Empiric Management of Suspected or Confirmed *Staphylococcus aureus* Bacteremia in Adults

Staphylococcus aureus (*S. aureus*) bacteremia is a life-threatening infection, which if untreated is associated with mortality rates of 20-40%. Infiltration of *S. aureus* into the bloodstream is often secondary to invasive instrumentation (intravenous line, central catheter, etc.) or spread from a local infection (osteomyelitis, cellulitis, pneumonia, etc.). *S. aureus* has a propensity to "seed" heart valves and cause endocarditis, further worsening patient outcomes. Delays in treatment are associated with worse outcomes.

The optimal management of *S. aureus* bacteremia is an area of ongoing study; therefore, clinicians should strongly consider enrollment of patients with *S. aureus* bacteremia in ongoing clinical trials at the MUHC. Further consultation with Infectious Diseases is recommended to guide workup and management. The goal of this guideline is for the initial management of *S. aureus* bacteremia in adult patients at the MUHC.

INITIAL SUSPICION based on PRELIMINARY CULTURES

Blood cultures showing growth of Gram-positive cocci in cluster formation:

- Other *staphylococcus sp* (coag-negative Staphylococci) may present as a Gram-positive cocci in clusters. **Not all of these will require therapy, as they may represent contamination**.
    - Blood culture contamination rates at the MUHC are in the range of 3-4%.
- Preliminary species identification (*S. aureus* vs coag-neg Staphylococcci) is usually available **within a few hours** after the blood culture bottle is flagged as positive. All cases of *S. aureus* in blood cultures should be treated as true bloodstream infection until proven otherwise. Interpretation of positive blood culture is based on number of positive blood culture bottles as a function of the total number collected, and clinical considerations. If multiple blood cultures are positive, true bloodstream infection is likely.
- **Proportion *S. aureus* blood culture isolates that are methicillin (oxacillin)-susceptible at MUHC: 85% (n = 131 blood isolates in 2023)**
- **IMPORTANT diagnostic considerations for true S. aureus bacteremia:**
    - **History and physical exam to determine most probable source of infection**
    - **Repeat 2 sets of blood culture (BC: one peripheral, one from central line if applicable) before starting antibiotics; repeat daily BC x 3d to document clearance (may be extended if persistently positive)**
    - **Obtain additional specimens for microbiological culture as appropriate**
    - **True bloodstream infection (BSI) will require imaging to r/o infective endocarditis; may be requested within a few days after establishing the diagnosis of BSI**
    - **ID consultation is recommended to guide additional investigations and duration of treatment**

PHARMACOLOGIC MANAGEMENT[1]:

Suspected true *S. aureus* bacteremia, susceptibility pending	
Hemodynamically stable, not known MRSA colonized	**Cefazolin**[1] 2 g IV q8h
Hemodynamically unstable, or known MRSA colonized	**Cefazolin**[1] **2g IV q8h *AND* Vancomycin**[2] **25 mg/kg IV x1 then 15 mg/kg IV q12h** (dosage will be adjusted by pharmacy) *If severe hypersensitivity reaction to cephalosporins*, **Vancomycin** 25 mg/kg IV x1 then 15 mg/kg IV q12h and **consult ID**

[1]Cefazolin to be changed, as per MUHC guidelines, if source of infection identified. Cefazolin can be given in case of penicillin hypersensitivity reaction

[2]Vancomycin: see vancomycin Therapeutic Drug Monitoring guideline; consult Pharmacy for patient specific dosing.

Known Susceptibility[1] results:		
	No CNS involvement	**CNS involvement (+/- epidural abscess)**
MSSA	**Cefazolin**[2] 2 g IV q8h (if randomized to trial, choose drug selected in randomization)	**Cloxacillin** 2 g IV q4h *If severe hypersensitivity reaction to penicillin:* **Meropenem** 2 g IV q8h and consult ID
MRSA	**Vancomycin**[3] 25 mg/kg IV x1 then 15 mg/kg IV q12h (dosage will be adjusted by pharmacy); **CONSULT ID**	

[1]Susceptibility to Oxacillin predicts susceptibility to Methicillin, Cefazolin and Cloxacillin.
[2]Cefazolin to be changed, as per MUHC guidelines, if source of infection identified.
[3]Consult Pharmacy for patient specific dosing. See Vancomycin Therapeutic Drug Monitoring guideline.

DURATION OF THERAPY

- *If uncomplicated bacteremia* (**all** of the following must be met: no endocarditis or other metastatic sites of infection, no implanted prostheses/endovascular material, follow-up blood cultures obtained 2-4 days after initial positive culture are negative, defervescence within 72h of antibiotics): 2 weeks of treatment
- For all other scenarios, ID to determine duration of treatment.

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