Preventing *Staphylococcus aureus* skin and soft-tissue infections in military trainees

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Infectious Diseases Division
University of Toledo College of Medicine and Life Sciences
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Outline

- Background
- Natural history study
- Targeted mupirocin trial
- IDCRP-001 (Quantico)
- IDCRP-055
- IDCRP-074
- IDCRP-090
- Questions
Objectives

- Describe the efforts of Department of Defense (DoD) researchers to understand the epidemiology and develop effective prevention strategies against staphylococcal skin and soft-tissue infections.

- Describe the opportunities and challenges of working in military recruit populations.
Skin and soft-tissue infections (SSTI)
- 1,600+ hospital admissions in active duty DoD
- 65,000 ambulatory clinic visits for abscess/cellulitis in active duty DoD\(^1\)

Military trainees are at higher risk for SSTI

No. 2 cause of ID hospitalization within first 2 years of service\(^2\)

Estimated $14-32M direct cost to Army
- Estimated $3K/SSTI\(^3\)

Cellulitis - knee
Abscess- knee

Study number: 2155
Date: 5 Nov 2013
Anatomic site: Knee
Community-acquired Methicillin-resistant *Staphylococcus aureus* among Military Recruits

Craig E. Zinderman,* Byron Conner,* Mark A. Malakooti,† James E. LaMar,* Adam Armstrong,‡ and Bruce K. Bohnker†

We report an outbreak of 235 community-acquired methicillin-resistant *Staphylococcus aureus* (MRSA) infections among military recruits. In this unique environment, the close contact between recruits and the physical demands of training may have contributed to the spread of MRSA. Control measures included improved hygiene and aggressive clinical treatment.
Fifteen-Year Study of the Changing Epidemiology of Methicillin-Resistant *Staphylococcus aureus*

Nancy F. Crum, MD, MPH,a Rachel U. Lee, MD,a Scott A. Thornton, MS,b O. Colin Stine, PhD,c Mark R. Wallace, MD,a Chris Barrozo,d Ananda Keefer-Norris,c Sharon Judd, RN,a Kevin L. Russell, MD, MTM&Hd

aInfectious Diseases Division, Naval Medical Center San Diego, San Diego, Calif; bNavy Environmental and Preventive Medicine Unit 6 (NEPMU6), Pearl Harbor, Hawaii; cUniversity of Maryland School of Medicine, Baltimore, Md; dNaval Health Research Center,
Figure 1. Rates of incident diagnoses of cellulitis/abscess, by demographic/military characteristics, active components, U.S. Armed Forces, by calendar year, 2002-2005.
Natural History of Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Colonization and Infection in Soldiers

Michael W. Ellis,¹ Duane R. Hospenthal,¹ David P. Dooley,¹ Paula J. Gray,² and Clinton K. Murray¹

Departments of ¹Medicine and ²Preventive Medicine, Brooke Army Medical Center, Fort Sam Houston, Texas
CA-MRSA Natural History

Infection

812 Participants

CA-MRSA
24 (3%)

- 9 Infections (38%)
  - CA-MRSA abscess - 4
  - Abscess (no culture) - 4
  - Cellulitis - 1

Admissions
CA-MRSA abscess - 1*

MSSA
229 (28%)

- 8 Infections (3%)
  - CA-MRSA abscess - 2
  - Abscess (no culture) - 3
  - Cellulitis - 3

Admissions
CA-MRSA abscess - 1*

No S. aureus
559 (69%)

- 12 Infections (2%)
  - CA-MRSA abscess - 5
  - Abscess (no culture) - 3
  - Cellulitis - 4

Admissions
CA-MRSA abscess - 3*
CA-MRSA abscess - 1
Abscess (no culture) - 1

Targeted Intranasal Mupirocin To Prevent Colonization and Infection by Community-Associated Methicillin-Resistant *Staphylococcus aureus* Strains in Soldiers: a Cluster Randomized Controlled Trial

Michael W. Ellis, Matthew E. Griffith, David P. Dooley, Joseph C. McLean, James H. Jorgensen, Jan E. Patterson, Kepler A. Davis, Joshua S. Hawley, Jason A. Regules, Robert G. Rivard, Paula J. Gray, Julia M. Ceremuga, Mary A. DeJoseph, and Duane R. Hospenthal

Departments of Medicine (Infectious Diseases), Preventive Medicine, and Pathology and Area Laboratory Services, Brooke Army Medical Center, Fort Sam Houston, Texas, and Departments of Pathology and Medicine (Infectious Diseases), University of Texas Health Science Center, San Antonio, Texas
Eligible Screened (n = 3447)

Excluded (n = 3313)
CA-MRSA Not Recovered on Nares Culture (n = 3313)

CA-MRSA Colonized Participants Randomized (n = 134)

Assigned to Placebo Treatment (n = 66)
Received Placebo (n = 62)
Refused Placebo (n = 4)

Lost to Follow-up (n = 1) a
Reason: Removed from Course for Military Discipline Reasons.

Analyzed (n = 65)
Excluded from Analysis (n = 1)
Reason: Lost to Follow-up and did not have Terminal Nares Culture.

Assigned to Mupirocin Treatment (n = 68)
Received Mupirocin (n = 64)
Refused Mupirocin (n = 4)

Lost to Follow-up (n = 2) a
Reasons: Removed from Course for Military Discipline Reasons.

Analyzed (n = 66)
Excluded from Analysis (n = 2)
Reason: Lost to Follow-up and did not have Terminal Nares Culture.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value for group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo</td>
</tr>
<tr>
<td>No. of participants completing follow-up&lt;sup&gt;a&lt;/sup&gt;</td>
<td>65</td>
</tr>
<tr>
<td>No. of infections/no. of participants (%)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>5/65 (7.7)</td>
</tr>
<tr>
<td>Total abscesses</td>
<td>4</td>
</tr>
<tr>
<td>CA-MRSA abscess</td>
<td>2</td>
</tr>
<tr>
<td>MSSA abscess</td>
<td>0</td>
</tr>
<tr>
<td>Abscess not cultured&lt;sup&gt;c&lt;/sup&gt;</td>
<td>2</td>
</tr>
<tr>
<td>Folliculitis</td>
<td>0</td>
</tr>
<tr>
<td>Cellulitis</td>
<td>1</td>
</tr>
<tr>
<td>No. of hospital admissions</td>
<td>0</td>
</tr>
</tbody>
</table>
Infectious Diseases Clinical Research Program (IDCRP)

Mission

Design, conduct, and publish collaborative clinical Infectious Disease research of importance to the DoD and NIAID through an effective research network that rapidly responds to evolving Infectious Diseases threats.
Chlorhexidine-Impregnated Cloths to Prevent Skin and Soft-Tissue Infection in Marine Recruits: A Cluster-Randomized, Double-Blind, Controlled Effectiveness Trial

Timothy J. Whitman, DO; Rachel K. Herlihy, MD, MPH; Carey D. Schlett, MPH; Patrick R. Murray, PhD; Greg A. Grandits, MS; Anuradha Ganesan, MD; Maya Brown, BA; James D. Mancuso, MD, MPH; William B. Adams, MD; David R. Tribble, MD, DrPH
Randomized by Platoon
(n=1562)

Eligible Platoons (n=44)
Recruits (n=2572)

Enrollment

Declined Participation (n=1010)

Randomized by Platoon (n=1562)

Allocated to Chlorhexidine Platoons (n=23)
Recruits (n=781)

Withdrawn from study
Recruits (n=305)

Completed the study (6 weeks)
Recruits (n=486, 62%)

Allocated to Comfort Bath® Platoons (n=21)
Recruits (n=781)

Withdrawn from study
Recruits (n=251)

Completed the study (6 weeks)
Recruits (n=546, 70%)

IDCRP-055:
Evaluating strategies to prevent methicillin-resistant
*Staphylococcus aureus* skin and soft-tissue
infections in military trainees
CONCISE COMMUNICATION

Evaluation of Methicillin-Resistant Staphylococcus aureus Skin and Soft-Tissue Infection Prevention Strategies at a Military Training Center

Stephanie M. Morrison, MPH;¹
Carl R. Blaesing, MS, MPH;² Eugene V. Millar, PhD;³
Uzo Chukwuma, MPH;⁴ Carey D. Schlett, MPH;³
Kenneth J. Wilkins, PhD;³ David R. Tribble, MD, DrPH;³
Michael W. Ellis, MD⁵
Hygiene Strategies to Prevent Methicillin-Resistant *Staphylococcus aureus* Skin and Soft Tissue Infections: A Cluster-Randomized Controlled Trial Among High-Risk Military Trainees

Michael W. Ellis,¹ Carey D. Schlett,² Eugene V. Millar,² Kenneth J. Wilkins,³ Katrina B. Crawford,² Stephanie M. Morrison-Rodriguez,² Laura A. Pacha,⁴ Rachel J. Gorwitz,⁵ Jeffrey B. Lanier,⁶ and David R. Tribble²

¹Department of Medicine and ²Infectious Disease Clinical Research Program, Department of Preventive Medicine and Biometrics, Uniformed Services University of the Health Sciences, ³National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland; ⁴US Army Public Health Command, Army Institute of Public Health, Aberdeen Proving Ground, Maryland; ⁵Centers for Disease Control and Prevention, Atlanta, and ⁶Martin Army Community Hospital, Fort Benning, Georgia
IDCRP-055

Results

Progression of Trainees through the Hygiene-based SSTI Prevention Trial

Eligible
30,209

Randomized by Battalion to Intervention

Study Group

<table>
<thead>
<tr>
<th>Group</th>
<th>Eligible</th>
<th>Developed an SSTI</th>
<th>Lost to Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>9,315</td>
<td>319 (3.4%)</td>
<td>1,160 (12.5%)</td>
</tr>
<tr>
<td>Enhanced Standard</td>
<td>10,864</td>
<td>478 (4.4%)</td>
<td>1,614 (14.9%)</td>
</tr>
<tr>
<td>Chlorhexidine</td>
<td>10,030</td>
<td>485 (4.8%)</td>
<td>1,184 (11.8%)</td>
</tr>
</tbody>
</table>

Attrition

<table>
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<tr>
<th>Group</th>
<th>Lost to Follow-up</th>
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<td>Standard</td>
<td>1,160 (12.5%)</td>
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</tbody>
</table>

Primary Endpoint

<table>
<thead>
<tr>
<th>Group</th>
<th>Developed an SSTI</th>
<th>Declined</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall SSTI 303</td>
<td>319 (3.4%)</td>
<td>16 (5.0%)</td>
</tr>
<tr>
<td>MRSA SSTI 86</td>
<td>303 (28.4%)</td>
<td></td>
</tr>
<tr>
<td>MRSA SSTI 135</td>
<td>439 (30.8%)</td>
<td></td>
</tr>
<tr>
<td>Overall SSTI 461</td>
<td>485 (4.8%)</td>
<td>24 (4.9%)</td>
</tr>
<tr>
<td>MRSA SSTI 95</td>
<td>461 (20.6%)</td>
<td></td>
</tr>
</tbody>
</table>

SSTI: Skin and Soft Tissue Infection; MRSA: methicillin-resistant *Staphylococcus aureus*
Conclusion: Hygiene-based interventions did not prevent overall SSTI and MRSA SSTI

Adapted from Clin Infect Dis. 2014;58: 1540.
Conclusion: Beneficial trend from chlorhexidine against MRSA during summer

Adapted from Clin Infect Dis. 2014;58: 1540.
IDCRP-055
Secondary Objectives and Supplemental Efforts

- Determine impact on *S. aureus* nasal colonization rates
- Describe the molecular characteristics of *S. aureus* study isolates
  - Chlorhexidine resistance
  - Clinical and colonizing strain concordance
- Determine pre-existing humoral immunity to *S. aureus* antigens
- Determine microbiome associated with SSTI and MRSA SSTI
- Evaluate study impact on: acute respiratory illness, and GI illness
- Evaluate cost-effectiveness of hygiene-based strategies
- Assess SSTI knowledge and personal hygiene practices
IDCRP-074

Skin and soft-tissue infection in military trainees: epidemiology and economic burden of disease
Objective: Determine SSTI rates, clinical presentations, outcomes, recurrence rates, and risk factors

Secondary objectives:
- Determine molecular characteristics of S. aureus isolates
- Determine direct medical and indirect costs of S. aureus SSTI

Design: Prospective observational study

Participants: Infantry Trainees

Primary endpoint: Incidence of SSTI and MRSA SSTI

Study period: July 9 2012- Dec 2014
IDCRP-074
Supplemental efforts

- Determine the etiology of nonpurulent SSTI (aspirate)
- Assess humoral immune responses during active SSTI
- Assess cellular immune responses during active SSTI
- Virulence gene expression in SSTI samples
- *S. aureus* colonization among military trainees
- Determine microbiome associated with SSTI and MRSA SSTI
- Determine pre-existing antibodies to staphylococcal and determine whether it is associated with risk of SSTI
IDCRP-090:

Natural history of *Staphylococcus aureus* colonization, infection, and immune response in military trainees
IDCRP-090

S. aureus cohort study

• Study questions:
  • Is there protective immunity to colonization?
  • Is there protective immunity to infection?
  • Is there a protective microbiome?

• Study design:
  • Observational cohort
  • Approximately 600 soldiers (2 company cohorts x 2 summers)
  • Study dates spring/summer 2015-2016
Discussion
Conclusions and future directions

- DoD SSTI prevention efforts
  - Robust
  - Integrated between services-IDCRP
  - Significant contributions
    - Prevention
    - Epidemiology (molecular)
    - Microbiome
    - Immunology

- Fort Benning is a unique and valuable research site
  - Personnel
    - Research staff
    - Research participants
  - Infrastructure
Questions

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