TACKLING THE MRSA EPIDEMIC

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Evolution of Drug Resistance in S. aureus

Penicillin

S. aureus  Penicillin-resistant S. aureus

[1950s] [1960s]

Methicillin

Methicillin-resistant S. aureus (MRSA)

[1960s]
METHICILLIN RESISTANCE IN S. AUREUS

- 1961: First reports in Europe
- 1965: First hospital outbreak in US

Barrett. NEJM. 279:441, 1965

METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS

- Contains mecA gene for PBP-2a
- PBP-2a has low affinity for all -lactams:
  - Penicillins
  - Cephalosporins
  - Carbapenems
- mecA gene located on mobile element
  - integrates into specific site of chromosome

Evolution of Drug Resistance in S. aureus

Penicillin-resistant S. aureus (1950s)

Methicillin-resistant S. aureus (MRSA) [1960s]

Vancomycin-resistant intermediate-resistant S. aureus (VISA) [1997]

Vancomycin-resistant enterococci (VRE) [1990s]
HEALTH-CARE ASSOCIATED MRSA

**Prevalence of MRSA**

Proportion of *S. aureus* Nosocomial Infections Resistant to Oxacillin (MRSA)
Among Intensive Care Unit Patients, 1989-2004

*Source: NNIS System.*

Centers for Disease Control and Prevention Web site.

**METHICILLIN RESISTANT STAPHYLOCOCCUS AUREUS**

- Classical hospital-acquired ORSA
  - Contains SCCmec Types I, II, or III
  - Usually shows resistance to:
    - Tetracyclines
    - Macrolides
    - Quinolones
    - Rifampin
    - Aminoglycosides
HA-MRSA

- Strains show multi-drug resistance
- Not spread in the community setting
  - Slower growth than OSSA
  - Lack of antibiotic pressure in environment

Risk Factors for MRSA

<table>
<thead>
<tr>
<th>Setting</th>
<th>Risk Factors for Infection and Colonization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospitals</td>
<td>Previous hospital stay&lt;sup&gt;1,2&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Prolonged length of stay prior to infection&lt;sup&gt;7&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Surgical procedure(s)&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Enteral feeding&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Levofloxacin use&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Long-Term Care Facilities</td>
<td>Presence of decubitus ulcer&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td>Prior Antibiotic Exposure&lt;sup&gt;4,5&lt;/sup&gt;</td>
<td>Presence of wounds&lt;sup&gt;1&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Third-generation cephalosporins&lt;sup&gt;4&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td>Fluoroquinolones&lt;sup&gt;1,4&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Risk Factors Associated Independently with MRSA Infection

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR</th>
<th>95% CIs</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levofloxacin use</td>
<td>8.01</td>
<td>3.15, 20.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Enteral feeding</td>
<td>2.55</td>
<td>1.37, 4.72</td>
<td>0.003</td>
</tr>
<tr>
<td>Surgery</td>
<td>2.24</td>
<td>1.19, 4.22</td>
<td>0.01</td>
</tr>
<tr>
<td>Previous hospitalization</td>
<td>1.95</td>
<td>1.02, 3.76</td>
<td>0.04</td>
</tr>
<tr>
<td>Length of stay before culture</td>
<td>1.03</td>
<td>1.0, 1.07</td>
<td>0.05</td>
</tr>
</tbody>
</table>
HA-MRSA INFECTIONS BY ORGAN SYSTEM

Naimi TS et al. JAMA. 2003;290:2976-2984

Mortality Associated with Bacteremia Due to MRSA vs. MSSA

<table>
<thead>
<tr>
<th>Outcome</th>
<th>MRSA-infected Patients</th>
<th>MSSA-infected Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovered</td>
<td>70.4%</td>
<td>86.4%</td>
</tr>
<tr>
<td>Died of other causes</td>
<td>17.8%</td>
<td>8.5%</td>
</tr>
<tr>
<td>Died of infection*</td>
<td>11.8%</td>
<td>5.1%</td>
</tr>
</tbody>
</table>

*P<0.001


S. aureus Surgical Site Infections: Impact of Methicillin Resistance on Outcomes

Independent effect of MRSA: OR 3.4 (95% CI 1.5-7.2, P = 0.003)
After adjusting for age, ASA score, duration of surgery

ASA Score: American Society of Anesthesiologists score of preoperative physical fitness
COMMUNITY ASSOCIATED MRSA

COMMUNITY ASSOCIATED MRSA (CA-MRSA)

• Different from HA-MRSA
  – Epidemiologically
  – Clinically
  – Genetically

CDC Definition of CA-MRSA

• Diagnosis of MRSA
  – made in the outpatient setting OR
  – culture positive for MRSA ≤ 48 hr of hosp admission

• No medical history of MRSA colonization or infection

www.cdc.gov
CDC Definition of CA-MRSA

- No medical history in the past year of:
  - Hospitalization
  - Admission to nursing home, SNF or hospice
  - Dialysis
  - Surgery
- No indwelling catheters or medical devices that pass through the skin

MRSA AS COMMUNITY PATHOGEN

- Associated with SSTI

CA-MRSA

- Skin soft tissue 74%
- Urinary tract 6%
- Respiratory 7%
- Other 8%
- Bloodstream 4%
- Otitis media externa 1%
MRSA AS COMMUNITY PATHOGEN

- Associated with SSTI
- Genetically different than HA-MRSA
  - SCCmec Type IV

CA-MRSA TOXINS

- Panton-Valentine leukocidin
- Superantigen enterotoxin H
- 15 additional unique superantigen genes
  - 11 exotoxin genes
  - 4 enterotoxin genes
- Strain MW2 demonstrated 10 times stronger human-T cell proliferation than other S. aureus strains
  - May correlate with high virulence

RISK FACTORS FOR CA-MRSA

- IVDU
- MSM
- Correctional institutions
- Homelessness/marginally housed

CA-MRSA in CORRECTIONAL FACILITIES

- Los Angeles County Jail (N=165,000)
  - 2002: 928 inmates with MRSA infections
    - 66 hospitalized, most with SSTI
    - 10 with invasive disease (bacteremia, endocarditis, osteomyelitis)
  - 2003: 1849 cases
  - 2004: 2480 cases

MMWR. 2003;52(5):88
Ngo V, et al. Abstract 32, SHEA, 2005
CA-MRSA in CORRECTIONAL FACILITIES

- Folliculitis, furuncles, boils, abscesses
- “Spider bites”
- Risks:
  - previous antibiotics, skin trauma, sharing soap, hand-washing clothes, self-draining boils, recent arrival to facility

MMWR. 2003;52(5):88
Tobin et al. IDSA 2003

CA-MRSA in COMPETITIVE ATHLETES

- Wrestlers (Indiana)
  - 2 wrestlers from different weight groups
- Fencing club (Colorado)
  - Skin abscesses, paraspinal myositis, bacteremia
  - Risks:
    - sharing sensor wires
    - shared clothing

MMWR. 2003;52(5):88

CA-MRSA in COMPETITIVE ATHLETES

- Collegiate football players in Pennsylvania, Wisconsin, California
- Professional football players
  - Miami Dolphins
  - St. Louis Rams
    - 5 of 58 players (9%); 8 infections
    - Lineman or linebackers

MMWR. 2003;52(5):88
NEJM 2005; 352:468-475
### RISK FACTORS FOR CA-MRSA

- IVDU
- MSM
- Correctional institutions
- Homelessness/marginally housed
- Athletes
- Post-influenza pneumonia

### Clinical Implications of CA-MRSA

**Outpatient & Emergency Dept settings**

Consider medical practice modification in areas with high prevalence of CA-MRSA:
- More frequent C & S testing of potential *S. aureus* skin infections, especially in pediatrics
- Surgical drainage of infection, when appropriate
- Careful selection of empiric antibiotics for suspected staphylococcal infections when treatment is indicated
- Careful patient and laboratory follow-up

*Naimi et al. JAMA 2003;290:2976-84*

### THERAPEUTIC OPTIONS

- Community-acquired MRSA
  - Frequently sensitive to multiple drugs
  - Old, inexpensive drugs such as TMP/SMX, tetracycline, clindamycin can often be used
THERAPEUTIC OPTIONS

• Community-acquired MRSA
  – Frequently sensitive to multiple drugs
  – Old, inexpensive drugs such as
    TMP/SMX, tetracycline, clindamycin can
    often be used
• Hospital-acquired MRSA
  – Usually multi-drug resistant

THERAPEUTIC OPTIONS

• Glycopeptides (Vancomycin)
• Streptogramins (Synercid)
• Oxazolidinones (Linezolid)
• Daptomycin
• Tigecycline (Glycylcycline)

COMING NEW DRUGS

• Telavancin
• Ceftibiprole
PREVENTION OF MRSA

Impact of Hand Hygiene on Hospital Infections

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Setting</th>
<th>Impact on Infection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1977</td>
<td>Casewell</td>
<td>adult ICU</td>
<td>Klebsiella decreased</td>
</tr>
<tr>
<td>1982</td>
<td>Maki</td>
<td>adult ICU</td>
<td>decreased</td>
</tr>
<tr>
<td>1984</td>
<td>Massanari</td>
<td>adult ICU</td>
<td>decreased</td>
</tr>
<tr>
<td>1990</td>
<td>Simmons</td>
<td>adult ICU</td>
<td>no effect</td>
</tr>
<tr>
<td>1992</td>
<td>Doebbeling</td>
<td>adult ICU</td>
<td>decreased with one versus another hand hygiene</td>
</tr>
<tr>
<td>1994</td>
<td>Webster</td>
<td>NICU</td>
<td>MRSA eliminated</td>
</tr>
<tr>
<td>1995</td>
<td>Zafar</td>
<td>nursery</td>
<td>MRSA eliminated</td>
</tr>
<tr>
<td>1999</td>
<td>Pittet</td>
<td>hospital</td>
<td>MRSA decreased</td>
</tr>
</tbody>
</table>


Link to: Improving hand hygiene

FINAL THOUGHTS ON MRSA

• CA-MRSA is spreading rapidly and may become the dominant strain soon both in hospitals and community
• No new oral drugs will be released in the near future
• High index of suspicion and good hand hygiene are key to treatment and prevention
Human destiny is bound to remain a gamble, because at some unpredictable time and in some unforeseeable manner, nature will strike back.

*Mirage of Health*, Rene Dubos, 1959

THANK YOU