Staphylococcus aureus complex (LTR81523)

Edit Approved By: Van der Walt, Peet (09/27/2023) **Revision: 7.00**

Organism

Staphylococcus aureus complex

- *S. aureus*
- *S. argenteus*

Clinical

S. aureus may colonize the nose and/or skin of humans. It is associated with skin/soft tissue, bone/joint infections, wound infections, endocarditis, catheter-related bacteremia, septicemia, and nosocomial infections (pneumonia, surgical wound infections) both in immunocompetent and immunocompromised patients. *S. argenteus* causes a similar spectrum of disease as *S. aureus*.

Usual susceptibility pattern

Most strains are resistant to penicillin. Oxacillin/cloxacillin resistance is most commonly associated with an altered penicillin binding protein (PBP2') which results in resistance to all beta-lactam agents. This resistance, encoded by the *mec*A gene or *mec*C gene, may be homogeneous, affecting all cell populations or heterogeneous, affecting only a sub population.

Rarely, low-level oxacillin resistance can be due to hyper-beta-lactamase producers (BORSA (borderline oxacillin resistant *S. aureus*)), producing very large amounts of penicillinase or modification in other penicillin binding proteins (other than PBP2') and are referred to as MODSA (modified/moderate oxacillin resistant *S. aureus*). Current guidelines recommend reporting all oxacillin resistant *S. aureus* strains, regardless of the mechanism, as being resistant to all beta-lactam antibiotics

Rare strains of S. aureus can produce a penicillinase able to hydrolyze cefazolin at high inoculum (in infections such as osteomyelitis, endocarditis, medical device related infections, abscesses). This may lead to clinical failure of cefazolin (but not cloxacillin) in MSSA.

S. aureus are usually susceptible to vancomycin and linezolid. Rare isolates with vancomycin resistance (intermediate) have been reported and linezolid resistance has also been described. Resistance to clindamycin may be inducible. Resistance to erythromycin, TMP-SMX and tetracycline is variable. Although most strains appear susceptible to quinolones, resistance develops very quickly by selection of resistant mutants.

Although the rates of resistance seem to be lower in *S. argenteus* than in *S. aureus* methicillin resistant strains have been reported.

Staphylococcus aureus complex, Continued

Susceptibility method VITEK2. Additional tests include disc diffusion or E test method.

Disc diffusion:		Mueller-Hinton agar incubated in ambient air at 35°C for 16-18 hours.
Cefoxitin disc screen		Mueller-Hinton agar incubated in ambient air at 35°C for 16- 18 hours. Use 0.5 McFarland suspension in saline.
Etest:	Oxacillin	Mueller-Hinton agar with 2% NaCl incubated in ambient air at 35°C for 24 hours. Use 1.0 McFarland suspension in saline.
	Vancomycin	Mueller-Hinton agar incubated in ambient air at 35°C for 24 hours. Use 0.5 McFarland suspension in saline.
	Other	Mueller-Hinton agar incubated in ambient air at 35ºC for 16-20 hours. Use 0.5 McFarland suspension in saline.
Note: Testing at temperatures > 35°C may not detect methicillin resistance.		

Susceptibility testing of atypical / small-colony variant (SCV) *Staphylococcus aureus*:

For isolates of *S. aureus* that do not grow well on unsupplemented Mueller-Hinton agar (i.e. SCV), testing on other media (i.e. MH with 5% sheep blood (MHS) or BAP), does not reliably detect *mecA*-mediated resistance. Susceptibility testing of other antibiotics may also be problematic.

SCV are characterized by colonies about 1/10 the size of those produced by typical wild-type *S. aureus*. They may also display reduced pigmentation and decreased hemolysis or coagulase activity.

Subculturing of these strains should be minimized as this may result in reversion to the wild-type phenotype and the susceptibility results for the SCV cannot be assumed to be the same as the wild-type parent.

IF …	**THEN** …
S. aureus SCV	• setup cefoxitin (CFOX) disc on MHS **and** BAP • if additional antibiotics are requested by physician consult microbiologist prior to testing

Staphylococcus aureus complex, Continued

Susceptibility reporting

	CSF/ Brain	Blood/ Endo Vascular Catheter	Sterile Body Site	Deep Wound	PJI (see Note)	Urine	Eye (See Note)	Nasal (See Note)	Sputum ETT Aspirate	Other	Comments
Amoxicillin-clavulanate (oral)				*		*			*	*	* Report (same as ox/clox) if *Haemophilus/ Moraxella / S. pneumoniae/* Amp S Enterococci or anaerobes co-isolated
Cefazolin		✓	✓	✓	✓	✓	✓	✓	✓	✓	Report same as ox/clox
Clindamycin			✓	✓	✓		✓	✓	✓	✓	**See Special Considerations**
Daptomycin		2	2		2						2nd line if vanco I/R Etest method **See Special Considerations**
Doxycycline			✓*	✓*	✓*	✓*	✓*	✓*	✓*	✓*	If tetra S - report doxy S If tetra I/R - do doxy disc *If patient < 8 y report only if MRSA **and** TMP-SMX I/R - see **Special Considerations**
Erythromycin			*	*	*		*	*	*	*	* Test but do not report – **See Special Considerations**
Levofloxacin					✓		✓				Do not report in patients < 18 y (exception eye specimens)
Moxifloxacin							✓				Do not report in patients < 18 y (exception eye specimens)
Linezolid	2	2	2	2	2				2		2nd line if ox/clox R or vanco I/R. If linezolid R see **Special Considerations**
Mupirocin	*	*	*	*	*	*	*	*	*	*	**See Special Considerations**
Nitrofurantoin						✓					
Oxacillin/ cloxacillin	✓*	✓*	✓*	✓*	✓*	✓	✓*	✓	✓	✓	Refer to *Staphylococcus Oxacillin Reporting Flowchart* (Doc ID: MIC - 37934) ***See Special Considerations**
Rifampin	*	*	*	*	✓	*	*	*	*	*	* Report on physician request only – see **Special considerations**
TMP-SMX			✓	✓	✓	✓	✓	✓	✓	✓	If TMP-SMX R see **Special Considerations** Do not report if patient <2 months
Vancomycin	2	2	2	2	2	2	2	2	2	2	2nd line if ox/clox R If VTK2 vanco ≥2 **or** ox/clox R refer to *Detection of Vancomycin Resistance in S. aureus Flowchart* (Doc ID: MIC–14944)

Staphylococcus aureus complex, Continued

Notes:

<table>
<tr><td>Deep eye specimens:</td><td>Perform susceptibility test if:
<table>
<tr><td>• vitreous fluid</td><td>• canaliculitis</td><td>• corneal ulcer / scrapings</td></tr>
<tr><td>• chamber aspirate</td><td>• endophthalmitis</td><td>• contact lens related infections</td></tr>
<tr><td>• intraocular fluid</td><td>• donor sclera</td><td>• ophthalmology clinic/ward</td></tr>
<tr><td>• keratitis</td><td>• chorioretinitis</td><td>• history of failure of therapy</td></tr>
<tr><td>• injury/surgery</td><td>• cornea</td><td>• preseptal/orbital cellulitis</td></tr>
</table></td></tr>
<tr><td rowspan="2">Superficial eye specimens:</td><td>Screen for oxacillin/cloxacillin resistance using cefoxitin disc testing:
Refer to Staphylococcus Oxacillin Reporting Flowchart (Doc ID: MIC - 37934)</td></tr>
<tr><td>Susceptibility testing of superficial eye specimens not routinely performed.
• Add comment:
“Susceptibility testing of topical antibiotics is not standardized and is not routinely performed on superficial eye infections”.&A89</td></tr>
<tr><td rowspan="2">Nasal specimens:</td><td>Screen for oxacillin/cloxacillin resistance using cefoxitin disc testing:
Refer to Staphylococcus Oxacillin Reporting Flowchart (Doc ID: MIC - 37934)</td></tr>
<tr><td>Susceptibility testing should only be performed upon physician request.</td></tr>
<tr><td>Prosthetic joint infections (PJI)</td><td>For S. aureus isolated from joint fluids with prosthetic joint/implant associated infections (PJI), joint tissues, or foreign bodies from joints.
Refer to Staphylococcus spp. Doxycycline, Levofloxacin, SXT and Rifampin Reporting Flowchart (Doc ID: MIC – 14945).</td></tr>
</table>

Special considerations

<table>
<tr><td><u>Clindamycin/ Erythromycin:</u></td><td>If clindamycin S/I and erythromycin I/R this may indicate inducible resistance.
<table>
<tr><th>IF…</th><th>THEN….</th></tr>
<tr><td>VITEK2 ICR is positive</td><td>• Report clindamycin R
• Add comment:
“This isolate is presumed to be resistant to clindamycin based on the detection of inducible clindamycin resistance in vitro”. #A139</td></tr>
<tr><td>VITEK2 ICR is negative</td><td>• Report clindamycin as tested</td></tr>
</table></td></tr>
<tr><td rowspan="2"><u>Daptomycin:</u></td><td>Daptomycin is inactivated by surfactant in the lungs. Therefore this antibiotic should not be used for the treatment of respiratory infections.

Blood isolates where Daptomycin is reported, add comment:
“Daptomycin is inactivated by lung surfactant and should not be used for respiratory infections.” (21127)</td></tr>
<tr><td>S. aureus should be susceptible to this antibiotic. Consult microbiologist if not susceptible.
If ‘nonsusceptible’, the organism ID and susceptibility should be confirmed by repeat testing. If confirmed, consider submitting isolate to a reference laboratory.</td></tr>
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Staphylococcus aureus complex, Continued

Special considerations (continued)

Doxycycline:	If reporting doxycycline and patient < 8 y add comment: "Doxycycline can now be prescribed for children <8y for short-course (<21d) therapy: OTHER tetracyclines are still contraindicated for this age group." **(25)**
Linezolid:	*S. aureus* are usually susceptible to this antibiotic. • If VITEK2 linezolid R confirm with disc diffusion • If linezolid S by disc diffusion report linezolid S and add comment: "Current testing methods may not detect resistance. Infectious diseases consultation is recommended if clinical failure or delayed response to therapy." **(free text)** • Consult microbiologist if confirmed as R.
Mupirocin:	Send to reference laboratory for mupirocin testing at physician request or if *S. aureus* (MRSA or MSSA*)* isolated from a nasal screen of a pre-operative patient undergoing cardiothoracic surgery.
Oxacillin/ Cloxacillin:	For **MSSA (oxacillin/cloxacillin susceptible)** isolates from **Sterile Body Sites / Deep Wounds,** if vancomycin reported add comment**:** "For methicillin (cloxacillin) susceptible Staphylococcus aureus infections requiring parenteral therapy, anti-staphylococcal beta lactam agents (e.g. cloxacillin, cefazolin) are more effective than vancomycin." #A347
	Very rare strains of MRSA may not be detected by automated systems as they retain low MICs to both cloxacillin and cefoxitin. If documented clinical failure of cloxacillin for serious *S. aureus* infection, consult microbiologist regarding *mec*A gene testing.
Rifampin:	If rifampin result reported, add comment "Rifampin should only be used in combination therapy" **(21282)**
TMP-SMX:	Automated systems may overcall resistance to TMP-SMX in S. aureus. If VITEK 2 TMP-SMX R confirm with disc diffusion. Report SXT disc diffusion results.

Interpretation

For Etest, report actual MIC result. For interpretation (S, I, or R) report according to the nearest higher doubling dilution **(Appendix 1)**.

Use **CLSI** interpretive document for **Staphylococcus spp.** using *S. aureus* breakpoints

For oxacillin and cefoxitin: Refer to *Staphylococcus Oxacillin Reporting Flowchart* (Doc ID: MIC - 37934)

For vancomycin: Rapid automated systems may not be reliable to detect vancomycin heteroresistance.
Refer to *Detection of Vancomycin Resistance in S. aureus Flowchart* (Doc ID: MIC – 14944)