Evaluating the Role of MRSA Nasal Swabs

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Pharmacy Grand Rounds
February 28, 2017
Objectives

• Identify the pathophysiology of MRSA nasal colonization

• Discuss current evidence for the utility of MRSA nasal swabs in specific patient populations

• Describe the clinical considerations associated with MRSA nasal swabs
The burden of infection

- Mortality
- MRSA
- Cost
- Drug consequences

Pathophysiology

- Primary reservoir of *S. aureus* is the vestibulum nasi
  - Shown to be highest colonization site

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- *S. aureus with ClfB*
- Loricrin


*ClfB: clumping factor B*
Pathophysiology

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  - Shown to be highest colonization site

- *S. aureus with ClfB*

- Loricrin

*ClfB*: clumping factor B

Epidemiology

<table>
<thead>
<tr>
<th>Rates of Nasal Colonization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>MSSA</td>
</tr>
<tr>
<td>MRSA</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk Factors for Nasal Colonization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotic use within 3 months</td>
</tr>
<tr>
<td>Diagnosis of SSTI</td>
</tr>
<tr>
<td>Advanced age</td>
</tr>
</tbody>
</table>


SSTI: skin or soft-tissue infection
## Culture vs. PCR

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Time to results (h)</th>
<th>Cost</th>
<th>Required skill level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culture</td>
<td>Low</td>
<td>100%</td>
<td>18-48</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>PCR</td>
<td>High</td>
<td>&lt;100%</td>
<td>4-12</td>
<td>High</td>
<td>Moderate to high</td>
</tr>
</tbody>
</table>

What gene detected by PCR is associated with methicillin-resistant S. aureus?

A. Loricrin
B. *mecA*
C. VISA
D. ClfB
Universal screening

**Design**
- Prospective, interventional case-control study
- Two community hospitals approximately 175 beds

**Population**
- 15,049 adults
- All adults admitted during study period

**Objective**
- Evaluate the clinical effectiveness and cost-benefit of universal versus targeted screening for MRSA to prevent hospital-acquired MRSA infections

**Intervention**
- 9-month baseline: targeted screening for both hospitals
- 5-month intervention: universal screening at intervention hospital

Universal screening

• Universal screening was associated with:
  • Increase in MRSA detection (P < 0.01)
  • Non-significant decline in hospital-acquired MRSA infections (P = 0.34)
  • Benefit-to-cost ratio of 0.50

Consequences of screening

- Costly
- Isolation precautions
- Laborious
- Requires infrastructure
Is screening a poor use of resources?

- No Screening
  - Universal Screening
    - Targeted Screening
  - Screening
- Start
Is screening a poor use of resources?

Cost in Euros (millions)

Universal Screening
No Screening
Targeted Screening

# MRSA pneumonia

<table>
<thead>
<tr>
<th></th>
<th>CAP</th>
<th>HAP</th>
</tr>
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<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>2-9%</td>
<td>20-40%</td>
</tr>
<tr>
<td><strong>Risk Factors</strong></td>
<td>Prior influenza, ESRD</td>
<td>Hospitalization where &gt;20% isolates are MRSA, high risk for mortality</td>
</tr>
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<td></td>
<td>Prior antibiotic therapy, IVDA, tobacco use, COPD, HIV infection</td>
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<tr>
<td><strong>Mortality</strong></td>
<td>29-55%</td>
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**Notes:**
- IVDA: intravenous drug abuse
- ESRD: end-stage renal disease
- COPD: chronic obstructive pulmonary disease
- HIV: human immunodeficiency virus

References:
<table>
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<tr>
<th>The value of prediction</th>
</tr>
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</table>

| Design                  | • Retrospective review study  
                          | • 850-bed three-hospital healthcare organization |
|-------------------------|--------------------------------------------------------------------------------|
| Population              | • 5,779 nasal MRSA tests from patients in either ICU or chronic care units |
| Objective               | • Examine whether MRSA nasal colonization predicts MRSA involvement in a patient with positive cultures from site of suspected infection |
| Inclusion               | • MRSA PCR nasal swab performed within a 24-h period before or after a clinical culture showed the growth of any organism |

The value of prediction

• Results
  • Total number of clinical cultures (+)MRSA – 5.6%
  • Positive MRSA PCR nasal swab in setting of MRSA clinical cultures – 217/323 patients (67.2%)

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<thead>
<tr>
<th>Infectious Source</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
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<tr>
<td>Total</td>
<td>67</td>
<td>90</td>
<td>27</td>
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<td>Respiratory</td>
<td>75</td>
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<td>Bloodstream</td>
<td>74</td>
<td>88</td>
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<td>70</td>
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<td>89</td>
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<td>Urine</td>
<td>77</td>
<td>87</td>
<td>11</td>
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Definitions

• *Sensitivity*
  • Probability that a test result will be positive when the disease is present (true positive rate)

• *Specificity*
  • Probability that a test result will be negative when the disease is not present (true negative rate)

• *Positive predictive value*
  • Probability that the disease is present when the test is positive

• *Negative predictive value*
  • Probability that the disease is not present when the test is negative
The value of prediction

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Prediction in the ICU

| Design          | • Prospective cohort study  
|                 | • 1252-bed urban teaching hospital |
| Population      | • 749 consecutive patients admitted to the medical ICU |
| Objective       | • Test whether ICU nasal screening for MRSA predicts the presence or absence of MRSA infections requiring antimicrobial treatment |
| Intervention    | • Nasal swabs were obtained at ICU admission and weekly thereafter for MRSA detection |

Prediction in the ICU

• Results
  • Rate of MRSA nasal colonization – 24.4%
  • Confirmed MRSA PNA – 13.4%

<table>
<thead>
<tr>
<th>Infection</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PNA</td>
<td>24.2</td>
<td>78.5</td>
<td>17.7</td>
<td>84.4</td>
</tr>
<tr>
<td>BSI</td>
<td>23.1</td>
<td>78.2</td>
<td>11.0</td>
<td>89.7</td>
</tr>
<tr>
<td>Either PNA or BSI</td>
<td>25.2</td>
<td>79.2</td>
<td>27.4</td>
<td>77.3</td>
</tr>
</tbody>
</table>

LRTI: lower respiratory tract infection
BSI: bloodstream infection
PNA: pneumonia

## Utility in pneumonia

| Design          | • Retrospective cohort study  
|                 | • 244-bed academic tertiary care hospital |
| Population      | • 435 patients from both ICU and general floor |
| Objective       | • Describe the diagnostic characteristics of the nasal swab MRSA PCR test in predicting culture-confirmed pneumonia |
| Inclusion       | • Patients with confirmed pneumonia who had nasal swab MRSA PCR test and culture specimen obtained |

Utility in pneumonia

• Results
  • Rate of colonization – 14.3%
  • Positive blood cultures – 25 cases (5.7%)

<table>
<thead>
<tr>
<th>Pneumonia Type (n)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Positive Predictive Value (%)</th>
<th>Negative Predictive Value (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (435)</td>
<td>88.0</td>
<td>90.1</td>
<td>35.4</td>
<td>99.2</td>
</tr>
<tr>
<td>CAP (149)</td>
<td>77.8</td>
<td>90.7</td>
<td>35.0</td>
<td>98.4</td>
</tr>
<tr>
<td>HCAP (238)</td>
<td>100.0</td>
<td>88.9</td>
<td>34.2</td>
<td>100.0</td>
</tr>
<tr>
<td>HAP (48)</td>
<td>66.7</td>
<td>95.6</td>
<td>50.0</td>
<td>97.7</td>
</tr>
</tbody>
</table>
CAP guidelines 2007

No discussion of utility of MRSA nasal swab culture or PCR technology

HAP/VAP guidelines 2016

• “Observational data suggest that concurrent or recent positive MRSA screens increase the likelihood that clinical infection is due to MRSA.”

• “…negative MRSA surveillance studies need to be interpreted within the context of the local prevalence of MRSA.”

• “There is also some evidence suggesting that a positive MRSA screen…may increase the risk of MRSA being cultured from respiratory samples, but not enough evidence to definitively list this as a risk factor for MRSA pneumonia.”

Is MRSA detection and de-escalation effective?

| Design       | • Retrospective analysis  
|              | • Assessed two 1-month periods prior to and following initiation of MRSA PCR swab protocol |
| Population   | • Patients receiving vancomycin or linezolid for pneumonia pre- and post-PCR protocol |
| Intervention | • MRSA PCR nasal swab ordered on all patients with suspected pneumonia started on vancomycin or linezolid  
|              | • Provider notified of PCR results to make decision of therapy |
| Outcomes     | • 1°: Duration of MRSA-targeted therapy  
|              | • 2°: Length of hospital stay; mortality after conclusion of initial MRSA-targeted regimen |

Is MRSA detection and de-escalation effective?

366 patients on vancomycin or linezolid

Indication not pneumonia: 263

Pre-PCR Group: 71

MRSA nasal culture: 41
Died during treatment: 3

Pre-PCR Group: 27

PCR Group: 32

Died during treatment: 2

PCR Group: 30

Is MRSA detection and de-escalation effective?

<table>
<thead>
<tr>
<th></th>
<th>Pre-PCR (n = 27)</th>
<th>PCR (n = 30)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of MRSA-Targeted Therapy (days)</td>
<td>4.0 ± 2.0</td>
<td>2.13 ± 0.86</td>
<td>P = &lt;0.0001</td>
</tr>
<tr>
<td>Days to Clinical Improvement</td>
<td>1.78 ± 2.52</td>
<td>2.27 ± 3.34</td>
<td>P = 0.54</td>
</tr>
<tr>
<td>Incidence of AKI</td>
<td>7 (26%)</td>
<td>1 (3.3%)</td>
<td>P = 0.02</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>11.04 ± 9.5</td>
<td>8.2 ± 7.8</td>
<td>P = 0.22</td>
</tr>
<tr>
<td>Mortality</td>
<td>4 (14.8%)</td>
<td>2 (6.7%)</td>
<td>P = 0.41</td>
</tr>
</tbody>
</table>

AKI: acute kidney injury  
LOS: length of stay  

There is evidence to support de-escalating antimicrobial therapy based on MRSA nasal swab results in pneumonia.

A. True
B. False
Surgical populations

- *S. aureus* is the most common pathogen causing surgical site infections (SSIs)
- *S. aureus* nasal colonization:
  - Occurs in ~25% of individuals
  - Increases risk of SSI 2-14 fold
- Screening for MRSA colonization may play a role in:
  - Identifying candidates for decolonization
  - Informing the selection of optimal prophylactic antimicrobials

### SCIP guidelines

- Universal use of mupirocin for nasal decolonization is discouraged

<table>
<thead>
<tr>
<th>Cardiac Procedures</th>
<th>Orthopedic Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>45% reduction in <em>S. aureus</em> SSIs with the use of perioperative mupirocin among patients known to be colonized with <em>S. aureus</em></td>
<td>Mupirocin decolonization has shown significant decreases in nasal MRSA carriage and overall SSIs</td>
</tr>
</tbody>
</table>

Mupirocin should be given intranasally to all patients with documented *S. aureus* colonization (SOE = A)

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SCIP: surgical care improvement project

Skin and soft tissue infections

- MRSA nasal colonization is a risk factor
- Predictive value increases significantly when paired with MRSA swab from another site
- Decolonization may play a role in recurrent SSTIs
- Limited data exists

A 51 year-old male presents to the ED with a 2-day history of fever, shortness of breath, and cough and no other PMH.

CXR shows new bilateral infiltrates, and he is diagnosed with community-acquired pneumonia.

The patient resides at home with his wife and two children, has no recent hospitalizations or antibiotics, and no other risk factors for MRSA pneumonia.

He is admitted to the hospital and started on ceftriaxone and azithromycin.

An MRSA PCR nasal swab, ordered in the ED, returns positive for MRSA colonization the next morning.

On rounds, the attending states she would like to start IV linezolid. What is your response?
A. Recommend starting IV vancomycin due to cost considerations

B. Oblige and go check Pyxis to confirm linezolid is available

C. Recommend adding oral MRSA coverage with doxycycline

D. Discuss likelihood of MRSA pneumonia being present based on patient’s presentation, risk factors and the PPV of the nasal swab PCR
Take home points

- MRSA nasal swabs should not be used to direct antibiotic therapy alone

<table>
<thead>
<tr>
<th>Cardiac and Orthopedic Surgery</th>
<th>Strong Negative Predictor</th>
<th>Risk Factor vs. Definitive Diagnostic Tool</th>
</tr>
</thead>
</table>
Evaluating the Role of MRSA Nasal Swabs

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CA-Pneumonia and Influenza Correlation
Sensitivity = \frac{A}{A + C}

Specificity = \frac{D}{B + D}

Positive Predictive Value = \frac{A + B}{A + C}

Negative Predictive Value = \frac{D + C}{B + D + C}
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