Decolonization and Prophylaxis for *S. aureus* (MR&SSA) Infection Prevention in Surgical Patients

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Seattle, WA
**S. Aureus Nasal Carriage**

Persistent carriers 20%
   Always carry one strain of S. aureus

Intermittent carriers 60%
   Carry different strains of S. aureus intermittently

Noncarriers 20%

# S. Aureus Nasal Carriage Usual Prevalence

<table>
<thead>
<tr>
<th>Group</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>General population</td>
<td>37%</td>
</tr>
<tr>
<td>Health care workers</td>
<td>27%</td>
</tr>
<tr>
<td>Patients on adm</td>
<td>36%</td>
</tr>
<tr>
<td>Patients with IDDM</td>
<td>56%</td>
</tr>
<tr>
<td>Hemodialysis patients</td>
<td>52%</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>21%</td>
</tr>
<tr>
<td>I.V. drug users</td>
<td>55%</td>
</tr>
</tbody>
</table>

Nasal Colonization and *S. aureus* SSI

<table>
<thead>
<tr>
<th>Colony Count</th>
<th>N</th>
<th>Percent of Carriers</th>
<th>Infection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>345</td>
<td>--</td>
<td>8%</td>
</tr>
<tr>
<td>&lt; $10^3$</td>
<td>14</td>
<td>13%</td>
<td>7%</td>
</tr>
<tr>
<td>&gt; $10^3$</td>
<td>92</td>
<td>87%</td>
<td>21%</td>
</tr>
</tbody>
</table>

White. AAC 1963; 161: 667-70
### Nasal Colonization and S. aureus SSI – Ortho Implants

<table>
<thead>
<tr>
<th>Nares Culture</th>
<th>N</th>
<th>Infection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neg</td>
<td>199</td>
<td>3 (1.5%)</td>
</tr>
<tr>
<td>Pos</td>
<td>73 (27%)</td>
<td>6 (8%)</td>
</tr>
<tr>
<td>- Heavy</td>
<td>63%</td>
<td></td>
</tr>
<tr>
<td>- Light</td>
<td>37%</td>
<td></td>
</tr>
</tbody>
</table>

Multivariate analysis – only heavy colonization was significantly associated with Staph infection (p=0.002)

Kalmeijer. ICHE 2000; 21: 319-23
Mupirocin for Eliminating *S. aureus* Nasal Colonization

Mupirocin nasal application twice daily (444 carriers):

- 3-5 doses: 83% elimination
- 6 doses: 93% elimination
- Placebo: no elimination

Perl. NEJM 2002;346:1871-7
Nasal Colonization with *S. aureus*

Risk of *S. aureus* SSI in patients with nasal colonization:

- Mupirocin: 3.7%
- Placebo: 5.9%

Odds ratio: 0.49 (0.25 – 0.92)

*p* = 0.02

Perl. NEJM 2002;346:1871-7
Mupirocin vs Control to Prevent *S. aureus* SSI in Carriers

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Mupirocin n/N</th>
<th>Control n/N</th>
<th>Risk Ratio M-H,Fixed,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Garcia 2003</td>
<td>1/31</td>
<td>3/34</td>
<td></td>
</tr>
<tr>
<td>Kalmeijer 2002</td>
<td>2/95</td>
<td>5/86</td>
<td></td>
</tr>
<tr>
<td>Konvalinka 2006</td>
<td>5/130</td>
<td>4/127</td>
<td></td>
</tr>
<tr>
<td>Perl 2002</td>
<td>16/432</td>
<td>26/439</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>688</strong></td>
<td><strong>686</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 24 (Mupirocin), 38 (Control)
Heterogeneity: Chi² = 1.69, df = 3 (P = 0.64); I² = 0.0%
Test for overall effect: Z = 1.79 (P = 0.073)

0.63 [ 0.38, 1.04 ]

Van Rijen. Cochrane Review, 2009, Issue 1
Mupirocin vs Control to Prevent S. aureus Nosocomial Infections in Carriers

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Mupirocin n/N</th>
<th>Control n/N</th>
<th>Risk Ratio M-H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boelaert 1989</td>
<td>1/17</td>
<td>6/18</td>
<td></td>
</tr>
<tr>
<td>Garcia 2003</td>
<td>1/31</td>
<td>3/34</td>
<td></td>
</tr>
<tr>
<td>Harbarth 1999</td>
<td>3/48</td>
<td>7/50</td>
<td></td>
</tr>
<tr>
<td>Kalmeijer 2002</td>
<td>2/95</td>
<td>5/86</td>
<td></td>
</tr>
<tr>
<td>Konvalinka 2006</td>
<td>5/130</td>
<td>4/127</td>
<td></td>
</tr>
<tr>
<td>Mup Study Group 1996</td>
<td>32/134</td>
<td>68/133</td>
<td></td>
</tr>
<tr>
<td>Perl 2002</td>
<td>17/430</td>
<td>34/439</td>
<td></td>
</tr>
<tr>
<td>Wertheim 2004b</td>
<td>21/793</td>
<td>23/809</td>
<td></td>
</tr>
</tbody>
</table>

**Total (95% CI)**

<table>
<thead>
<tr>
<th></th>
<th>Mupirocin</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events</td>
<td>1678</td>
<td>1696</td>
</tr>
</tbody>
</table>

Total events: 82 (Mupirocin), 150 (Control)
Heterogeneity: Chi² = 7.24, df = 7 (P = 0.40); I² = 3%
Test for overall effect: Z = 4.77 (P < 0.00001)

0.55 [ 0.43, 0.70 ]

Van Rijen. Cochrane Review, 2009, Issue 1
Effectiveness of Eradication in S. aureus Positive Patients

- 5 Hospitals
- 6771 patients screened
- 1270 (18.8%) positive for S. aureus
- 917 randomized to eradication or no eradication

Bode. NEJM 2010; 362: 9-17
Effectiveness of Eradication in *S. aureus* Positive Patients

- Mupirocin ointment applied to nares twice daily for 5 days
- Chlorhexidine gluconate soap (Hibiclens) used on entire body once daily for 5 days

Bode. NEJM 2010; 362: 9-17
# Effectiveness of Eradication in *S. aureus* Positive Patients

<table>
<thead>
<tr>
<th></th>
<th>Mup/CHG</th>
<th>Cont</th>
<th>RR (95% Conf Int)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>504</td>
<td>413</td>
<td></td>
</tr>
<tr>
<td>Any <em>S. aureus</em> infect</td>
<td>17 (3.4%)</td>
<td>32 (7.7%)</td>
<td>0.42 (0.23-0.75)</td>
</tr>
<tr>
<td>Surgical patients</td>
<td>441</td>
<td>367</td>
<td></td>
</tr>
<tr>
<td>Deep SSI</td>
<td>4 (0.9%)</td>
<td>16 (4.4%)</td>
<td>0.21 (0.07-0.62)</td>
</tr>
<tr>
<td>Superficial SSI</td>
<td>7 (1.6%)</td>
<td>13 (3.5%)</td>
<td>0.45 (0.18-1.11)</td>
</tr>
<tr>
<td>Any SSI</td>
<td>11 (2.5%)</td>
<td>29 (7.95)</td>
<td>0.32 (0.16-0.62)</td>
</tr>
</tbody>
</table>

**NOT ADDRESSED:** How long before surgery to start. What to do with patients who require operation immediately.

Bode. NEJM 2010; 362: 9-17
Effectiveness of Eradication in *S. aureus* Positive Patients

- 90% of the surgical patients were admitted the day before operation and received one or two decolonization treatments prior to the operation.

- Decolonization treatments were then continued for a duration of five days.

- Most of the remaining 10% of patients were operated at some later time.

Effectiveness of Eradication in S. aureus Positive Patients

- Number needed to screen to prevent one S. aureus infection = 250
- Number of carriers needed to treat to prevent one S. aureus infection = 23

Bode. NEJM 2010; 362: 9-17
S. aureus eradication?

So, should we just treat every surgical patient with mupirocin?
Low Level Mupirocin Resistance and Genotypic Chlorhexidine Resistance
Effect on MRSA Persistence

Mupirocin MIC

Sensitive \( \leq 4 \text{ mg/L} \)
Low-level resistance \( 8-256 \text{ mg/L} \)
High-level resistance \( \geq 512 \text{ mg/L} \)

CHG resistance
2-4-fold increase in MIC

Low Level Mupirocin Resistance and Genotypic Chlorhexidine Resistance Effect on MRSA Persistence

- Univ Geneva Hospitals has had an MRSA decolonization program since 1999
- Mupirocin resistance has increased from 9% to 81% in 2008
- 99% of resistant MRSA have low level resistance

Low Level Mupirocin Resistance and Genotypic Chlorhexidine Resistance Effect on MRSA Persistence

- 75 patients were found who had persistence or recurrence of MRSA after decolonization = decolonization failure
- These were matched with patients who did not have persistence

Low Level Mupirocin Resistance and Genotypic Chlorhexidine Resistance
Independent Risk Factors for Decolonization Failure

O.R.

Combined mupirocin & CHG resistance 3.4
Age (per 1-year increase) 1.04
Prior hospitalization (2 years) 2.4
Wound or pressure sore 5.7
Exposure to MRSA-inactive antibiotic 3.1
Central venous catheterization 5.7

All elective orthopedic surgery patients since January 2005 undergo MRSA screening (nose, throat, and groin)

All positive cases get a five-day decolonization program (mupirocin/fusidic acid with polymyxin nasally three-times daily for 5 days; CHG bodywash for 5 days)

Can’t go to surgery until MRSA screen negative

Must be admitted for operation within 3 months of negative screen

MRSA Colonization and subsequent Risk of Infection


All operated patients received cefuroxime as their prophylactic antibiotic.

Odds of a SSI were markedly increased in patients who were MRSA screen positive:
- OR 7.06 total hip
- OR 18.65 total knee

Fig. 1
## Vancomycin vs Cefazolin Prophylaxis in a Cardiac Surgery Unit with High Prevalence of MRSA

<table>
<thead>
<tr>
<th></th>
<th>Cefaz (433)</th>
<th>Vanco (452)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSI, any</td>
<td>39 (9.0%)</td>
<td>43 (9.5%)</td>
</tr>
<tr>
<td>SSI 2º to MSSA</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>SSI 2º to MRSA</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>SSI 2º to Gram neg rods</td>
<td>20</td>
<td>21</td>
</tr>
<tr>
<td>BSI, any</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>BSI 2º to MSSA</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>BSI 2º to MRSA</td>
<td>4</td>
<td>2</td>
</tr>
</tbody>
</table>

Vancomycin vs B-lactam Prophylaxis in Cardiac Surgery and Arthroplasty
22,549 Procedures in Victoria, Australia

Adjusted Odds Ratio for any SSI

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proc. Duration, min</td>
<td>1.003</td>
<td>1.002-1.004</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASA score &gt; 3</td>
<td>1.71</td>
<td>1.42-2.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vancomycin proph</td>
<td>1.40</td>
<td>1.02-1.93</td>
<td>0.04</td>
</tr>
</tbody>
</table>

### Vancomycin vs B-Lactam Prophylaxis in Cardiac Surgery and Arthroplasty

22,549 Procedures in Victoria, Australia

#### Adjusted Odds Ratio for SSI with MSSA

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
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<td>Proc. Duration, min</td>
<td>1.003</td>
<td>1.002-1.004</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASA score &gt; 3</td>
<td>1.89</td>
<td>1.30-2.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Vancomycin proph</td>
<td>2.79</td>
<td>1.60-4.87</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Glycopeptides and MRSA

Studies evaluated between 1990 and 2008

Only 14 trials met inclusion criteria – too heterogeneous for a meta-analysis

Only one of the 12 trials that reported 30-day SSI rates showed that glycopeptides reduced infection rates as compared to non-glycopeptides

Only two trials reported MRSA infection and neither found a reduction in infection rates

Findings consistent with prior study by Bolon et al (Clin Infect Dis. 2004) that there is no evidence that glycopeptides are more effective than beta-lactams for prophylaxis of SSI.

Many trials reviewed were small, poor quality, or both.

Glycopeptide versus Non-Glycopeptide Outcome – 30-day SSI Rate

Conclusion: This systematic review did not find any evidence to support the use of glycopeptides in preference to other antibiotics for the prevention of MRSA infections and SSIs. The limitations of the evidence make it difficult to identify a threshold at which a switch from non-glycopeptide to glycopeptide prophylaxis should be recommended.
High risk for MRSA defined as: 1) Coming from setting with high endemic rates of MRSA; 2) From extended care facility or nursing home; 3) On dialysis; 4) Prior history of MRSA colonization/infection; 5) IV drug abuse; 6) Transferred from acute care where residing >48 hours; 7) Requiring chronic wound care; 8) Patient undergoing valve surgery.

*May use Cefuroxime instead of Cefazolin when indicated.
New Prophylaxis Guidelines from ASHP/SIS/IDSA/SHEA

For patients at risk for MRSA infection use:

Vancomycin
and
Cefazolin

Bratzler. Am J Health Syst Pharm 2013;70:195-283
Who do you screen?

Patient characteristics

- Obesity
- Age
- Diabetes
- Immune suppression
Who do you screen?

Patient history

- Prior colonization
- Prior infection
- Dialysis
- Open wounds
- History of IV drug use
- Recently in hospital (how recent?)
- Recently in long-term care facility (how recent?)
- Received antibiotics within ___ days
- Other
Who do you screen?

Specific operative procedure

- Median sternotomy
- Arthroplasty
- Implantation of prosthetic device (mesh, pacemaker, screws, etc)
- Other
What site do you screen?

- Nares*
- Throat*
- Axilla
- Perineum
- Open wounds*
- Some combination of the above
For what organisms do you screen?

- MRSA
- MSSA
- MDRO
How do you screen?

- PCR
- Agar
- Other
When do you screen?

- How early is too early?
- How late is too late to do anything with the information?
Should Screening Depend on Incidence of MRSA?

• Is there a level of MRSA in the community that should lead to screening all patients?

• If so should this level be % of patients with SSI secondary to MRSA or proportion of *S. aureus* that are MRSA in the entire community?
Is It “Cost Effective” to Screen for MRSA, MSSA, Other?

• Screen all – Treat positives
• Screen as many as you can – Treat positives or
• Treat positives and those you couldn’t screen
• Treat everyone – Don’t bother to screen
Should We Worry About Resistance to Mupirocin and/or Chlorhexidine?

Will extensive use of mupirocin and CHG lead to increased resistance and loss of efficacy for those who need it the most?
Nasal Mupirocin vs. Povidone Iodine, both with CHG in Spine and Arthroplasty Patients

Deep SSI

Mupirocin (n=761)  5  (0.7%)
Pov Iod (n=776)  0

PreOp S.A. colonization associated with S.A. SSI (p=0.002)

Phillips. ID Week 2012. Abstract LB3