear to be associated with increased mortality, compared to use in patients with low-vancomycin MICs (<1.5 mg/L) in the treatment of MRSA bacteremia [Evidence Level B-2].\(^15\)
    • vancomycin use in patients with high-vancomycin MICs (2 mg/L) doesn’t appear to be associated with increased mortality, recurrence of disease, or hospital readmissions, compared to use in patients with low-vancomycin MICs (<2 mg/L) in the treatment of *Staph aureus* bacteremia (~50% of the isolates were MRSA) [Evidence Level B-3].\(^16\)
• **Daptomycin** is also an initial treatment option.\(^1,6,8\) However, daptomycin has NOT been shown to be more effective than vancomycin.\(^10\) Daptomycin is also much more expensive (~$650/day) compared to vancomycin (~$35/day).\(^4\)
o Avoid daptomycin if the original source of infection is pneumonia, as pulmonary surfactants inactivate daptomycin.\(^8\) |
| **How should persistent MRSA bacteremia be treated?** | • Most experts define persistent MRSA bacteremia as continued positive blood cultures after seven days of antibiotic therapy at effective doses. However, also take into account the patient’s response to therapy, pharmacokinetic monitoring, susceptibility testing results, and whether or not the source of the initial infection has been removed.\(^1,11\)
• Consider a switch to **daptomycin** if MRSA bacteremia persists after about five to seven days of vancomycin therapy. Switch earlier if patients are getting worse or if cultures are positive after three days PLUS vancomycin MICs are ≥2 mg/L.\(^8,10\)
o Check daptomycin susceptibilities. Resistance to daptomycin may develop with previous vancomycin therapy.\(^11\)
o Start with daptomycin 8 to 10 mg/kg IV once every 24 hours in most patients.\(^1,6,8\) Use adjusted body weight to calculate doses for patients who are obese (e.g., BMI ≥30 kg/m\(^2\)).\(^13,14,17\) Even though 8 to 10 mg/kg is higher than FDA-approved dosing (6 mg/kg), data support that these doses are usually safe and effective.\(^20\)
• Monitor for daptomycin dose-dependent toxicities (e.g., myopathy [muscle pain/weakness], elevated creatinine phosphokinase [CPK]), especially in patients who are obese.\(^3,9,11\) Obese patients:\(^17\)
o experience higher AUC and maximum concentrations of daptomycin compared to non-obese patients.
o may experience an increased risk of CPK elevations with daptomycin therapy. |

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### Clinical Question

<table>
<thead>
<tr>
<th>What salvage treatments should be used for MRSA bacteremia?</th>
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</tr>
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<td>Salvage therapy for MRSA bacteremia is needed when there is treatment failure with vancomycin and daptomycin. No data are available to compare salvage therapies to one another. Salvage therapy options are listed in order of preference, based on amount of available data and clinical experience.</td>
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| - **Ceftaroline (Teflaro):** consider ceftaroline for most patients when salvage therapy is needed to treat MRSA bacteremia.\(^6,11\)
  - Ceftaroline can be used alone or in combination with first-line therapy (e.g., daptomycin, vancomycin).\(^3,8,11\)
  - Limited data support the use of ceftaroline alone. However, combination therapy with daptomycin or vancomycin appears to be synergistic.\(^11\)
  - Though ceftaroline product labeling for other approved indications specifies every 12-hour dosing, data and protocols support using ceftaroline 600 mg IV **every eight hours** for MRSA bacteremia.\(^6,8,9,11\)
  - Ceftaroline costs about $600/day of therapy.\(^9\)
| - **Telavancin (Vibativ):** Limited data support the use of telavancin (monotherapy) when salvage therapy is needed to treat MRSA bacteremia.\(^6,8,10\)
  - Typical doses range from 7.5 to 10 mg/kg (max 750 mg) IV once daily.\(^6,8\)
  - Reduce the dose for patients with a creatinine clearance ≤50 mL/min.\(^9\)
  - Telavancin costs about $450/day of therapy.\(^9\)
| - **Linezolid (Zyvox):** Limited data support the use of linezolid when salvage therapy is needed to treat MRSA bacteremia.\(^8\)
  - Linezolid has been used alone or in combination with a carbapenem.\(^11\)
  - Use of linezolid may be limited to uncomplicated MRSA bacteremia. Linezolid is associated with an increased risk of thrombocytopenia when used for longer than two weeks.\(^6,11\)
  - Linezolid dosing is 600 mg IV twice daily.\(^1\)
  - Linezolid costs about $60/day of therapy.\(^1\)
| - There are not data to support use of delafloxacin (**Baxdela**), dalbavancin (**Dalvance**), or oritavancin (**Orbactiv**) as salvage therapy for MRSA bacteremia at this time. |

### What is an appropriate duration of therapy for MRSA bacteremia?

- Treatment durations are calculated from the first negative blood culture (i.e., day one).\(^6,12\)
  - Treat **uncomplicated MRSA bacteremia** for at least two weeks.\(^1,6,12\)
  - Treat **complicated MRSA bacteremia** for at least four to six weeks, depending on the site of infection.\(^1,6,12\) For example:
    - treat complicated MRSA bacteremia with endocarditis for at least six weeks.\(^1\)
    - treat complicated MRSA bacteremia with osteomyelitis for at least eight weeks.\(^1\)
### Clinical Question

Can **oral therapy** be used to complete treatment for MRSA bacteremia?

- Despite guideline recommendations to use IV antibiotics to treat MRSA bacteremia, some prescribers consider switching patients from IV to oral therapy after ten days.\(^{18}\)
- Preliminary and limited data suggest that use of oral antibiotics (most commonly trimethoprim/sulfamethoxazole [TMP/SMX] or linezolid) to complete the full treatment duration may have similar outcomes (composite endpoint including 90-day recurrence, deep-seated MRSA infection, or all-cause mortality) compared to using IV antibiotics for the full course of treatment [Evidence Level B-3].\(^{18}\) However, more studies are needed to:
  - confirm the safety and effectiveness of completing treatment for MRSA bacteremia with oral antibiotics.
  - define the optimal time to convert patients from IV to oral antibiotics.
- Until more data are available, avoid routinely converting patients from IV to oral antibiotic therapy to complete the full treatment duration of MRSA bacteremia.
  - Limit use of oral antibiotics to complete therapy to situations such as when home IV therapy is not an option, especially in patients with uncomplicated cases who responded rapidly to vancomycin.\(^{8,12}\)

### Pertinent Information/Clinical Pearls

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### What should be done to **prevent transmission** of MRSA?

- See our chart, *MRSA: Prevention and Decolonization*, for strategies to prevent MRSA transmission.

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*Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.*
Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the LEVEL OF EVIDENCE for the clinical recommendations we publish.

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<thead>
<tr>
<th>Level</th>
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<th>Study Quality</th>
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</table>
| A     | Good-quality patient-oriented evidence.* | 1. High-quality RCT  
2. SR/Meta-analysis of RCTs with consistent findings  
3. All-or-none study |
| B     | Inconsistent or limited-quality patient-oriented evidence.* | 1. Lower-quality RCT  
2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings  
3. Cohort study  
4. Case control study |
| C     | Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening |

*Outcomes that matter to patients (e.g., morbidity, mortality, symptom improvement, quality of life).

RCT = randomized controlled trial; SR = systematic review


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References


