

# Reductions in Workload and Reporting Time by Use of Methicillin-Resistant *Staphylococcus aureus* Screening with MRSASelect Medium Compared to Mannitol-Salt Medium Supplemented with Oxacillin<sup>∇</sup>

Philippe R. S. Lagacé-Wiens,<sup>1,2\*</sup> Michelle J. Alfa,<sup>1,2,3</sup>  
Kanchana Manickam,<sup>2,3</sup> and Godfrey K. M. Harding<sup>1,2,3</sup>

Department of Medical Microbiology and Infectious Diseases, University of Manitoba, Winnipeg, Manitoba, Canada<sup>1</sup>;  
Clinical Microbiology, Saint-Boniface General Hospital, Winnipeg, Manitoba, Canada<sup>2</sup>; and Diagnostic Services of  
Manitoba, Winnipeg, Manitoba, Canada<sup>3</sup>

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**Methicillin-resistant *Staphylococcus aureus* (MRSA) is a significant pathogen in both nosocomial and community settings, and screening for carriers is an important infection control practice in many hospitals. In this retrospective study, we demonstrate that the implementation of an MRSA screening protocol using a selective chromogenic medium (MRSASelect) reduced the workload for this screening test by 63.7% overall and by 12.6% per specimen and reduced the turnaround time for reporting by an average of 1.33 days for all MRSA screening specimens, 1.97 days for MRSA-positive specimens, and 1.3 days for MRSA-negative specimens compared to standard mannitol-salt agar supplemented with 6 mg of oxacillin/liter.**

Methicillin-resistant *Staphylococcus aureus* (MRSA) is an important pathogen affecting all areas of hospital practice and is increasingly being recognized as an important pathogen in the community (5). The timely and cost-effective identification and isolation of MRSA carriers in an effort to reduce the intra- and interfacility spread of this pathogen remains an important infection control issue in many hospitals (4). The steady increase in prevalence of MRSA combined with increased infection control awareness of MRSA has led to a dramatic increase in microbiology laboratory workload in the form of increased staff, space, and material requirements (4, 5). Furthermore, adequate infection control measures require rapid turnaround time (TAT) and accurate results in order to optimize hospital resources and reduce the spread of MRSA (4, 5). Therefore, MRSA screening methods need to be studied with respect to workload and reporting time, as well as accuracy.

Selective (e.g., mannitol salt agar with oxacillin) media are advocated for MRSA screening (4, 7, 10). These selective and differential media are incubated for 24 to 72 h and examined for suspect colonies. More rapid alternative methods for screening for MRSA carriers have been developed, including traditional and real-time PCR and chromogenic media, which have been shown to be comparable or superior in sensitivity and specificity to traditional selective media such as mannitol-salt agars (MSA) supplemented with antimicrobials (1–3, 6, 9–11). These selective chromogenic media contain colorless proprietary molecules (chromogens) chemically resembling substrates of specific bacterial enzymes but releasing visible dyes when hydrolyzed by microorganisms possessing the required enzymes (9). Chromogens can be tailored to enzymes

relatively specific to certain organisms, for example, on MRSASelect, only *S. aureus* colonies produce a pink color within the recommended incubation period and other staphylococci are white or colorless. In addition, these media contain multiple antimicrobial agents that serve to inhibit the growth of methicillin-susceptible strains of *S. aureus* and other commensal organisms. The purpose of this study was to determine whether a reduction in workload and TAT could be observed by implementing a protocol using MRSASelect chromogenic medium as a “rapid” MRSA screening method compared to traditional MSA-based culture.

(Part of the data included here was presented in abstract form at the 2007 AMMI/CACMID general meeting in Halifax, Nova Scotia, Canada.)

## MATERIALS AND METHODS

**Study design.** The number of specimens and workload generated by tests performed on the specimens that are processed were tracked automatically by the Delphic Laboratory Information System (Sysmex, Auckland, New Zealand). The workload unit (WLU) is defined as 1 min of time, and the number of WLUs assigned to a test reflects the actual hands-on time (in minutes) needed to complete the test. WLUs are set by the Standards for Management Information Systems in Canadian Health Service Organizations for all common laboratory tests; WLUs are based on time studies and are periodically updated to ensure they are accurate and current as new methods are developed. A base number of WLUs are assigned for specimen accessioning, setup, and initial read, and additional tests are deemed “extra” WLUs. The total WLUs for specific tests (such as MRSA screening) are compiled by the electronic system as additional tests are ordered for suspect organisms. Workload associated with an MRSA screening method based on MSA supplemented with 6 mg of oxacillin/liter (MSA/Ox) (Fig. 1) was reviewed January to June 2005 using the laboratory information system. In this protocol, specimens were directly inoculated to the medium and examined for suspect colonies after 18 to 24 h of incubation. Suspect colonies were confirmed as *S. aureus* by using a 24-h tube coagulase test, and methicillin resistance was confirmed after overnight susceptibility testing with the Vitek susceptibility card, followed by a commercial MecA latex agglutination test. Negative plates were reincubated, and negative results were reported if plates remained negative after 48 h. After the implementation of an MRSASelect-based MRSA screening protocol (Fig. 1), the workload generated by this new method was tracked for another 6-month period (July to December 2006). In this protocol, specimens

\* Corresponding author. Mailing address: Clinical Microbiology, Saint-Boniface General Hospital, Winnipeg, Manitoba R2H 2A6, Canada. Phone: (204) 237-2053. Fax: (204) 237-6065. E-mail: plagacewiens@hotmail.com.

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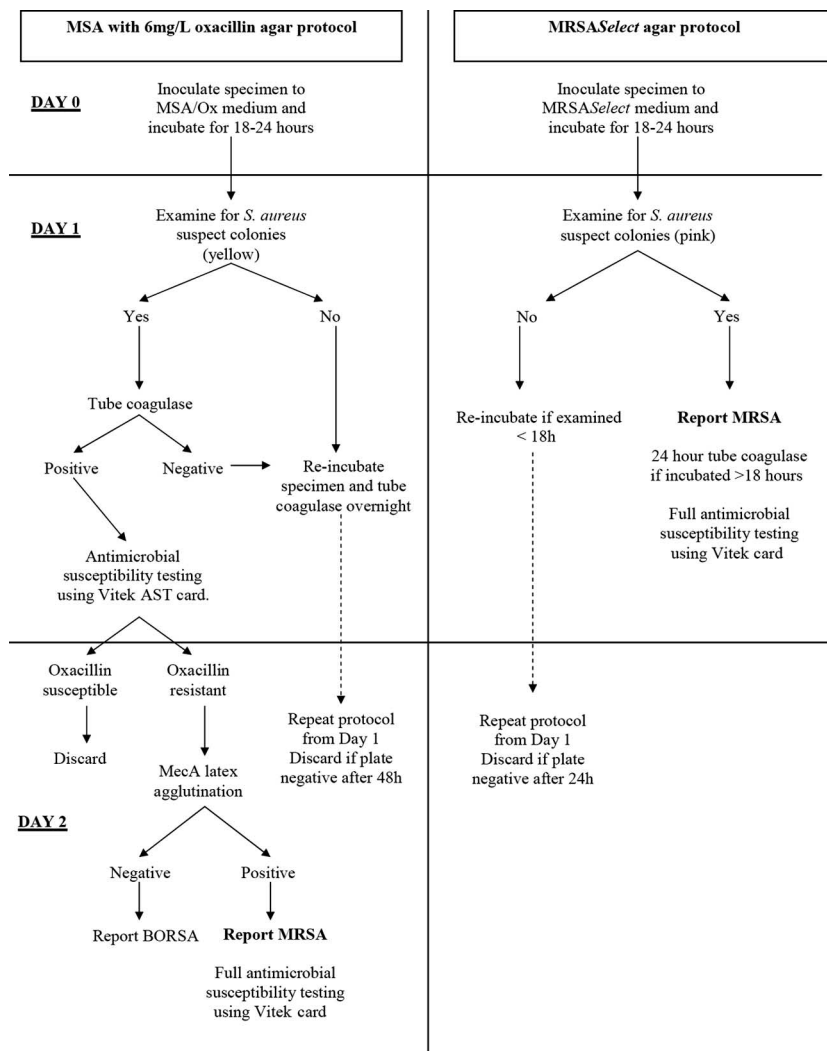


FIG. 1. Comparison of process flow for MSA/Ox and MRSASelect protocols. Specimens from previously known MRSA carriers were also concomitantly plated to nonselective media (sheep blood agar) in the MSA/Ox protocol or inoculated into enrichment broth in the MRSASelect protocol (broth only worked-up if direct plated specimens negative at 24 h).

were directly inoculated into the media and incubated for 18 to 24 h. The growth of any pink colonies on the MRSASelect within this incubation period was reported as MRSA without additional testing. Because the manufacturer of MRSASelect warns that coagulase-negative staphylococci may appear pink after prolonged incubation, pink colonies observed after the recommended 24-h incubation period were confirmed as *S. aureus* using a 24-h tube coagulase test. Negative plates that were examined before 18 h of incubation were re-incubated, and suspect colonies later identified were confirmed as *S. aureus* using a tube coagulase test. Negative results were reported if plates were negative after 24 h of incubation. The TAT was also compared for both protocols. A total of 500 consecutive specimens from the start of each study period were analyzed, and the reporting times were compared. TAT has been defined as the time from specimen receipt in the laboratory (accessioning) to the time the result was phoned (i.e., positive for MRSA) or to the time the report was printed and sent to the ward (i.e., negative specimens). The accessioning time, phoned report times, and final printed report times are automatically recorded by the electronic system, allowing for accurate determination of TAT for MRSA screening regardless of whether they were positive or negative.

**Specimens.** Specimens submitted for MRSA surveillance, including swabs of the nares, wounds, respiratory, urine, intravascular catheter sites, and rectum or stool, were included in the present study. Diagnostic specimens were not included since these are not directly inoculated on to MRSA screening media. Swabs for MRSA screening were transported in M40 sterile transport systems

(Copan Innovations, Corona, CA) to the laboratory, where they were plated onto media according to the protocol in place at the time.

**Media.** MSA/Ox was produced in-house by using MSA powder (BD, Oakville, Ontario, Canada), oxacillin (Sigma, Oakville, Ontario, Canada) and following manufacturer's instructions. Sheep's blood agar (SBA) was produced in-house with tryptic soy agar powder (BD) and sheep blood (Quad Five, Ryegate, MT). Chromogenic media (MRSASelect) was purchased from the manufacturer (Bio-Rad, Montreal, Quebec, Canada). All media were subjected to internal quality control using oxacillin-resistant *S. aureus* (ATCC 43300) and oxacillin-sensitive *S. aureus* (ATCC 29213).

When specimens were from known MRSA carriers, SBA was coinoculated with MSA/Ox (under the MSA/Ox protocol) because it increased the sensitivity of MRSA detection in our MRSA-positive hospital population (data not shown). Selective enrichment broth (brain heart infusion broth supplemented with ceftiozime [5 µg/ml] and aztreonam [75 µg/ml]) (12) was inoculated during the period when MRSASelect for the same population. Our laboratory had previously shown that broth enrichment only improved the sensitivity of direct plating for known MRSA-positive patients and that a combined approach using MRSASelect was as sensitive as molecular amplification of MRSA-specific targets from specimens (data not shown). This effect is likely due to the common practice of using antimicrobials for MRSA decolonization of patients in our center.

TABLE 1. TAT for final reporting results of MRSA screening specimens by specimen type<sup>a</sup>

Specimen group	MRSASelect (n = 500)		MSA/Ox (n = 500)		P
	n	Mean TAT (days)	n	Mean TAT (days)	
MRSA positive	25	1.56	30	3.53	<0.0001
MRSA negative	473	1.66	470	2.96	<0.0001
All specimens	500	1.66	500	3.00	<0.0001
Nares	296	1.68	201	2.69	<0.0001
Wound	89	1.65	65	2.97	<0.0001
Rectal	3	1.33	177	3.42	0.0003
Intravenous catheter site	92	1.55	48	2.79	<0.0001
Respiratory	14	1.56	8	2.63	0.001
Urine	6	2.67	1	5.00	— <sup>b</sup>

<sup>a</sup> n, Number of specimens.

<sup>b</sup> Insufficient data for statistical analysis.

**Statistical analysis.** The Student *t* test was used to compare means in the reporting time analysis.

## RESULTS

**Reduction in workload.** The workload for MRSA screening was retrospectively evaluated for two-different 6-month periods. The total workload went down from 168,950 to 61,295 WLUs (−63.72%). The reduction was most evident in “extra” WLUs (slide agglutination, tube coagulase, catalase tests, antimicrobial disk diffusion, and subculturing), which were reduced from 34,081 to 3,102 WLUs (−90.90%). The specimen number was also less in the second period (from 13,276 to 5,513). Nevertheless, there was a workload reduction of 1.61 WLUs/specimen (−12.63% per specimen), which was also primarily due to a reduction in extra WLUs from 2.57 to 0.56 per specimen (−78.08%). The anticipated impact for a large clinical laboratory such as ours that processes 11,000 MRSA screening specimens per year tending to a population with ca. 5% MRSA carriage would be approximately 300 h of technological time.

**Reporting time.** The reporting times for both study periods are summarized in Table 1. Overall, the reporting time for MRSA screening specimens went from 3 days with the MSA/Ox protocol to 1.66 days with the MRSASelect protocol (−44.7%, *P* < 0.0001). The reduction in TAT was relatively larger in MRSA-positive specimens (3.53 days to 1.56 days, −55.8%) than for MRSA-negative specimens (2.96 to 1.66 days, 43.9%), but statistically significant reductions in TAT were observed in both positive and negative specimens (*P* < 0.0001). The reporting time was significantly improved for all specimen types (wounds, nares, rectal, respiratory, and intravascular line specimens). Urine specimens were too few for statistical analysis. The number of MRSA-positive screening specimens in the 500 specimens selected from each study period was not significantly different (30 of 500 [6%] during the MSA/Ox protocol and 25 of 500 [5.0%] during the MRSASelect protocol, *P* = 0.49). The broth enrichment identified 5 (20%) of the positive MRSA cases that would have been missed if direct plating to MRSASelect alone had been used to screen previously positive patients. Using subgroup analysis of our data, a universal broth enrichment protocol under the

MRSASelect protocol would increase the overall TAT from 1.66 to 2.12 days. However, the overall TAT would still be improved over an MSA/Ox direct plating protocol (2.12 days versus 2.98 days, *P* < 0.001).

## DISCUSSION

The sensitivity and specificity of MRSASelect medium (97.3 and 99.8%) has already been studied and compared to MSA/Ox (80.2 and 79.0%, respectively) for MRSA screening (9). Although MRSASelect compares favorably or is superior to other solid screening media in terms of sensitivity and specificity, some authors have questioned the screening sensitivity of direct plating on chromogenic media and have demonstrated that preincubation in enrichment broth increased detection by 16 to 24% in several chromogenic media, but the postenrichment sensitivity of MRSASelect was not analyzed (8). We found that parallel testing of both media with broth enrichment and direct PCR in our laboratory for validation purposes corroborated published data but showed similar sensitivity rates with or without broth enrichment for routine screening, with improved sensitivity only being seen in known MRSA-positive patients. Although the sensitivity and specificity of chromogenic MRSA screening media has been well studied, the use of chromogenic media for streamlining workflow and rapid result reporting has not been well studied. Our data showed that the protocol using MRSASelect medium requires fewer additional tests, subcultures, and confirmatory tests than the protocol based on MSA/Ox. This resulted in a significant reduction in workload, both overall and per specimen plated. This workload reduction was shown to be primarily due to a reduction in “extra” workload (subcultures catalase, coagulase etc.). Furthermore, due to the distinct color difference between *S. aureus* (pink) and coagulase-negative staphylococci (white) on MRSASelect, our data demonstrated there was a less frequent need to subculture and repeat susceptibility or identification tests. While the elimination of confirmatory tests (e.g., *mecA* PCR or PBP2' latex agglutination) might be expected to result in a greater number of false-positive MRSA screening tests when the MRSASelect protocol was used, parallel runs in our laboratory using latex agglutination confirmatory testing under both protocols revealed that the chromogenic medium did not produce any false positives (data not shown). The high specificity of the MRSASelect medium has also been previously described (99.8 to 100%), and confirmatory testing is not required according to the manufacturer. This recommendation, based on high specificity, is also supported by a number of independent studies (1, 8, 9). Since confirmatory testing is not apparently required with the MRSASelect protocol, workload reduction is expected to be even greater where the prevalence of MRSA carriage is higher than in our center (~6%).

The reporting time for both positive and negative MRSA screening specimens was significantly reduced with MRSASelect. Our reporting time of 1.66 days for MRSASelect was similar to those published by others (8). The reduction in TAT was most significant for MRSA-positive specimens, which suggests that hospitals with higher rates of MRSA would benefit most from adopting a similar protocol. For negative specimens, the reduction was primarily due to the MRSASelect medium providing comparable specificity results to the MSA/Ox medium after

18 to 24 h of incubation instead of the 48 h of incubation required for MSA/Ox before a negative result can be issued. For MRSA-positive specimens, the reduced TAT was partly due to a reduction in subculturing and repeating susceptibility testing for coagulase-negative staphylococci that were inadvertently inoculated onto the Vitek susceptibility card (this occurred when coagulase-negative staphylococcus was growing on MSA/Ox but not for MRSASelect). Furthermore, the high specificity of MRSASelect reported in the literature, as well as in our own hands effectively eliminated the need for confirmatory testing using *mecA* PCR or PBP2' latex agglutination. This resulted in a further reduction of TAT for positive specimens. Another possibility for the observed reduction in reporting time was a change in the provincial infection control guidelines that occurred between the two study periods that eliminated the need for routine screening of stool and urine for MRSA. Fewer specimens contaminated with endogenous flora (such as stool) may have reduced the overall processing time. To evaluate this, we analyzed reporting time by specimen type and determined that the reporting time was significantly reduced for all specimen types. Therefore, it is unlikely that the specimen source was a major confounder of our findings.

Although premanufactured chromogenic media for MRSA screening are more costly than routine media produced in-house, the significant reduction in workload, the ability to report MRSA based on pink color at 18 to 24 h without confirmatory tests and the reduced TAT resulted in the use of MRSASelect being a cost-effective alternative for screening MRSA in our laboratory. Indeed, the MRSA screening workload was reduced whereby the work that required two full-time technologists to complete using MSA/Ox could now be handled by one full-time technologist using MRSASelect. However, not all hospital laboratories would benefit from this or a similar protocol. Hospitals not required to or choosing not to screen for MRSA would clearly not benefit. Furthermore, screening is not cost-effective in areas where MRSA prevalence is so high as to make contact isolation of carriers prohibitively expensive. Lastly, although subgroup analysis of our data revealed that universal broth enrichment with subsequent use of MRSASelect agar still provided a reduction in TAT over direct plating on MSA/Ox, laboratories that choose enhanced screening with universal broth enrichment may not observe as significant a reduction in TATs. Nevertheless, there is increasing government pressure in both Canada and the United States to increase efforts to screen and identify MRSA carriers in the hospital setting. This is evidenced by recent provincial and

state mandates recommending enhanced screening for MRSA. Our findings suggest that where screening for MRSA using solid media is desired or mandated, MRSASelect may be superior to MSA/Ox for routine screening since it has a faster TAT and is less labor-intensive.

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