Just Be*CAUSE* :

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Infectious Diseases Consultation for *Staphylococcus aureus* Bacteremia

By Mary Banoub, PharmD, CPP, BCIDP and Vera Luther, MD, FIDSA

Staphylococcus aureus bacteremia (SAB) is a serious infection associated with high morbidity and mortality. While the incidence of SAB ranges from 4.3 to 38.2 per 100,000 person-years for North America, the **reported mortality rate is upwards of 30%**.[1] Frequently, SAB is associated with complications including deep-seated metastatic sites of infection (i.e. infective endocarditis, device-associated infection, osteoarticular metastases, and pleuropulmonary involvement). SAB can impact a variety of patient populations with common risk factors including prolonged or recent hospitalization, catheter placement, injection drug use, and immunocompromise.

The high morbidity and mortality of SAB can be attributed to the vast arsenal of virulence factors employed by *S. aureus* to cause severe invasive disease including toxins, immune-modulatory factors, and exoenzymes.[2] *S. aureus* is especially adept at forming biofilms, causing difficult-to-eradicate infections of indwelling medical devices as well as native tissue surfaces, such as the cardiac valves. Frequently occurring antibiotic resistance has led to an increase in methicillin -resistant *S. aureus* (MRSA) infections, which account for greater than 50% of *S. aureus* isolates in the United States, and is associated with even higher mortality than methicillin-susceptible *S. aureus* (MSSA) isolates.

The **majority of SAB cases are complicated, with patients meeting criteria necessitating longer antibiotic treatment courses (4-6 weeks) for the infection.** Indeed, most patients do not meet criteria for uncomplicated infection (Table 1).[3]

Table 1: IDSA 2011 MRSA Guideline's Criteria for Deeming SAB Uncomplicated
Exclusion of endocarditis
No implanted prostheses
Follow-up blood cultures performed on specimens obtained 2–4 days after the initial set that do not grow MRSA/MSSA
Defervescence within 72 h of initiating effective therapy
No evidence of metastatic sites of infection

One large study assessing 5,063 cases of SAB found only 213 (4.2%) patients could be classified as having an uncomplicated infection.[4] Given the virulence of this organism, high morbidity and mortality, and frequent complication rate, studies have aimed to assess ways to improve management of SAB. **One of the major components found to be associated with improved outcomes in SAB is bedside infectious diseases (ID) consultation.**

Image: https://www.cdc.gov/antibiotic-use/

See page 2 for references

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ID consultation ensures thorough evaluation of the source, recommendations for source control, and serial examination of the patient dedicated to the evaluation of potentially evolving metastatic sites of infection. One of the first studies to assess the impact of ID consultation in SAB was published in 1998; Fowler, et al. prospectively evaluated outcomes for 244 hospitalized patients with SAB and followed them for 12 weeks after their first positive blood culture.[5] Patients for whom ID's recommendations were followed were more likely to be cured of their *S. aureus* infection and less likely to relapse (P < .01), as compared to patients for whom ID's recommendations were not followed. This was despite significantly more metastatic infections (P > .01) in the group which followed ID's recommendations. Since then, multiple studies have corroborated these findings[6,7,8], including a **systematic review and meta-analysis ultimately assessing 5,337 patients with SAB**. This study **showed reduced 90-day mortality** (relative risk (RR) 0.77 [95% CI 0.64-0.92]) and **relapse risk** (RR 0.62 [95% CI 0.39-0.99]); **improved appropriateness of anti-staphylococcal agent use** (RR 1.14 [95% CI 1.08-1.20] and **treatment duration** (RR 1.85 [95% CI 1.39-2.46]); and **more frequent follow-up blood cultures** (RR 1.35 [95% CI 1.25-1.46] and **echocardiography** (RR 1.98 [95% CI 1.66-2.37]) **with ID consultation.**[9] The positive effect of ID consultation has not necessarily translated to telephone ID consultation with one retrospective study showing 90-day mortality for telephone-consultation patients was higher (OR 2.31 [95% CI 1.22-4.38]) as compared to bedside ID consultation.[10]

In practice, ID consultation should be obtained even if *S. aureus* is isolated from a single blood culture bottle. Importantly, ***S. aureus* should <u>never</u> be considered a contaminant**.[11] Blood cultures should also be obtained if urine cultures grow *S. aureus*, as this often signifies hematogenous spread to the urinary tract. Notably, concepts discussed above regarding *S. aureus* also apply to *Staphylococcus lugdunensis*, a coagulase-negative staphylococcus with a similar propensity for causing aggressive infections like *S. aureus.*[12] *S. lugdunensis* is unlike other coagulase-negative staphylococci species, such as *Staphylococcus epidermidis* or *Staphylococcus hominis*, which are more likely to be skin flora contaminants.

Utilization of the BioFire® FilmArray® Blood Culture Identification Panel (BCID) 2 panel can help detect *S. aureus* (and *S. lugdunensis)* as well as resistance genes that identify methicillin resistance (mecA/C and MREJ resistance genes) before blood culture growth is finalized. Utilization of results from this rapid diagnostic technology is encouraged to facilitate transition to targeted antibiotics as well as more timely ID consultation for SAB and *S. lugdunensis* bacteremia.

In conclusion, *S. aureus* (and *S. lugdunensis*) can and often do cause complicated disease and are associated with high morbidity and mortality. ID consultation for SAB is an evidence-based practice shown to ensure quality measures are achieved (e.g. echocardiography, repeat blood cultures, removal of infectious foci, and appropriate antibiotic therapy) and to reduce poor outcomes (e.g. 90-day mortality and relapse risk) in SAB.

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BIOFIRE® Joint Infection (JI) Panel

By Courtney Jackson, PharmD

About the JI panel

The BIOFIRE® Joint Infection (JI) Panel:[1]

- Multiplex polymerase chain reaction test that amplifies DNA targets directly from synovial fluid
- Permits rapid identification of 39 pathogens and 8 antimicrobial resistance genes (Table 1)
- Highly sensitive and specific to detect pathogens included as targets on the panel
- Local turnaround time is ~4 hours

Table 1: JI Panel Pathogens and Resistance Genes Detected[1]

Gram Positive (+) Bacteria	Gram Negative (-) Bacteria
*Anaerococcus prevotii/vaginalis**	*Bacteroides fragilis**
*Clostridium perfringens**	*Citrobacter*
*Cutibacterium avidum/granulosum**	*Enterobacter cloacae complex*
Enterococcus faecalis	*Escherichia coli*
Enterococcus faecium	*Haemophilus influenzae*
*Finegoldia magna**	*Kingella kingae*
*Parvimonas micra**	*Klebsiella aerogenes*
*Peptoniphilus**	*Klebsiella pneumoniae* group
*Peptostreptococcus anaerobius**	*Morganella morganii*
Staphylococcus aureus	*Neisseria gonorrhoeae*
Staphylococcus lugdunensis	*Proteus spp.*
Streptococcus spp.	*Pseudomonas aeruginosa*
Streptococcus agalactiae	*Salmonella spp.*
Streptococcus pneumoniae	*Serratia marcescens*
Streptococcus pyogenes	
Yeast	**Gram Negative (-) Resistance Genes**
Candida spp.	Carbapenemases:
Candida albicans	IMP
Gram Positive (+) Resistance Genes	KPC
Methicillin Resistance:	NDM
mecA/C and MREJ (MRSA)	OXA-48-like
Vancomycin Resistance:	VIM
vanA/B	Extended Spectrum Beta-Lactamases (ESBL):
	CTX-M

*anaerobic targets

Table 1. Note: The JI panel is ONLY capable of detecting organisms and resistance genes included in the list above. Organisms not included on the panel as targets cannot be detected, and a negative JI panel does not necessarily indicate that there is not an infectious pathogen present. Notable potential pathogens that are **NOT** included in the joint panel include ***Cutibacterium acnes*** and coagulase-negative staphylococci other than *Staphylococcus lugdunensis,* such as ***Staphylococcus epidermidis***.

Why the JI panel?

While synovial culture remains a gold-standard for microbiologic diagnosis of joint infections, culturing techniques have several important limitations including longer turn-around times, and false-negative results in patients on antibiotic therapy or with organisms that are difficult to grow in culture.

Who can benefit from the JI panel?

The JI panel should be **considered in patients with suspected native joint septic arthritis or prosthetic joint infection in conjunction with synovial fluid culture** and can be used to more rapidly inform decision making when transitioning to targeted antimicrobial therapy.

1. BioFire® Joint Infection Panel [product labeling: instructions for use]. bioMérieux. Salt Lake City, UT. Updated August 2023

BIOFIRE® Joint Infection (JI) Panel

By Courtney Jackson, PharmD

Specimen type and collection

The JI panel is **only validated for synovial fluid,** which can be collected via arthrocentesis or during surgery in a sterile container or non-heparinized syringe. The JI panel order may be canceled for insufficient quantity (requires at least 0.2 mL), invalid results from the BIOFIRE® FILMARRAY ® TORCH instrument, or if the synovial fluid specimen is too viscous, which may impede performance of the assay.

Ordering the JI Panel and cultures

The **JI panel (LAB8783 Joint Infection Panel, NAAT) must be ordered in conjunction with or as an add on to synovial fluid culture** (LAB5563 Synovial Culture (Aerobic)). Synovial fluid culture is especially important to recover organisms for susceptibility testing, identify organisms not included in the JI panel, and further identify organism species when the JI panel only identifies the genus, complex, or group. Synovial fluid culture (aerobic) specimens are incubated for up to 14 days for detection of other organisms including other coagulase-negative Staphylococci and *Cutibacterium acnes*. Other synovial cultures may be appropriate to order based on the suspected causative organism (e.g. anaerobic, acid-fast, fungal).

Making antimicrobial decisions based on the JI panel results

The JI panel may be used to tailor antimicrobial therapy for suspected native joint septic arthritis and prosthetic joint infection. However, the JI panel results should be evaluated in conjunction with patient-specific criteria such as severity of illness, clinical syndrome, risk factors for antimicrobial resistance or history of antimicrobial resistance, allergies, organ dysfunction, and other factors. Additionally, the diagnosis of native joint septic arthritis and prosthetic joint infection should be made in conjunction with other clinical and laboratory findings including synovial fluid testing (cell count and differential, crystal identification), histological evaluation of tissue, intraoperative inspection, and radiographic results if available.

Synovial fluid cultures should continue to be monitored for pathogens which may not be detected from the JI panel. Antimicrobial therapy should also be re-evaluated when organism identification and susceptibility results return. Additionally, it is possible that pathogens detected on the panel may not be isolated in subsequent culture. For example, this may occur when samples are collected after initiation of antibiotic therapy. **Infectious Diseases consultation is recommended to guide management of native joint septic arthritis or prosthetic joint infection.**

Limitations and additional considerations

The JI panel may result negative due to:

- Joint infection with pathogens that are not detected by the panel
- If the pathogen quantity is below the limit of detection
- No pathogens present

Therefore, a negative JI panel result does not rule out joint infection depending on the clinical scenario. Rarely, polymicrobial specimens with four or more organisms detected are possible. In this instance, retesting of the sample is recommended to confirm the polymicrobial result. The JI panel has not been validated for testing specimens other than synovial fluid and cannot be used on swabs or tissue samples. The JI panel is not intended to monitor effectiveness of treatment and should not be performed as a test of cure.

Questions

- Contact Microbiology lab (6-2658) or CAUSE (secure chat group: WFMC CAUSE Antimicrobial Stewardship Approval) for questions or discrepancies between the panel and culture results
- Check out the BIOFIRE® Joint Infection (JI) Panel Guidance document on the CAUSE website

1. BioFire® Joint Infection Panel [product labeling: instructions for use]. bioMérieux. Salt Lake City, UT. Updated August 2023

Prescribing Doxycycline Postexposure Prophylaxis (DoxyPEP) for Bacterial Sexually Transmitted Infections (STIs)

By Olivia Randazza PharmD, CPP, BCIDP, AAHIVP

Who may benefit most from DoxyPEP?

- DoxyPEP reduces syphilis and chlamydia infections by >70% and gonococcal infections by ~50%.[1] The CDC clinical guidelines on the use of DoxyPEP for bacterial STI prevention recommend provider counseling on DoxyPEP in specific high risk populations:

CDC Recommendations[1]
Counsel all **gay, bisexual, and other men who have sex with men (MSM) and transgender women (TGW)** with a **history of at least one bacterial STI (specifically, syphilis, chlamydia or gonorrhea) during the past 12 months** about the benefits/harms of using DoxyPEP and offer DoxyPEP through shared decision-making.
No recommendation can be given at this time on the use of DoxyPEP for cisgender women, cisgender heterosexual men, transgender men, and other queer and nonbinary persons. This is due to insufficient evidence to assess the balance of benefits and harms of the use of DoxyPEP in these populations.

How should I prescribe and counsel on DoxyPEP?[1]

Doxycycline (oral immediate release)

- Take 200 mg (two 100 mg pills) by mouth once as needed *ideally* within 24 hours of oral, vaginal, or anal sex but no later than 72 hours. Do not exceed 200 mg per 24 hours.
- Prescription quantity and refills: based on individual behavior assessment between patient and prescriber

DoxyPEP Patient Counseling

- Key side effects:
  - Esophagitis — Take with a full glass of water and avoid lying down for 30 minutes after taking
  - Gastrointestinal intolerance (nausea, vomiting, diarrhea) — Take on a full stomach to reduce GI side effects
  - Photosensitivity — Wear sunscreen or protective clothing if planning to be in the sun for long periods
- Key drug-drug and drug-food interactions:
  - Cations — Bind to doxycycline resulting in reduced absorption. Separate doxycycline by at least 2 hours from dairy products, antacids, and supplements that contain calcium, iron, magnesium, or sodium bicarbonate
  - Review patient's medication list to assess for other potential drug-drug interactions
- Benefits, risks, and considerations:
  - Studies have shown DoxyPEP is effective in reducing the risk of chlamydia, gonorrhea, and syphilis
  - DoxyPEP does **not** protect against viral STIs (e.g. HIV, Mpox, HSV, HPV) or prevent pregnancy; therefore, other prevention strategies should still be employed (e.g. condoms, HIV PrEP, hormonal birth control)
  - DoxyPEP may have unknown long-term effects including potential for development of antimicrobial resistance in other pathogens or commensal organisms and changes in a patient's gut microbiome

1. Bachmann LH, Barbee LA, Chan P, et al. CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024. MMWR Recomm Rep 2024;73(No. RR-2):1–8. DOI: http://dx.doi.org/10.15585/mmwr.rr7302a1

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By Olivia Randazza PharmD, CPP, BCIDP, AAHIVP

Lab Screening and Visits[1]

CDC Considerations for Clinical Services for Persons receiving DoxyPEP for Prevention of Syphilis, Chlamydia, and Gonorrhea	
Initial Visit	• Screen for STIs at anatomic sites of exposure and treat as indicated per CDC guidelines (see below)[1-3] • Counsel on use of risk reduction / prevention strategies including condom use, consideration of reducing the number of partners, and accessing HIV PEP, PrEP or HIV treatment as indicated • Counsel on DoxyPEP (page 5)
Follow-Up Visits	• Generally, should be seen and screened every 3-6 months • Screen for STIs at anatomic sites of exposure and treat as indicated per CDC guidelines (see below)[1-3] • Assess for side effects from doxycycline • Re-assess continued need for DoxyPEP and refill as needed • Re-enforce counseling on risk reduction / prevention strategies • Refer for comprehensive services as needed (e.g. primary care, mental health, substance use) • Confirm linkage to HIV care for persons living with HIV

STI Screening per CDC Guidelines[1-3]	**Men who have Sex with Men (MSM) and Transgender Women (TGW)**
	Every 3-6 months (screen sooner if patient is symptomatic or other concern for STI):
	• Gonorrhea, chlamydia, syphilis (all anatomical sites)
	• HIV:
	  • For persons without HIV infection not receiving HIV PrEP, consider screening for HIV infection every 3-6 months[2]
	  • For persons without HIV infection receiving HIV PrEP, screen per CDC HIV PrEP guidelines[3]
	• Consider screening for hepatitis B and C infection, and vaccinate / treat as appropriate

Key Considerations

- Refer to the CDC DoxyPEP clinical guidelines for comprehensive recommendations[1]
- DoxyPEP should be considered in specific high risk populations, including gay, bisexual, and other men who have sex with men (MSM) and transgender women (TGW), with a history of at least one bacterial STI (specifically, syphilis, chlamydia or gonorrhea) during the past 12 months
- All patients should be counseled on appropriate doxycycline administration, side effects, drug interactions, and potential benefits / risks of DoxyPEP
- All patients should have routine follow-up and screening for STIs

1. Bachmann LH, Barbee LA, Chan P, et al. CDC Clinical Guidelines on the Use of Doxycycline Postexposure Prophylaxis for Bacterial Sexually Transmitted Infection Prevention, United States, 2024. MMWR Recomm Rep 2024;73(No. RR-2):1–8. DOI: http://dx.doi.org/10.15585/mmwr.rr7302a1
2. https://www.cdc.gov/std/treatment-guidelines/default.htm
3. https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf

CAUSE Guideline Highlight

Did You Know?

- Institutional Diagnostic Guidelines are available on the CAUSE website that review several rapid diagnostic tools
- Includes:
  - **New** BIOFIRE® Joint Infection (JI) Panel Guidance
  - **Updated** BIOFIRE® Blood Culture Identification 2 Panel (BCID2)® Guidance
  - BIOFIRE® FilmArray® Pneumonia Panel® Educational Handout

Atrium Health Wake Forest Baptist
Center for Antimicrobial Utilization, Stewardship, and Epidemiology

CAUSE Resources

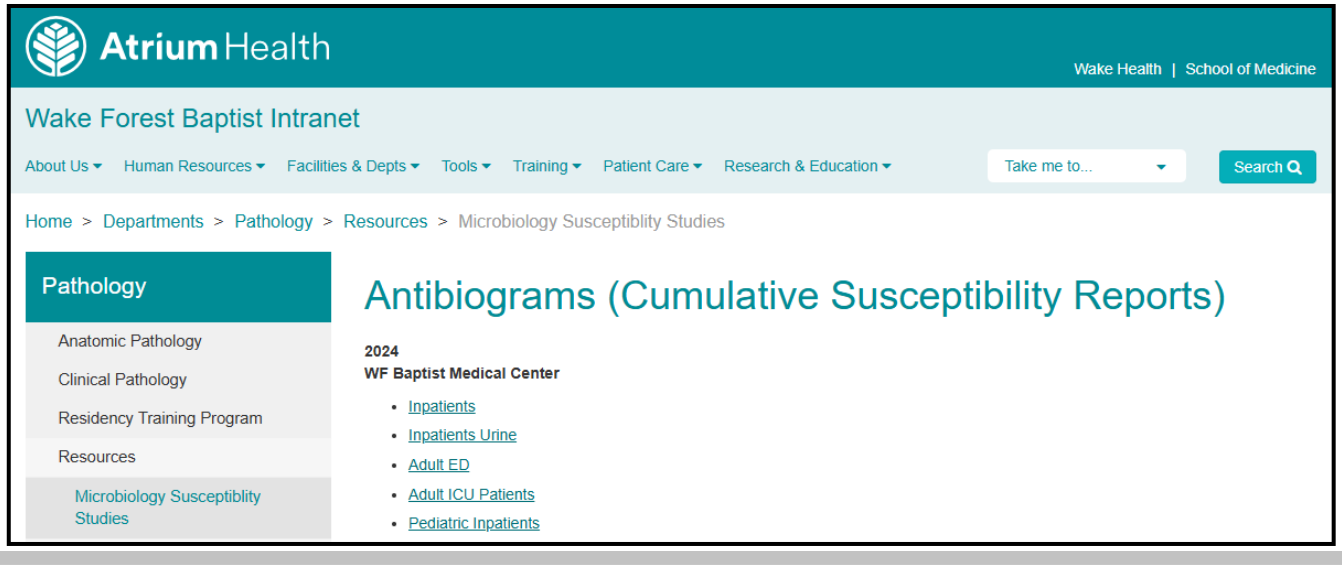
CAUSE Website

CLICK HERE

Access to:

- Adult and pediatric infectious diseases resources:
  - Treatment guidelines
  - Antimicrobial dosing guidelines
  - Rapid diagnostic guidance
- Antimicrobial stewardship curriculum:
  - Didactic lectures
  - Exam questions
  - Small group activities
- Overview of the institution's antibiotic support team (AST)
- Adult and pediatric prior authorization processes and institutional restricted antimicrobials

Access all current and historical Wake Market Antibiograms on the Atrium Health Wake Forest Baptist Intranet by searching "Antibiograms"



Meet the CAUSE Staff

The Center for Antimicrobial Utilization, Stewardship, and Epidemiology (CAUSE) is the Antimicrobial Stewardship Program of Atrium Health Wake Forest Baptist (AHWFB). CAUSE was established in 2000 to promote, administrate, and implement antimicrobial stewardship. Daily operation of CAUSE is directed by a core group of clinicians designated as CAUSE staff.

CAUSE activities are consistent with the IDSA/SHEA Antibiotic Stewardship Guidelines. In addition, CAUSE is compliant with TJC standards and the CDC Core Elements of Hospital Antibiotic Stewardship Programs.

It is CAUSE's philosophy to support and work through the clinicians practicing in various areas throughout the health-system. The program goals are to:

- Prevent or slow the emergence of antimicrobial resistance
- Optimize selection, dose, and duration of antimicrobial treatment
- Reduce adverse drug events
- Reduce morbidity and mortality
- Reduce length of stay
- Reduce health care expenditures

The CAUSE Advisory Board (CAB) is a committee that serves to advise, approve, and communicate CAUSE activities and medical staff concerns. It is composed of CAUSE staff, medical staff from selected clinical services, and pharmacy, nursing, and informatics representatives from all Wake Forest market facilities.

CAUSE Staff Members	
Vera Luther, MD, FIDSA CAUSE Medical Director ID Attending Physician	Christopher Ohl, MD, FIDSA CAUSE Associate Medical Director ID Attending Physician
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Image: https://www.idsociety.org/clinical-practice/antimicrobial-stewardship/index.html