CA-MRSA a new problem in Indonesia?

Latre Buntaran
Clinical Microbiologist Consultant
Indonesia Coordinator of ANSORP Study
Secretary General of INASIC
Community Associated MRSA

- Papua New Guinea
- Asia
- Europe
- United Kingdom
- Ireland
- Canada
- United States of America
- Central America
- South America

Latre Buntaran. 2011, ANSORP.
MRSA in Western Australia

MRSA increasing in prevalence in the WA community

Annual Notification of Community and healthcare-associated MRSA

Latre Buntaran. 2011, ANSORP.
nosocomial
community-acquired with risk factors
community-acquired without risk factors

CA-MRSA: an emerging threat in USA

* 14-year study at Driscoll Children’s Hospital, Texas

Purcell K et al. Arch Pediatr Adolesc Med. 159;980-985, 2005
CA-MRSA : an emerging threat in USA


<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>% MRSA</td>
<td>71.5</td>
<td>73.5</td>
<td>76.4</td>
<td>0.008</td>
</tr>
</tbody>
</table>

- 95.6% of CA-MRSA: Skin and soft tissue infections
- 62% of skin and soft tissue infections: CA-MRSA

Kaplan SL et al. Clin Infect Dis. 40;1785-91, 2005
CA-MRSA in Taiwan

- 464 children with *S. aureus* infections between 1997-2001 in NTUH

- Incidence of CA-MRSA:
  
  CA-MRSA / total community *S. aureus* infections   59 / 80 (74 %)
  CA-MRSA / total MRSA infections                       59 / 373 (15.8 %)

- CA-MRSA with risk factors: only 51 % of CA-MRSA infections

- Major infections by CA-MRSA: SSTI (92 %), bacteremia (7 %), osteomyelitis (3 %), pneumonia (2 %)

Worldwide CA-MRSA clone

Canada
ST8-IV, PVL+ (USA 300)
ST1-IV, PVL + (USA 400)

USA
ST8-IV, PVL+(USA300)
ST1-IV, PVL+(USA400)

Europe
ST80-IV, PVL+(European)
ST398-V,PVL-(Pig-associated)
ST152-V, PVL+(Balkan region)

South America
ST30-IV, PVL+(SWP)

East Asia
ST59-VI,L,PVL+(Taiwan)
ST30-IV, PVL + (SWP)

Oceania
ST1-IV,PVL-(WA-MRSA-1)
ST129-IV,PVL-(WA-MRSA-2)
ST93-IV,PVL+(Queensland)
ST30-IV,PVL+(SWP)

Latre Buntaran. 2011, ANSORP.

Results of multiplex PCR SCC\textit{mec} gene typing in MRSA and MSSA
Results of simple PCR VISA gene on MRSA and MSSA
Characteristics of specimens with Scc mec typing, plasmid pub 110 and beta-lactam antibiotic sensitivity pattern

<table>
<thead>
<tr>
<th>NO. SAMPLE</th>
<th>SPECIMENS</th>
<th>Scc mec</th>
<th>pub 110</th>
<th>AMC</th>
<th>CXM</th>
<th>OX</th>
<th>CTX</th>
<th>CRO</th>
<th>CAZ</th>
<th>FEP</th>
<th>IPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>URINE</td>
<td>IV</td>
<td>+</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>9</td>
<td>SPUTUM</td>
<td>II</td>
<td>+</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>11</td>
<td>Throat Swab</td>
<td>II</td>
<td>+</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>10</td>
<td>PUS</td>
<td>II</td>
<td>-</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
<td>R</td>
</tr>
<tr>
<td>1</td>
<td>Blood</td>
<td>-</td>
<td>-</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>2</td>
<td>Blood</td>
<td>-</td>
<td>-</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>3</td>
<td>Bronchial discharge</td>
<td>-</td>
<td>-</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>5</td>
<td>Blood</td>
<td>-</td>
<td>-</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>6</td>
<td>Urine</td>
<td>-</td>
<td>-</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>7</td>
<td>Urine</td>
<td>-</td>
<td>-</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>8</td>
<td>Urine</td>
<td>-</td>
<td>-</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>
Characteristics of specimens with Scc mec typing, plasmid pub 110 and beta-lactam antibiotic sensitivity pattern

<table>
<thead>
<tr>
<th>NO. SAMPLE</th>
<th>SPECIMENS</th>
<th>Scc mec</th>
<th>pub 110</th>
<th>SXT</th>
<th>CC</th>
<th>AN</th>
<th>CIP</th>
<th>LVFX</th>
<th>VA</th>
<th>TEC</th>
<th>TGC</th>
<th>FOS</th>
<th>LZ</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>URINE</td>
<td>IV</td>
<td></td>
<td></td>
<td>R</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>9</td>
<td>SPUTUM</td>
<td>II</td>
<td></td>
<td></td>
<td>R</td>
<td>R</td>
<td>S</td>
<td>R</td>
<td>R</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>R</td>
</tr>
<tr>
<td>11</td>
<td>Throat Swab</td>
<td>II</td>
<td></td>
<td></td>
<td>R</td>
<td>R</td>
<td>S</td>
<td>R</td>
<td>R</td>
<td>S</td>
<td>S</td>
<td>R</td>
<td>S</td>
</tr>
<tr>
<td>10</td>
<td>PUS</td>
<td>II</td>
<td></td>
<td></td>
<td>R</td>
<td>R</td>
<td>S</td>
<td>R</td>
<td>R</td>
<td>S</td>
<td>S</td>
<td>R</td>
<td>S</td>
</tr>
<tr>
<td>1</td>
<td>Blood</td>
<td>-</td>
<td></td>
<td></td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>2</td>
<td>Blood</td>
<td>-</td>
<td></td>
<td></td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>3</td>
<td>Bronchial discharge</td>
<td>-</td>
<td></td>
<td></td>
<td>R</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>R</td>
<td>S</td>
</tr>
<tr>
<td>5</td>
<td>Blood</td>
<td>-</td>
<td></td>
<td></td>
<td>R</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>R</td>
<td>S</td>
</tr>
<tr>
<td>6</td>
<td>Urine</td>
<td>-</td>
<td></td>
<td></td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>7</td>
<td>Urine</td>
<td>-</td>
<td></td>
<td></td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
<tr>
<td>8</td>
<td>Urine</td>
<td>-</td>
<td></td>
<td></td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>
### Characterization of clinical specimens related to VISA gene and plasmid pub 110

<table>
<thead>
<tr>
<th>SPECIMENS</th>
<th>No.</th>
<th>MRSA/MSSA</th>
<th>pub 100</th>
<th>vraA</th>
<th>vraG</th>
<th>vraF</th>
<th>vraR</th>
<th>fruA</th>
<th>fruB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>1</td>
<td>HA-MSSA</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Blood</td>
<td>2</td>
<td>CA-MSSA</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Bronchial discharge</td>
<td>3</td>
<td>HA-MSSA</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Urine</td>
<td>4</td>
<td>CA-MRSA</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Blood</td>
<td>5</td>
<td>CA-MSSA</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Urine</td>
<td>6</td>
<td>CA-MSSA</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Urine</td>
<td>7</td>
<td>CA-MSSA</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Urine</td>
<td>8</td>
<td>CA-MSSA</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Sputum</td>
<td>9</td>
<td>HA-MRSA</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Pus</td>
<td>10</td>
<td>HA-MRSA</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Throat Swab</td>
<td>11</td>
<td>HA-MRSA</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>TOTAL</td>
<td>11</td>
<td>11</td>
<td>27%</td>
<td>91%</td>
<td>45%</td>
<td>36%</td>
<td>36%</td>
<td>100%</td>
<td>64%</td>
</tr>
</tbody>
</table>
Relationship between antibiotics use and **MRSA/MSSA** at 3 private hospitals (%) (2008–2010)

<table>
<thead>
<tr>
<th>Isolat <em>S. aureus</em> (+)</th>
<th>MRSA (+)</th>
<th>MSSA (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB (+)</td>
<td>18 (6%)</td>
<td>270 (94%)</td>
</tr>
<tr>
<td>AB (-)</td>
<td>0 (0%)</td>
<td>23 (8%)</td>
</tr>
</tbody>
</table>

Latre, 2011
### Relationship between antibiotics use and MRSA at 3 private hospitals (%)(2008 – 2010)

<table>
<thead>
<tr>
<th>Isolat MRSA (+)</th>
<th>HA-MRSA (+)</th>
<th>CA-MRSA (+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 (6%)</td>
<td>12 (67%)</td>
<td>6 (33%)</td>
</tr>
<tr>
<td>AB (+)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>AB (-)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The proportion of CA-MRSA to all MRSA isolates

- Proportion = CA-MRSA / CA-MRSA + Nosocomial MRSA

- Proportion of CA-MRSA: \( \frac{6}{6+12} = 33\% \)
The proportion of CA-MRSA to all community MSSA and MRSA isolates

- Proportion = CA-MRSA / CA-MRSA + CA-MSSA

- Proportion CA-MRSA : \( \frac{6}{6+162} = 0.04 \) or 4%
Types of CA-MRSA

- CA-MRSA strains are resistant to mono betalactam or betalactam and erythromisin
- Usually infect healthy patients who get MRSA had no predisposing factors
- MLST type: 1-1-1-1-1-1-1, spa type 131 and SCCmec type IV

- CA-MRSA strains derived from individuals who have risk factors
- MLST types: 3-3-1-1-4-4-16 and 3-3-1-1-4-4-3, spa types: 1 & 7, dan SCCmec type IV
Community-Acquired MRSA

- MRSA is an emerging community-acquired pathogen among patients without established risk factors for MRSA
  - No recent hospitalization
  - No recent surgery
  - No residence in a long-term care facility
  - No injecting drug use

Four pediatric deaths from community-acquired MRSA. MMWR. 1999;48:707.
Community-Acquired MRSA (cont’d)

- Almost 90% of cases are skin infections, often first detected as clusters of abscesses (“spider bites”)
- Various epidemiologic settings
  - Sports participants
  - Jails, military recruits
  - Men who have sex with men
A Few CA-MRSA Strains Cause Most Community Outbreaks

- Pneumonia (AL, AR, IL, MD, TX, WA)
- Missouri
- California
- Pennsylvania
- Colorado
- Mississippi
- Texas
- Georgia
- Tennessee
- Texas
- Missouri
- California
- USA300-114
- USA100
- USA200
- Community
- Hospital Strain
- Hospital Strain

SAFER • HEALTHIER • PEOPLE™
Community-Acquired MRSA (cont’d)

- The proportion of all community-acquired MRSA strains in the US ranges from 9–20%, depending on the geographic region.
- In the US, one PFGE type (“USA 300 strain”) is found throughout the country.
- Community-acquired MRSA has smaller resistance gene (SCCmecIV).
- Community-acquired MRSA has gene for Panton-Valentine leukocidin (PVL), a necrotizing cytotoxin.
Classification of MRSA According to *meca* type

<table>
<thead>
<tr>
<th>Type</th>
<th>Size (Kb)</th>
<th>Source</th>
<th>Ribotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>34.3</td>
<td>Hospital</td>
<td>Conserved</td>
</tr>
<tr>
<td>II</td>
<td>53.0</td>
<td>Hospital</td>
<td>Conserved</td>
</tr>
<tr>
<td>III</td>
<td>66.9</td>
<td>Hospital</td>
<td>Conserved</td>
</tr>
<tr>
<td>IV</td>
<td>21-24</td>
<td>Community</td>
<td>Variable</td>
</tr>
</tbody>
</table>

### CA-MRSA vs HA-MRSA: Toxin Genes

<table>
<thead>
<tr>
<th>Toxin</th>
<th>CA-MRSA (%+)</th>
<th>HA-MRSA (%+)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PVL</td>
<td>77</td>
<td>4</td>
</tr>
<tr>
<td>SEA</td>
<td>58</td>
<td>4</td>
</tr>
<tr>
<td>SEG</td>
<td>19</td>
<td>96</td>
</tr>
<tr>
<td>SEH</td>
<td>65</td>
<td>4</td>
</tr>
<tr>
<td>SEB</td>
<td>23</td>
<td>4</td>
</tr>
</tbody>
</table>

Toxin Analysis

- PVL Pneumonia
  - Mortality rate
    - 32% with PVL positive strains
    - 6% for PVL negative strains

### Factors Associated With Lethality

- **Hemoptysis**: 42%
  - Median survival time with hemoptysis: 2 days
  - Median survival time in absence of hemoptysis: 35 days
  - \( p < 0.01 \)

- **Multivariate analysis**
  - RR 2.81 (1.29 – 6.11) \( p = 0.006 \)
Risk Factors for CAMRSA Infection

“The Five C’s”

- Compromised (broken) skin
- Contact (skin - to - skin)
- Contaminated items or surfaces
- Crowding
- Difficulty keeping clean (poor hygiene)
Recognition of CAMRSA Infections

- "Spider bites": pimples or pustules
- Boils: abscesses
- Cellulitis: diffuse skin infection
- Common signs: redness, swelling and warmth of skin
- Common symptoms: tenderness of skin, pain or itching
CAMRSA Skin Infections
“Spider Bites”
CAMRSA Skin Infections
Boils (Abscesses)
CAMRSA Skin Infections
Draining Abscesses
Cellulitis

Mild

Severe
Treatment of CAMRSA Infections

- Drainage: most important aspect of treatment of abscesses
- Antibiotics: may not be needed for all infections
- Wound care
Treatment Options for MRSA

CA-MRSA
- Clindamycin
- Tetracyclines
- Vancomycin
- Quinupristin-dalfopristin
- Linezolid
- Daptomycin*
- Tigecycline
  - *Teicoplanin

HA-MRSA
- Vancomycin
- Quinupristin-dalfopristin
- Linezolid
- Daptomycin*
- Tigecycline
  - *Teicoplanin

* Daptomycin is not recommended for treating pneumonia.
Conclusion

1. In one of the Indonesia study:

   1. The prevalence of CA-MRSA and HA-MRSA were 2% and 4% respectively.

   2. UTI with risk factors are predominant in CA-MRSA, while in HA-MRSA is pneumonia.

   3. CA-MRSA still sensitive to clindamycin whereas HA-MRSA are very sensitive to vancomycin, teicoplanin and oxazolidinone.

   4. SCC _mec_ type II (HA-MRSA) are more frequent (75%) than type IV (CA-MRSA) (25%).

Thank You