



**M061-2 Nares: MRSA - Methicillin-resistant *Staphylococcus aureus* –**

**HISTORY.** This sample was submitted to A and B laboratories as a swab from an 18-year old trauma patient admitted to hospital who had a boil. Laboratories were requested to set up and process as per their laboratory protocol. Participants were notified that results would be graded based on CMPT's Clinical Relevancy scale. It was expected that laboratories would screen for the presence of *Staphylococcus aureus* (and further test for MRSA), even in the absence of a specific request.

**CMPT QA.** Internal validation yielded 4+ growth of methicillin-resistant *Staphylococcus aureus* and coagulase-negative staphylococcus, both viable for 8 days.

**CLINICAL RELEVANCY GRADING (maximum grade = 4)**

As 14 out of 15 (93%) reference laboratories correctly identified this organism as an MRSA this challenge was considered suitable to grade. The remaining reference laboratory chose to reject the sample with a comment only (see Table 1). Antimicrobial susceptibility testing (AST) was not requested, nor graded. An additional aspect was added to this challenge to determine the extent to which laboratories notify infection prevention and control practitioners when an MRSA is discovered. This aspect was not graded but the results are provided for laboratory interest. In future surveys as part of clinical relevancy, this aspect will be graded.

**-GRADING—(MAXIMUM = 4)**

**CLINICAL RELEVANCY REPORTING:** 93% (69/74) of category A laboratories and 98% (41/42) of category B laboratories received a grade of 4/4.

**NOTES**

- In future surveys, as part of Clinical Relevancy, the extent to which laboratories notify infection prevention and control practitioners when an MRSA is discovered will be graded.**
- Isolation of an MRSA positive patient as early as possible in hospital is important to prevent spread to other patients in the hospital setting.

Overall, 97 % (70/72) of category A laboratories and 98% (41/42) of category B laboratories reported *S. aureus*. Only 3 laboratories (2A, 1B) failed to isolate and report the *S. aureus* (MRSA) present in this sample. These laboratories should review their isolation and identification methodologies. One category A laboratory that correctly identified the isolate as *S. aureus* but did not indicate that it was referred for further testing received a grade of zero. Three laboratories did not process the sample and submitted comments only as per their laboratory protocol. These labs were also given a grade of 0. Two laboratories (1A, 1B) indicated they do not process nose

swabs. These two laboratories were not graded, but this challenge was intended as a screening test, rather than an anatomical site-specific challenge. If nothing else, when the rates of MRSA are increasing in Canada, these samples should be examined at least for MRSA. The fact that this patient also was indicated to have a boil should prompt a culture. Finding a *S. aureus* in a trauma patient admitted to hospital should generate an investigation of the possibility of MRSA. Results received and grades assigned for clinical relevancy reporting are shown in Table 1.

**Table 1. M061-2 Clinical Relevancy reporting results and grades assigned to category A and B laboratories.**

Result	A labs	B labs	Total (% out of 114)	Grade
Methicillin-resistant <i>Staphylococcus aureus</i> MRSA +/- refer, presumptive	68 (94%)	39 (93%)	107 (94%)	4
<i>S. aureus</i> , oxacillin referred (1A); <i>S. aureus</i> , refer for MRSA testing (1B); <i>S. aureus</i> , refer for AST (resistant to all antibiotics x 2) 1B	1	2	3	4
<i>S. aureus</i>	1	0	1	0
No <i>S. aureus</i> isolated (1A, 1B); No MRSA isolated (1A)	2	1	3	0
“Routine bacterial cultures of nasal swabs are not performed because results are not predictive of disease. Healthy adults are often colonized with <i>S. aureus</i> .” (Reference 1A); Specimen rejected; nose swabs are cultured for carrier status only and must be accompanied by appropriate clinical history (1A); reject specimen without specific MRSA/ <i>S. aureus</i> request (1B)	2	1	3	0
Do not routinely process nose samples	1	1	2	ungraded
<b>Total</b>	75	44	119	

**Identification of *Staphylococcus aureus*.** Performance on this sample was excellent. A variety of commercial and classic methods were used to successfully identify MRSA; these included slide and tube coagulase, slide latex agglutination, automated and semi-automated systems (e.g., Vitek, MicroScan, Phoenix, Rapid Staph, Staph Plus, API) and ATB. Classical testing for *S. aureus* was mostly by tube coagulase using commercial reagents.

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Some laboratories have reported difficulties in obtaining consistent sources of rabbit plasma for performing slide and tube coagulase tests, and now use commercial slide agglutination procedures for differentiation of *S. aureus* from coagulase-negative staphylococci. A number of these commercial tests were reported earlier to have reduced sensitivity for MRSA strains<sup>1,2</sup>. Newer tests have incorporated anti-capsular antibodies to *S. aureus* to increase the sensitivity of the tests<sup>3</sup>. However, “small colony variants” and the Ontario strain<sup>4,5</sup> have emerged that have smaller colony morphology and unreliable latex/coagulase activity. The tube coagulase test is the only test that will reliably identify these variants as *S. aureus*.

**Identification, susceptibility testing and screening of MRSA** Methicillin resistance among *S. aureus* strains is mediated by the production of a unique penicillin-binding protein (PBP) called either PBP2' or 2a. This is a 78kD protein with a low affinity for binding with  $\beta$ -lactam antimicrobials. The *mecA* gene encodes this novel PBP and is present on the chromosome of all isolates of MRSA. Automated systems, e.g., MicroScan, Vitek, and Vitek 2, and oxacillin or cefoxitin screens are commonly used to identify *S. aureus* strains as MRSA.

A number of methods have been used with good sensitivity and specificity for screening MRSA. The oxacillin screen plate contains 6 mg/L of oxacillin and added 4% NaCl. Screening for MRSA may require prolonged incubation because of the heteroresistant nature of the population of cells. *S. aureus* strains must be incubated for a full 24 hours on this medium before discard. In strains that have not been sub-cultured in the laboratory, the automated systems may occasionally either under- or over-call oxacillin resistance<sup>7,8</sup>. Newer updates to the automated systems have been designed to take this issue into account. The manufacturer of E-test recommends that Mueller Hinton agar supplemented with 2% NaCl should be used to test for oxacillin resistance by that method. For Kirby Bauer testing, either a 1  $\mu$ g oxacillin disk or 30  $\mu$ g cefoxitin disk is used on Mueller Hinton agar without added NaCl. The zone diameter breakpoint for resistance using oxacillin is  $\leq$  10mm; for cefoxitin the breakpoint is  $\leq$  19 mm. Some strains of MRSA may show larger zones of inhibition around the oxacillin disk with tiny colonies within the zone of inhibition. Careful examination using transmitted light may be necessary to identify them. Disk diffusion testing with cefoxitin has been shown to be more reliable with fewer discrepant strains<sup>9,10</sup>. **No single definitive test will capture all strains of MRSA. When discrepancies between methods occur, those strains should be submitted to a reference laboratory for *mecA* analysis.**

A number of screening agar media have also become available commercially that have good sensitivity and specificity. These media incorporate either oxacillin or cefoxitin as the selective agent and have either mannitol salt or chromogens to facilitate selective identification of MRSA. These media are relatively similar in sensitivity and specificity<sup>11,12</sup>.

**Notification of MRSA to Infection Control** A total of 38 category A and 13 category B laboratories indicated that they would notify infection control of the positive MRSA finding. The laboratories that reported MRSA, either presumptive or refer, indicated only that they would refer the sample so it is difficult to determine if they would notify infection control when the final result was determined. This practice would result in delays in reporting. Laboratories are encouraged to report “presumptive MRSA” to infection control when they have sufficient information to suggest that the isolate will be confirmed. This would include, sufficient growth within 24 hours on an MRSA screening agar, and confirmation that the isolate was coagulase positive (Latex Agglutination or tube coagulase). Testing for PBP2a<sup>10</sup> or PCR for the *mecA* gene can be a secondary procedure that can be performed once the organism has been subcultured. Isolation of an MRSA positive patient as early as possible in hospital is important to prevent spread to other patients in the hospital setting.

**TREATMENT** Physicians would not consider using penicillin or ampicillin for nasopharyngeal colonization of MRSA and reporting of vancomycin on an MRSA from this source might encourage the inappropriate use of vancomycin. Mupirocin has been shown to be effective in some patients for nasal decontamination of MRSA<sup>13,14</sup> but standardized susceptibility testing methods for this agent are not available and resistance with widespread use in selected settings has been reported<sup>15</sup>. Antimicrobial susceptibility testing need not be routinely performed or reported from this sample. There were several treatment or decolonization comments added by some laboratories in this challenge. These may be confusing to clinicians, and may not reflect the susceptibility of the individual strain of MRSA. Local knowledge of susceptibility to agents such as rifampin, fusidic acid or mupirocin would be required to provide accurate information for clinical use. In most cases that is not necessary or helpful.

**CLINICAL SIGNIFICANCE** MRSA is an important nosocomial pathogen in Canada. The most common reservoirs of MRSA are infected or colonized patients, and most harbor the organism for many months. Hospital personnel can also serve as reservoirs to transmit to other patients. Nasal carriage<sup>16</sup> or a break in the skin<sup>17</sup> have been identified as sources of prolonged carriage and infections. In most instances, standard precautions as described in the “*Guidelines for Isolation Precaution in Hospitals*”<sup>18</sup> or in local hospital infection prevention and control documents should be used to control the spread of MRSA.

Community-acquired MRSA infections have also become more prevalent in the last few years. As reported recently in the Canadian Medical Association Journal, community-associated MRSA in certain populations can have increased morbidity and mortality<sup>19</sup>. Community-acquired MRSA usually are less resistant to other antibiotics<sup>20</sup>. This could be due

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to less exposure to other antibiotics, unlike patients that have been hospitalized for some time. Finally, the greater concerns are the reduced susceptibility to vancomycin<sup>21</sup> and resistance to fluoroquinolones<sup>22</sup>. The production of newer antibiotics may be required to meet the challenge of treating patients with drug resistant MRSA infections.

Colonization and infection with MRSA in Canada have become more widespread in recent years, and laboratories need to have on hand standard screening methods for early identification. Vigilance in the laboratory is necessary to ensure that such strains are identified accurately and quickly to prevent their spread in hospitals.

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