Methicillin-Resistant
Staphylococcus aureus
Nasal Swabs as a Tool in Antimicrobial Stewardship

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PGY2 Infectious Diseases Pharmacy Resident
HSHS St. John’s Hospital

Objectives: Pharmacists
• Identify patients at risk and recommended empiric therapies for MRSA pneumonia
• Discuss the relationship between MRSA nasal swabs and MRSA pneumonia
• Explain how using MRSA nasal swabs can be a beneficial tool in antimicrobial stewardship

Objectives: Technicians
• Describe the impact of MRSA pneumonia on patient care
• Explain the purpose of using MRSA nasal swabs
• Discuss the benefits of decreasing unnecessary vancomycin use

Terminology
• CAP = community acquired pneumonia
• HAP = hospital acquired pneumonia
• HCAP = healthcare associated pneumonia
• VAP = ventilator associated pneumonia
• MSSA = methicillin-susceptible Staphylococcus aureus
• MRSA = methicillin-resistant Staphylococcus aureus
• ICU = intensive care unit
• MDR = multidrug resistant
• PCR = polymerase chain reaction
• PPV = positive predictive value
• NPV = negative predictive value

Disclosures
• N. Tucker: No actual or potential conflicts of interest to disclose
• T. Dietrich: No actual or potential conflicts of interest to disclose
• May be discussing off-label uses

EVIDENCE BEHIND MRSA NASAL SWABS IN PREDICTING MRSA PNEUMONIA
Significance of MRSA Pneumonia

- MRSA accounts for:
  - 20-40% of HAP & VAP, with 56% mortality
  - 27% of HCAP, with 20% mortality
- Increase in annual incidence of MRSA causing HAP & VAP
  - 2008: 11.3 cases per 100,000 patient days
  - 2012: 15.5 cases per 100,000 patients days
- National prevalence survey reported 4.1% MRSA colonization in inpatients

Risk Factors for MDR Pathogens: 2016

<table>
<thead>
<tr>
<th>MDR HAP</th>
<th>MDR VAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior IV antibiotics within 90 days</td>
<td>Prior IV antibiotics within 90 days</td>
</tr>
<tr>
<td>Septic shock at time of diagnosis</td>
<td>Septic shock at time of diagnosis</td>
</tr>
<tr>
<td>Acute respiratory distress syndrome preceding diagnosis</td>
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</tr>
<tr>
<td>Hospitalization ≥ 5 days prior to diagnosis</td>
<td>Hospitalization ≥ 5 days prior to diagnosis</td>
</tr>
<tr>
<td>Acute renal replacement therapy prior to onset</td>
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</tr>
</tbody>
</table>

MRSA Risk Factors: 2016

- Presence of the following indicate MRSA coverage:

<table>
<thead>
<tr>
<th>HAP</th>
<th>VAP</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDR risk factors present</td>
<td>MDR risk factors present</td>
</tr>
<tr>
<td>&gt;20% of cultures of methicillin resistant</td>
<td>&gt;20% of cultures of methicillin resistant</td>
</tr>
<tr>
<td>MRSA prevalence unknown</td>
<td>MRSA prevalence unknown</td>
</tr>
<tr>
<td>High mortality risk*</td>
<td>High mortality risk*</td>
</tr>
</tbody>
</table>

*Ventilator support or septic shock

Risk Factors for MDR Organisms: 2005

- Hospitalization ≥ 2 days in preceding 90 days
- Nursing home, Extended care facility
- Home infusion therapy
- Chronic dialysis within 30 days
- Home wound care
- Family member with MDR pathogen
- Antimicrobial therapy within 90 days
- Immuno-suppression

MDR VAP Risk Factor Analysis

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior IV antibiotic use within 90 days</td>
<td>OR = 12.3 (95% CI: 6.48 – 23.35)</td>
</tr>
<tr>
<td>Septic shock at time of diagnosis</td>
<td>OR = 2.01 (95% CI: 1.12 – 3.61)</td>
</tr>
<tr>
<td>ARDS preceding diagnosis</td>
<td>OR = 3.1 (95% CI: 1.88 – 5.1)</td>
</tr>
<tr>
<td>Hospitalization ≥ 5 days prior to diagnosis</td>
<td>Not reported</td>
</tr>
<tr>
<td>Acute renal replacement therapy prior to onset</td>
<td>OR = 2.5 (95% CI: 1.14 – 5.49)</td>
</tr>
</tbody>
</table>

ARDS = acute respiratory distress syndrome

Empiric Treatment for MRSA

- Vancomycin
- Linezolid
- Strong recommendation, moderate quality evidence
Patient Case

• DW is a 67 year old male
  – Chronic obstructive pulmonary disease
  – End-stage renal disease on hemodialysis
• Presents with shortness of breath, productive cough with purulent sputum, and fever
• Recently prescribed oral azithromycin for bronchitis

Patient Case

• Chest x-ray with diffuse infiltrates
• Admitted with septic shock & pneumonia

<table>
<thead>
<tr>
<th>Tmax</th>
<th>RR</th>
<th>BP</th>
<th>HR</th>
<th>WBC</th>
<th>SCr</th>
<th>Lactate</th>
</tr>
</thead>
<tbody>
<tr>
<td>39.6</td>
<td>26</td>
<td>72/44</td>
<td>112</td>
<td>17.6</td>
<td>4.6</td>
<td>4.6</td>
</tr>
</tbody>
</table>

Assessment

Which of the following would indicate that DW requires empiric therapy for MRSA?

A. COPD  
B. Septic shock  
C. Hemodialysis  
D. Oral azithromycin within 90 days

Patient Case, cont.

• Upon admission, DW receives a nasal swab to screen for MRSA colonization

Current Use of MRSA Nasal Swabs

FDA Indication  
• Detect MRSA colonization

Illinois Law
• MRSA Screening and Reporting Act

HSHS St. John’s Hospital Policy  
• Screen on ICU admission

Chromogenic Agar

• Qualitative test for detection of MRSA  
• Selective agents in agar suppress growth of all non-MRSA organisms  
• Results in 18 – 24 hours
PCR Screening

- Qualitative diagnostic test for detection of MRSA DNA from nasal swabs in patients at risk for nasal colonization
- Uses PCR for MRSA DNA amplification and detection
- Results in 3 hours

Predictive Value of Screening

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Chan 2012</th>
<th>Rimawi 2014</th>
<th>Dangerfield 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective</td>
<td>Chan 2012</td>
<td>Rimawi 2014</td>
<td>Dangerfield 2014</td>
</tr>
<tr>
<td>Intervention</td>
<td>Chan 2012</td>
<td>Rimawi 2014</td>
<td>Dangerfield 2014</td>
</tr>
<tr>
<td>Patients</td>
<td>Chan 2012</td>
<td>Rimawi 2014</td>
<td>Dangerfield 2014</td>
</tr>
<tr>
<td>Results</td>
<td>Chan 2012</td>
<td>Rimawi 2014</td>
<td>Dangerfield 2014</td>
</tr>
<tr>
<td>Limitations</td>
<td>Chan 2012</td>
<td>Rimawi 2014</td>
<td>Dangerfield 2014</td>
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</tbody>
</table>

Active MRSA Surveillance in ICU Patients with VAP

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Prospective observational study in 388 VAP patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective</td>
<td>Determine performance characteristics of active surveillance cultures as predictors of MRSA VAP</td>
</tr>
<tr>
<td>Intervention</td>
<td>Cultures on ICU admission, every 7 days, &amp; on ICU discharge, nares, oropharynx, or trachea &amp; open wounds</td>
</tr>
<tr>
<td>Patients</td>
<td>Median days to VAP: 6 Mean days hospitalization: 39.4 MRSA colonization: 14%</td>
</tr>
<tr>
<td>Results</td>
<td>PPV: 48.1% Sensitivity: 70.3% NPV: 96.7% Specificity: 92% 11 (29.7%) with negative colonization and positive cultures</td>
</tr>
<tr>
<td>Limitations</td>
<td>VAP diagnostic criteria Chromogenic agar</td>
</tr>
</tbody>
</table>

Negative PCR may not Rule Out MRSA Pneumonia?

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Retrospective review in 275 MICU patients with pneumonia, 165 with MRSA pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective</td>
<td>Investigate data on MRSA pneumonia in patients with MRSA nasal colonization</td>
</tr>
<tr>
<td>Patients</td>
<td>HCAP: 86% CAP: 14% MRSA colonization: 45%</td>
</tr>
<tr>
<td>Results</td>
<td>PPV: 97.4% NPV: 54.3% 91 (55%) patients with negative nasal PCR and positive cultures</td>
</tr>
<tr>
<td>Limitations</td>
<td>No hospital-acquired pneumonias High prevalence of MRSA CAP (17%) &amp; MRSA colonization</td>
</tr>
</tbody>
</table>

Putting the MRSA Nasal Swab to Work

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Retrospective cohort of 435 confirmed pneumonia patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective</td>
<td>Describe diagnostic characteristics of MRSA PCR in predicting culture-confirmed MRSA pneumonia</td>
</tr>
<tr>
<td>Intervention</td>
<td>MRSA PCR nasal swab</td>
</tr>
<tr>
<td>Patients</td>
<td>HCAP: 54.7% CAP: 34.3% HAP/VAP: 11% ICU: 43.6% MRSA colonization: 14.3%</td>
</tr>
<tr>
<td>Results</td>
<td>PPV: 35.4% Sensitivity: 88% NPV: 99.2% Specificity: 90.1%</td>
</tr>
<tr>
<td>Limitations</td>
<td>Mix of sputum, BAL, &amp; blood cultures MRSA PCR not standard of care at institution May have larger immunocompromised population</td>
</tr>
</tbody>
</table>

A Not-So-Good Study

<table>
<thead>
<tr>
<th>Study Type</th>
<th>Retrospective study of 72 patients with MRSA nasal PCR + lower respiratory tract sample with S. aureus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Objective</td>
<td>Determine if absence of MRSA nasal colonization can predict absence of MRSA in lower respiratory tract secretions</td>
</tr>
<tr>
<td>Patients</td>
<td>ICU: 68.1% Mortality: 30.6% MRSA colonization: 38.9%</td>
</tr>
<tr>
<td>Results</td>
<td>PPV: 93.3% Sensitivity: 93.3% NPV: 95.2% Specificity: 95.2% 2 (4.8%) patients with negative PCR and positive cultures</td>
</tr>
<tr>
<td>Limitations</td>
<td>Excluded hospital acquired pneumonias High MRSA colonization High mortality not explained</td>
</tr>
</tbody>
</table>
**HCAP & CAP Data**

**Study Type**
Retrospective cohort of 165 MICU patients

**Objective**
Correlation between MRSA nasal swab and MRSA lower respiratory tract infection

**Intervention**
Nasal swab + respiratory culture within 24 hours of admission

**Patients**
HCAP risk factor(s): 44.8%  
CAP: 55.2%
MRSA colonization: 17%

**Results**
PPV: 28.6%  
Sensitivity: 80%  
NPV: 98.5%  
Specificity: 87.1%
- 2 (1.2%) patients with negative swab and positive cultures

**Limitations**
- No hospital acquired pneumonias
- Chromogenic agar
- Poor patient descriptions


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**More HCAP & CAP Data**

**Study Type**
Retrospective cohort of 200 ICU & intermediate care patients with clinically confirmed pneumonia

**Objective**
Concordance between nasal PCR and respiratory cultures

**Patients**
CAP: 52.5%  
HCAP: 44%  
HAP/VAP: 3.5%
MRSA colonization: 27.5%

**Results**
PPV: 34.5%  
Sensitivity: 90.5%  
NPV: 98.6%  
Specificity: 79.9%
- 2 (1.4%) patients with negative swab and positive cultures
- 2 potentially preventable antibiotic days of therapy per patient

**Limitations**
- Few nosocomial pneumonias


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**The Latest Data**

**Study Type**
Retrospective study of 400 ICU patients with nosocomial pneumonia

**Objective**
Determine diagnostic performance characteristics of MRSA nasal PCR for prediction of MRSA pneumonia in critically ill

**Intervention**
Inservice presentations to ICU providers regarding MRSA nasal PCR as antimicrobial stewardship tool

**Patients**
HAP: 18%  
HCAP: 54%  
VAP: 28%
MRSA colonization: 22.8%

**Results**
PPV: 37.36%  
Sensitivity: 91.89%  
NPV: 99.03%  
Specificity: 84.3%
After 4th culture, NPV = 87.5%
Vancomycin de-escalated based on negative MRSA PCR: 42%


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**Summary of Trials**

<table>
<thead>
<tr>
<th></th>
<th>PPV</th>
<th>NPV</th>
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<tbody>
<tr>
<td>Chan et al.</td>
<td>48.1%</td>
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<td>Rimawi et al.</td>
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<td>Dangerfield et al.</td>
<td>35.4%</td>
<td>99.2%</td>
</tr>
<tr>
<td>Johnson et al.</td>
<td>93.3%</td>
<td>95.2%</td>
</tr>
<tr>
<td>Tilahun et al.</td>
<td>28.6%</td>
<td>98.5%</td>
</tr>
<tr>
<td>Giancola et al.</td>
<td>34.5%</td>
<td>98.6%</td>
</tr>
<tr>
<td>Smith et al.</td>
<td>37.4%</td>
<td>99%</td>
</tr>
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**Risks of Unnecessary Vancomycin**

- Vancomycin resistance (ex: VRE)
- Nephrotoxicity
- Adverse reactions
- Trough monitoring & costs

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**Patient Case, cont.**

- Upon admission, DW received a nasal swab to screen for MRSA colonization
- On day 2, DW’s MRSA nasal swab returns as negative
- On day 3, DW is much improved
- Sputum culture grows normal flora
Assessment

Based on DW’s improving condition and negative MRSA nasal swab, which of the following would you recommend?

A. Addition of second anti-MRSA agent
B. Continue current therapy
C. Convert to oral vancomycin
D. Discontinue vancomycin

Evidence Summary

• Majority of data in ICU patients with HCAP and CAP
• Negative MRSA nasal swabs show high NPV for MRSA pneumonia
  – Potential to use as antimicrobial stewardship tool

Impact of provider education on methicillin-resistant Staphylococcus aureus nasal swabs and antibiotic de-escalation

Tyson E. Dietrich, PharmD; Natalie R. Tucker, PharmD; Alexis L. Kasniunas, PharmD; Brandi D. Strader, PharmD, BCPS

Purpose

Evaluate the impact of MRSA nasal swabs as an antimicrobial stewardship instrument to assist with the de-escalation of empiric vancomycin coverage in the ICU

Study Site

• HSHS St. John’s Hospital
  – Regional acute care medical center
  – Springfield, IL

• 38 Bed ICU
  – Closed unit
  – Providers ➔ physicians/nurse practitioner/pharmacists(n=10)

Study Design

• Quasi-experimental pilot study
  – Initial phase
    • Pre-education electronic medical record review
      – November 1, 2014 to February 28, 2015
  – Intervention phase
    • Education of ICU providers
      – November 2016
  – Final phase
    • Post-education electronic medical record review
      – December 1, 2016 to February 28, 2017
Patient Criteria

Inclusion
- ≥18 years of age
- ICU patients
- Confirmed pneumonia
- MRSA nasal swab within 48 hours of ICU admission
- Vancomycin use
- *HSHS provider overseeing the care of the patient

Exclusion
- Concomitant infections requiring MRSA coverage
- Pregnancy

* Retrospective evaluated all ICU providers
  - Southern Illinois University
  - Springfield Clinic

Outcomes

- Primary
  - Time to de-escalation of empiric vancomycin therapy
- Secondary
  - PPV and NPV of MRSA PCR
  - Development of MRSA pneumonia
  - Provider acceptance
  - Mortality

Provider Education

- Impact can vary depending on delivery
  - Ex. Didactic vs. interactive

- Davis et al.
  - Using both interactive and didactic methods were associated with a positive effect on practice
  - SES = 0.67 (95% CI, 0.01-1.45)

Education Intervention

- Comprehensive and summary handout
- Background
  - HAP/VAP 2016 guidelines
  - NPV/PPV of MRSA nasal PCR
  - De-escalation
- Small group
  - 10-15 minutes
  - 1:1 or 1:2

Statistics

- Descriptive
- Inferential
  - Two tailed t-test
- Power analysis
  - 80% power = 17 patients per group
- P-value ≤ 0.05

Results
**Pre-education**

- 53 patients identified
- Exclusions:
  - Other infection (n=15)
  - Pre-operative/one time dose (n=11)
  - No swab (n=3)
  - Vancomycin after MRSA PCR (n=3)
  - No ICU provider (n=3)
  - Vancomycin started post-ICU (n=1)
- Median Age, years (IQR): 65 (51-81)
- Male: 11 (65%)
- Median APACHE II (IQR): 19 (16-22)
- Underlying Lung Disease: 7 (41%)
- History of MRSA: 1 (6%)
- Mechanical Ventilation: 13 (76%)
- HSHS Provider: 5 (29%)
- Pneumonia Classification: CAP 5 (29%), HCAP 7 (41%), HAP 4 (24%), VAP 1 (6%)
- Median Time to PCR Collection (IQR): 0 (0-12)
- Median Time to PCR Result (IQR): 22 (11-26)
- Time to De-escalation:
  - Median Hours of MRSA Coverage After Swab Result (IQR): 101 (49-178) 38 (23-59)
  - Excluding Outliers:
    - Median Hours of MRSA Coverage After Swab Result (IQR): 85 (48-151) 38 (24-65)
  - Median Hours of MRSA Coverage (IQR): 168 (72-202) 48 (35-99)
- Predictive Value of MRSA Nasal Swab for MRSA Pneumonia:
  - Positive: 35%
  - Negative: 65%
  - Provider Surveys:
    - To gage interest/involvement
    - Initial
      - Given immediately after education
    - Follow-up
      - Given 1 month after education
    - Responses
      - Strongly agree - agree - neutral - disagree - strongly disagree

**Post-education**

- 51 patients identified
- Exclusions:
  - Not HSHS provider (n=24)
  - Other infection (n=4)
  - Pre-operative/one time dose (n=6)
  - Vancomycin started post-ICU (n=2)
  - Vancomycin DC post ICU (n=1)
- Median Age, years (IQR): 67 (60-72)
- Male: 8 (57%)
- Median APACHE II (IQR): 20 (12-23)
- Underlying Lung Disease: 10 (71%)
- History of MRSA: 1 (7%)
- Mechanical Ventilation: 8 (57%)
- HSHS Provider: 14 (100%)
- Pneumonia Classification: CAP 7 (50%), HCAP 5 (36%), HAP 2 (14%), VAP 0 (0%)
- Median Time to PCR Collection (IQR): 0 (0)
- Median Time to PCR Result (IQR): 14 (10-20)
- Time to De-escalation:
  - Median Hours of MRSA Coverage After Swab Result (IQR): 38 (23-59)
  - Excluding Outliers:
    - Median Hours of MRSA Coverage After Swab Result (IQR): 38 (24-65)
  - Median Hours of MRSA Coverage (IQR): 48 (35-99)
- Provider Acceptance - Survey 1:
  - Found the information regarding MRSA nasal swabs as a de-escalation tool useful
    - Agreed
  - Comfortable with implementing MRSA nasal swab in my practice
    - Agreed
  - Will be implementing MRSA nasal swab in my practice
    - Agreed
  - Already incorporated the use MRSA nasal swabs into my current practice
    - Neutral
  - Typically wait for cultures to be finalized before de-escalation
    - Agreed
Provider Acceptance - Survey 2

- Using the education provided to help with de-escalation
  - Agreed

- Comfortable with implementing MRSA nasal swab in my practice
  - Agreed

Mortality and Development of MRSA Pneumonia

- No patient in either group developed MRSA pneumonia post de-escalation

- Mortality
  - 11/17 (65%) pre-education vs. 2/14 (14%) post-education (p=0.003)

Assessment Question

TH was admitted to your ICU 48 hours ago for respiratory failure and suspected pneumonia. His MRSA nasal swab is positive and cultures are still pending.

True or False

Based on his MRSA PCR result, antibiotics should continue because he will likely have MRSA pneumonia.

Limitations

- Differing provider groups
- Single center
  - Limits external validity
- Low patient numbers
- Potential for bias
- New guidelines
  - 2016 HAP/VAP guidelines

Conclusion

- Consistent with literature
  - PPV = 50%
  - NPV = 96%
- No development of MRSA pneumonia after de-escalation
- High provider acceptance
- MRSA nasal swabs can play a significant role in de-escalation

Future Implications

- Growth of MRSA nasal swab use
  - NOT just in “high risk” patients
  - Pharmacist interventions

- Expansion of education

- Continued data collection
  - Cost analysis
  - Patient harm
Methicillin-Resistant
*Staphylococcus aureus*
Nasal Swabs as a Tool in
Antimicrobial Stewardship

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