

Bad Bugs in the Blood:
Staphylococcus aureus bacteremia

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Disclosure Statement

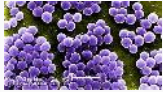
- I have had no financial relationship over the past 12 months with any commercial sponsor with a vested interest in this presentation.

Learning Objectives

<ul style="list-style-type: none">• Pharmacist<ul style="list-style-type: none">• Describe evidence-based practices for treatment of <i>Staphylococcus aureus</i> bacteremia• List alternative therapies to vancomycin for methicillin resistant <i>Staphylococcus aureus</i> (MRSA) bacteremia	<ul style="list-style-type: none">• Technician<ul style="list-style-type: none">• Describe the difference between methicillin susceptible (MSSA) and methicillin resistant <i>Staphylococcus aureus</i>• Recommend appropriate hygiene/precautions required for hospital personnel when entering a patient's room with MRSA precautions
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Staphylococcus aureus

- Gram positive cocci in clusters
- Two types:
 - Methicillin susceptible *S. aureus*
 - Methicillin resistant *S. aureus*
 - *mecA* gene = high level of resistance to methicillin



S. aureus bacteremia

- Once in bloodstream it can disseminate to cause infection in most organs
 - Associated mortality of approximately 20-40%
 - One-third of patients with *S. aureus* bacteremia develop local complications or distant metastases (bone & joint, heart valves, epidural space)
- Risk factors for complicated infection
 - Persistent bacteremia
 - Community acquisition
 - Skin lesions
 - Persistent fever
 - IV drug use

Del Rio A, et al. Clin Infect Dis 2007;48 (Suppl 4).

S. aureus bacteremia

- Uncomplicated bacteremia
 - Positive blood culture results with the following:
 - Exclusion of endocarditis
 - No implanted prostheses
 - Follow-up blood cultures (2-4 days after initial) are negative
 - Defervescence within 72 hours of initiating effective therapy
 - No evidence of metastatic infection
- Complicated bacteremia
 - Positive blood cultures that do not meet criteria for uncomplicated bacteremia


Lau C, et al. Clin Infect Dis 2011;52(3):18-55

Staphylococcus aureus bacteremia (SAB) Best Practices

Don't let it fool you	It is not a contaminant. ALWAYS treat <i>S. aureus</i> when isolated from the blood.
Document clearance	Obtain repeat blood cultures 48-96 hours after initial positive culture.
Nip it in the bud	Remove infected devices and evaluate for metastatic infection – source control!
BINGO!	Use the most appropriate anti-infective agents.
Timing is everything	Treat for an appropriate duration.
Check with the experts	Obtain an infectious disease consultation.

Hygiene Recommendations

- Precautions in the hospital setting for MRSA
 - Standard precautions (i.e. hand hygiene)
 - Wear a gown
 - Wear gloves
 - Additional precautions may be needed



CDC. Precautions to Prevent Spread of MRSA. Accessed 19 Jan 2017.

Source Control

Source Control

- Identify the source and extent of the infection
- Eliminate and/or debride sites of infection
- Transesophageal echocardiography (TEE) preferred to rule out endocarditis
 - Evaluate for valve replacement if large vegetation

Liu C, et al. Clin Infect Dis 2011;52(3):18-55.

Methicillin-susceptible *Staphylococcus Aureus*

Anti-infective Agents

Oxacillin 2 g IV every 4 hours **Or** Nafcillin 2 g IV every 4 hours **Or** Cefazolin 2 g IV every 8 hours

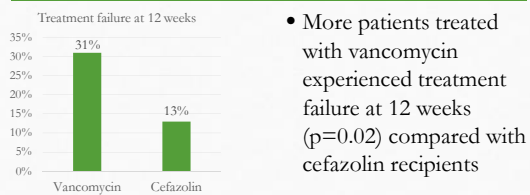
Rao SN, et al. WAC 2015;39(9):3232-38.
Oxacillin, nafcillin, cefazolin. Lexiscomp, Inc. Accessed 21 Jan 2018.

Vancomycin vs. cefazolin in MSSA

- Prospective cohort of hemodialysis-dependent patients from Sept 1994 through Aug 2001
- 123 patients included in the study
 - 77 (63%) received vancomycin
 - 46 (37%) received cefazolin

Sztybel M, et al. Clin Infect Dis 2007;44:190-6.

Vancomycin vs. cefazolin in MSSA



Sztybel M, et al. Clin Infect Dis 2007;44:190-6.

Nafcillin or cefazolin vs. vancomycin in MSSA

- Retrospective cohort study from January 2003 - June 2007
- 267 hospital admissions in final analysis
 - 38 – nafcillin or cefazolin alone
 - 135 – both vancomycin and either nafcillin or cefazolin
 - 94 – vancomycin alone
- 30 (11%) patients died within 30 days of culture collection

Schweizer et al. BMC Infectious Diseases 2011, 11:279.

Nafcillin or cefazolin vs. vancomycin in MSSA

Antibiotics received	Cumulative mortality incidences
Only nafcillin or cefazolin	3% (1/38)
Both vancomycin and nafcillin or cefazolin	7% (10/135)
Only vancomycin	20% (19/94)

- Patients who received nafcillin or cefazolin were significantly less likely to die compared to patients who received only vancomycin.*

*After statistically adjusting for propensity score

Schwartz et al. BMC Infectious Diseases 2011, 11:279

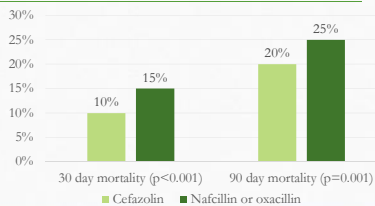
Cefazolin vs. nafcillin or oxacillin

- Retrospective cohort study from 2003 – 2010
- 3167 patients received definitive therapy with cefazolin, nafcillin, or oxacillin
 - 1163 (37%) patients received cefazolin
 - 2004 (63%) patients received nafcillin or oxacillin

McDanel SJ, et al. Clin Infect Dis 2017;65(1):100-6.

Cefazolin vs. nafcillin or oxacillin

- Primary Outcomes: 30-day all-cause mortality and 90-day mortality



McDanel SJ, et al. Clin Infect Dis 2017;65(1):100-6.

Methicillin-resistant
Staphylococcus aureus

Anti-infective Agents

Vancomycin IV 15-20 mg/kg/dose to target trough concentrations of 15-20 mg/L **Or** Daptomycin IV 6 mg/kg/dose once daily target trough concentrations of 15-20 mg/L

Liu C, et al. Clin Infect Dis 2011;52(3):18-55

Adjuvant beta-lactam therapy with vancomycin

- Retrospective, multicenter cohort study
- 97 patients included
 - 40 (41%) patients in standard treatment group (STAN)
 - 57 (59%) patients in combination treatment group (COMBO)
- Primary outcome: clinical failure*

*composite end-point including (1) 30-day mortality, (2) persistent bacteremia (≥ 7days), (3) bacteremia relapse, and/or (4) change from COMBO or STAN or addition of anti-MRSA antibiotic necessitated by lack of infection response

Causapou AM, et al. Pharmacotherapy 2017;37(11):1347-56.

Adjuvant beta-lactam therapy with vancomycin

Clinical Outcomes	STAN (n=40)	COMBO (n=57)	p value
Clinical failure	12 (30%)	14 (24.6%)	0.552
Persistent bacteremia	6 (15%)	2 (3.6%)	0.062
30-day all-cause mortality	6 (15%)	12 (21.2%)	0.597
Duration of bacteremia (median #days)	4	3	0.048

Caupao AM, et al. Pharmacotherapy 2017;37(11):1547-56.

MRSA Alternative Agents to vancomycin

When should you use an alternative agent ?

- MIC > 2mg/L (vancomycin)
- Vancomycin treatment failure with persistent bacteremia at or around 7 days of therapy

What agents should you use?

- High dose daptomycin
- Quinupristin-dalfopristin
- TMP-SMX
- Linezolid
- Telavancin
- Ceftaroline*

Liu C, et al. Clin Infect Dis 2011;52(3):18-53.
Kallar R, et al. J Antimicrob Chemother 2016;71:576-86. *Not from guidelines

Treatment Duration

Uncomplicated bacteremia

—————→ **≥ 2 weeks***

Complicated bacteremia

—————→ **4-6 weeks***

*from date of first negative blood cultures

Liu C, et al. Clin Infect Dis 2011;52(3):18-53.

Infectious Disease Consultation

Outcome	Consult	Jenkins 2008	Rieg 2009	Saunderson 2015
90-day mortality	Yes	6/100 (6%)	83/300 (28%)*	39/183 (21%)*
	No	12/134 (9%)	56/131 (43%)	89/294 (30%)
Relapse of bacteremia	Yes	4/100 (4%)	15/221 (7%)	4/183 (2.2%)
	No	10/134 (7%)	4/75 (5%)	12/294 (4.1%)
Appropriate agent	Yes	58/63 (92%)*	--	140/156 (90%)
	No	56/84 (67%)	--	170/193 (88%)
Appropriate duration	Yes	51/69 (74%)*	231/350 (66%)*	--
	No	41/97 (42%)	54/171 (32%)	--

*statistically significant

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Additional Unknowns

- Oral vs. IV antibiotic therapy throughout treatment duration
- Continuous infusion
- Hardware (i.e. joint replacements)
- Echocardiography

Summary

- Don't let it fool you
- Document clearance
- Nip it in the bud
- BINGO!
- Timing is everything
- Check with the experts

HW is a 70-year-old male on empiric vancomycin for gram positive cocci in the blood. Two days later his blood culture results with methicillin-susceptible staphylococcus aureus. What should you do?

- A. Recommend an infectious disease consult
- B. Recommend continuing with vancomycin therapy for at least 14 days
- C. Recommend switching to daptomycin for at least 21 days
- D. Recommend de-escalating to cefazolin therapy for at least 14 days
- E. A & D

RPh

After how many days of vancomycin treatment with persistent MRSA bacteremia should you generally consider alternative therapy?

- A. 3 days
- B. 5 days
- C. 7 days
- D. 10 days

RPh

Vancomycin is the recommended treatment for methicillin-resistant *Staphylococcus aureus* bacteremia

A. True
B. False

Tech

What would be appropriate hygiene/precautions when entering a patient room when MRSA precautions are in place?

A. Gown
B. Gloves
C. Hand sanitizer upon entering and leaving the room
D. All of the above

Tech

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Questions?
