Emergence and Epidemiology of Community-Associated Methicillin-Resistant Staphylococcus aureus in the United States

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Overview

- Background / Terminology
- Outbreak Investigations
- Community emergence
- Reasonable approaches to prevention and control (Expert Panel Summary)


Community-Associated Methicillin Resistant Staphylococcus Aureus
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MRSA is an emerging community pathogen among patients without established risk factors for MRSA infection (e.g., recent hospitalization, recent surgery, residence in a long-term-care facility, or injecting-drug use).

**MMWR** 48:707; 1999

Four Pediatric Deaths from Community-acquired Methicillin-Resistant *S. aureus* -- Minnesota and North Dakota, 1997-1999

**Terminology**

- Terminology has been inconsistent
- Community-Onset (CO) MRSA: infection diagnosed or index culture collected in community
- Established risk factors (RFs): recent hospitalization, surgery, dialysis, long-term care; indwelling catheter or percutaneous medical device; history of MRSA
- Community-Acquired MRSA: Used for CO infections or CO infections in patients without established RFs, but difficult to establish with certainty where acquisition occurred
- Community-Associated MRSA: CO infections in persons without established RFs

**Bacteriologic Differences in CA-MRSA and HA-MRSA Isolates**

<table>
<thead>
<tr>
<th>Antimicrobial resistance</th>
<th>CA-MRSA</th>
<th>HA-MRSA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Few agents</td>
<td>Multiple agents</td>
<td></td>
</tr>
<tr>
<td>SCCmec (genetic element carrying mecA resistance gene)</td>
<td>Type IV</td>
<td>Type II</td>
</tr>
<tr>
<td>PFGE Types</td>
<td>USA 300, 400</td>
<td>USA 100, 200</td>
</tr>
<tr>
<td>PVL toxin gene</td>
<td>Common</td>
<td>Rare</td>
</tr>
</tbody>
</table>

**Panton-Valentine Leukocidin (PVL) Toxin**

- Necrotizing cytotoxin
- Associated with abscesses and severe pneumonia
- Also found in some methicillin-susceptible *S. aureus* (MSSA) isolates

**Terminology**

- “CA-MRSA” now sometimes used to refer to MRSA strains with certain bacteriologic properties
- However:
  - No definitive bacteriologic criteria for community strains
  - Attributes may change over time, particularly if community strains become established in healthcare settings or vice versa (differences in selective pressures, interchange of genetic material)
  - Eventually may be impossible to distinguish CA-MRSA and HA-MRSA

**CA-MRSA Outbreaks**
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CA-MRSA Outbreaks
• Often first detected as clusters of abscesses or “spider bites”
• Various settings
  – Sports participants: football, wrestlers, fencers
  – Correctional facilities: prisons, jails
  – Military recruits
  – Daycare and other institutional centers
  – Newborn nurseries and other healthcare settings
  – Men who have sex with men

Competitive Sports

August 22, 2003 / 52(33);793-795

CA-MRSA Abscesses among Professional Football Players
(Kazakova et al NEJM 2005;352:468-75)
• MRSA abscesses in 5/58 players at sites of turf burns
• Association with:
  – BMI>30
  – Lineman/Linebacker
  – Recent antibiotic use
• Abx use
  – 2.6 scripts/yr for Rams
  – 0.2 scripts/yr for gen pop’n
• No MRSA on colonization survey or environmental sampling

CA-MRSA Abscesses among Professional Football Players
(Kazakova et al NEJM 2005;352:468-75)
• Observational:
  – Trainers providing wound care had no access to hand hygiene
  – Towels frequently shared
  – Players often did not shower before using whirlpool
  – Weight-training equipment not regularly cleaned
• Transmission controlled with improved wound care, targeted therapy, enhanced hygiene

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Turf Burns

Prevention and Control

- Cover all wounds
- Train athletes in first aid for wounds and signs of infection
- Encourage good hygiene
- Discourage sharing of items
- Establish routine cleaning schedules for shared equipment
- Encourage players to report skin lesions

Correctional Facilities

Methicillin-Resistant *Staphylococcus aureus* Skin or Soft Tissue Infections in a State Prison – Mississippi, 2000 (MMWR 2001 50:919-22)

- 59 skin infections in 3000 inmate prison
- Case-patients frequently reported: helping or being helped by other inmates with wound care, lancing own or other inmates' boils with fingernails or tweezers, sharing potentially contaminated personal items (linen, pillows, clothing, tweezers)
- High nasal carriage rate of MRSA (4.9%)

MRSA Outbreaks in Correctional Facilities

- Georgia
- California
- Texas

Intervention to Reduce the Incidence of MRSA Skin Infections in a Correctional Facility in Georgia (Wooten et al ICHE 2004;25:402-7)

- 16 cases of MRSA skin lesions in 200-bed detention center
- Prior to intervention:
  - Co-pay required for clinic visit
  - Lesions treated with warm compresses and topical antibiotics (no capacity for I&D)
  - Soap kept in locked drawers
- Rates declined significantly after implementing measures to improve skin disease screening, personal hygiene, wound care, and antimicrobial therapy
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Contributing Factors to MRSA Spread in Correctional Facilities
• Barriers to routine hygiene
  – Access to soap limited
  – Mental health problems contributed to poor adherence
  – Improper handling of laundry
• Barriers to inmates accessing the medical system
  – Cost
  – Language and literacy
  – Fear
• Barriers within the medical system
  – Frequent medical staff turnover and understaffing
  – Limited services available (e.g., no I & D)
  – Lack of coordination between facilities
• Unrecognized cause of skin infections
  – Cultures rarely performed; lesions attributed to spider bites
• Crowding

Prevention and Control
• Collaborated with Bureau of Prisons*
  – Implement skin infection screening and monitoring
  – Culture suspect lesions and provide targeted therapy
  – Improve inmate hygiene (education, availability of soap, etc)
  – Improve access to wound care and trained healthcare staff
  – Additional interventions (antiseptic washes, nasal decolonization) to be considered in consultation with public health


Military Trainees

Military Training Facility, 2001-2003 Cases of CA-MRSA Soft Tissue Infections

Zinderman, Emerg Infect Dis Vol 10, May 2004 941-944

Military Training Facility, 2001-2003 Cases of CA-MRSA Soft Tissue Infections

Zinderman, Emerg Infect Dis Vol 10, May 2004 941-944

Other Outbreaks

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Skin Infections in a Religious Community

- 24 confirmed or probable cases
- Antibiotic use in past year and use of community sauna were independently associated with disease
- MRSA (different from outbreak strain) isolated from sauna
- Transmission interrupted with multifaceted intervention and closing sauna

Skin Infections in a Religious Community

Tattoo Recipients

- Outbreaks reported in several states associated with licensed and unlicensed tattooing
- Investigations underway
- Tattoo parties, improvised equipment

Hospital Transmission of CA-MRSA

- Hospital transmission of CA-MRSA among post-partum women, NY (Saiman L, CID, 2003;37:1313-9)
- CA-MRSA in a NICU, TX (Healy CM, CID, 2004;39:1460-6)

CA-MRSA outbreaks among otherwise healthy full-term newborns

- Clusters of MRSA skin infections among newborns delivered at a common facility
- Onset of symptoms in 1st few weeks of life – usually about a week after discharge from term nursery
- No risk factors for acquisition following discharge identified
- Resolved after reinforcement of nursery infection control practices and, in some cases, decolonization of colonized health care workers

CA-MRSA Causing Infections In the Hospital – Uruguay 2002-2004

- Number of infections by quarter for Asocacion Espanola, Uruguay
Benoit, Estivariz EIS Uruguay Trip Report July 2002-July 2004
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CA-MRSA Outbreaks: Summary

A Few CA-MRSA Strains Cause Most Community Outbreaks

CA-MRSA: Factors for Transmission

Transmission Dynamics CA-MRSA Outbreaks

CA-MRSA Outbreak Control Measures

- Multi-component strategies used (difficult to assess individual contribution of each)
- Strategies focusing on increased awareness, early detection and appropriate management, enhanced hygiene, and maintenance of a clean environment appear to have been successful at interrupting transmission

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CA-MRSA: Emergence in the Community

Methicillin-Resistant Staphylococcus aureus in Three Communities

- Fridkin SK. NEJM 2005;352:1436-44.
- Emerging Infections Program – Active Bacterial Core Surveillance (ABCs)
  - 2001-2002
  - Atlanta, Baltimore, Minnesota
  - Laboratory-based surveillance, all culture-confirmed (invasive and non-invasive) infections in surveillance area
  - Determined absence of established risk factors by record review, patient interview

CA-MRSA Prevalence Varies by Region

- Healthcare-Associated MRSA
- Community-Associated MRSA

CA-MRSA Prevalence in Three Sites – ABCS/EIP

Incidence of CA-MRSA Disease in Atlanta and Baltimore, According to Race and Age Group

- Atlanta, 2001-2002
- Baltimore, 2002

CA-MRSA Incidence Varies by Race

- African American
- White
- Total

Incidence of CA-MRSA by Race, ABCS/EIP

CA-MRSA Predominantly Causes Skin Disease

<table>
<thead>
<tr>
<th>Disease Syndrome</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<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>
</tr>
</tbody>
</table>
Infecting Strain of CA-MRSA Often Resistant to Prescribed Antimicrobial

- 73% of CA-MRSA infections treated initially with an antimicrobial to which the infecting strain was resistant
- Among patients with SSTIs, therapy to which the infecting strain was resistant did not appear to be associated with adverse outcomes

CA-MRSA in Hawaii, 2001-2003

- Retrospective chart review of patients with MRSA infection, 2001-2003
- Four health-care facilities (40% of acute care beds):
  - Children and woman’s center
  - Private urban clinic
  - County urban hospital
  - Rural community hospital

Increase in CA-MRSA Infections, Hawaii 2001-03

Estivariz EIS ‘03

CA-MRSA Prevalence Varies by Age, Hawaii 2001-2003

Estivariz EIS ‘03

Race Distribution of Case-patients Hawaii, 2001-2003

- P<0.05 for CA-MRSA vs expected
- Data from 2001 Hawaii Health Survey, HI State DOH

S. aureus Community-Acquired Pneumonia Following Influenza-Like Illness, 2003-4

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median [range]</td>
<td>21 (8 mos.-62 yrs)</td>
</tr>
<tr>
<td>Sex, female</td>
<td>9 (52)</td>
</tr>
<tr>
<td>MRSA</td>
<td>15 (88)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>10 (59)</td>
</tr>
<tr>
<td>Black</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Underlying disease*</td>
<td>5 (29)</td>
</tr>
<tr>
<td>MRSA risk factors</td>
<td>4 (24)</td>
</tr>
<tr>
<td>Documented influenza vaccination</td>
<td>1 (6)</td>
</tr>
</tbody>
</table>

*One each: Diabetes, multiple sclerosis, abdominal wall malformation, cystic fibrosis, chronic lung disease
S. aureus Community-Acquired Pneumonia Following Influenza-Like Illness, 2003-4

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No./ (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence of preceding influenza illness</td>
<td>n=17</td>
</tr>
<tr>
<td>Clinical symptoms only</td>
<td>5 (29)</td>
</tr>
<tr>
<td>Laboratory Confirmed</td>
<td>12 (71)</td>
</tr>
<tr>
<td>Rapid antigen test</td>
<td>10 (59)</td>
</tr>
<tr>
<td>Paired serology</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Fluorescent antibody staining</td>
<td>1 (6)</td>
</tr>
<tr>
<td>Hypotension (systolic&lt;90mmHg)</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Leukopenia (WBC &lt; 3,500/mm^3)</td>
<td>4 (24)</td>
</tr>
<tr>
<td>Thrombocytopenia (&lt;150,000/mm^3)</td>
<td>4 (24)</td>
</tr>
<tr>
<td>Hospitalization</td>
<td>16 (94)</td>
</tr>
<tr>
<td>ICU (8 intubated)</td>
<td>13 (81)</td>
</tr>
<tr>
<td>Death (Median Age = 28)</td>
<td>5 (29)</td>
</tr>
</tbody>
</table>

Eight Indistinguishable MRSA Patterns from CAP Patients

<table>
<thead>
<tr>
<th>State</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Texas</td>
<td></td>
</tr>
<tr>
<td>Arkansas</td>
<td></td>
</tr>
<tr>
<td>Maryland</td>
<td></td>
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<tr>
<td>Maryland</td>
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<tr>
<td>Maryland</td>
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<tr>
<td>Washington</td>
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<tr>
<td>Alabama</td>
<td></td>
</tr>
<tr>
<td>Illinois</td>
<td></td>
</tr>
<tr>
<td>Maryland</td>
<td></td>
</tr>
</tbody>
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S. aureus Colonization
NHANES Nasal Swab Survey 2001-2, Kuehnert et al.

CA-MRSA Prevention and Control

CA-MRSA Expert Panel Summary

Rachel J. Gorwitz, MD MPH
Division of Healthcare Quality Promotion
National Center for Infectious Diseases

Prevention and Control of Community-Associated Methicillin-Resistant Staphylococcus aureus

CA-MRSA Transmission

Community Group Setting

- MRSA
  - Differs from hospital strains
  - PVL toxin +
  - Resistant to standard therapy

- Skin Abscesses
  - Crowding
  - Contaminated items or environment
  - Contact
  - Compromised skin
  - Cleanliness

- MRSA
- No. (%)
Clinical Considerations

MRSA belongs in the differential diagnosis of skin and soft tissue infections (SSTI's) compatible with S. aureus infection:
- Abscesses, pustular lesions, “boils”
- “Spider bites”
- Cellulitis?

Clinical Considerations - Evaluation

Increase Awareness

Clinical Considerations - Evaluation

Collect Diagnostic Specimens

Obtain material for culture
- Guides clinical management
- Contributes to knowledge of local prevalence, epidemiology, susceptibility patterns

Clinical Considerations - Management

Incision and Drainage Should Be Routine

Primary therapy for abscesses
- May be adequate sole therapy in some circumstances
- Provider education / refreshers on appropriate technique may be necessary

Adequate Follow-Up Must be Maintained

Develop follow-up plan for all non-hospitalized patients
- Instructions to return if:
  - Develop systemic symptoms
  - Worsening local symptoms
  - No improvement in 48-72 hours
Clinical Considerations - Management

Empiric Antimicrobial Therapy May Be Needed for SSTIs

- Significant associated cellulitis
- Systemic signs of illness
- Associated co-morbidities

Antimicrobial Selection

- Beta-lactams still appropriate first-line therapy for SSTIs in some circumstances?
- Take into account:
  - Local prevalence of MRSA
  - Severity of illness
  - Patient co-morbidities

Antimicrobial Selection (SSTIs)

- Alternate agents:
  - Clindamycin
  - TMP/SMX
  - Tetracyclines
  - Rifampin (in combination with other agent)
  - Linezolid
- More data needed to establish effectiveness!

Inducible Clindamycin Resistance

- Mediated by \textit{erm} gene
- Isolates appear macrolide (erythromycin)-resistant and clindamycin-susceptible on routine susceptibility testing
- In vitro resistance to clindamycin can occur during a course of therapy
- Detected by a D-test, or double disk diffusion test
- Clinical implications of positive D-test unclear, but should check for inducible resistance and avoid clindamycin if detected

Not optimal for MRSA:

- Macrolides
- Fluoroquinolones
- High prevalence of resistance or potential for rapid development of resistance

Use Local Data for Treatment

- MRSA prevalence and susceptibility to alternate agents vary geographically
- Local epidemiologic risk factors may be useful in assessing likelihood of MRSA in a given patient

DRAFT
Clinical Considerations

**Patient Education**

- Critical component of case management
  - Wound care
  - Hygiene
    - Hand washing
    - Regular bathing
  - Avoid sharing of potentially contaminated objects

**Management of Household Clusters and Recurrent Disease**

- Education is critical
- Instruct patients and household members to seek care early so that prompt appropriate treatment of new infections can be provided
- Decolonization???

Clinical Considerations

**Decolonization Regimens**

- Topical Nasal Agents
  - Mupirocin, Others
- Antiseptic Body Washes
  - Chlorhexidine, Others
- Oral antimicrobials
  - TMP/SMX + Rifampin, Others
  - Infected individuals only
- Single, short courses

**Management of Household Clusters and Recurrent Disease: Decolonization**

- Data from healthcare settings (pre-op, dialysis, long-term care):
  - Regimens can be effective in eliminating colonization, at least in the short term
  - Effectiveness in preventing disease less clear
- Almost no data on effectiveness in community setting
- Resistance can emerge
- Basic strategies should be optimized first

Public Health Intervention

**When to Investigate**

- Consider investigation when culture-proven MRSA cases have been detected in a cluster among epidemiologically-linked individuals in the community
Public Health Intervention

**When to Investigate**

- Decision to investigate should take into account various factors
  - Number of cases and temporal proximity of the cluster
  - Setting in which transmission is occurring
  - Severity of illness among cases
  - Presence of ongoing transmission or recurrent illness among cohort members
  - Host factors of those likely to be infected
  - Likelihood that an intervention could be successfully implemented

**Components of Interventions**

- Enhance surveillance
- Target empiric therapy to the pattern of the outbreak strain
- Educate on wound care and wound containment
- Promote enhanced personal hygiene and limit sharing of personal items
- Consider excluding patients from certain activities
- Achieve and maintain a clean environment

Risk Factor Study?

- Can be labor and resource intensive
- Not always necessary for outbreak management
- Consider when:
  - Cluster occurs in a new setting
  - Results are likely to:
    - Directly impact control efforts
    - Contribute to general understanding of the disease and future prevention efforts

Colonization Swab Surveys?

- Have been used in many published investigations
- Yield has often been low
- Not generally necessary to direct control and prevention efforts
- May be useful:
  - To determine extent of or identify risk factors for transmission (“carrier-control” study)
  - To contribute to the understanding of CA-MRSA epidemiology (non-nasal colonization sites)

Decolonization?

- No data to support efficacy in preventing disease transmission in the community; trials are needed.
- Control of previous outbreaks has been achieved without use of decolonization
- Emphasis should be placed on basic control strategies first

Conclusions

- Various studies are underway and more are needed to determine best methods for control and prevention of MRSA in the community
- Strategies focusing on increased awareness, early detection and appropriate management, enhanced hygiene, and maintenance of a clean environment appear to have been successful
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CA-MRSA Working Group Meeting
Participants, July 2004

Gordon L. Archer
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Elizabeth Bancroft
Henry F. Chambers
Robert S. Daum
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Monica Farley
James Hadler
Jim Jorgensen
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Newton E. Kendig
Kathleen Harriman
Franklin D. Lowy
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J. Kathryn MacDonald
Loren Miller

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John H. Powers
L. Barth Reller
Nalini Singh
Marcus Zervos
Craig Zinderman

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Roberta Carey
Rachel Gorwitz
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