Community Associated MRSA
Dr. Rachel Gorwitz, CDC
A Webber Training Teleclass

Community-Associated MRSA: What’s Up and What’s Next?

Rachel Gorwitz, MD, MPH
Division of Healthcare Quality Promotion
Centers for Disease Control and Prevention

Hosted by Paul Webber
paul@webbertraining.com

Staphylococcus aureus
- Common human colonizer and pathogen throughout history
- Transmitted by direct or indirect contact
- MRSA:
  - 1st described 1960s
  - Resistant to all currently available β-lactam agents (penicillins, cephalosporins)
  - Historically linked to healthcare settings
  - 1990s: Distinct MRSA strains emerged in the community as cause of infection in otherwise healthy people

Community-Associated MRSA
- Defined epidemiologically as MRSA infections with community onset in persons that lack significant healthcare exposure
- Predominantly skin infections
- Transmission associated with:
  - Frequent skin-to-skin contact
  - Compromised skin
  - Sharing contaminated objects / surfaces
  - Crowding
  - Lack of cleanliness
  - Prior antibiotic use
  - Lack of access to healthcare

National Database of MRSA Pulsed-Field Types
(Highlighted PFTs: historically community-associated)

A Single Pulsed-Field Type (USA300) has Accounted for Most Community-Associated MRSA Infections in the U.S.

Learning Objectives
- Describe the changing epidemiology of MRSA in community settings
- Discuss important findings from recent studies of CA-MRSA prevalence, incidence, risk factors, and virulence factors
- Describe emerging antimicrobial resistance in CA-MRSA and discuss implications for clinical management of skin infections
- Identify current and future strategies to prevent CA-MRSA infections

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**CA-MRSA Infections are Mainly Skin Infections**

<table>
<thead>
<tr>
<th>Disease Syndrome</th>
<th>(%)</th>
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<tr>
<td>Skin/soft tissue</td>
<td>1,266 (77%)</td>
</tr>
<tr>
<td>Wound (Traumatic)</td>
<td>157 (10%)</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>64 (4%)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>61 (4%)</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>43 (3%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>31 (2%)</td>
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*Fridkin et al NEJM 2005;352:1436-44*

**MRSA Was the Most Commonly Identified Cause of Purulent Skin Infections Among Adult ED Patients (EMERGEency ID Net), August 2004**

<table>
<thead>
<tr>
<th>Disease Syndrome</th>
<th>(%)</th>
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<tbody>
<tr>
<td>Skin/soft tissue</td>
<td>54%</td>
</tr>
<tr>
<td>Wound (Traumatic)</td>
<td>59%</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>39%</td>
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<tr>
<td>Sinusitis</td>
<td>15%</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>51%</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>74%</td>
</tr>
<tr>
<td>Other</td>
<td>68%</td>
</tr>
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*Moran et al NEJM 2006;355:666-674*

**Increase in Ambulatory Care Visits for Skin Infections Typical of S. aureus**

*LF McCaig et al, APHA 2008*

2005/06: 15.2 million visits annually in the United States

**Increased Emergency Department Visits for Skin Infections Typical of S. aureus**


**Hospitalizations for S. aureus Skin Infections Increasing Dramatically**


*JAMA 2007;298:1763-71*

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Active Bacterial Core Surveillance Areas (Invasive MRSA)

Total Population: ~ 16.3 million

MRSA Case Categorization (ABCs Population-Based Surveillance)
- Healthcare-associated:
  - Hospital-onset: Cases with positive culture obtained >48 hrs after hospital admission (may also have risk factors)
  - Community-onset: Cases with at least 1 of the following risk factors:
    - Invasive device at time of admission; h/o MRSA infection or colonization; h/o surgery, hospitalization, dialysis, or residence in a LTC facility in 12 mos preceding culture
- Community-associated: Cases with community-onset and none of above risk factors documented

Most Invasive MRSA Infections are Healthcare-Associated

National estimates:
94,360 infections; 18,650 deaths
31.8 cases & 6.3 deaths per 100,000 persons

Klevens et al. JAMA 2007;298:1763-71

Invasive Hospital-Onset MRSA Infections are Decreasing while Community-Associated Infections are Increasing, Connecticut

Petit S et al. Presented March 17, 2008 at the International Conference on Emerging Infectious Diseases, Atlanta, GA

Distribution of Clinical Syndromes: Invasive CA-MRSA

Infectious Syndrome* | %
---|---
Bacteremia +/- other syndromes | 77%
Pneumonia (mostly bacteremic) | 16%
SSTI (mostly bacteremic) | 26%
Endocarditis (metastatic complication) | 13%
Osteomyelitis | 10%
Bacteremia without other syndrome | 24%

*Categories not mutually exclusive
Fridkin SHEA 2008

Incidence of Invasive CA-MRSA Infections and Deaths by Age

Overall Incidence (all ages):
Infections: 4.6 per 100,000
Deaths: 0.5 per 100,000

Klevens et al JAMA 2007;298:1763-71
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Community-Acquired Pneumonia (CAP)
- S. aureus is a recognized cause of CAP (~3% of cases with pathogen identified)
  - Associated with preceding influenza infection
  - Rapid progression; Case-fatality 29-60%
- Several recent case series of severe MRSA CAP
  - Median age: late teens
  - ~50% with antecedent or concurrent viral illness
  - 43% empirically treated with antimicrobial agents recommended for MRSA CAP (vancomycin, linezolid)
  - Replacing MSSA or adding to overall burden?

Prevalence of MRSA Nasal Colonization by Age and Survey Cycle (N=18,626)
National Health and Nutrition Examination Survey, 2001-04

USA300 / USA400: 19.7%
1.5%
0.8%

Prevalence of MRSA Nasal Colonization
Low, Proportion MRSA in S. aureus Infections High
- Transmission via direct inoculation from exogenous source?
- Limited subset of population affected?
- High attack rate?
- Intermittent or low-level colonization?
- Predilection of USA300 for non-nasal colonization?

Non-Nasal MRSA Colonization?
- LA inpatients & outpatients with CA-MRSA infection1:
  - 40% colonized with MRSA in any of 4 sites
  - 26% nares, 8% axilla, 20% inguinal, 15% rectum
- Boston community clinic2:
  - 4.7% of 532 MRSA+ nares; 2.0% of 508 peri-anal & nares
- Atlanta VA HIV Clinic (preliminary)3:
  - 70 (12%) of 578 patients MRSA+ in nose or groin
  - 33 (47%) both, 26 (37%) nose only, 11 (16%) groin only
- Similar studies in healthcare settings (USA300 not prevalent) describe increases in sensitivity when adding rectal or peri-anal cultures to nasal cultures4,5

Vaginal MRSA Colonization
- S. aureus vaginal colonization in 5-20% of women of child-bearing age
- Recent studies have detected MRSA in vaginal-rectal swabs obtained for group B strep screening
  - Chen et al. Ob & Gyn 2006;108:482-7: 0.5% of 2963 cultures (“community” strains)
  - Andrews et al. Ob & Gyn 2008;111:113-8: 3.5% of 5732 cultures (no strain typing done)
- No increased incidence of vertically transmitted early-onset neonatal infections due to MRSA

Clindamycin Resistance Among MRSA Isolates, Texas Children’s Hospital, Houston Texas,2001-2004

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Multi-Drug Resistant USA300
- Resistance to multiple classes of antimicrobial agents described in MRSA USA300 isolates containing a conjugative plasmid
  - ermC (erythromycin), mupA (mupirocin) – conjugative plasmid
  - resistomycin resistance (resK) – separate plasmid
  - resistance to fluoroquinolones – chromosomal
  - Susceptible to TMP/SMX
- Initially described in isolates from adult clinic patients in Boston and San Francisco
- Association with self-identifications as a man-who-has-sex-with-men
- CDC isolate database (N>2000): 10 isolates from 5 states; 3/10 in women
- Sexually-transmitted infection?!
  - Can be transmitted by skin-skin contact during sex, but does not meet classical criteria for an STI

Potential Virulence Factors
- Panton-Valentine leukocidin (PVL) toxin
  - Associated with more severe clinical manifestations in some reports (osteomyelitis, invasive infections, CAP)
  - Conflicting results from animal model studies using isogenic PVL+ and PVL- MRSA strains
- Arginine catabolic mobile element (ACME)
  - Identified in USA300-0114, some isolates of USA100 (US), ST197 & ST1 (UK)
  - Products of this gene cluster may enhance survival at low pH on human skin and within phagocytic cells
- Phenol-soluble modulin (PSM) peptides
  - Described in MRSA USA300, USA400
  - Recruit, activate, & lyse human neutrophils
- In mouse model, PSM+ strains of USA300/400 had increased ability to produce skin lesions and increased mortality compared to isogenic PSM- strains

MRSA in Animals
- Food Animals
  - MRSA ST398 in pigs (Europe, Canada, U.S.), pig farmers (Europe, Canada), retail pork (Europe)
  - Health risks of MRSA in food products unknown
- Non-Food Animals
  - Strains reflect predominant human strains
  - Transmission between humans and animals (both directions) described – small % of human infections
  - Pets may play role in sustained household transmission
  - Little evidence to support antimicrobial decolonization in animals, but colonization is typically short-lived

Primary Prevention
- Hygiene and wound care remain cornerstones of primary prevention
  - Keep cuts / scrapes clean and covered
  - Avoid direct and indirect contact with wound drainage
  - Clean hands and shower regularly, particularly after skin-skin contact and contact with shared environmental surfaces

Primary Prevention
- Most extensively tested vaccine (Nabi StaphVAX) showed promise initially but was found ineffective in confirmatory trial
- A number of novel antigens being tested for potential inclusion in vaccine
- Development of a vaccine with levels of protection similar to other commonly administered vaccines unlikely to occur in near future
- Target population?

Controlling Transmission
- Promptly identify & manage new infections
- Use local data to guide empiric therapy
- Educate on wound care / containment
- Promote enhanced personal hygiene and limit sharing of personal items
- Exclude patients from direct-contact activities if unable to contain wound drainage
- Achieve and maintain a clean environment
- Use standard precautions in ambulatory care
- Use antibiotics appropriately

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#### Environmental Management
- Role of environment in spread of MRSA is unclear
  - Not naturally found in the environment
  - Can survive on surfaces for months, depending on conditions
- Cover infected skin to avoid contaminating surfaces
- Focus cleaning on surfaces frequently touched by people’s bare skin and surfaces that could come in contact with infected skin (e.g., benches in weight room)
- Use barriers between skin and shared surfaces, and clean skin after use
- Protect difficult to clean surfaces such as keyboards with covers that can be removed and cleaned

#### Cleaning & Disinfecting Environmental Surfaces
- Cleaners: Lift soil, organic matter, microorganisms, etc from surface so they can be rinsed away with water
- Disinfectants: Chemical products that destroy or inactivate microorganisms
  - Can use after cleaning for surfaces that have visible drainage from infected skin
- Read label instructions for how to apply, contact time, safety for the surface, precautions to protect skin, etc
- More information:  
  [CDC website](http://www.cdc.gov/ncidod/dhqp/ar_mrsa_Enviro_Manage.html)

#### Colonization Screening and Decolonization
- In general, colonization cultures of infected or exposed persons in community settings are not recommended.
- “Decolonization” = Use of antimicrobial regimens to suppress or eliminate *S. aureus* colonization
  - Goal is to prevent infection in high-risk patient or to prevent transmission
  - Effectiveness in community settings not established

#### Use of Decolonization in Community Settings
- R Raz et al. *Arch Int Med* 1996: Fewer recurrences of MSSA SSTIs in patients that received monthly mupirocin
- M Wiese-Posselt et al. *CID* 2007: Termination of MSSA furunculosis outbreak in German village following multi-component decolonization strategy of colonized or infected persons & family members
- MW Ellis et al. *Antimicrob Agents Chemo* 2007: RPCT of mupirocin decolonization of MRSA-colonized military trainees – no impact on MRSA infection or transmission

#### Decolonization: Current Guidance
- May be reasonable to administer, *after treating active infections and reinforcing hygiene and appropriate wound care, when*:
  - Individual patient has recurrent infections
  - Ongoing transmission in a closely-associated cohort (e.g., household)
- Appropriate regimens (agents and schedules) not established for community settings

#### Strategies for Clinical Management of MRSA in the Community

[ CDC website](http://www.cdc.gov/ncidod/dhqp/ar_mrsa_ca.html)
Management of Skin Infections in the Era of CA-MRSA

- Consider MRSA in differential diagnosis
- Drain purulent skin lesions*
- Obtain material for culture
  - Molecular typing, toxin testing not recommended to guide clinical management
- Consider antimicrobial therapy
  - Systemic symptoms, severe local symptoms, immune suppression, failure to respond to drainage
  - Variety of oral treatment options – use local data to inform empiric therapy
- Educate patients on wound management and hygiene
- Maintain adequate follow-up

*Fitch et al. Abscess incision and drainage. NEJM 2007;357:e20

Conclusions

- S. aureus has long been a cause of localized and invasive infections in the community.
- MRSA has emerged as a cause of these infections, and may be contributing to increased burden and severity.
- Strains of MRSA identified in community and healthcare settings were initially distinct, but are becoming less so.
- Invasive infections are a minority of CA-MRSA infections, but risk factors are not well understood.
- While optimal prevention strategies have yet to be defined, strategies focusing on increased awareness, early detection and appropriate management, enhanced hygiene, and maintenance of a clean environment have been successful in controlling clusters / outbreaks of infection.

Additional Resources

- UNC Public Health Grand Rounds (April 2005)
  - www.publichealthgrandrounds.unc.edu
- Health Departments
  - www.lapublichealth.org
  - www.doh.wa.gov
  - www.toh.state.tx.us
- NCAA
  - www.ncaa.org

CA-MRSA Working Group Meeting Participants, July 2004

<table>
<thead>
<tr>
<th>Gordon L. Archer</th>
<th>Gregory Moran</th>
<th>CDC</th>
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<tbody>
<tr>
<td>Carol L. Baker</td>
<td>Olga Nuno</td>
<td>DBJ</td>
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<td>Elizabeth Bancroft</td>
<td>John H. Powers</td>
<td>JCB</td>
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<td>Henry F. Chambers</td>
<td>L. Barth Reiller</td>
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<td>Robert S. Daum</td>
<td>Nalini Singh</td>
<td>RC</td>
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<td>Jeffrey S. Duchin</td>
<td>Marcus Zervos</td>
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<td>Monica Farley</td>
<td>Craig Zinderman</td>
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<td>James Hadler</td>
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<td>Jim Jorgensen</td>
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<td>Sheldon K. Kaplan</td>
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<td>Newton E. Kendig</td>
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<td>Kathleen Hartman</td>
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<td>JTW</td>
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<td>Franklin D. Lowy</td>
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<td>Ruth Lynfield</td>
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<td>J. Kathryn MacDonald</td>
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<td>Loren Miller</td>
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*Meeting Co-Chair

CDC / AMA/ IDSA Treatment Algorithm for Skin Infections

Additional Resources

http://www.cdc.gov/mrsa

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Thank-you!!
Questions?

The Next Few Teleclasses

<table>
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<tr>
<th>Date</th>
<th>Topic</th>
<th>Speaker/Details</th>
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<tr>
<td>22 Jul. 06</td>
<td>Free British Teleclass Progress Report from the Chief Nursing Officer</td>
<td>Christine Beasley, Bristol Department of Health</td>
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<tr>
<td>7 Aug. 06</td>
<td>Free Teleclass: Contribution &amp; Stimulation: Current Issues &amp; New Research</td>
<td>Dr. William Ruby, University of North Carolina</td>
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<td>14 Aug. 06</td>
<td>Free Teleclass: Extended Spectrum Beta Lactamase and Infection Control</td>
<td>Dr. David Patterson, Broadcast live from New Zealand infection control conference</td>
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<tr>
<td>11 Sep. 06</td>
<td>How to Prevent Healthcare-Associated Infection</td>
<td>Gary Phillips, Northwoll Training &amp; Development</td>
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<tr>
<td>16 Sep. 06</td>
<td>LTC: Surveillance in Long Term Care</td>
<td>Mary Andrus, CDC</td>
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<tr>
<td>16 Sep. 06</td>
<td>Nursing Teleclass: Cephalosporin sp: Prevention is Better Than Cure</td>
<td>Prof. Mark Rifas, Leeds University</td>
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