Do Staphylococcal Decolonization Strategies Work?
Dr. Andrew Simor, University of Toronto
A Webber Training Teleclass

Do Staphylococcal Decolonization Strategies Work?

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University of Toronto, Toronto, ON

Hosted by Nicole Kenny

www.webbertraining.com

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I have no disclosures to make with regards to this presentation.

Objectives

• to understand the rationale for staphylococcal decolonization
• to review evidence for decolonization as a strategy for staphylococcal infection prevention
• to consider recommendations for S. aureus decolonization

S. aureus Colonization

• major ecologic niche is the anterior nares
• other sites may include pharynx, axillae, perineum, skin lesions or wounds

Prevalence of S. aureus Nasal Colonization, 2003-04

<table>
<thead>
<tr>
<th>Carriage</th>
<th>S. aureus</th>
<th>MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence (%)</td>
<td>28.6</td>
<td>1.5</td>
</tr>
<tr>
<td>Estimated no. (in millions)</td>
<td>78.9</td>
<td>4.1</td>
</tr>
</tbody>
</table>


S. aureus Nasal Carriage

<table>
<thead>
<tr>
<th>Carriage</th>
<th>% (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Persistent</td>
<td>20 (12-30)</td>
</tr>
<tr>
<td>Intermittent</td>
<td>30 (16-70)</td>
</tr>
<tr>
<td>Non-carriers</td>
<td>50 (16-69)</td>
</tr>
</tbody>
</table>


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**S. aureus Colonization Risk Factors**
- chronic skin conditions (atopic)
- diabetes mellitus (insulin)
- dialysis
- IVDU
- HIV

**Significance of S. aureus Nasal Carriage**
Nasal carriage of *S. aureus* is a risk for infection in hospital (usually same strain):
- nosocomial bacteremia (RR 30; 95% CI 2.9-4.7) (von Eiff, NEJM 2001; Wertheim, Lancet 2004)
- BSI, exit site infection in dialysis patients (Luzar, NEJM 1990; Kluytmans, ICHE 1996)
- SSI (2-9 X increased risk) (Kluytmans, JID 1995; Perl, NEJM 2002; Kamejaj, CID 2002)
- ICU-acquired infection (2-5 X increased risk) (Honda, ICHE 2010)

**Significance of MRSA Colonization**
Colonization with MRSA associated with a greater risk of subsequent infection:
- Nasal carriers of MRSA 3.9 times more likely to develop nosocomial staphylococcal bacteremia than were MSSA carriers (Pujol, Am J Med 1996)
- MRSA colonization at ICU admission associated with higher risk of ICU-acquired *S. aureus* (MRSA) infection; RR 4.1 (Honda, Infect Control Hosp Epidemiol 2010)

**Risk of MRSA Colonization Becoming an Infection**
- 60 of 209 (29%) adults with newly identified colonization developed a subsequent MRSA infection during 18 months of follow-up (Huang, CID 2003)
- 8 of 38 (21%) with newly identified colonization developed MRSA infection in 1 year of follow-up (Davis, CID 2004)

**Decolonization**
treatment to eradicate staphylococcal carriage

**S. aureus Decolonization**

- **Topical Agents**
  - mupirocin
  - bacitracin
  - triclosan
  - chlorhexidine
  - retapamulin
  - lysostaphin
  - tea tree oil
  - bacterial interference
  - *S. aureus* 502A

- **Systemic Agents**
  - rifampin
  - TMP/SMX
  - ciprofloxacin
  - tetracyclines
  - novobiocin
  - vancomycin

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Reasons to Consider Staphylococcal Decolonization

1. to prevent infection in a colonized patient (MSSA/MRSA)
2. to prevent transmission (primarily MRSA) to others

MRSA Decolonization

<table>
<thead>
<tr>
<th>short-term</th>
<th>long-term</th>
</tr>
</thead>
<tbody>
<tr>
<td>surgery</td>
<td>dialysis</td>
</tr>
<tr>
<td>? ICU</td>
<td>recurrent SSTI</td>
</tr>
<tr>
<td>infection control</td>
<td></td>
</tr>
</tbody>
</table>

S. aureus Decolonization

- surgical patients
- non-surgical patients
- ICU patients
- dialysis patients
- recurrent SSTIs
- MRSA decolonization

Mupirocin for S. aureus Decolonization in HCWs

MSSA
Reagan, Ann Intern Med 1991
Doebbeling, Clin Infect Dis 1993
Fernandez, J Antimicrob Chemother 1995

MRSA
Casewell, J Antimicrobial Chemother 1986
Scully, Arch Intern Med 1992

Staphylococcal Decolonization – Surgical Patients

- ↓ S. aureus carriage in CHG-treated group
- ↓ nosocomial infections, esp. LRTI and deep SSI (20% vs 26%; ARR 6.2%; 95% CI 1.1-11.7; p=0.002)

Segers, JAMA 2006

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Mupirocin Surgical Prophylaxis

- in most RCTs, peri-operative mupirocin had no effect on SSI or *S. aureus* SSI rates  

Mupirocin Surgical Prophylaxis - RCTs

<table>
<thead>
<tr>
<th>Reference; All SSI (%)</th>
<th>S. aureus SSI (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery (No.)</td>
<td>mupirocin</td>
</tr>
<tr>
<td>1 elective (3,864)</td>
<td>7.9</td>
</tr>
<tr>
<td>2 orthopedic (614)</td>
<td>3.8</td>
</tr>
<tr>
<td>3 G.I. (395)</td>
<td>14.5</td>
</tr>
<tr>
<td>4 cardiac (263)*</td>
<td>13.8</td>
</tr>
<tr>
<td>5 CV, GI, ortho(808)*</td>
<td>2.5</td>
</tr>
</tbody>
</table>

* all *S. aureus* carriers

Mupirocin Surgical Prophylaxis

808 surgical patients

<table>
<thead>
<tr>
<th>441 Mup-CHG</th>
<th>367 placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>RR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>4 (0.9)</td>
<td>deep SSI</td>
</tr>
<tr>
<td>7 (1.6)</td>
<td>superficial SSI</td>
</tr>
<tr>
<td>6 (1.2)</td>
<td>other infection</td>
</tr>
</tbody>
</table>

Bode, N Engl J Med 2010

Mupirocin to Prevent Infections in non-Surgical Patients (RCTs)

<table>
<thead>
<tr>
<th>Reference (No.)</th>
<th>Patients</th>
<th>Infection rate (%)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mupirocin</td>
<td>placebo</td>
<td></td>
</tr>
<tr>
<td>1 (1,627)</td>
<td>colonized inpatients, the Netherlands</td>
<td>2.6</td>
<td>2.8</td>
</tr>
<tr>
<td>2 (98)</td>
<td>MRSA inpatients, Geneva</td>
<td>1.5</td>
<td>2.8</td>
</tr>
<tr>
<td>3 (127)</td>
<td>colonized LTCF, USA 50% MRSA</td>
<td>5</td>
<td>15</td>
</tr>
</tbody>
</table>


Study Limitations

- real-time PCR for prompt initiation of intervention  
- no MRSA (all MSSA)  
- decreased *S. aureus* SSI rates, but no data on overall SSI rates

Bode, N Engl J Med 2010

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S. aureus Decolonization - ICU

- quasi-experimental before-after study, medical ICU; real-time PCR screening; mupirocin + CHG baths
- ICU-acquired S. aureus infections decreased: 3.5 to 1.3 per 1,000 pt-days (RR 0.37, 95% CI 0.14-0.90)

Fraser, Infect Control Hosp Epidemiol 2010

MRSA in the ICU

Prevalence of MRSA on admission to ICU:
8% (range: 5-20%)

Rate of MRSA acquisition in ICU:
5% (range: 2-12%)

1 Lucet, Arch Intern Med 2003; Huang, J Infect Dis 2007; Ridenour, Infect Control Hosp Epidemiol 2007

MRSA Decolonization in the ICU

- Before-after observational studies in ICUs and NICUs using mupirocin and/or CHG body wash have shown reduced MRSA infection rates
(Muller, Crit Care 2005; Sandh, Infect Control Hosp Epidemiol 2006; Ridenour, Infect Control Hosp Epidemiol 2007; Milstone, Infect Control Hosp Epidemiol 2010; Batra, Clin Infect Dis 2010)

MRSA Decolonization

- A cluster randomized trial to prevent MRSA infections in ICUs (45 hospitals):
  - ASC + Contact Precautions
  - ASC + Precautions + Decolonization
  - Universal decolonization

Platt, Medical Care 2010

Staphylococcal Decolonization - Dialysis Patients

Meta-analysis: Mupirocin Prophylaxis in Dialysis Patients

↓ 78% S. aureus BSI
↓ 66% S. aureus peritonitis

Tacconelli, Clin Infect Dis 2003

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### S. aureus Decolonization in Hemodialysis (RCTs)

<table>
<thead>
<tr>
<th>Reference (No.)</th>
<th>Treatment</th>
<th>S. aureus infections</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (44)</td>
<td>RFP + Bac</td>
<td>11.1%</td>
<td>0.61 (0.41-0.90)</td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>46.2%</td>
<td></td>
</tr>
<tr>
<td>2 (34)</td>
<td>Mupirocin</td>
<td>1.0/100 mos</td>
<td>0.24 (0.03-1.9)</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>4.1/100 mos</td>
<td></td>
</tr>
<tr>
<td>3 (36)</td>
<td>Mupirocin</td>
<td>0.35/1000days</td>
<td>0.06 (0.01-0.46)</td>
</tr>
<tr>
<td></td>
<td>None</td>
<td>5.95/1000days</td>
<td></td>
</tr>
</tbody>
</table>


### S. aureus Decolonization in Peritoneal Dialysis (RCTs)

<table>
<thead>
<tr>
<th>Reference (No.)</th>
<th>Treatment</th>
<th>S. aureus infections</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (267)</td>
<td>Mupirocin</td>
<td>0.1/100 mos</td>
<td>0.66 (0.47-0.92)</td>
</tr>
<tr>
<td></td>
<td>Placebo</td>
<td>0.2/100 mos</td>
<td></td>
</tr>
<tr>
<td>2 (133)</td>
<td>Mupirocin</td>
<td>0.52/pt-yr 0.34/pt-yr</td>
<td>P=0.03</td>
</tr>
<tr>
<td></td>
<td>Gentamicin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*overall peritonitis rates*


### Use of Mupirocin + Antiseptics in a Furunculosis Outbreak due to Methicillin-Susceptible S. aureus (PVL+)

Wiese-Posselt, Clin Infect Dis 2007

### Failure of Mupirocin Decolonization in a CA-MRSA Outbreak

- CA-MRSA outbreak among members of a high school football team
- only 36% compliance with recommended treatment
- mupirocin failed to prevent subsequent infections

Rihn, Pediatr Infect Dis J 2005

### Mupirocin to Prevent Recurrent SSTIs (RCTs)

<table>
<thead>
<tr>
<th>Reference (No.)</th>
<th>Patients</th>
<th>Infection rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MSSA; monthly treatment X 1 yr</td>
<td>26</td>
</tr>
<tr>
<td>1 (34)</td>
<td>CA-MRSA, military recruits</td>
<td>10.6</td>
</tr>
</tbody>
</table>


MRSA isolated in the abscess

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MRSA Decolonization

• many observational studies with mupirocin or other agents, as part of infection control measures in hospitals and nursing homes
• retrospective observational study, 3 Chicago hospitals, MRSA screening on admission, decolonization at MD’s discretion: transient eradication of MRSA, but no reduced risk of subsequent infection (Robicsek, ICHE 2009)

MRSA Decolonization

“...there is insufficient evidence to support use of topical or systemic antimicrobial therapy for eradicating MRSA”
Loeb, Cochrane Database Syst Rev 2003

MRSA Decolonization

Can decolonization with mupirocin be improved by adding?
• antiseptic body wash (CHG)
• systemic antibiotics (Simor, Clin Infect Dis 2007)
• decolonization of household contacts or hot water laundering of clothes and bedding

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Variables Associated with MRSA Persistence/Re-colonization

<table>
<thead>
<tr>
<th>Variable</th>
<th>Risk</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRSA at &gt;1 site$^1$</td>
<td>HR=1.73</td>
<td>1.04-2.87</td>
<td>0.035</td>
</tr>
<tr>
<td>Fluoroquinolone exposure</td>
<td>HR=1.81</td>
<td>1.01-3.26</td>
<td>0.048</td>
</tr>
<tr>
<td>Mupirocin-resistance$^2$</td>
<td>RR=9.37</td>
<td>2.76-31.87</td>
<td>0.0003</td>
</tr>
<tr>
<td>Decolonization therapy</td>
<td>RR=0.12</td>
<td>0.04-0.36</td>
<td>0.0002</td>
</tr>
<tr>
<td>Residence in a LTCF$^3$</td>
<td>OR=1.8</td>
<td>1.1-3.2</td>
<td>0.03</td>
</tr>
<tr>
<td>Decubitus ulcer</td>
<td>OR=2.3</td>
<td>1.2-4.4</td>
<td>0.01</td>
</tr>
<tr>
<td>Mupirocin-resistance</td>
<td>OR=4.1</td>
<td>1.6-10.7</td>
<td>0.003</td>
</tr>
</tbody>
</table>


Reasons for Failure to Eradicate MRSA Colonization

• use of drugs with marginal activity, or that induce resistance (ciprofloxacin, fusidic acid)
  (Peterson, Arch Intern Med 1990; Chang, Diagn Microbiol Infect Dis 2000)
• intranasal therapy ineffective for GI reservoir of the organism (Bruce, J Clin Microbiol 2005)
• Host factors (skin lesions, catheters, medical devices, comorbidities

Mupirocin Resistance in S. aureus

• mupirocin resistance rates increasing globally, especially in MRSA (Cookson, J Antimicrob Chemother 1998; Yoo, Antimicrob Agents Chemother 2006)
• resistance is associated with extensive mupirocin use (Miller, ICHE 1996; Vasquez, ICHE 2000; Vivoni, ICHE 2005)
• resistance (high-level) associated with treatment failure (Cookson, J Antimicrob Chemother 1998; Walker, ICHE 2002; Simor, Clin Infect Dis 2007)
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### Decolonization Practices among IDSA Members (1)
- IDSA Emerging Infections Network survey, April 2005, to determine decolonization use (483 [57%] responses)
- 17% routine pre-op decolonization of *S. aureus* carriers (63% cardiac surgery); 94% with mupirocin
- 20% MRSA decolonization for infection control (47% in outbreaks; 38% all colonized); 92% with mupirocin

*West, Infect Control Hosp Epidemiol 2007*

### Decolonization Practices among IDSA Members (2)
- 85% used decolonization for patients with recurrent furunculosis due to CA-MRSA
- Most used mupirocin + antiseptic body wash; 55% also used oral antimicrobial agent
- No data on outcome/efficacy

*West, Infect Control Hosp Epidemiol 2007*

### MRSA Decolonization in European ICUs and Surgical Units
- Routine antiseptic washing (eg. chlorhexidine) in 66%
- Routine decolonization with mupirocin in 63%

*Hansen, Infection 2010*

### S. aureus Decolonization Recommendations
- No routine decolonization pre-op or in nonsurgical patients; perhaps consider in surgical patients known to be *S. aureus* carriers
- Consider in dialysis patients, but risk of mupirocin resistance in the long-term

*S. aureus Decolonization Recommendations*

### S. aureus Decolonization Recommendations
- Possibly useful in patients with recurrent skin/soft tissue infection (need more data for CA-MRSA)
- Mupirocin susceptibility testing should be done prior to use for decolonization
- MRSA as an infection control measure needs to be studied; consider in outbreaks or select patients

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