CMPT Clinical Bacteriology Program

Innovation, Education, Quality Assessment, Continual Improvement

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# Challenge M153-5

November 2015

## Heart valve swab: Methicillin Resistant *Staphylococcus aureus* (MRSA)

## HISTORY

A simulated OR heart valve swab collected from 28 year old IV drug user was sent to category A laboratories.

Participants were expected to isolate and identify MRSA. Participants were also expected to perform susceptibility testing and report isolate to infection control (IC)/public health (PH).

## CMPT QA/QC/STATISTICS

All simulated samples are produced at CMPT according to CMPT internal protocols. The sample contained a pure culture of MRSA.

*The samples are assessed for homogeneity and stability using in-house quality control methods and random selection of samples before and during production, and post sample delivery. The number of random samples selected is 15% of the total production batch.*

The challenge sample lot was confirmed to be homogeneous and stable for at least **16** days.

The presence of MRSA and its susceptibility profile were confirmed by a reference laboratory.

*All challenge components have in-house assigned values based on the most clinically appropriate result; the most clinically appropriate result is determined by expert committee evaluation. No further statistical analysis is performed on the results beyond that described under "Suitability for grading."*

## SURVEY RESULTS

Reference laboratories

**Identification:** 13/13 (100%) laboratories reported methicillin resistant *Staphylococcus aureus* (MRSA).

**Report to Infection Control**: 13/13 (100%) laboratories indicated they would report the isolate to IC.

**Susceptibility**

Oxacillin: 13/13 (100%) laboratories reported the strain resistant.

**MAIN EDUCATIONAL POINTS from M153-5**

1. Infective endocarditis can be a complication of injection drug use, particularly with gram positive organisms such as MRSA.
2. Appropriate labelling of the isolate as MRSA and correct reporting to Infection Control or Public Health is important to prevent the transmission of MRSA.
3. The antimicrobial cornerstone of native-valve MRSA infective endocarditis treatment is vancomycin in susceptible isolates, and timely, accurate susceptibility testing is critical for effective patient management.

Vancomycin: 13/13 (100%) laboratories reported the strain susceptible.

Clindamycin: 12/13 (92%) laboratories reported the isolate resistant; one laboratory did not report.

Trimethoprim-sulfamethoxazole: 10/12 (83%) laboratories reported the organism resistant; 2 laboratories did not report, 1 referred.

Only 8 laboratories reported susceptibility results for erythromycin (resistant); 3 for tetracycline (susceptible), and 1 for gentamicin (susceptible).

Participants

**Identification** (Table 1): 56/57 (98%) laboratories reported MRSA and were graded 4. One participant reported *Staphylocccus aureus* and was graded 1.

**Infection Control notification** (Table 2): 57/57 (100%) laboratories indicated they would report the isolate to IC and were graded 4.

### Grading

**Maximum grade: 24**

Reporting MRSA was graded 4. Reporting only S. aureus was graded 1.

Reporting the isolate to IC/PH was graded 4. Not reporting was graded 0.

Reporting the isolate resistant to oxacillin, clindamycin was graded 4 for each component.

Reporting the strain susceptible to vancomycin was graded 4; not reporting results was graded 0.

Reporting the isolate susceptible to SXT was graded 4.

Reporting results using the incorrect identifier is graded 0.

**Table 1. Identification results**

| Reported | Total | Grade |
|---|---|---|
| methicillin resistant *Staphylococcus aureus* (MRSA), ± refer | 55 | 4 |
| cloxacillin resistant (MRSA) *Staphylococcus aureus*, refer | 1 | 4 |
| *Staphylococcus aureus* (reported oxacillin R and notified IC/PH) | 1 | 1 |
| Sample not normally processed, ± refer | 5 | ungraded |
| **Total** | **62** | |

**Table 2**. Report to IC / PH

| Reported | Total | Grade |
|---|---|---|
| yes | 57 | 4 |
| snnp | 5 | ungraded |
| **Total** | **62** | |

### Susceptibility

For grading see Table 3A-D and comment on results section

Four laboratories reported susceptibility results using the incorrect identifier and were graded 0 for each graded component.

### *Suitability for Grading*

*A challenge is considered suitable for grading if agreement is reached by 80 percent of selected reference group and at least 50 percent of the participants.*

Organism identification, report to IC, and susceptibility to oxacillin, vancomycin, clindamycin, and SXT were correctly performed by at least 80 percent of reference laboratories and greater than 50 percent of all laboratories and was thus, determined to be suitable for grading.

## COMMENTS ON RESULTS

All participating laboratories correctly identified MRSA and notified infection control or public health as per local protocol and were graded 4. With respect to antimicrobial susceptibility testing, the vast majority of laboratories performed very well.

All laboratories correctly identified oxacillin resistance and were graded 4. 52/57 (91%) of laboratories tested the vancomycin as susceptible, and were graded 4.

51/56 (91%) of laboratories tested the clindamycin as resistant, and were graded 4. 42/54 (78%) laboratories tested the SXT as susceptible and were graded 4. The laboratory providing no report for vancomycin was graded 0. Laboratories providing no report for clindamycin or SXT were ungraded. While clindamycin and SXT are Group A antibiotics for the testing and reporting of *S. aureus* isolates, it would be reasonable to omit them from reporting in the context of a known infective endocarditis case, where those antibiotics would not be first nor second-line therapies. Laboratories that do not routinely process this specimen were not graded.

**Tables 3A-3D.** Susceptibility results

| 3A - Oxacillin/Cloxacillin | Total | Grade |
|---|---|---|
| Resistant +/- comment* | 53 | 4 |
| Reported using incorrect identifier | 4 | 0 |
| sample not normally processed | 5 | ungraded |
| **Total** | **62** | |
| **3B - Vancomycin** | **Total** | **Grade** |
| Susceptible | 52 | 4 |
| Reported using incorrect identifier | 4 | 0 |
| no report | 1 | 0 |
| snnp | 5 | ungraded |
| **Total** | **62** | |
| **3C - Clindamycin** | **Total** | **Grade** |
| Resistant | 51 | 4 |
| Reported using incorrect identifier | 4 | 0 |
| no report | 1 | ungraded |
| refer, snnp | 6 | ungraded |
| **Total** | **62** | |
| **3D - SXT** | **Total** | **Grade** |
| Susceptible | 42 | 4 |
| Reported using incorrect identifier | 4 | 0 |
| no report | 8 | ungraded |
| refer, snnp | 8 | ungraded |
| **Total** | **62** | |

* lab reported isolate as methicillin resistant S.aureus and added comment "Oxacillin-resistant staphylococci are resistant to all currently available Beta-lactam antimicrobial agents, ie, penicillins, Beta-lactam/Beta-lactamase inhibitor combinations, cephalosporins, and carbapenems".

Labelling the isolate as MRSA is important for Infection Control and management reasons; laboratories that failed to do so were downgraded to 1.

The purpose of reporting to Infection Control or Public Health is to ensure appropriate infection control measures are implemented. In hospitals that do not have regular infection control staff, a laboratory report should include instructions to ward staff to have the patient placed on contact isolation.

## ISOLATION and IDENTIFICATION

Infectious endocarditis (IE) is characterized by continuous bacteremia, thus, cultures do not need to be timed with peaks of fever. [1]

In order to help separate contaminants from true causing organisms, at least 3 sets of blood cultures obtained from different venipuncture sites should be obtained. [2]

90% of infectious endocarditis will yield positive blood cultures, however, about 10% of patients with show no growth from blood cultures. The administration of antibiotics before the extraction of blood cultures, infection with fastidious bacteria or fungi are some of the causes of culture negative endocarditis.

A causative organism can be identified in about two-thirds of patients by performing serological testing for *Coxiella* and *Bartonella*, and if negative, testing for *Brucella, Mycoplasma, Legionella*, and *Chlamydia*. Extended blood culture after 7 days provides no further useful yield, even for the HACEK bacteria, which are characteristically slow-growing. [1]

## CLINICAL RELEVANCE

The cardiac endothelium is normally resistant to transient bacteraemia caused by daily activities such as chewing and tooth brushing. However, damage to the endothelium can be caused by valve sclerosis, rheumatic valvulitis, or by direct bacterial activity (particularly from *Staphylococcus aureus*). [1]

Individuals using intravenous drugs (IDU) have a significantly higher incidence of infective endocarditis as injected particulate matter causes endothelial damage, which is followed by infection from high injected bacterial loads associated with relative immune suppression. [3]

80-90% of infective endocarditis are caused by gram positive cocci *Staphylococcus*, *Streptococcus*, and *Enterococcus* species. [1, 3]

*S. aureus* is the most common cause of IE in much of the developed world and rates of MRSA infection have been increasing. [4]

In non-IDUs, *S aureus* IE involves primarily the left side of the heart and is associated with high mortality rates (25% to 40%). On the other hand, *S aureus* IE in IDUs occurs in the right side of the heart and often involves the tricuspid valve; right side infectious endocarditis (RSIE) also has higher cure rates (>85%). [2] The diagnosis of RSIE often requires a high index of suspicion, since respiratory, rather than systemic signs of IE predominate.

## ANTIMICROBIAL SUSCEPTIBILITY

The antimicrobial cornerstone of native-valve MRSA infective endocarditis treatment is vancomycin in susceptible isolates, while patients whose MRSA isolates exhibit higher MIC's to vancomycin or are intolerant should be treated with daptomycin.

Optimized vancomycin therapy in MRSA bacteremia is determined with vancomycin $AUC_{24}$:MIC > 400.[5] Kullar and colleagues demonstrated that patients with complicated MRSA bacteremia (including infective endocarditis) had significantly improved outcomes when their vancomycin $AUC_{24}$:MIC was greater than 421. To achieve this $AUC_{24}$:MIC with vancomycin serum trough levels of 15mg/L, vancomycin MIC's had to be less than 1mg/L. [6] Therefore, it is critical in serious MRSA infections such as MRSA IE, to have accurate, timely testing and reporting of vancomycin MICs. Clindamycin in *S. aurues* IE is associated with clinical relapse, and is not recommended. SXT has been shown to be inferior to vancomycin in *S. aureus* IE, but can be used in certain salvage situations under consultation with infectious diseases specialists.

**MIC** (*minimum inhibitory concentration*) – The minimum concentration of antibiotic to inhibit the growth of an organism.

**AUC** (*area under the curve*) – The total exposure of an antibiotic to an organism

**AUC:MIC** — The rate of bacterial killing is both related to the amount of time the concentration of the antibiotic is above the MIC and the total exposure of antibiotic to the organism.

## REFERENCES

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