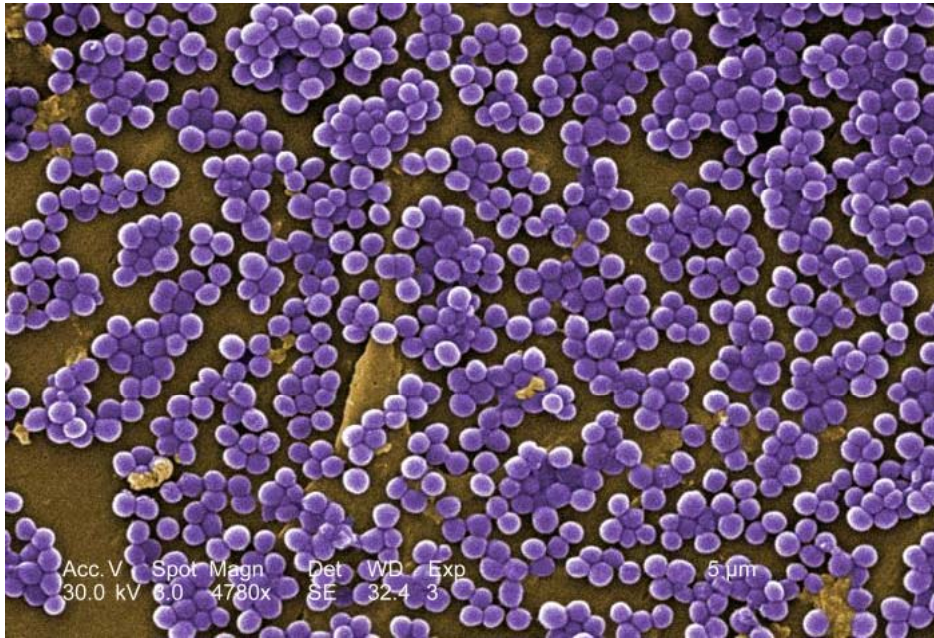
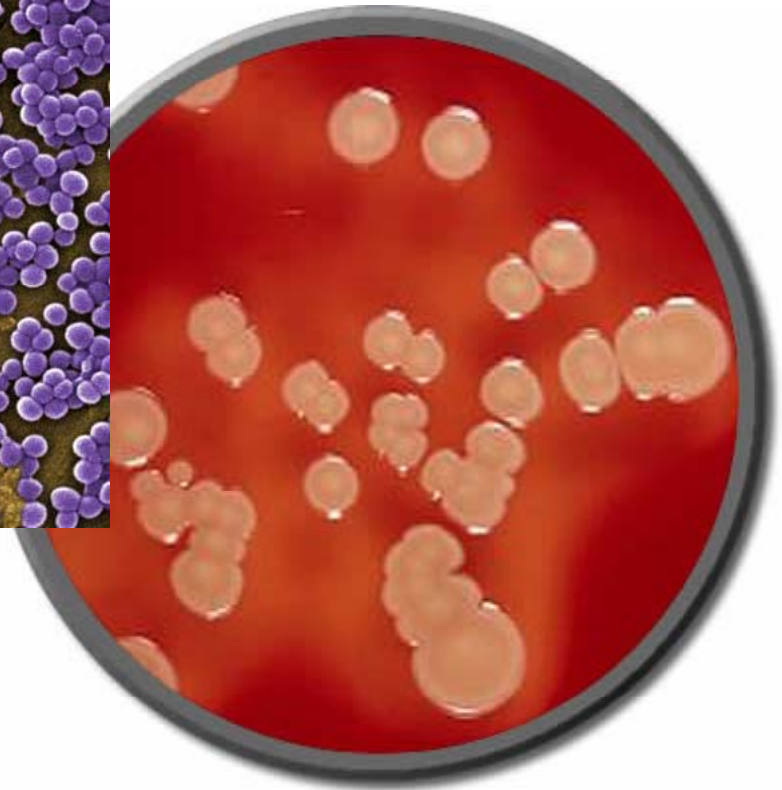


Approach to the Patient
with *Staphylococcus aureus*
Bacteremia

William Muth, MD
21 August 2009



Staphylococcus



aureus

Learning Objectives

1. To understand the importance of *Staphylococcus aureus* infections, their diverse natures, and the organism's inherent virulence.
2. To understand how to distinguish between *Staph aureus* bacteremia and endocarditis.
3. To understand when to use echocardiography in evaluating *Staphylococcus aureus* bacteremia
4. To understand currently available antibiotic therapies of *Staph aureus* bacteremia/endocarditis.
5. To understand appropriate duration of therapy for *Staphylococcus aureus* bacteremia/endocarditis.

Why is it important to understand about
Staphylococcus aureus bacteremia?

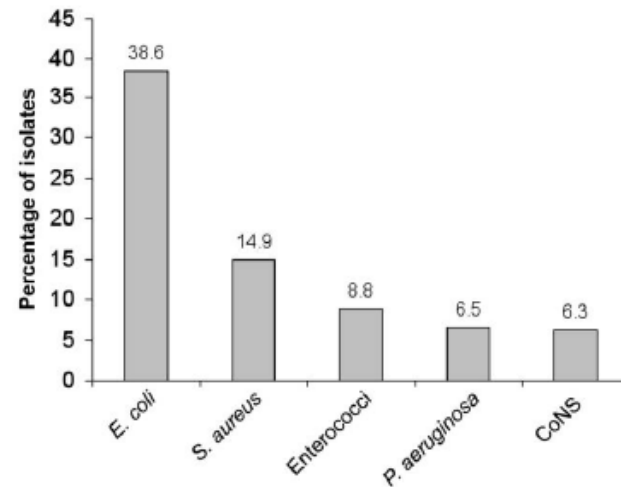
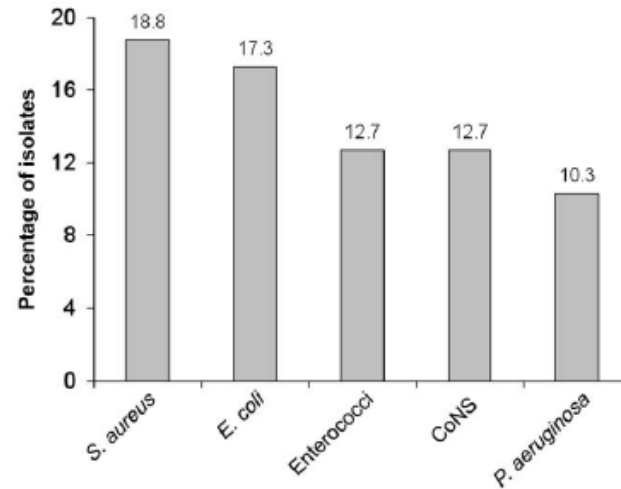
1. It is common.
2. The organism is virulent.
3. The organism can be multi-drug resistant.
4. It can have all sorts of endovascular and metastatic complications.

Staphylococcal aureus Bacteremia (SAB) is Common

- Overall frequency of *Staph aureus* bacteremia is increasing.
 - From 1980-89 rates of SAB went up by 283% as reported to NNIS by non-teaching hospitals; by 176% in large teaching hospitals
 - By 1998 *Staph aureus* had become the second most common bloodstream isolate.
- Increasing use of invasive procedures, prosthetic devices, and intravascular catheters likely underlies the increased incidence of this disease.

Staph aureus Infections are Common

The 5 most frequently occurring bacteria (*Escherichia coli*, *Staphylococcus aureus*, enterococci, *Pseudomonas aeruginosa*, and coagulase-negative staphylococci [CoNS]) identified in 3,209,413 clinical isolates from hospital inpatients (*top*) and outpatients (*bottom*) in the United States from 1988 through March 2005.



Staphylococcus aureus is very resourceful and virulent

DeLeo et al, ID Clinics of NA, 23:1, 17-34, 2009

Table 1
***Staphylococcus aureus* molecules that contribute to immune evasion or alter host immune function**

Gene(s)	Protein or Molecule	Function/Effect on Immune System
<i>ahpC, ahpF</i>	Alkyl hydroperoxide reductase subunits C and F, AhpC and AhpF	Promotes resistance to reactive oxygen species (ROS)
<i>aur</i>	Zinc metalloproteinase aureolysin, Aur	Degrades LL-37
<i>cap5</i> or <i>cap8</i> genes	Capsular polysaccharide	Inhibits phagocytosis
<i>katA</i>	Catalase, KatA	Detoxifies hydrogen peroxide
<i>chp</i>	Chemotaxis inhibitory protein of <i>Staphylococcus aureus</i> , chemotaxis inhibitory protein of <i>S aureus</i>	Inhibits chemotaxis
<i>clfA</i>	Clumping factor A, ClfA	Inhibits phagocytosis, causes platelet activation
<i>crtM, crtN</i>	Carotenoid pigment, staphyloxanthin	Promotes resistance to ROS
<i>dlt</i> operon	Dlt operon, DltABCD	Promotes resistance to cationic antimicrobial peptides (AMPs) and group IIA phospholipase A ₂
<i>eap</i>	Extracellular adherence protein, Eap	Inhibits leukocyte adhesion
<i>ecb</i>	Extracellular complement-binding protein, Ecb	Inhibits C5a generation
<i>efb</i>	Extracellular fibrinogen-binding protein, Efb	Inhibits C5a generation
<i>fnbA, fnbB</i>	Fibronectin-binding proteins A and B, FnbA and FnbB	Cause platelet activation
<i>hla, hly</i>	Alpha-hemolysin (α -hemolysin), Hla	Causes host cell lysis
<i>hld</i>	Delta-hemolysin, Hld	Causes host cell lysis
<i>hlgA, hlgB, hlgC</i>	Gamma-hemolysin subunits A, B, and C; HlgA, HlgB, HlgC; two-component leukocidin	Causes leukocyte and erythrocyte lysis
<i>icaA, icaD, icaB, icaC, icaR</i>	Polysaccharide intercellular adhesin, PIA	Resistance to cationic AMPs
<i>isdA, isdB</i>	Iron-regulated surface determinants of <i>S aureus</i> , IsdA and IsdB	Resistance to AMPs, skin fatty acids, and neutrophil ROS
<i>lukS-PV, lukF-PV</i>	Leukocidin S-PV and F-PV subunits; LukS/F-PV; PVL; two-component leukocidin	Causes phagocyte lysis
<i>lukD, lukE</i>	Leukocidin D and E; LukD and Luke; two-component leukocidin	Causes leukocyte lysis

(continued on next page)

Staphylococcus aureus is very resourceful and virulent

Table 1
Staphylococcus aureus molecules that contribute to immune evasion or alter host immune function

Gene(s)	Protein or Molecule	Function/Effect on Immune System
<i>mprF</i>	Multiple peptide resistance factor, MprF	Promotes resistance to cationic AMPs
<i>psm</i>	Phenol-soluble modulin-like peptides, PSMs	Cause leukocyte lysis
<i>sak</i>	Staphylokinase	Inhibits host α -defensins
<i>sbi</i>	IgG-binding protein, Sbi	Sequesters host IgG
<i>scn</i>	Staphylococcal inhibitor of complement, SCIN	Inhibits complement
<i>sea, seb, sec_n, sed, see, seg, seh, sei, sej, sek, sel, sep</i>	Staphylococcal enterotoxins; SEA, SEB, SEC _n , SED, SEE, SEG, SEH, SEI, SEJ, SEK, SEL, and SEP	Activate T-cells
<i>sodA, sodM</i>	Superoxide dismutase, SodA, SodM	Promotes resistance to ROS
<i>spa</i>	Protein A	Sequesters host IgG, inhibits phagocytosis
<i>ssl5</i>	Staphylococcal superantigen-like 5, SSL5	Binds PSGL-1 and inhibits neutrophil rolling
<i>ssl7</i>	Staphylococcal superantigen-like 7, SSL7	Binds to C5a and IgA
<i>tst</i>	Toxic shock syndrome toxin-1, TSST1	Activates T-cells

Function of each molecule was determined based upon published studies. (Available at: PubMed, <http://www.ncbi.nlm.nih.gov/sites/entrez/>). See also the review by T.J. Foster.⁵⁷

Staphylococcus aureus Infections - Pathogenesis

Staphylococcus aureus has evolved numerous means to avoid destruction by the human innate immune system, including those that block almost all of the key antimicrobial functions of phagocytic leukocytes. It has the ability to up-regulate virulence factors under stressful stimuli (e.g., host immune response or circulating antibiotics).

- **Adhesion and colonization** – ability to adhere to/colonize the nares, damaged skin or the surfaces of implanted devices or prostheses.
- **Tissue Invasion** – ability to secrete exfoliative toxins, hemolysins, other enzymes.
- **Immune Evasion** - ability to secrete anti-opsonizing proteins, leukotoxins (e.g. Panton-Valentine leukocidin), superantigens
- **Biofilms** – ability to elaborate slimy biofilms on damaged skin, fitted medical devices, and healthy or damaged heart valves.

Staphylococcus aureus is increasingly Multi-drug Resistant

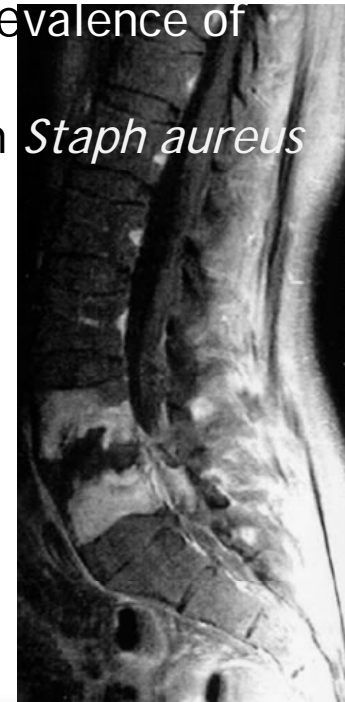
- Sixty percent of ICU *Staphylococcus aureus* isolates as reported to NNIS are now methicillin resistant (MRSA)
- Vancomycin intermediate (VISA) and Vancomycin resistant (VRSA) strains of *Staphylococcus aureus* have been encountered clinically.

TABLE 192-5 Mechanisms of *Staphylococcus aureus* Resistance to Major Classes of Antibiotics

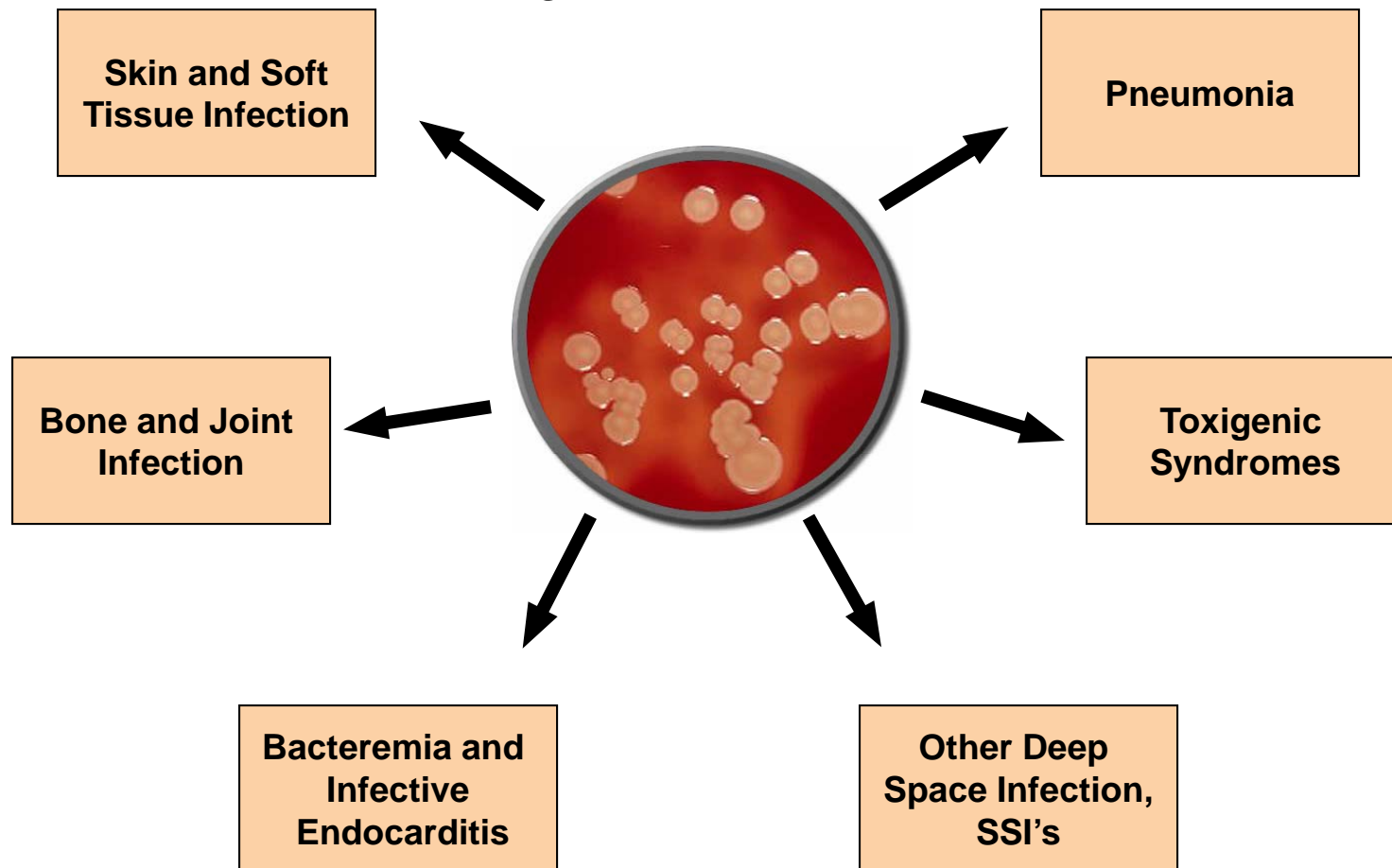
Antimicrobials	Resistance Mechanisms			Resistance Gene		
	Target Modification ^(a)	Drug Inactivation ^(b)	Decreased Accumulation ^(c)	Nature [*]	Origin	Location [*]
<i>β</i>-Lactams						
Penicillinase-S	Yes ^(a)	Yes ^(b)	No	Penicillinase ^(b)	Acquired	Plasmid
Penicillinase-R	Yes ^(a)	No	No	PBP2A ^(a) PBP2A ^(a)	Acquired Acquired	SCC <i>mec</i> (chromosome) SCC <i>mec</i> (chromosome)
<i>Glycopeptides</i>						
Intermediate-R	Yes ^(a)	No	No	Mutations in wall-building genes ^(a)	Intrinsic	Chromosome
Fully-R	Yes ^(a)	No	No	<i>vanA</i> and <i>vanH</i> ^(a)	Acquired	Tn1546 (chromosome)
<i>Macrolide-Lincosamide-Streptogramin B</i>						
Macrolides	Yes ^(a)	No	Yes ^(c)	<i>erm</i> ^(a) <i>msrA</i> ^(c)	Acquired Acquired	Plasmid or chromosome Plasmid
Lincosamide [‡]	Yes ^(a)	Yes ^(b)	No	<i>erm</i> ^(a) <i>linA</i> ^(b)	Acquired Acquired	Plasmid or chromosome Plasmid or chromosome
Streptogramin B [‡]	No	Yes ^(b)	Yes ^(c)	<i>erm</i> ^(a) <i>vgb</i> ^(b) (rare) <i>msrA</i> ^(c) (rare)	Acquired Acquired Acquired	Plasmid or chromosome Plasmid or chromosome Plasmid or chromosome
Streptogramin A	No	Yes ^(b)	Yes ^(c)	<i>vat</i> , <i>vatA</i> ^(b) (rare) <i>vga</i> , <i>vgaB</i> ^(c) (rare)	Acquired Acquired	Plasmid or chromosome Plasmid or chromosome
Quinupristin-dalfopristin	Yes ^(a)	Yes ^(b)	Yes ^(c)	Combinations of above (rare)	Acquired	Plasmid or chromosome
<i>Other Classes</i>						
Linezolid	Yes ^(a)	No	No	Mutation in 23S rRNA gene ^(a)	Intrinsic	Chromosome
Tetracyclines	Yes ^(a)	No	Yes ^(c)	<i>tet(M)</i> , <i>tet(O)</i> ^(c) <i>tet(K)</i> and <i>tet(L)</i> ^(c)	Acquired Acquired	Plasmid or chromosome Plasmid or chromosome
Gentamicin	No	Yes ^(b)	Yes ^(c)	<i>aac(6')</i> - <i>aph(2'')</i> ^(b) Respiratory chain mutants ^(c)	Acquired Acquired	Plasmid or chromosome Chromosome
Chloramphenicol	No	Yes ^(b)	No	<i>cat</i> ^(b)	Acquired	Plasmid or chromosome
Fusidic acid	Yes ^(a)	No	Yes ^(c)	<i>fusA</i> mutation ^(a) pUB101 ^(c)	Intrinsic Acquired	Chromosome Plasmid
Rifampin	Yes ^(a)	No	No	<i>rpoB</i> mutation ^(a)	Intrinsic	Chromosome
Fluoroquinolones	Yes ^(a)	No	Yes ^(c)	<i>griA</i> and <i>gyrA</i> ^(a) <i>norA</i> ^(c)	Intrinsic Intrinsic	Chromosome Chromosome
Trimethoprim	Yes ^(a)	No	No	<i>dfrA</i> mutation ^(a) <i>dfrA</i> ^(a)	Intrinsic Acquired	Chromosome Plasmid or chromosome
Sulfamethoxazole	Yes ^(a)	No	No	<i>dpsA</i> ^(a)	Intrinsic Acquired	Chromosome Plasmid (probable) (acts by mutation or overproduction)

Staph aureus Bacteremia can have “Protean” Endovascular and Distant Complications.

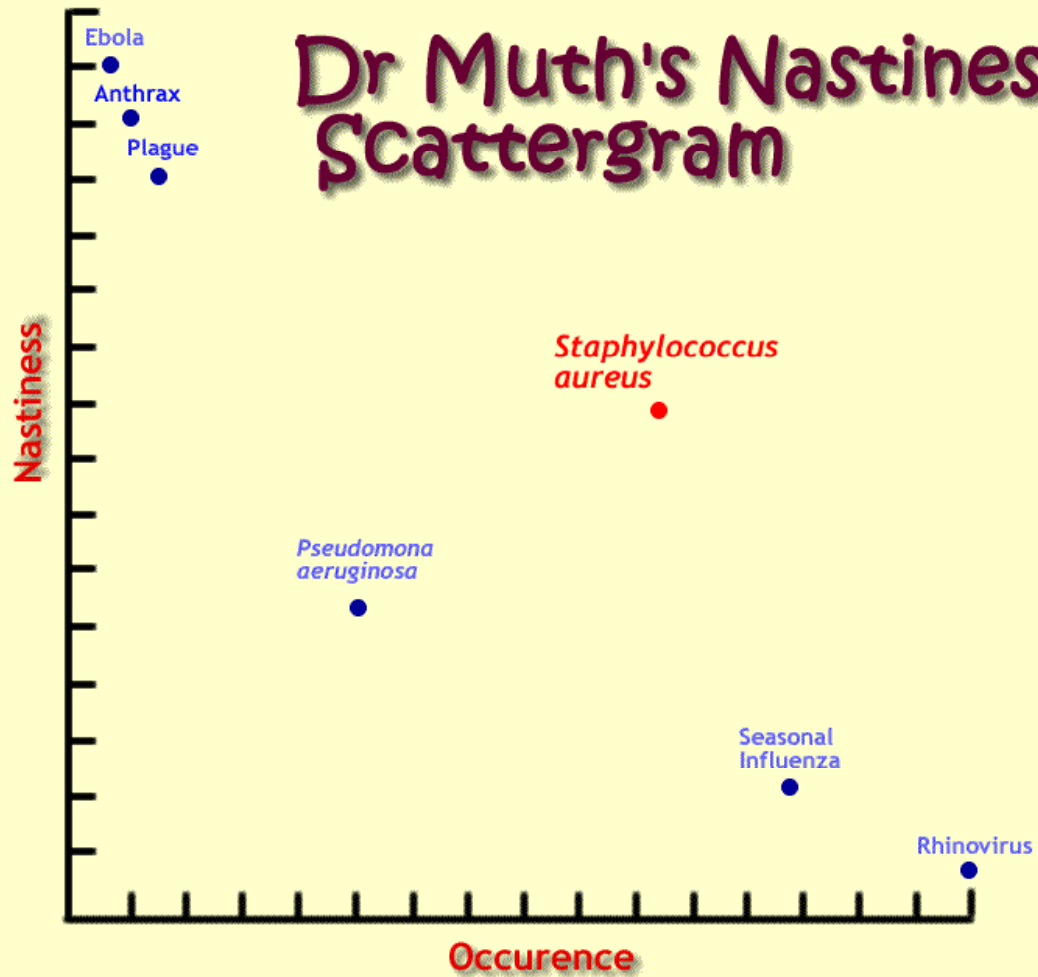
- Rates of infective endocarditis due to *Staph aureus* are increasing
 - Majority of cases still community acquired but healthcare-associated cases rising likely due to increasing prevalence of implantable devices, interventional procedures
- Common metastatic sites of infection associated with *Staph aureus* bacteremia include:
 - Septic arthritis
 - Hematogenous osteomyelitis (kids)
 - Vertebral osteomyelitis/discitis
 - Hepatosplenic abscesses
 - Brain abscesses



Staphylococcus aureus - Clinical Syndromes



Dr Muth's Nastiness Scattergram



Case #1

45 y.o. white female with Crohn's disease in the hospital receiving TPN via a central line becomes acutely febrile. Blood cultures 12 hrs later are reportedly positive for *Staphylococcus aureus*. She promptly becomes afebrile after IV antibiotics are begun and the line removed. Repeat BCs are negative.

Questions

1. What is the antibiotic of choice?
2. How long should she be treated with IV antibiotics?
3. Does she need an echocardiogram to rule out infective endocarditis? If so, what type (TTE vs TEE)?

Case #2

75 y.o. white female, previously healthy, admitted to the hospital with a three day history of shaking chills and fever without otherwise localizing findings. Blood cultures 12 hours later are reportedly positive for MSSA. Despite prompt initiation of IV nafcillin, blood cultures on day 3 and five of her hospitalization remain positive.

Questions

1. What is the antibiotic of choice?
2. How long should she be treated with IV antibiotics?
3. Does she need an echocardiogram to rule out infective endocarditis? If so, what type (TTE vs TEE)?

Approach to the Potentially Bacteremic Patient - Obtaining Blood Cultures

1. Do cultures before antibiotics!
2. Skin antisepsis – 70% isopropyl alcohol
3. Never do just one blood culture!
 - A. Less chance of isolating the culprit
 - B. Won't demonstrate continuous bacteremia
 - C. Can't distinguish contaminant from true bacteremia
4. Optimal number and volume – unknown but three cultures, each 20 cc may be “ideal” in adults
5. Optimal timing of blood cultures
 - A. Likely virulent pathogen – blood cultures q 5”
 - B. Less virulent – blood cultures over several hours
6. Peripheral venipuncture preferred

Types of Bacteremias

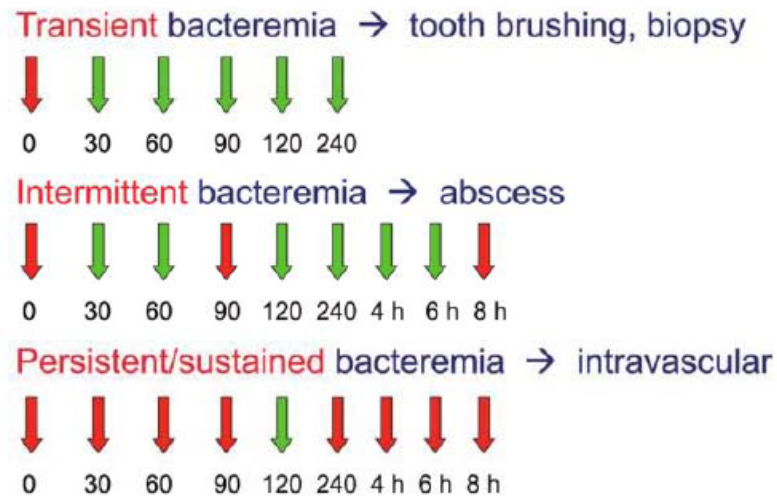
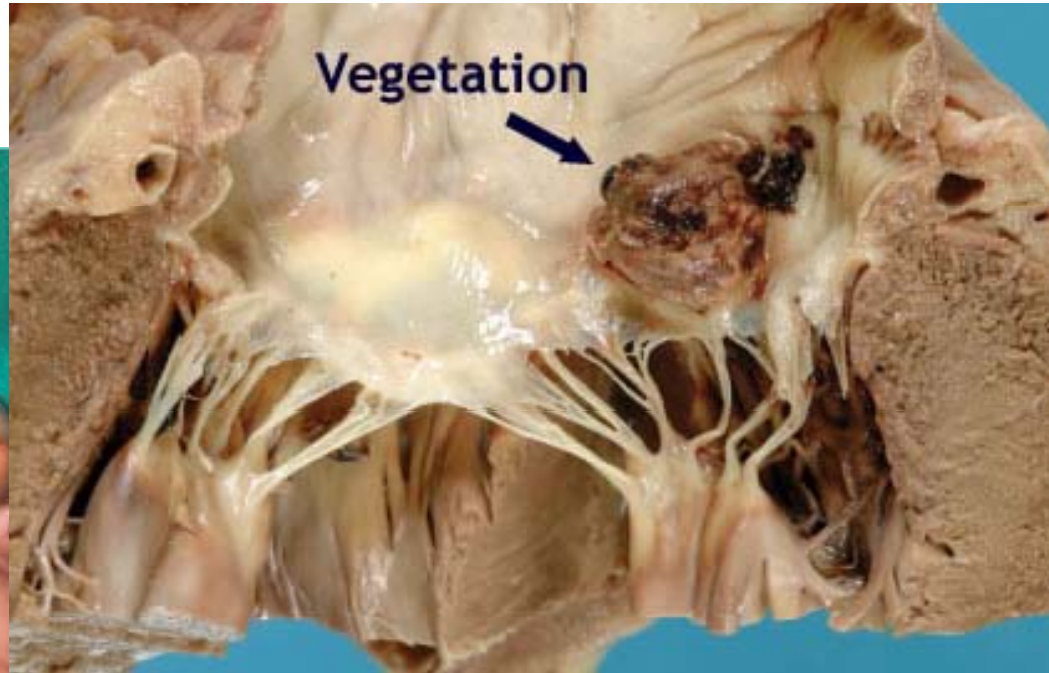


Figure 1. Commonly used classification of bacteremias into 3 categories: transient (bacteremia lasts for a short amount of time and can be caused by actions such as brushing of teeth or after gastrointestinal biopsy), intermittent (recurring bacteremia due to discontinuous seeding of the same organisms, which can be caused by infections such as abscesses), and persistent or sustained (bacteremia occurring over a prolonged period that is usually associated with infections such as infective endocarditis). Red and green arrows indicate the presence and absence, respectively, of bacteria in blood cultures obtained at different time points (in minutes, unless hours [h] is specified).



Infective
Endocarditis

How Do You Diagnose Infective Endocarditis versus "Simple" Bacteremia?



Staphylococcus aureus Bacteremia - Risk Factors for Endocarditis

Table 2. Risk factors for infective endocarditis after *Staphylococcus aureus* bacteremia

Reference	Year	No. of patients	Risk factor
Fowler et al. [35]	2003	724	Community acquisition, persistent fever, persistent bacteremia, and skin examination findings that suggest acute systemic infection
Chang et al. [38]	2003	505	Valvular heart disease, prosthetic valve, previous infective endocarditis, injection drug use, unknown source of bacteremia, persistent bacteremia, nonwhite race, and community acquisition
El-Ahdab et al. [39]	2005	51 ^a	Persistent fever and persistent bacteremia
Hill et al. [40]	2007	132	Unknown source of bacteremia, prosthetic valve, persistent fever, and persistent bacteremia

^a All of these patients had prosthetic valves.

Staphylococcus aureus Bacteremia - Is it Endocarditis?

1. Risk factors for IE and metastatic disease
 - A. “Oslerian” physical findings
 - B. Cardiac valvular disease
 - C. Prosthetic implants
 - D. Community acquired bacteremia
 - E. Older age
 - F. Persistent bacteremia
2. Unfortunately the above factors will not identify a significant proportion of those with *Staph aureus* IE –
 - A. “Oslerian” findings very insensitive
 - B. *Staph aureus* can cause IE in patients without VHD

Infective Endocarditis - Diagnosis

TABLE 1A. Definition of Infective Endocarditis According to the Modified Duke Criteria

Definite infective endocarditis

Pathological criteria

Microorganisms demonstrated by culture or histological examination of a vegetation, a vegetation that has embolized, or an intracardiac abscess specimen; or

Pathological lesions; vegetation or intracardiac abscess confirmed by histological examination showing active endocarditis

Clinical criteria

2 major criteria; or

1 major criterion and 3 minor criteria; or

5 minor criteria

Possible IE

1 major criterion and 1 minor criterion; or

3 minor criteria

Rejected

Firm alternative diagnosis explaining evidence of IE; or

Resolution of IE syndrome with antibiotic therapy for ≤ 4 days; or

No pathological evidence of IE at surgery or autopsy, with antibiotic therapy for ≤ 4 days; or

Does not meet criteria for possible IE as above

Modifications shown in boldface. Reprinted with permission from Clinical Infectious Diseases.²⁵ Copyright 2000, The University of Chicago Press.

TABLE 1B. Definition of Terms Used in the Modified Duke Criteria for the Diagnosis of Infective Endocarditis

Major criteria

Blood culture positive for IE

Typical microorganisms consistent with IE from 2 separate blood cultures: Viridans streptococci, *Streptococcus bovis*, HACEK group, *Staphylococcus aureus*; or community-acquired enterococci in the absence of a primary focus; or

Microorganisms consistent with IE from persistently positive blood cultures defined as follows: At least 2 positive cultures of blood samples drawn >12 h apart; or all of 3 or a majority of ≥ 4 separate cultures of blood (with first and last sample drawn at least 1 h apart)

Single positive blood culture for *Coxiella burnetii* or anti-phase 1 IgG antibody titer $>1:800$

Evidence of endocardial involvement

Echocardiogram positive for IE (**TEE recommended for patients with prosthetic valves, rated at least "possible IE" by clinical criteria, or complicated IE [paravalvular abscess]; TTE as first test in other patients**) defined as follows: oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or abscess; or new partial dehiscence of prosthetic valve; new valvular regurgitation (worsening or changing or preexisting murmur not sufficient)

Minor criteria

Predisposition, predisposing heart condition, or IDU

Fever, temperature $>38^{\circ}\text{C}$

Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, and Janeway's lesions

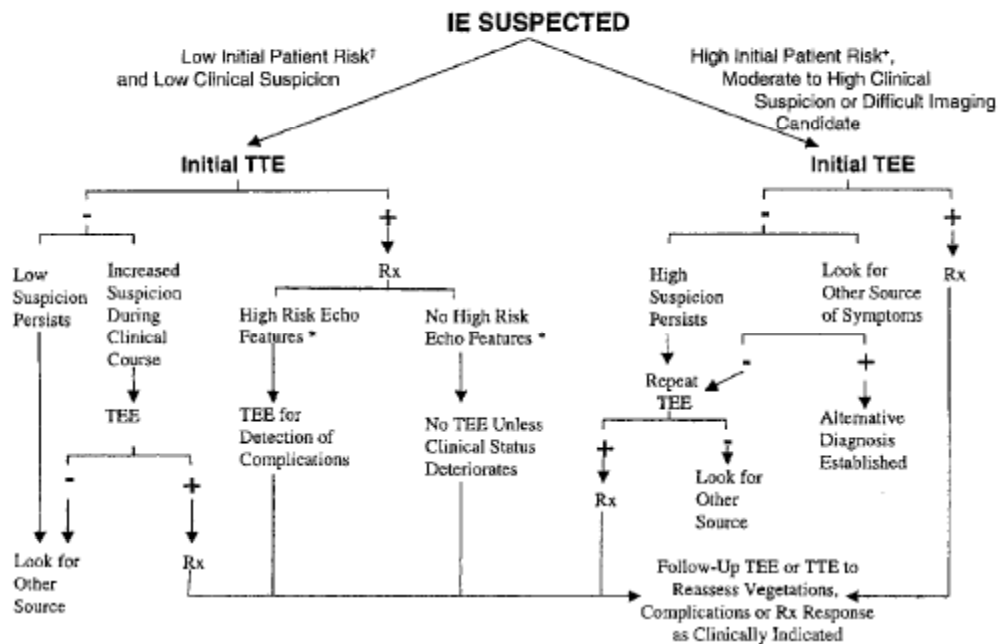
Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor

Microbiological evidence: positive blood culture but does not meet a major criterion as noted above* or serological evidence of active infection with organism consistent with IE

Echocardiographic minor criteria eliminated



Echocardiography in Assessing Likelihood of Infective Endocarditis



An approach to the diagnostic use of echocardiography (echo). *High-risk echocardiographic features include large and/or mobile vegetations, valvular insufficiency, suggestion of perivalvular extension, or secondary ventricular dysfunction (see text). †For example, a patient with fever and a previously known heart murmur and no other stigmata of IE.

+High initial patient risks include prosthetic heart valves, many congenital heart diseases, previous endocarditis, new murmur, heart failure, or other stigmata of endocarditis. Rx indicates antibiotic treatment for endocarditis. Reproduced with permission from: Bayer AS, Bolger AF, Taubert KA, Wilson W, Steckelberg J, Karchmer AW, Levison M, Chambers HF, Dajani AS, Gewitz MH, Newburger JW, Gerber MA, Shulman ST, Pallasch TJ, Gage TW, Ferrieri P. Diagnosis and Management of Infective Endocarditis and Its Complications. *Circulation*. 1998;98:2936-2948.

Role of Echocardiography in Evaluating *Staphylococcus aureus* Bacteremia

1. Echocardiography has a crucial role in excluding endocarditis
 - A. A negative TEE in patient without prosthetic heart valves has excellent negative predictive value.
2. Trans-thoracic versus trans-esophageal echo
 1. TEE more sensitive than TTE but “invasive,” costly
 2. TEE indicated in patients with valvular prostheses
 3. IDSA recommends TEE in all patient with catheter related SAB:

If not contraindicated, TEE should be done to rule out vegetations in patients with catheter-related Staphylococcus aureus bloodstream infection because of recently reported high rates of complicating endocarditis (B-II) [27–30]; if TEE is not available and results of transthoracic echocardiography are negative, the duration of therapy should be decided clinically for each patient.

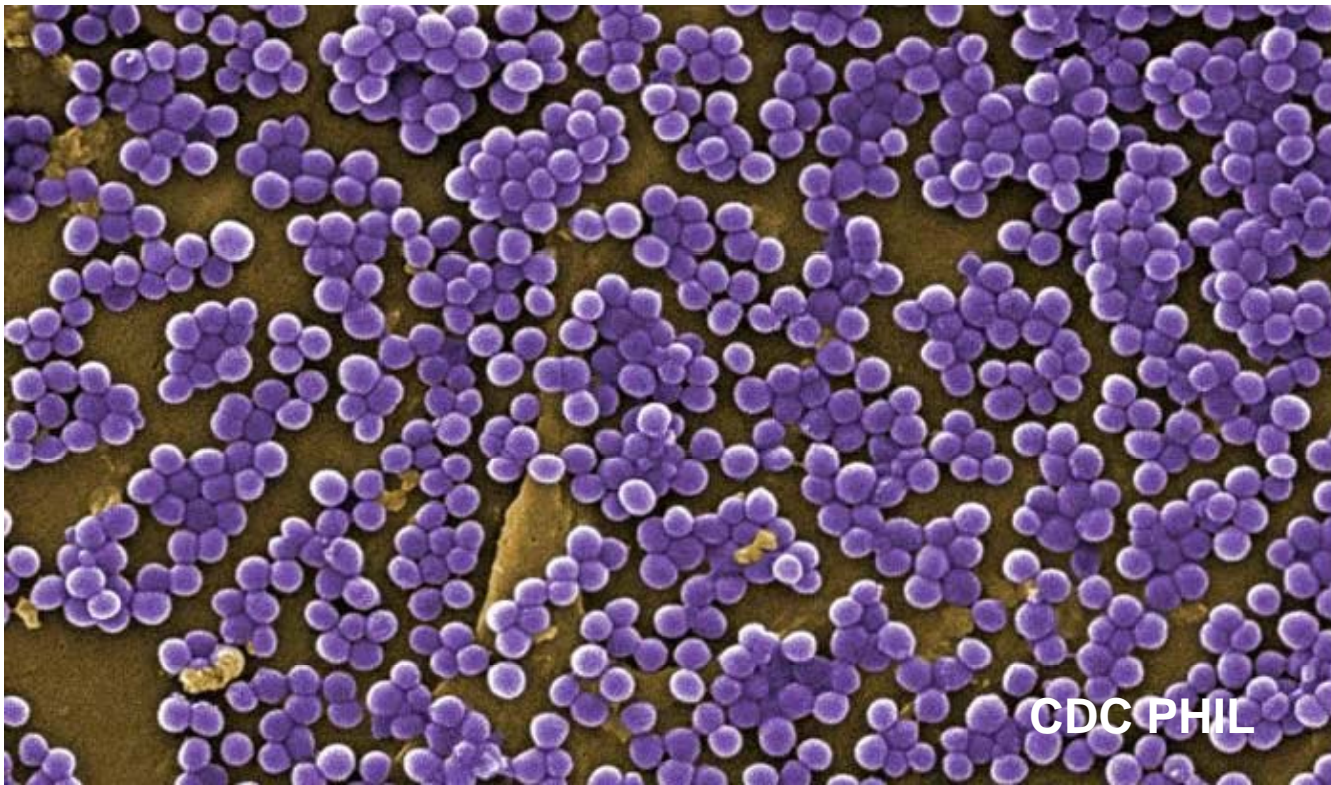
Guidelines for the Management of Intravascular Catheter–Related Infections

"Guidelines for the Management of Intravascular Catheter-Related Infections" - 2009

Staphylococcus aureus

78.	Patients with <i>S. aureus</i> CRBSI should have the infected catheter removed, and they should receive 4–6 weeks of antimicrobial therapy, unless they have exceptions listed in recommendation 80	B-II	[139, 144]
79.	Patients who are being considered for a shorter duration of therapy should have a transesophageal echocardiograph (TEE) obtained	B-II	[142, 150]
80.	Patients can be considered for a shorter duration of antimicrobial therapy (i.e., a minimum of 14 days of therapy) if the patient is not diabetic; if the patient is not immunosuppressed (i.e., not receiving systemic steroids or other immunosuppressive drugs, such as those used for transplantation, and is nonneutropenic); if the infected catheter is removed; if the patient has no prosthetic intravascular device (e.g., pacemaker or recently placed vascular graft); if there is no evidence of endocarditis or suppurative thrombophlebitis on TEE and ultrasound, respectively; if fever and bacteremia resolve within 72 h after initiation of appropriate antimicrobial therapy; and if there is no evidence of metastatic infection on physical examination and sign- or symptom-directed diagnostic tests	A-II	[135]
81.	If a TEE is performed, it should be done at least 5–7 days after onset of bacteremia to minimize the possibility of false-negative results	B-II	[152]
82.	Short-term catheters should be removed immediately for patients with <i>S. aureus</i> CRBSI	A-II	[139, 144]
83.	For <i>S. aureus</i> CRBSI involving long-term catheters, the catheters should be removed unless there are major contraindications (e.g., there is no alternative venous access, the patient has significant bleeding diathesis, or quality of life issues take priority over the need for reinsertion of a new catheter at another site)	A-II	[139, 144]

Antibiotic Therapy - *Staphylococcus aureus* Bacteremia/Endocarditis



Remember – Source Control!

Antibiotic Therapy of *Staph aureus* Bacteremia (Methicillin Sensitive)

- Semi-synthetic penicillins – nafcillin or oxacillin are the drugs of choice.
- First generation cephalsporins such as cefazolin are alternatives for persons with penicillin allergy
- Vancomycin can be used for persons with severe penicillin allergy.
- Static drugs such as clindamycin would not be preferred in SAB.

Antibiotic Therapy *Staph aureus* Endocarditis, Native Valve

TABLE 7. Therapy for Endocarditis Caused by Staphylococci in the Absence of Prosthetic Materials

Regimen	Dosage* and Route	Duration	Strength of Recommendation	Comments
Oxacillin-susceptible strains				
Nafcillin or oxacillin†	12 g/24 h IV in 4–6 equally divided doses	6 wk	IA	For complicated right-sided IE and for left-sided IE; for uncomplicated right-sided IE, 2 wk (see text)
<i>with</i> Optional addition of gentamicin sulfate‡	3 mg/kg per 24 h IVIM in 2 or 3 equally divided doses <i>Pediatric dose</i> §: Nafcillin or oxacillin 200 mg/kg per 24 h IV in 4–6 equally divided doses; gentamicin 3 mg/kg per 24 h IVIM in 3 equally divided doses	3–5 d		Clinical benefit of aminoglycosides has not been established
For penicillin-allergic (nonanaphylactoid type) patients:				
Cefazolin	6 g/24 h IV in 3 equally divided doses	6 wk	IB	Consider skin testing for oxacillin-susceptible staphylococci and questionable history of immediate-type hypersensitivity to penicillin Cephalosporins should be avoided in patients with anaphylactoid-type hypersensitivity to β -lactams; vancomycin should be used in these cases§
<i>with</i> Optional addition of gentamicin sulfate	3 mg/kg per 24 h IVIM in 2 or 3 equally divided doses <i>Pediatric dose</i> : cefazolin 100 mg/kg per 24 h IV in 3 equally divided doses; gentamicin 3 mg/kg per 24 h IVIM in 3 equally divided doses	3–5 d		Clinical benefit of aminoglycosides has not been established
Oxacillin-resistant strains				
Vancomycin	30 mg/kg per 24 h IV in 2 equally divided doses <i>Pediatric dose</i> : 40 mg/kg per 24 h IV in 2 or 3 equally divided doses	6 wk	IB	Adjust vancomycin dosage to achieve 1-h serum concentration of 30–45 μ g/mL and trough concentration of 10–15 μ g/mL (see text for vancomycin alternatives)

*Dosages recommended are for patients with normal renal function.

†Penicillin G 24 million U/24 h IV in 4 to 6 equally divided doses may be used in place of nafcillin or oxacillin if strain is penicillin susceptible (minimum inhibitory concentration ≤ 0.1 μ g/mL) and does not produce β -lactamase.

‡Gentamicin should be administered in close temporal proximity to vancomycin, nafcillin, or oxacillin dosing. See Table 4 for appropriate dosage of gentamicin.

§Pediatric dose should not exceed that of a normal adult.

||For specific dosing adjustment and issues concerning vancomycin, see Table 4 footnotes.

Antibiotic Therapy *Staph aureus* Endocarditis, Prosthetic Valve

TABLE 8. Therapy for Prosthetic Valve Endocarditis Caused by Staphylococci

Regimen	Dosage* and Route	Duration, wk	Strength of Recommendation	Comments
Oxacillin-susceptible strains				
Nafcillin or oxacillin <i>plus</i> Rifampin <i>plus</i> Gentamicin†	12 g/24 h IV in 6 equally divided doses 900 mg per 24 h IV/PO in 3 equally divided doses 3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses <i>Pediatric dose‡:</i> nafcillin or oxacillin 200 mg/kg per 24 h IV in 4–6 equally divided doses; rifampin 20 mg/kg per 24 h IV/PO in 3 equally divided doses; gentamicin 3 mg/kg per 24 h IV/IM in 3 equally divided doses	≥6 ≥6 2	IB	Penicillin G 24 million U/24 h IV in 4 to 6 equally divided doses may be used in place of nafcillin or oxacillin if strain is penicillin susceptible (minimum inhibitory concentration ≤0.1 μg/mL) and does not produce β-lactamase; vancomycin should be used in patients with immediate-type hypersensitivity reactions to β-lactam antibiotics (see Table 3 for dosing guidelines); cefazolin may be substituted for nafcillin or oxacillin in patients with non-immediate-type hypersensitivity reactions to penicillins
Oxacillin-resistant strains				
Vancomycin <i>plus</i> Rifampin <i>plus</i> Gentamicin	30 mg/kg 24 h in 2 equally divided doses 900 mg/24 h IV/PO in 3 equally divided doses 3 mg/kg per 24 h IV/IM in 2 or 3 equally divided doses <i>Pediatric dose:</i> vancomycin 40 mg/kg per 24 h IV in 2 or 3 equally divided doses; rifampin 20 mg/kg per 24 h IV/PO in 3 equally divided doses (up to adult dose); gentamicin 3 mg/kg per 24 h IV or IM in 3 equally divided doses	≥6 ≥6 2	IB	Adjust vancomycin to achieve 1-h serum concentration of 30–45 μg/mL and trough concentration of 10–15 μg/mL (see text for gentamicin alternatives)

*Dosages recommended are for patients with normal renal function.

†Gentamicin should be administered in close proximity to vancomycin, nafcillin, or oxacillin dosing. See Table 4 for appropriate dosage of gentamicin.

‡Pediatric dose should not exceed that of a normal adult.

Endocarditis – Indications for Surgery

TABLE 3. Echocardiographic Features That Suggest Potential Need for Surgical Intervention

Vegetation

Persistent vegetation after systemic embolization
Anterior mitral leaflet vegetation, particularly with size >10 mm*
≥1 embolic events during first 2 wk of antimicrobial therapy*
Increase in vegetation size despite appropriate antimicrobial therapy*†

Valvular dysfunction

Acute aortic or mitral insufficiency with signs of ventricular failure‡
Heart failure unresponsive to medical therapy†
Valve perforation or rupture†

Perivalvular extension

Valvular dehiscence, rupture, or fistula†
New heart block‡‡
Large abscess or extension of abscess despite appropriate antimicrobial therapy†

See text for more complete discussion of indications for surgery based on vegetation characterizations.

*Surgery may be required because of risk of embolization.

†Surgery may be required because of heart failure or failure of medical therapy.

‡Echocardiography should not be the primary modality used to detect or monitor heart block.

Infection with certain micro-organisms including Staph aureus is a relative indication for valve replacement as are all cases of prosthetic valve endocarditis.

Duration of Antibiotic Therapy for *Staph aureus* bacteremia, not Endocarditis

1. “Simple bacteremia,” negative TEE – can be as short as two weeks
2. Uncomplicated SAB, no TEE – four weeks
3. Complicated SAB (presence of metastatic sites of infection, etc.) – four to six weeks of Rx along with “source control”

Simple Bacteremia - A Bit More

- Catheter-associated infection and removal of the catheter
- Negative result of follow-up blood culture
- Defervescence within 72 h
- Normal findings on transesophageal echocardiogram*
- No prosthetic material in the joints or intravascular space
- No symptoms suggestive of metastatic infection

Complicated *Staph aureus* Bacteremia

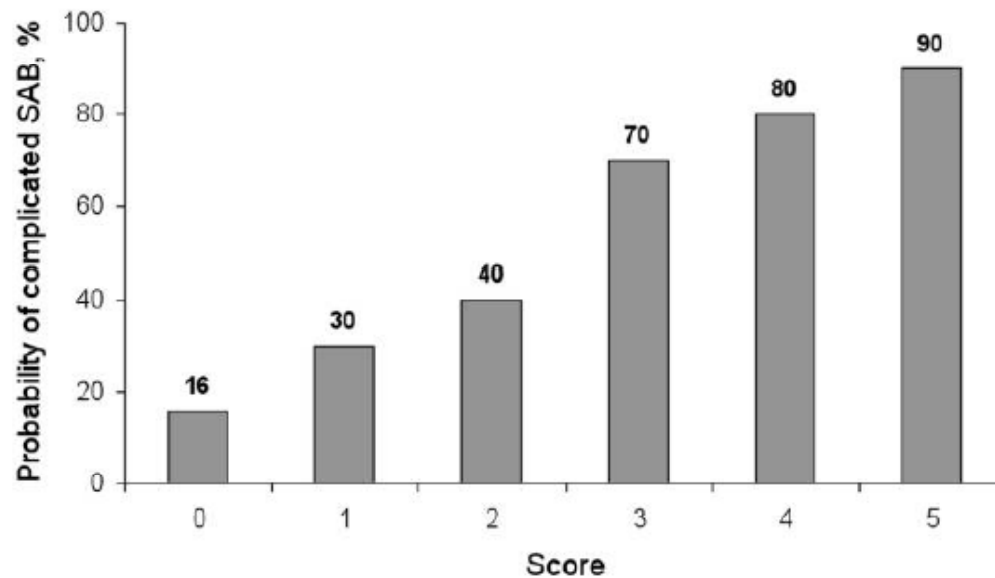


Figure 1. Association between the *Staphylococcus aureus* bacteremia (SAB) score and the probability of complicated SAB [9]. One point each is assigned for community-acquired infection, skin findings suggestive of acute systemic infection, and persistent fever at 72 h, and 2 points is assigned for a positive result of follow-up blood culture at 48–96 h.

Therapy of MRSA Bacteremia

1. Vancomycin generally the drug of choice
 - A. Slower cidal activity
 - B. Heterogeneous strains
2. Daptomycin (*Cubicin*) – probably good. Avoid in MRSA pneumonia
3. Linezolid (*Zyvox*) – static, some failures in treatment of IE – *Avoid* in bacteremic illness
4. Tigecycline (*Tygacil*) – low serum levels – *Avoid* in bacteremic illness

Case #1

45 y.o. white female with Crohn's disease in the hospital receiving TPN via a central line becomes acutely febrile. Blood cultures 12 hrs later are reportedly positive for *Staph aureus*. She promptly becomes afebrile after IV antibiotics are begun and the line removed. Repeat BCs are negative.

Questions

1. What is the antibiotic of choice?
2. How long should she be treated with IV antibiotics?
3. Does she need an echocardiogram to rule out infective endocarditis? If so what type (TTE vs TEE)?

Case #2

75 y.o. white female, previously healthy admitted to the hospital with a three day history of shaking chills and fever without otherwise localizing findings. Blood cultures 12 hours later are reportedly positive for MSSA. Despite prompt initiation of IV nafcillin, blood cultures on day 3 and five of her hospitalization remain positive.

Questions

1. What is the antibiotic of choice?
2. How long should she be treated with IV antibiotics?
3. Does she need an echocardiogram to rule out infective endocarditis? If so what type (TTE vs TEE)?



*Thank you for
your attention!*

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