Using MRSA nasal swab PCR to guide de-escalation of empiric MRSA therapy: Does Swabbing Nares Do Well, or Is There Nary a Use?

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March 13th, 2020

Learning Objectives:
1. Describe the importance of de-escalation of methicillin-resistant Staphylococcus aureus (MRSA) therapy
2. Discuss and evaluate the primary literature assessing the use of MRSA nasal swab culture and PCR in guiding treatment
3. Formulate an evidence-based recommendation regarding the clinical utility of MRSA nasal swab
I. *Staphylococcus aureus*
   
   A. History
   
   1. Initially discovered in 1880
      a) Identified by Sir Alexander Ogston from a surgical abscess
   2. Penicillin discovered in 1928 by Alexander Fleming
      a) Penicillin resistant *S. aureus* / Methicillin-susceptible *S. aureus* (MSSA) appeared in 1942
   3. Methicillin introduced in 1959 for the treatment of penicillinase-producing *Staphylococcus*
      a) MRSA appeared within the next two years

   Figure 1: Timeline of Penicillin and *S. aureus*

   Initially discovered in 1880 and identified by Sir Alexander Ogston from a surgical abscess
   Penicillin discovered in 1928 by Alexander Fleming
   Penicillin resistant *S. aureus* / Methicillin-susceptible *S. aureus* (MSSA) appeared in 1942
   MRSA appears in 1951 after broad use of methicillin

   B. Common colonizer in humans
   
   1. Can normally be found on the skin
   2. Up to 30% of the human population is colonized with *S. aureus*

   C. *S. aureus* is a primary cause of multiple infectious etiologies
   
   1. Commonly seen in complex disease states such as endocarditis
      a) Accounts for 15-40% of all infectious endocarditis cases and for the majority of cases in patients who inject drugs
      b) *S. aureus* endocarditis is associated with an in-hospital mortality rate of 20-30%
   2. Seen in patients with both hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP)
      a) *S. aureus* accounts for 20-40% of all HAP and VAP and is associated with an all-cause mortality rate of 55.5%
      b) Seen in patients with community-acquired pneumonia (CAP) who have risk factors for MRSA
      1) MRSA has been identified as a potential pathogen in 8.9% of all CAP cases
   3. A common cause of skin and soft tissue infections (SSTIs)
      a) Common skin infections that involves *S. aureus* include cellulitis, abscesses, diabetic foot infections, and necrotizing fasciitis
      1) Between 8-25% of all SSTIs are thought to be due to *S. aureus*

   D. Virulence of *S. aureus*
   
   1. There are five stages in the pathogenesis of *S. aureus* infections
      a) Colonization, local infection, systemic dissemination, metastatic infection, toxinosis
      1) Colonization of the skin is completely asymptomatic and is not a cause for concern.
      2) Local infection with *S. aureus* can be caused by a cut or break in the skin which can lead *S. aureus* to begin invading the body through the dermis.
After entering the body and reaching the bloodstream, *S. aureus* can easily disseminate throughout the body due to it being easily able to “stick” in different places in the body.

Describe the importance of de-escalation of MRSA therapy

Once spread throughout multiple areas of the body, *S. aureus* can more easily potentiate its toxins in order to damage the host.

Several virulence factors also aid in the pathogenicity of *S. aureus*.

- Staphylocoagulase-proteins activate prothrombin which converts fibrinogen to fibrin, leading to blood clotting
  - This can lead to the creation of vegetation in bacterial endocarditis which is aided by fibrin barriers that decrease *S. aureus* clearance by leukocytes
- Von Willebrand factor binding proteins exhibit non-proteolytic prothrombin activator activity and leads to the creation of a prothrombin complex similar to staphylocoagulase which can lead to clotting

**Antibiotic resistance**

1. Resistance to penicillin is due to the *blaZ* gene which encodes for a beta-lactamase that breaks down penicillin
2. Resistance to methicillin is due to a binding site change in the penicillin-binding protein 2A (PBP2A) caused by the *mecA* gene
   - The *mecA* gene also confers resistance to almost all beta-lactam antibiotics
3. Penicillin resistance is observed in 80% of all *S. aureus* isolates
   - Of the resistant strains, 60% are reported to be MRSA, and 40% are stated to be MSSA
   - However, MRSA rates have started to drop in recent years.
     - Studies have shown MRSA having a decrease in resistance to antimicrobial agents from on average 4.5 antibiotics in 2000 to 3.7 antibiotics in 2014.

**MRSA risk factors**

- Prior hospitalization within 12 months, history of MRSA infection, infection within the last three months, intravenous drug use, history of Vancomycin-resistant *Enterococci* (VRE), antibiotic use within the last 90 days, diabetes, and chronic renal failure

**Treatment overview**

1. Penicillin-susceptible *S. aureus* (PSSA)
   - Anti-staphyloccocal penicillins are the drugs of choice
     - Higher 30-day mortality with cephalosporins treatment compared to anti-staphylococcal penicillins (39% vs 10%) (P=0.004)
2. MSSA
   - Anti-staphyloccocal penicillins (i.e. oxacillin and nafcillin)
     - Preferred first-line agents in several guidelines due to large amounts of data supporting their efficacy
   - Cephalosporins (i.e. cefazolin)
     - Newer data have shown similar efficacy when compared to oxacillin/nafcillin for treatment of MSSA infections. Treatment failure rates of 15% for nafcillin vs 15% for cefazolin have been observed when treating MSSA bacteremia
3. MRSA
   - Primarily treated with Vancomycin
     - While other treatments exist, vancomycin is seen as the standard of treatment for MRSA
Treatment affected by toxicities and monitoring requirements

(a) Current guidelines suggest a trough goal of 15-20 mcg/mL for vancomycin in the setting of severe infections such as pneumonia, bacteremia, or endocarditis. 21
(b) Current guidelines suggest a trough goal of 10-15 mcg/mL for S. aureus cellulitis, SSTI, and UTI 21
(c) Nephrotoxicity may affect up to 43% of all patients taking vancomycin depending on the length of treatment. 22

b) Some alternatives to vancomycin include daptomycin and linezolid

(1) Daptomycin
   (a) Not appropriate for treatment of pneumonia due to deactivation by pulmonary surfactant.
   (b) Increases creatinine phosphokinase levels and may lead to rhabdomyolysis 23

(2) Linezolid
   (a) Comes as an oral agent, which may facilitate outpatient treatment
   (b) Increases the risk of myelosuppression and serotonin syndrome 24

II. Importance of appropriate de-escalation of antibiotics

A. Mortality
   1. Studies have shown that treating MSSA with anti-staphylococcal penicillins had a significantly lower risk of mortality (7%) when compared to using vancomycin (20%) (95% CI 0.01, 0.76) 25

B. Resistance
   1. Unnecessary use of anti-MRSA therapy increases resistance in S. aureus
      a) Vancomycin-intermediate S. aureus (VISA) has been shown to possibly be linked to previous vancomycin use
         (1) 54% of patients who have been diagnosed with VISA have been treated with vancomycin within the previous month. 26
   2. Use of narrow therapy decreases resistance rates
      a) The implementation of an electronic program for infectious disease (ID) consulting service in Melbourne, Australia led to a decrease in the use of broad-spectrum antibiotics. This in turn translated into a 10% decrease in the rates of MRSA 27

C. Toxicities
   1. Use of MRSA agents can put patients at a high risk for toxicities

<table>
<thead>
<tr>
<th>Table 1: Common MRSA drugs and adverse effects 28</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vancomycin</strong></td>
</tr>
<tr>
<td><strong>Daptomycin</strong></td>
</tr>
<tr>
<td><strong>Linezolid</strong></td>
</tr>
</tbody>
</table>
III. Diagnostic tools for MRSA
   A. Diagnostic tests
      1. Culture-based testing
         a) Used to detect microbial growth in the blood, urine, tracheal aspirate, fluid collections, wound, or other miscellaneous sources
            (1) On average, *S. aureus* begins to grow after about 24-48 hours in blood cultures

      2. Molecular detection
         a) Platforms such as Verigene or Biofire extract nucleic acid can check for specific bacteria and resistance markers through polymerase chain reaction (PCR)
            (1) These tests are quick and can return results in less than 2 ½ hours, but will only test for the bacteria that are selected on the panel
               (a) If a panel for gram-positive bacteria is checked but a gram-negative bacteria is growing, the panel will show fully negative

   B. Considerations for diagnostic tests
      1. See appendix A for definitions of sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).
      2. Culture-based testing
         a) Blood cultures can be contaminated by bacteria that are not truly causing an infection
            (1) The likelihood that a blood culture growth is a contaminant depends on the type of bacteria that grows
               (a) Bacteria such as *S. aureus* have a very low likelihood of being a contaminant (1%), compared to coagulase-negative *Staphylococcus* has a high likelihood of being a contaminant (82%)  
         b) Cultures may also not be accurate if the patient received antibiotics prior to a culture being obtained
            (1) Using antibiotics prior to obtaining cultures has shown to decrease positive blood cultures in CAP patients by half (5.2% vs 2.6%)  

   3. Rapid diagnostic tests
      a) Molecular detection
         (1) Specific sensitivities and specificities differ between molecules that are being tested  
            (a) Gilman et al. 2015 showed Verigene had a sensitivity and specificity for *Staphylococcus* species of 100%
         (2) Rapid diagnostic testing in suspected MRSA patients being tested for the mecA gene has shown sensitivity of 93.9% and specificity of 98.6%.  
            (a) Since this test has a higher specificity, a negative result would likely be truly negative
            (b) However, mecA is not only found in *S. aureus*. It is also found in *Staph epidermidis* which is a common contaminant.

IV. MRSA nare tests
   A. Initially, MRSA nares tests were done to help decrease the spread of MRSA by placing patients with positive MRSA nares on contact precautions and treating patients with mupirocin
   B. A test where the nasal cavity is cultured to determine if MRSA is present within the nares
      1. Is either tested using culture-derived means or through PCR
a) MRSA nasal swabs have shown to have different sensitivities and specificities depending on if they are grown in a culture or PCR

<table>
<thead>
<tr>
<th>Table 2: Differences between MRSA Nasal PCR and MRSA Nasal Culture</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of nares test</strong></td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Sensitivity</td>
</tr>
<tr>
<td>Time to growth</td>
</tr>
</tbody>
</table>

C. Use in current practice
1. The 2014 IDSA skin and soft tissue infections guidelines reference using MRSA nasal colonization as a risk factor warranting the use of vancomycin in patients with cellulitis, erysipelas, or surgical site infections.  
2. Previous HAP and VAP IDSA guidelines mention positive MRSA nares increase the risk of MRSA being cultured from respiratory samples but not enough data was available to make a recommendation.
   a) The guidelines do reference a study showing that using MRSA nares in critically ill patients had poor specificity, sensitivity, PPV, and NPV.
3. The 2019 IDSA CAP guidelines do have an update for the use of MRSA nasal swabs stating that MRSA nasal swabs can be used to withhold MRSA therapy when swabs are negative.
   a) The guidelines state that positive MRSA nasal swabs are not indicative of pneumonia due to MRSA

D. Previous studies from the mid to late 2000’s and the early 2010's had conflicting evidence on when to use MRSA nares to guide therapy. Some studies showed high NPV for pneumonias, but there was not enough data to make a strong stance on using MRSA nares as a diagnostic tool.

E. While prior studies showed the clinical utility of MRSA nasal swabs for de-escalation of therapy in patients with pneumonia, new data suggest that using MRSA nasal swabs could help with de-escalation of antibiotics in treatment of other infections as well.
Clinical Question: Can negative MRSA nasal swab be used to de-escalate empiric MRSA therapy?


Objectives

- Determine if MRSA nares tests could be used to rule out MRSA infections
- Determine if MRSA nares could be used to rule in MRSA infections
- Determine if MRSA nasal-colonization could be used as a marker of antibiotic resistance

Methods

Retrospective, cohort study conducted between August 1, 2005 - January 31, 2007 at the Evanston Northwestern Healthcare system in Chicago, Illinois

Patient population

Inclusion Criteria:
- Patients who had a clinical culture positive for any pathogen

Exclusion Criteria:
- Viral cultures
- Surveillance clinical cultures that were unlikely to represent sites where MRSA disease is a significant consideration (ex. stool cultures, vaginal cultures)

Intervention

- MRSA nares were collected using BD-GeneOhm real-time PCR test, and the results were compared to cultures collected
- Only the first positive clinical culture in a 30-day period was used for each patient
- True MRSA infections were defined as:
  - Bloodstream infection - requires a positive blood culture
  - Respiratory tract infection - requires a positive respiratory culture, positive chest X-ray, and a decision to treat
  - Urinary tract infection - requires a positive urine culture + decision to treat OR >100,000 CFU/mL + at least 50 leukocytes per high power field
  - All other sites required a positive culture and a decision to treat
    - Other sites in this study were most frequently taken from the abdominal wall, buttock, or breast.
## Baseline Characteristics

### Table 3a: Prevalence of culture sites

<table>
<thead>
<tr>
<th>Culture Site</th>
<th>Number of cultures taken (% total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloodstream</td>
<td>1012 (17.5%)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>426 (7.3%)</td>
</tr>
<tr>
<td>Extremity</td>
<td>457 (7.9%)</td>
</tr>
<tr>
<td>Ulcer</td>
<td>72 (1.2%)</td>
</tr>
<tr>
<td>Urine</td>
<td>2948 (51.0%)</td>
</tr>
<tr>
<td>Other</td>
<td>864 (14.9%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>5779 (100%)</td>
</tr>
</tbody>
</table>

## Results

- \( n = 5779 \)

### Table 3b: Sensitivity, Specificity, and PPV for MRSA nares

<table>
<thead>
<tr>
<th>Diagnostic characteristic</th>
<th>Result of analysis to predict MRSA positive culture (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>67% (62% - 72%) (95% CI)</td>
</tr>
<tr>
<td>Specificity</td>
<td>90% (89% - 90%) (95% CI)</td>
</tr>
<tr>
<td>PPV</td>
<td>27% (24% - 31%) (95% CI)</td>
</tr>
</tbody>
</table>

- MRSA nares screens were positive for 13.7% of the population
- MRSA was positive in 5.5% of all clinical cultures

### Table 3c: Predictive values for MRSA nares PCR based on culture site

<table>
<thead>
<tr>
<th>MRSA culture site</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>PPV (95% CI)</th>
<th>NPV (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloodstream</td>
<td>0.74 (0.59, 0.85)</td>
<td>0.88 (0.86, 0.90)</td>
<td>0.21 (0.15, 0.29)</td>
<td>0.99 (0.98, 0.99)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>0.75 (0.55, 0.88)</td>
<td>0.90 (0.86, 0.92)</td>
<td>0.30 (0.20, 0.43)</td>
<td>0.98 (0.97, 0.99)</td>
</tr>
<tr>
<td>Extremity</td>
<td>0.61 (0.52, 0.70)</td>
<td>0.94 (0.92, 0.96)</td>
<td>0.76 (0.65, 0.84)</td>
<td>0.90 (0.86, 0.92)</td>
</tr>
<tr>
<td>Ulcer</td>
<td>0.70 (0.48, 0.86)</td>
<td>0.89 (0.77, 0.95)</td>
<td>0.70 (0.48, 0.86)</td>
<td>0.89 (0.77, 0.95)</td>
</tr>
<tr>
<td>Urine</td>
<td>0.77 (0.65, 0.86)</td>
<td>0.87 (0.86, 0.89)</td>
<td>0.11 (0.09, 0.15)</td>
<td>0.99 (0.99, 1.00)</td>
</tr>
<tr>
<td>Other</td>
<td>0.60 (0.49, 0.70)</td>
<td>0.96 (0.95, 0.97)</td>
<td>0.61 (0.49, 0.71)</td>
<td>0.96 (0.95, 0.97)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>0.67 (0.62, 0.72)</td>
<td>0.90 (0.89, 0.90)</td>
<td>0.27 (0.24, 0.31)</td>
<td>0.98 (0.97, 0.98)</td>
</tr>
</tbody>
</table>

- The NPV for half of the obtained cultures was high, with urine, bloodstream, and respiratory cultures having an NPV of \( \geq 98\% \)
- However, the NPV for cultures obtained from extremities or from ulcers were low (NPV ≤ 90%)
- Cultures for “Other” had an NPV of about 96%. However, due to the lack of more specific data as to where these cultures originate from, conclusions cannot be drawn from these results.
**Authors’ conclusions**

The absence of nasal MRSA colonization was useful for ruling out MRSA involvement only if the prevalence of MRSA as a pathogen in the type of infection being assessed was low (e.g., < 10%).

**Reviewer’s Critique**

<table>
<thead>
<tr>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>● Large sample size</td>
<td>● Study did not clarify exact numbers or types of cultures obtained from the “other” category</td>
</tr>
<tr>
<td>● Study has in-depth analysis of the relationship between MRSA nares and clinical cultures</td>
<td>● Relatively small portion of positive cultures were MRSA (5.5% of positive cultures were MRSA)</td>
</tr>
<tr>
<td>● Study used only nasal PCR</td>
<td>● Only the first positive culture in a 30-day period was used for each patient (a urine culture that was positive for <em>E. coli</em> may have overridden a possible MRSA infection in the blood).</td>
</tr>
</tbody>
</table>

**Take-home points**

- While an older study, this study did show a possible high NPV for MRSA nares regarding MRSA clinical cultures.
- Negative MRSA nares may be used to rule out MRSA infections
- Positive MRSA nares should not be used to rule in MRSA infections

Objective
Describe the diagnostic characteristics of nasal-swab screening in predicting MRSA infections in hospitalized patients receiving empiric treatment with IV vancomycin

Methods
Retrospective, observational chart review between January and October 2015 for patients of the Peter Lougheed Centre in Calgary, Alberta

Patient population

Inclusion Criteria:
- Age > 18 years old
- Initiated on empiric IV vancomycin (first dose within 48 hours)
- Documented nasal swab and culture within 48 hours of admission
- Culture from either blood, sputum, wound, bronchoalveolar lavage (BAL), or endotracheal (ET) tube within 48 hours of admission

Exclusion Criteria:
- Patients with cultures collected after receiving the first dose of vancomycin
- Patients on long-term dialysis therapy (due to higher risk of non-MRSA infections requiring vancomycin therapy such as coagulase-negative Staphylococcus line infections)
- The patient was previously included in the trial

Baseline Characteristics

Table 4a: Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%) of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of Patients</td>
<td>273</td>
</tr>
<tr>
<td>Sex, male</td>
<td>176 (64.5)</td>
</tr>
<tr>
<td>Age (years) (mean ± SD)</td>
<td>55.8 ± 17.7</td>
</tr>
<tr>
<td>History of recent admission</td>
<td>73 (26.7)</td>
</tr>
<tr>
<td>Admitting service</td>
<td></td>
</tr>
<tr>
<td>Internal Medicine</td>
<td>146 (53.5)</td>
</tr>
<tr>
<td>Hospitalist</td>
<td>69 (25.3)</td>
</tr>
<tr>
<td>Intensive care</td>
<td>27 (9.9)</td>
</tr>
<tr>
<td>Cultures</td>
<td>334</td>
</tr>
<tr>
<td>Blood Culture</td>
<td>266 (79.6)</td>
</tr>
<tr>
<td>Wound Culture</td>
<td>36 (10.8)</td>
</tr>
<tr>
<td>ET aspirate</td>
<td>22 (6.6)</td>
</tr>
</tbody>
</table>

- Total of 334 cultures included in the study; 60 patients had 2 or more culture sites
Results

Table 4b: Sensitivity, Specificity, and PPV for MRSA nares

<table>
<thead>
<tr>
<th>Diagnostic characteristic</th>
<th>Result of analysis to predict MRSA positive culture (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>58.3% (28.6% - 83.5%)</td>
</tr>
<tr>
<td>Specificity</td>
<td>93.9% (90.0% - 96.3%)</td>
</tr>
<tr>
<td>PPV</td>
<td>30.4% (14.1% - 53.0%)</td>
</tr>
</tbody>
</table>

- MRSA nares screens were positive for 8.4% of all nasal cultures
- 4.4% of all patients had a positive MRSA clinical culture

Table 4c: Negative predictive value of MRSA nares in newly admitted patients treated with empiric vancomycin

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>NPV% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cultures</td>
<td>98.0 (95.1 - 99.3)</td>
</tr>
<tr>
<td>Recently admitted</td>
<td>98.4 (90.5 - 99.9)</td>
</tr>
<tr>
<td>Not recently admitted</td>
<td>97.8 (94.2 - 99.3)</td>
</tr>
<tr>
<td>Blood culture</td>
<td>99.2 (96.7 - 99.9)</td>
</tr>
<tr>
<td>Non-blood culture</td>
<td>87.5 (70.1 - 95.9)</td>
</tr>
</tbody>
</table>

Authors’ conclusions

The high NPV of MRSA nasal-swab screening in a low prevalence settings suggest that a negative result on MRSA nasal-swab screening significantly reduces the probability of MRSA infection.

Reviewer’s Critique

Strengths
- Study had a large portion of patients with blood cultures, which makes this easily generalizable for bacteremia
- This study gives solid data regarding the NPV value of MRSA nasal swabs in comparison to both blood culture and non-blood culture results

Limitations
- MRSA nares were done with cultures and not PCR
- Small sample size
- Excluding dialysis patients does decrease the generalizability of this trial when discussing dialysis patients who are at a higher risk of MRSA infections
- Significantly less cultures from non-blood sources, makes it difficult to generalize to other cultures

Take-home points
- MRSA therapy may be de-escalated when treating bloodstream infections in the presence of a negative MRSA nares culture.
Table 5: Mergenhagen KA, Starr KE, Wattengel BA et al. Determining the utility of methicillin-resistant *Staphylococcus aureus* nares screening in antimicrobial stewardship. *Clin Infec Dis.* 2019 42

**Objective**

Determine the NPV of MRSA screening in the determination of subsequent positive clinical cultures for MRSA

**Methods**

Retrospective, cohort study between January 2007 and January 2018, across VA medical centers

**Patient population**

**Inclusion Criteria:**
- Age ≥ 18 years old
- MRSA nares tested upon admission or transfer to a VA inpatient facility

**Exclusion Criteria:**
- Discharged nares results
- Rectal swabs for VRE
- Autopsy results
- Cultures with disparate results (blood culture labeled as abscess) or where the collection type was missing

**Intervention**

- Positive and negative cultures were identified and classified into their culture source (e.g. blood, urine, wound), and then categorized to their most closely identified subcategory (e.g. urine catheter, sterile respiratory, peripheral blood)
- Positive MRSA cultures were defined as cultures taken after but within 7 days of MRSA nasal swab, that contained MRSA
- Negative MRSA cultures were defined as cultures taken after but within 7 days of MRSA nasal swab, that did not contain MRSA

**Baseline characteristics**

**Table 5a: Baseline Characteristics**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of clinical cultures taken</td>
<td>561,325</td>
</tr>
<tr>
<td>Number of unique patients</td>
<td>245,833</td>
</tr>
<tr>
<td>MRSA nares with PCR performed (%)</td>
<td>73.7</td>
</tr>
<tr>
<td>MRSA nares with standard culture (%)</td>
<td>26.3</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>96.3%</td>
</tr>
<tr>
<td>Age (years) (mean ± SD)</td>
<td>68.2 ± 12.3</td>
</tr>
<tr>
<td>Cultures (most frequent)</td>
<td></td>
</tr>
<tr>
<td>Urine (%)</td>
<td>40</td>
</tr>
<tr>
<td>Wound (%)</td>
<td>24.7</td>
</tr>
<tr>
<td>Respiratory (%)</td>
<td>16.2</td>
</tr>
<tr>
<td>Blood (%)</td>
<td>12.5</td>
</tr>
<tr>
<td>MRSA incidence (%)</td>
<td>8.3</td>
</tr>
</tbody>
</table>
Results

Table 5b: Sensitivity, Specificity, and PPV for MRSA nares including best and worst % by site

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Result of analysis to predict MRSA positive culture (95% CI)</th>
<th>Culture with highest value (%)</th>
<th>Culture with lowest value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>67.4% (67.0% - 67.9%)</td>
<td>Peripherally Inserted central catheter lines (79.1)</td>
<td>Graft cultures (51.3)</td>
</tr>
<tr>
<td>Specificity</td>
<td>81.2% (81.1% - 81.3%)</td>
<td>Heart tissue cultures (93.7)</td>
<td>Eye tissue cultures (74.4)</td>
</tr>
<tr>
<td>PPV</td>
<td>24.6% (24.4% - 24.8%)</td>
<td>Device cultures (56.3)</td>
<td>Urine cultures (7.6)</td>
</tr>
</tbody>
</table>

- MRSA nares screens were positive for 22.9% of the cohort

Table 5c: Negative Predictive values for MRSA Nasal PCR + Nasal Culture

<table>
<thead>
<tr>
<th>Current location</th>
<th>NPV % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cultures</td>
<td>96.5% (96.4% - 96.52%)</td>
</tr>
<tr>
<td>All blood</td>
<td>96.5% (96.3% - 96.6%)</td>
</tr>
<tr>
<td>Respiratory tract</td>
<td>96.1% (95.9% - 96.2%)</td>
</tr>
<tr>
<td>Sterile Respiratory</td>
<td>96.1% (95.9% - 96.4%)</td>
</tr>
<tr>
<td>Urine Catheter</td>
<td>99% (98.9% - 99.1%)</td>
</tr>
<tr>
<td>Wound (unspecified)</td>
<td>93.1% (93% - 93.3%)</td>
</tr>
<tr>
<td>Wound (sterile)</td>
<td>93.5% (93.3% - 93.6%)</td>
</tr>
</tbody>
</table>

- Majority of cultures had relatively high NPV for MRSA of above 96% with the exception of wound cultures which had an NPV of less than 94% (Ex. Sterile wound of upper/lower extremity + foot 89% NPV, skin graft 89.6% NPV)

Table 5d: Negative Predictive values PCR vs. Nasal Culture

<table>
<thead>
<tr>
<th>Type</th>
<th>Number- PCR</th>
<th>NPV - PCR (95% CI)</th>
<th>Number Culture</th>
<th>NPV- Culture (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole cohort</td>
<td>413,664</td>
<td>96.9% (96.8% - 96.9%)</td>
<td>147,661</td>
<td>95.5% (95.4% - 95.6%)</td>
</tr>
<tr>
<td>Blood</td>
<td>51,928</td>
<td>96.8% (96.7% - 97.0%)</td>
<td>18,257</td>
<td>95.4% (95.2% - 95.7%)</td>
</tr>
<tr>
<td>Respiratory Tract</td>
<td>66,242</td>
<td>96.6% (96.5% - 96.8%)</td>
<td>24,670</td>
<td>94.6% (94.3% - 94.9%)</td>
</tr>
<tr>
<td>Renal System</td>
<td>145,777</td>
<td>99.3% (99.3% - 99.3%)</td>
<td>55,666</td>
<td>99.1% (99.0% - 99.2%)</td>
</tr>
<tr>
<td>Wound</td>
<td>101,423</td>
<td>93.9% (93.7% - 94.0%)</td>
<td>34,655</td>
<td>91.1% (90.9% - 91.4%)</td>
</tr>
</tbody>
</table>
Authors’ conclusions

This study suggests that a negative MRSA nares swab taken within 7 days of culture is useful for predicting the absence of MRSA in a subsequent clinical culture. It is not, however, appropriate to use MRSA nares as a tool to predict current MRSA infection. Use of MRSA nares screening may improve patient care by avoiding potential toxicities associated with the use of unnecessary or broad antibiotics.

Reviewer’s Critique

Strengths
- Very large trial
- Provided data on a state as well as on a national level
- Was done mostly with PCR
- Gave data regarding using MRSA nares with PCR vs. culture
- Broke down to useful subcategories

Limitations
- The study did not confound for positive cultures that may not have been true cultures
- Almost the entire population was male (96.3%)
- Large percentage of the positive cultures was from urinary sources, which is not a common source of MRSA
- No baseline characteristics other than ages and sex.

Take-home points
- Using MRSA nares as a negative predictive marker is appropriate depending on the likely source of infection
  - It would be appropriate for patients with pneumonia, bloodstream infections, or UTIs.
● Using MRSA nares to confirm the use of MRSA therapy is inappropriate
● Use of PCR for MRSA nares appears to have a slightly higher NPV compared to culture-based diagnostic tests.

V. Literature summary

Table 6: Literature Summary

<table>
<thead>
<tr>
<th>Study</th>
<th>Use of MRSA nares as a negative predictive marker may be appropriate; however, using it as a positive marker does not seem appropriate</th>
<th>Using MRSA nares as a negative predictive marker may be appropriate for bloodstream infections</th>
<th>Use of MRSA nares as a negative predictive marker seems appropriate for suspected urine, blood, and respiratory infections</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robicsek, et. al 2007</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rioux, et. al 2017</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mergenhagen, et. al 2019</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VI. Recommendations

A. The use of MRSA nares PCR testing as an antimicrobial stewardship tool to guide de-escalation of therapy in certain clinical situations may be appropriate
   1. Current data only supports de-escalation of therapy if MRSA prevalence is less than 10% at the institution

B. Due to the lack of baseline characteristics regarding patients with risk factors (ex. dialysis, IV drug use), clinical judgement should be used in combination with results to guide treatment

C. While use of MRSA nasal cultures will take longer than MRSA nasal PCR to be finalized as negative, a negative MRSA nasal swab from a culture can still be used as a negative predictive marker.

D. MRSA nares should not be used to guide treatment in patients with skin and soft tissue infections, wound infections, or VAP

Table 7: Summary of recommendations for using MRSA nares as a negative predictive tool

<table>
<thead>
<tr>
<th>Site of infection</th>
<th>Should negative MRSA nares be used to de-escalate therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bloodstream</td>
<td>Yes</td>
</tr>
<tr>
<td>Respiratory tract</td>
<td>Yes*</td>
</tr>
<tr>
<td>Urinary Tract</td>
<td>Yes**</td>
</tr>
<tr>
<td>Wound</td>
<td>No</td>
</tr>
<tr>
<td>Ulcer</td>
<td>No</td>
</tr>
<tr>
<td>Skin</td>
<td>No</td>
</tr>
</tbody>
</table>

* Due to prior evidence of low NPV in patients with VAP, MRSA nares should not be used to guide therapy.
**Empiric therapy with vancomycin may be appropriate should the patient have a history of gram positive UTI even if MRSA nares are negative
References:


# Definitions and formulas for predictive values

<table>
<thead>
<tr>
<th>Predictive Values</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value (PPV)</th>
<th>Negative Predictive Value (NPV)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Formula</strong></td>
<td>$\frac{T+}{T+ (+) F-}$</td>
<td>$\frac{T-}{T- (+) F+}$</td>
<td>$\frac{T+}{T+ (+) F+}$</td>
<td>$\frac{T-}{T- (+) F-}$</td>
</tr>
<tr>
<td><strong>Simplified meaning</strong></td>
<td>The ability to detect a disease if it is really present.</td>
<td>The ability to exclude persons who do not have the disease</td>
<td>How likely is a positive test to indicate that the person has the disease</td>
<td>How likely is a negative test to indicate that the disease is not present in the person</td>
</tr>
</tbody>
</table>

Key: (T+ - True positive), (T- - True negative), (F+ - False positive), (F- - False negative)