An Update on Skin Soft Tissue Infections - MRSA

Yi Guo, Pharm.D.

(Dr. Belinda Ostrowsky will present on behalf of Dr. Yi Guo on Feb 27, 2018)
Objectives

- Review the epidemiology and classification of skin and soft tissue infections (SSTIs)
- Review the characteristics and risk factors of MRSA-associated SSTIs
- Discuss the antimicrobial treatment options for MRSA SSTIs
- Describe opportunities for antimicrobial stewardship interventions
- Discuss patient cases
Epidemiology

- SSTIs accounted for 3.4 million ED visits (2.6% of all ED visits)
- Estimated prevalence of 7-10% for SSTIs among hospitalized patients
- Mean length of stay of 3.7 days with $18,299 per case
- SSTIs is the second most common type of infection among persons residing in long-term care facilities

2011 National Statistics of the Healthcare Cost and Utilization Project
**Staphylococcus aureus**

- *Staphylococcus aureus*: common cause of infection in the community and hospital

- Methicillin-resistant *Staphylococcus aureus* (MRSA):
  - Increasingly important cause of healthcare-associated infection since 1970s
  - Since 1990s, emerged as cause of infection in the community
Microbiology of Purulent SSTIs

- MRSA: 59%
- MSSA: 17%
- B-hemolytic strep: 3%
- non-B hemolytic strep: 4%
- Other: 8%
- Unknown: 9%

(97% USA 300)

# Characteristic of MRSA

<table>
<thead>
<tr>
<th>Prevalent genotypes</th>
<th>Healthcare-associated MRSA (HA-MRSA)</th>
<th>Community-acquired MRSA (CA-MRSA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>USA 100, USA 200</td>
<td>USA 300, USA 400</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antimicrobial resistance</th>
<th>Healthcare-associated MRSA (HA-MRSA)</th>
<th>Community-acquired MRSA (CA-MRSA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multiple agents (usually sensitive to vancomycin)</td>
<td>Few agents (usually sensitive to non-β-lactam antibiotics)</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
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<th></th>
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<tbody>
<tr>
<td>Types I-III</td>
<td>Types IV, V</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Panton-Valentine Leukocidin toxin gene</th>
<th>Healthcare-associated MRSA (HA-MRSA)</th>
<th>Community-acquired MRSA (CA-MRSA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rare</td>
<td></td>
<td>Common</td>
</tr>
</tbody>
</table>

Good News for Some Locations

The Journal of Infectious Diseases
SUPPLEMENT ARTICLE

Life After USA300: The Rise and Fall of a Superbug
Paul J. Planet

The community-associated methicillin-resistant Staphylococcus aureus (CA-MRSA) epidemic in the United States is largely attributable to the meteoric rise of a single clone, referred to as USA300. This strain not only spread across the United States in just a few years to become the predominant cause of staphylococcal disease, but it also appears to have increased the overall number of skin and soft-tissue infections (SSTIs), increasing the overall disease burden. While USA300 still constitutes a major public health burden, its prevalence may be decreasing in some parts of the United States. Other than an epidemic in South America due to a closely related strain, USA300 also seems to have been largely unable to establish itself as an endemic infection in other geographic locations. While there have been several hypotheses put forward to explain the enormous success of USA300, the reasons for its failures and its potential fall remain obscure. Far from being unique to USA300, the rise and fall of specific clones of S. aureus in human populations seems to be a common process that has occurred multiple times and in multiple locations. This review charts the rise of USA300 and the evidence that suggests that it may be in decline, and it considers how best to understand the future spread, containment, and possible extinction of CA-MRSA.

Keywords. MRSA; USA300; Staphylococcus aureus; phylogenomics; epidemic.
Worldwide Prevalence of MRSA

# National Estimates and Adjusted Incidence Rates of Invasive MRSA Infections

<table>
<thead>
<tr>
<th>Epidemiologic Category</th>
<th>Estimated Cases of Infection</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-Dialysis Patients</td>
<td>Dialysis Patients</td>
<td>Total</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Estimated No.</td>
<td>Incidence Rate (Confidence Interval)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Estimated No.</td>
<td>Incidence Rate (Confidence Interval)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Estimated No.</td>
</tr>
<tr>
<td>CA</td>
<td>16,522</td>
<td>5.18 (4.03-6.79)</td>
<td>0</td>
<td>0</td>
<td>16,522</td>
</tr>
<tr>
<td>HCA</td>
<td>44,627</td>
<td>14.01 (12.17-16.29)</td>
<td>10,517</td>
<td>2332.86 (1713.77-3152.92)</td>
<td>55,144</td>
</tr>
<tr>
<td>HCA-HO&lt;sup&gt;d&lt;/sup&gt;</td>
<td>10,130</td>
<td>3.18 (2.33-4.40)</td>
<td>803</td>
<td>178.12 (55.45-462.27)</td>
<td>10,933</td>
</tr>
<tr>
<td>HCA-HACO</td>
<td>34,497</td>
<td>10.83 (9.26-12.81)</td>
<td>9,714</td>
<td>2154.74 (1563.82-2935.10)</td>
<td>44,211</td>
</tr>
<tr>
<td>Overall&lt;sup&gt;e&lt;/sup&gt;</td>
<td>61,927</td>
<td>19.45 (17.16-22.18)</td>
<td>10,517</td>
<td>2332.86 (1713.77-3152.92)</td>
<td>72,444</td>
</tr>
</tbody>
</table>

<sup>a</sup> National Estimates and Incidence (no. per 100,000 population per year) are adjusted for age, race, gender and receipt of chronic dialysis using 2014 US Census Data.  
<sup>b</sup> National Estimates and Incidence (no. per 100,000 dialysis patients per year) for dialysis patients are adjusted for age, race and gender using 2013 USRDS point prevalence data.  
<sup>c</sup> Starting in 2011, confidence intervals on national estimates were calculated based on 72 age/race/gender/dialysis specific strata and summarized for an overall national estimate, accounting for variance across all strata producing a more conservative estimate (with wider confidence intervals) compared to estimates prior to 2011.  
<sup>d</sup> Non-dialysis and dialysis estimated number and incidence based on data from a sample of HO cases.  
<sup>e</sup> 47 cases could not be classified into an epidemiological category or category is unknown and therefore are counted in the overall estimate only.  

CA: community-associated (not linked to inpatient medical care, e.g. in a hospital, nursing home, dialysis facility, etc.)  
HCA: healthcare-associated (linked to receiving inpatient medical care, e.g. in a hospital, nursing home or dialysis facility, etc.)  
HCA-CO: healthcare-associated, community onset (these infections are linked to recent inpatient medical care (e.g. in a hospital or nursing home), but the infection was identified when the patient was back in the general community (e.g. at home))  
HCA–HACO: healthcare-associated, hospital onset (these infections were linked to and identified during recent inpatient medical care, e.g. in a hospital or nursing home, receiving dialysis)  

CDC, Active Bacterial Core Surveillance Report, Emerging Infections Program Network, MRSA, 2014
Definitions/Classification

Uncomplicated SSTI (uSSTI)
- Superficial skin infections that can be treated by surgical incision alone or in combination with oral antibiotics
- i.e. cellulitis, erysipelas, impetigo, small abscesses

Complicated SSTI (cSSTI)
- Skin infections either involving deeper soft tissue/fascia/muscle or requiring significant surgical intervention with antibiotics
- i.e. large abscess, necrotizing infection

Acute Bacterial Skin and Structure Infections (ABSSSI)
- Bacterial infection of the skin with a lesion size area of at least $75\text{cm}^2$ with variable clinical presentations
- i.e. cellulitis, erysipelas, major cutaneous abscesses (excluded diabetic foot infection, decubitus ulcers, infected burns, etc.)

Definitions/Classification

- SSTI
  - Nonpurulent
  - Purulent
Risk Factors

- Crowded living conditions
- Frequent skin-to-skin contact between individuals
- Compromised skin integrity
- Sharing of personal items that may become contaminated with wound drainage
- Poor hygiene
- Poorly controlled diabetes
- Peripheral vascular disease and pre-existing skin diseases that increase the risk of skin infections and abscesses
- Colonization with *S. aureus* and *S. pyogenes*

Case 1

• 60 years old female with 3 days of an enlarging, painful lesion on her right leg, looks like a boil that she attributes to a “spider bite.”

• T 98, BP120/70, P 80
What is the appropriate management of this patient?

A. Incision and drainage alone

B. Incision and drainage plus oral anti-MRSA antimicrobial agent

C. Oral anti-MRSA antimicrobial agent
Abscesses

- Incision and drainage is the primary treatment
  - I&D alone likely adequate for simple abscesses/boils

- Do antibiotics provide additional benefit?
  - Multiple, observational studies: high cure rates with or without antibiotics
  - 3 RCTs of uncomplicated skin abscesses

Conditions in Which Antibiotic Therapy is Recommended After Incision and Drainage

- Signs and symptoms of systemic illness
- Abscess in area difficult to drain completely
- Associated comorbidities or immuno-suppression
- Associated septic phlebitis
- Extremes of age
- Lack of response to incision and drainage alone
- Severe or extensive disease

Purulent SSTIs

- Cellulitis with purulent drainage/exudate
  - I&D is recommended
  - Empiric therapy for CA-MRSA is recommended
  - Empiric therapy for β-hemolytic strep unlikely needed
  - Duration: 5-7 days, based on clinical response

Management of SSTIs

Purulent

Mild
- Suspect CA-MRSA
  - I&D

Moderate
- Suspect CA-MRSA
  - I&D + PO
    - Clindamycin
    - Doxycycline
    - TMP/SMX
- Isolated MSSA
  - I&D + PO
    - Cephalexin
    - Dicloxacillin

Severe
- Suspected MRSA
  - I&D + IV
    - Ceftaroline
    - Daptomycin
    - Linezolid
    - Televancin
    - Vancomycin
- Isolated MSSA
  - I&D + IV
    - Cefazolin
    - Clindamycin
    - Oxacillin
    - Nafcillin

I&D= incision and drainage
IV= intravenous
PO= oral

Case 2

• 60 years old female presents with erythema of her right arm over the past 48 hours. It’s tender and warm to touch. There is no purulent drainage or abscess. No complaint of joint involvement.

• T 98.2, BP 130/72, P 77
What’s the appropriate management of this patient?

A. Clindamycin 450mg PO Q8H

B. Cephalexin 500mg PO Q6H, monitor clinical response and add TMP/SMX if no response

C. Cephalexin 500mg PO Q6H PLUS TMP/SMX 2 DS tablets PO Q6H
Nonpurulent SSTIs

- Cellulitis with no purulent drainage or exudate
  - Empiric treatment for $\beta$-hemolytic strep is recommended
    - Prospective study with 248 hospitalized patients
      - 73% due to $\beta$-hemolytic strep
      - 96% response rate to $\beta$-lactam antibiotics

- Multicenter, double-blind, randomized study with 500 patients
  - Clinical cure rate: cephalexin + TMP/SMX 84% vs. cephalexin 86%

Nonpurulent SSTIs

- Cellulitis with no purulent drainage or exudate
  - Add empiric treatment for MRSA if:
    - Fails to respond to $\beta$-lactam antibiotics
    - Patients with systemic infection
  - Duration: 5-7 days, based on clinical response

Management of SSTIs

Nonpurulent

Mild
- Suspect GAS
  - PO
    - Cephalexin
    - Clindamycin
    - Dicloxacillin
    - Penicillin VK

Moderate
- Suspect GAS
  - IV
    - Cefazolin
    - Ceftriaxone
    - Clindamycin
    - Penicillin G

- Isolated MRSA
  - IV
    - Ceftaroline
    - Daptomycin
    - Linezolid
    - Telavancin
    - Vancomycin

Severe
- Suspected MRSA and/or GNR and/or anaerobes
  - SD + IV
    - Vancomycin + imipenem
    - Vancomycin + meropenem
    - Vancomycin + piperacillin/tazobactam

- Isolated organism
  - SD + IV antibiotic accordingly

GAS = Group A β-hemolytic Streptococcus
GNR = gram-negative rods
IV = intravenous, PO = oral, SD = surgical debridement

Factors Affecting Antibiotic Selection

- Antibiotic allergies
- Vascular impairment-penetration of antibiotics
- Impaired renal function
- Antibiotic resistant patterns
- IV vs. PO
Factors Affecting Antibiotic Selection

- Clindamycin
  - Potential for inducible resistance (D-zone test)
  - Antitoxin effect
  - Higher risk of *C. difficile* associated colitis

Perform on erythromycin-resistant, clindamycin susceptible *S. aureus* isolates
Factors Affecting Antibiotic Selection

- TMP/SMX - Doesn’t provide good Group A strep isolates
- Tetracyclines - Not recommended for <8 years old, pregnancy
- Fluoroquinolones/Macrolides - Not optimal for MRSA (high prevalence of resistant or potential rapid development)
- Rifampin - Not as a single agent
Factors Affecting Antibiotic Selection

- Vancomycin - dosing based on actual body weight, monitor trough level (goal >10) and renal function
- Daptomycin - weekly CPK if prolonged duration
- Linezolid - check weekly CBC if duration >14 days, drug interaction with SSRI
- Dalbavancin/Oritavancin - $$$
Case 3

- 60 years old male with chronic venous dermatitis, poorly controlled DM, morbidly obese (wt 120kg), presenting with 1 week of left foot induration and tenderness. He reports no improvement with 1 week of TMP/SMX 1DS tablet daily. On exam, he is afebrile, WBC 10, stable, and has left foot cellulitis with an ulcer, open wound and draining serosanguinious fluid. Patient’s creatinine is 1.0.
What is the best regimen for this patient?

A. Vancomycin and Piperacillin/tazobactam
B. Vancomycin and Ampicillin/sulbactam
C. Cefazolin
D. TMP/SMX at a higher dose
# Montefiore Empiric Regimens

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Cellulitis                      | **Suspect MRSA:**  
|                                | - **PO:** Bactrim DS, Doxycycline, or Clindamycin  
|                                | - **IV:** Vancomycin (Add Ampicillin/sulbactam for lesion involving face/groin, bite, or ulcer)                                         |
| Purulent = Staph                | **Suspect Strep or MSSA:**  
| Non-purulent = Strep            | - **PO:** Cephalexin or Amox/clav  
|                                | - **IV:** Cephalexin or Ampicillin/sulbactam (if anaerobic coverage needed)                                                             |
|                                | *Local MMC MRSA rates = up to 50%                                                                                                         |
| Uncomplicated Diabetic Foot     | - See above options for PO options  
|                                | - If IV preferred, use Vancomycin for high local MRSA rates ≥ 50%; add Ampicillin/sulbactam if ulcer/open wound present                  |
| Severe Soft Tissue, OR         | **IV Vancomycin + Piperacillin/tazobactam**                                                                                             |
| Complicated Diabetic Foot (toxic, limb threatening, at risk for MDR infection) |                                                                                                                                 |
| Suspect Necrotizing Fasciitis  | **Call Surgery/ID, add Clindamycin IV to above regimen (narrow based on results)**                                                     |
## Antibiogram July 2015-June 2016

<table>
<thead>
<tr>
<th></th>
<th>No. tested (Mode)</th>
<th>CLINDA</th>
<th>GENT®</th>
<th>OXACILLIN</th>
<th>PEN G</th>
<th>VANCO</th>
<th>TETRA</th>
<th>TMP/SMX</th>
</tr>
</thead>
<tbody>
<tr>
<td>S. aureus (MSSA)²</td>
<td>724</td>
<td>411</td>
<td>79</td>
<td>73</td>
<td>100</td>
<td>100</td>
<td>91</td>
<td>93</td>
</tr>
<tr>
<td>S. aureus (MRSA)²</td>
<td>432</td>
<td>333</td>
<td>83</td>
<td>65</td>
<td>95</td>
<td>92</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Staphylococcus epidermidis²</td>
<td>118</td>
<td>240</td>
<td>55</td>
<td>52</td>
<td>100</td>
<td>98</td>
<td>51</td>
<td>32</td>
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<tr>
<td>Staphylococcus haemolyticus²</td>
<td>22</td>
<td>47</td>
<td>50</td>
<td>43</td>
<td>73</td>
<td>34</td>
<td>41</td>
<td>26</td>
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<tr>
<td>Staphylococcus lugdenensis²</td>
<td>143</td>
<td>25</td>
<td>80</td>
<td>88</td>
<td>99</td>
<td>100</td>
<td>100</td>
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<tr>
<td>Staphylococcus saprophyticus²</td>
<td>56</td>
<td>64</td>
<td>95</td>
<td>9</td>
<td>0</td>
<td>100</td>
<td>89</td>
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</table>
Role of Antimicrobial Stewardship
### SSTIs-Opportunities for Antimicrobial Stewardship

<table>
<thead>
<tr>
<th></th>
<th>Cellulitis (n=66)</th>
<th>Cutaneous Abscess (n=103)</th>
<th>STTI with Additional Complicating Factors (n=153)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anti-MRSA therapy</strong></td>
<td>56 (85)</td>
<td>80 (78)</td>
<td>124 (81)</td>
<td>&gt; 0.2</td>
</tr>
<tr>
<td><strong>Broad-spectrum gram-negative therapy</strong></td>
<td>40 (61)</td>
<td>69 (67)</td>
<td>123 (80)</td>
<td>0.004</td>
</tr>
<tr>
<td><strong>Anaerobic therapy</strong></td>
<td>49 (74)</td>
<td>75 (73)</td>
<td>127 (63)</td>
<td>0.11</td>
</tr>
<tr>
<td><strong>≥3 antibiotics</strong></td>
<td>34 (52)</td>
<td>41 (40)</td>
<td>74 (48)</td>
<td>&gt;0.2</td>
</tr>
<tr>
<td><strong>Total duration of therapy, median days (IQR)</strong></td>
<td>13 (10-14)</td>
<td>13 (10-16)</td>
<td>14 (11-17)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Positive culture result (n=150), 97% *S. aureus* or streptococci, 13% aerobic gram-negative bacteria

Lessons learned...

• Hospitalizations for SSTI were common (300-400 admissions annually)

• More than 50% of hospitalized patients were due to cellulitis or cutaneous abscess

• Frequent use of potentially unnecessary broad-spectrum antibiotic therapy

• Prolonged treatment course

• General overuse of radiographic procedures and laboratory testing
The Check List

- What are the most common empiric antibiotics prescribed for SSTIs at your facility?

- What are the susceptibility data according to antibiogram?

- Opportunity for antibiotic de-escalation or streamlining as per culture result?

- What is the average duration antimicrobial therapy for SSTI at your facility?

- If patient is transferring to a hospital from a long-term care facility, let the hospital know:
  - Name/duration of the antibiotic patient has been taking
  - Culture/susceptibility results
Opportunities for Antimicrobial Stewardship

1. What are the most commonly prescribed ABX for at your institution (i.e. SSTIs)?
   i.e. Vancomycin, TMP/SMX, Piperacillin/tazobactam, Levofloxacin, etc.

2. Perform an Medication Utilization Evaluation (MUE)

3. Access the appropriateness of antibiotic choices, duration dose/frequency, culture and susceptibility results

4. Communicate the outcomes/results to multidisciplinary team/committees

5. Form an Action Plan
Summary

• SSTIs are the most common causes of ambulatory visits and represent a substantial % of hospital admissions

• *S. aureus* remains the cardinal pathogen in SSTIs

• Guidelines with algorithms is helpful to select appropriate treatment options for SSTIs

• Antimicrobials stewardship plays important roles in ensuring the appropriateness of antimicrobial usage for SSTIs
COUNTERTHINK
MEET THE HOSPITAL STAPH

EMPLOYEES MUST WASH HANDS BEFORE RETURNING TO WORK.

CONCEPT: MIKE ADAMS
ART: DAN BERGER
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