TRENDS AND ANTIBIOTIC SUSCEPTIBILITY PATTERNS OF METHICILLIN-RESISTANT AND METHICILLIN-SENSITIVE STAPHYLOCOCCUS AUREUS IN AN OUTPATIENT DERMATOLOGY FACILITY

Marilyn Zabielinski, MD; Michael P. McLeod, MS; Cheryl Aber, MD; Jan Izakovic, MD; Lawrence A. Schachner, MD

Objectives: To determine whether the relative proportions of methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-sensitive S aureus (MSSA) were changing or stable in an outpatient dermatology clinic and to examine the antibiotic susceptibility profiles of S aureus isolates.

Design: Retrospective observational data were collected from skin culture isolates annually between January 1, 2005, and December 31, 2010, and monthly during the 6-month period of January 1, 2011, to June 30, 2011.

Setting: The University of Miami Hospital outpatient dermatology clinic.

Participants: A total of 387 S aureus isolates were analyzed between January 1, 2005, and June 30, 2011, from adult and pediatric patients.

Main Outcome Measures: The relative proportions of MRSA and MSSA skin culture isolates were measured, along with antibiotic sensitivity profiles.

Results: The overall relative proportion of MRSA was 35.7%. The overall relative proportion of MSSA was 64.3%. During the last 6 months of the study, the relative proportion of MRSA was 33.3%, while the relative proportion of MSSA was 66.7%. The relative proportion of MRSA from January 1, 2008, through December 31, 2010, was significantly higher than the relative proportion from January 1, 2005, through December 31, 2007 (45.3% vs 28.3%, P = .001). MRSA became more sensitive to ciprofloxacin, while MSSA became more resistant to ciprofloxacin, clindamycin, gentamicin sulfate, and trimethoprim-sulfamethoxazole.

Conclusions: The relative proportion of MRSA in the S aureus isolates increased by 17.0% during the last 3 years of our study. Despite this increase, MRSA became more sensitive to ciprofloxacin, while MSSA demonstrated increased antibiotic resistance to ciprofloxacin, clindamycin, gentamicin, and trimethoprim-sulfamethoxazole.

Published online January 16, 2013.

S TAPHYLOCOCCUS AUREUS IS THE most common cause of skin and soft-tissue infections in the United States and has been since the late 1970s, prior to which Streptococcus pyogenes caused the majority of these infections.1-3 Methicillin-sensitive S aureus (MSSA) and methicillin-resistant S aureus (MRSA) are the 2 major subtypes of S aureus, with methicillin resistance defined as an oxacillin sodium minimum inhibitory concentration of at least 4 µg/mL.4 According to the Centers for Disease Control and Prevention, a MRSA infection is designated as community associated (CA) if it develops in an individual without a history of MRSA isolation or if a positive culture is obtained in the outpatient setting or within 48 hours of hospitalization.5 In distinction to CA-MRSA, health care–associated MRSA is a strain isolated from a patient within 48 hours of hospitalization who has risk factors for a resistant infection, including dialysis, previous colonization, surgery during the past year, a permanent medical device or catheter, or hospital, hospice, or nursing home admission.6

In 1980, almost 2 decades after health care–associated MRSA was initially observed,7 the first case of a CA-MRSA infection was reported in the United States.8 Before 1987, MRSA isolation from outpatient dermatology clinic patients had not been reported.9 MRSA accounts for more than 50% of CA S aureus infections in many US centers.10,11 The reported prevalence and rise of CA-MRSA skin infec-
tion are variable and are largely dependent on the geographic regions in reference. For this reason and because of the limited data available on the trends of the incidence in outpatient dermatology clinics, our primary objective was to determine whether the relative proportions of MRSA and MSSA were changing or stable in our outpatient dermatology clinic in Miami, Florida. Secondly, we aimed to investigate the antibiotic susceptibility profiles of \textit{S} \textit{aureus} isolates to better guide empirical antibiotic choices.

### METHODS

#### STUDY DESIGN

Before data collection, the study was approved by the institutional review board at the University of Miami Miller School of Medicine. A retrospective observational study was then performed on data collected from skin culture isolates annually between January 1, 2005, and December 31, 2010, and monthly during the 6-month period of January 1, 2011, to June 30, 2011. Skin culture isolates were collected from patients seen at the University of Miami Hospital outpatient dermatology clinic. Antibiogram reports of these skin culture isolates were retrieved from the established laboratory accounts for this clinic (Quest Diagnostics and LabCorp). Additional similar data were obtained for January 1, 2008, through December 31, 2010, the antibiotic sensitivity profile of MRSA is summarized in Figure 1. During the last 6 months of the study, the relative proportion of MRSA was 33.3%, while the relative proportion of MSSA was 66.7% (Figure 1). The relative proportion of MRSA from January 1, 2005, through December 31, 2010, was significantly higher than the relative proportion from January 1, 2005, through December 31, 2007 (43.3% vs 28.3%, \(P = .001\)). The relative proportion of MRSA in the \textit{S} \textit{aureus} isolates increased by 17.0% during the last 3 years of our study compared with the previous 3 years.

#### STATISTICAL ANALYSIS

The relative proportions of MRSA and MSSA were calculated relative to \textit{S} \textit{aureus} skin culture isolates. Because of the non-parametric distribution of data, Mann-Whitney and Kruskal-Wallis tests were used to calculate statistically significant differences between the incidence and prevalence. In instances in which the Kruskal-Wallis test reached statistical significance, the post hoc Dunn test was used to determine individual statistical significance. To evaluate for a trend in the annual antibiotic sensitivity data, \(\chi^2\) test was used to calculate statistically significant differences. The relative proportions of MRSA were calculated for the most recent 3 years and were compared with the prior 3 years. Relative was defined with respect to MSSA skin culture isolates and vice versa with respect to MRSA skin culture isolates. Statistical significance was set at \(P < .05\) and in some instances at \(P < .01\). Statistical software (SPSS, version 19.0; SPSS Inc) was used for all calculations.

### RESULTS

#### DEMOGRAPHIC DATA

From the available data (\(n = 74\)), the mean (SD) patient age was 36.5 (22.2) years. Nine of 74 patients (12.2%) were children, while 65 of 74 patients (87.8%) were adults.

#### PREVALENCE AND RELATIVE PROPORTIONS OF MRSA AND MSSA

A total of 387 \textit{S} \textit{aureus} isolates were analyzed between January 1, 2005, and June 30, 2011. Of these total isolates during this period, the overall relative proportion of MRSA was 35.7%, and the overall relative proportion of MSSA was 64.3% (Figure 1). For January 1, 2008, through December 31, 2010, the relative proportion of MSSA was increased by 17.0% during the last 3 years of our study compared with the previous 3 years.

#### ANTIBIOTIC SENSITIVITY PROFILES

**MRSA and MSSA Antibiotic Sensitivity From January 1, 2005, Through December 31, 2010**

For the period January 1, 2005, through December 31, 2010, the antibiotic sensitivity profile of MRSA is summarized in Table 1. Additional results comparing the earlier years with the later years are shown in Figure 2. For the period January 1, 2005, through December 31, 2010, the antibiotic sensitivity profile of MSSA is summarized in Table 2. Additional results comparing the earlier years with the later years are shown in Figure 3.

Trend Data for MRSA and MSSA From January 1, 2005, Through December 31, 2010

For January 1, 2005, through December 31, 2007, and for January 1, 2008, through December 31, 2010, the trend data for MRSA are summarized in Table 3. For the same periods, the trend data for MSSA are summarized in Table 4.

### Antibiotic Sensitivity for MRSA and MSSA During the Last 6 Months of the Study

Antibiotic sensitivity data during the last 6 months of the study are given for MRSA in Table 1. These data for MSSA are given in Table 2.
Consistent with national data, the relative proportion of MRSA in this outpatient dermatology clinic in Miami has risen. For 3 years (2008-2010), the proportion of MRSA rose by 17.0% compared with the prior 3 years (2005-2007). The overall proportion of MRSA in our study was 35.7%. In another outpatient dermatology office, 21% of 135 cultures were MRSA.14 The proportion of MRSA in our study is not only higher than that among many other studies but also is increasing. These findings are similar to, albeit less dramatic than, the results of a large-scale retrospective study15 that analyzed trends in MRSA isolates and the prevalence in the United States using the Surveillance Network database (Eurofins Medinet) and the National Hospitalization Discharge Survey from 1998 to 2007. Among 1 711 991 S aureus isolates from patients seen in ambulatory settings in that study, the unadjusted MRSA annual prevalence increased by 79.5% from 1998 to 2007. These findings were corroborated by the results of a recent study16 from an outpatient dermatology clinic in Germany during the same period, which may suggest that the incidence of MRSA is increasing in multiple and geographically diverse regions.

Despite reports of an increase in MRSA skin isolates, other observations suggest that MRSA may not be rising in incidence as rapidly as once thought. In a North Carolina tertiary outpatient pediatric dermatology clinic, S aureus was recently recovered from 143 cultures, and 27.3% of those were MRSA, which was slightly decreased compared with S aureus cultures between 2005 and 2007, in which the proportion was 32.0%.15 Another study17 analyzing 240 cultures of S aureus from outpatient dermatology clinics noted a significant decrease in MRSA between 2005 and 2009, from 32.0% to 27.3%. Despite the decrease in the proportion of MRSA reported by Diamantis et al,17 they documented a rise in resistance to penicillin, methicillin sodium, erythromycin, clindamycin, and trimethoprim-sulfamethoxazole but not to vancomycin and gentamicin.

In addition to the rise in proportion of MRSA in our outpatient dermatology clinic, we observed a notable trend that MSSA is becoming more resistant to many antibiotics. Comparing the antibiogram results from 2008 to 2010 with those from 2005 to 2007, it was found that...
MSSA in the later period is significantly more resistant to ciprofloxacin, clindamycin, gentamicin, and trimethoprim-sulfamethoxazole. Comparing the same data for MRSA, the later period shows a statistically significant decrease in resistance to ciprofloxacin. It is possible that the increasing resistance of MSSA to these antibiotics is due to their popular use as empirical antibiotics, especially for MRSA, which can also convert to MSSA in vivo; furthermore, genetic recombination may be contributing to the increasing resistance that was observed because staphylococcal cassette chromosomes can be un-

### Table 2. Methicillin-Sensitive *Staphylococcus aureus* (MSSA) Antibiotic Sensitivity Profiles From 2005 to 2011

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>93.4</td>
<td>87.5</td>
<td>84.2</td>
<td>78.8</td>
<td>0.0</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>96.7</td>
<td>100.0</td>
<td>78.9</td>
<td>75.8</td>
<td>77.4</td>
<td>56.5</td>
<td>90.0</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>64.8</td>
<td>59.4</td>
<td>73.7</td>
<td>54.5</td>
<td>64.5</td>
<td>39.1</td>
<td>65.0</td>
</tr>
<tr>
<td>Gentamicin sulfate</td>
<td>97.8</td>
<td>100.0</td>
<td>89.5</td>
<td>84.8</td>
<td>83.8</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>94.5</td>
<td>87.5</td>
<td>NR</td>
<td>100.0</td>
<td>77.4</td>
<td>82.6</td>
<td>95.0</td>
</tr>
<tr>
<td>Rifampin</td>
<td>100.0</td>
<td>93.8</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>90.1</td>
<td>81.3</td>
<td>94.7</td>
<td>87.9</td>
<td>87.1</td>
<td>78.3</td>
<td>90.0</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>97.8</td>
<td>100.0</td>
<td>94.7</td>
<td>87.9</td>
<td>83.9</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Linezolid</td>
<td>NR</td>
<td>NR</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Total No. b</td>
<td>91</td>
<td>32</td>
<td>19</td>
<td>33</td>
<td>31</td>
<td>23</td>
<td>20</td>
</tr>
</tbody>
</table>

Abbreviation: NR, not reported.
*Six-month data for 2011.
Total number of MSSA isolates tested for each year from 2005 to 2010.

### Figure 3. Methicillin-sensitive *Staphylococcus aureus* antibiotic sensitivity from 2005 to 2007 compared with 2008 to 2010. *Denotes statistical significance in antibiotic sensitivity between 2005 to 2007 and 2008 to 2010 at $P < .01$.

### Table 3. Methicillin-Resistant *Staphylococcus aureus* Antibiotic Sensitivity Trend Data From 2005 to 2010

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Ciprofloxacin</td>
<td>90.8</td>
<td>29.9</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>95.1</td>
<td>71.3</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>64.8</td>
<td>54.0</td>
<td>.11</td>
</tr>
<tr>
<td>Gentamicin sulfate</td>
<td>97.2</td>
<td>88.5</td>
<td>.008</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>92.7</td>
<td>87.4</td>
<td>.20</td>
</tr>
<tr>
<td>Linezolid</td>
<td>100.0</td>
<td>100.0</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>88.7</td>
<td>85.1</td>
<td>.77</td>
</tr>
<tr>
<td>Trimethoprim-sulfamethoxazole</td>
<td>97.9</td>
<td>89.7</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>100.0</td>
<td>100.0</td>
<td>&gt;.99</td>
</tr>
</tbody>
</table>

The increasing resistance of MSSA to these antibiotics is due to their popular use as empirical antibiotics, especially for MRSA, which can also convert to MSSA in vivo; furthermore, genetic recombination may be contributing to the increasing resistance that was observed because staphylococcal cassette chromosomes can be un-
stable. A study\(^\text{18}\) reported that the conversion from MRSA to MSSA in vivo can occur because of a recombination between the recombinase genes \(crrC1\) allele 8 and \(crrC1\) allele 10. That MSSA is becoming increasingly resistant to antibiotics stresses the need to select antibiotics based on culture results.

The optimal empirical oral antibiotic therapy for CA-MRSA infections is often complicated by its increasingly resistant antibiotic profile. Our data suggest an exception to this trend. We found a significant increase in the sensitivity of MRSA to ciprofloxacin and a trend toward an increase (although not statistically significant) in its sensitivity to clindamycin, levofloxacin, rifampin, and tetracycline. The recent discontinued use of these antibiotics because of resistance has perhaps made them once again slightly more efficacious. Despite our favorable results with respect to the antibiotic sensitivity to CA-MRSA, other data document geographic regions with clindamycin resistance above 50% and with quinolone resistance above 80%.\(^\text{10-21}\) Trimethoprim-sulfamethoxazole is commonly considered the empirical antibiotic of choice for CA-MRSA, and our data confirm that CA-MRSA is highly sensitive to this antibiotic, with 90.0% of CA-MRSA isolates during the last 6 months of the study being sensitive. However, it is always best to base antibiotic therapy selection on the most recent antibiogram results.\(^\text{1}\)

Based on the results given in Tables 1 and 2 for our outpatient dermatology clinic, the best empirical antibiotic to cover both MRSA and MSSA is trimethoprim-sulfamethoxazole or tetracycline. However, a caveat to note is that when trimethoprim-sulfamethoxazole or tetracycline is empirically used to cover \(S\) aureus, an additional agent may be needed if infection by group A streptococci is a possibility. Clindamycin or erythromycin may be considered therapeutic options, but MRSA and MSSA are not as sensitive to these 2 antibiotics; in fact, erythromycin is a poor choice for MRSA.\(^\text{22-24}\) When a MRSA isolate is erythromycin resistant but clindamycin sensitive, it is important to perform a D-zone test\(^\text{25}\) to detect the presence of \(erm\) genes before beginning therapy with clindamycin.\(^\text{19,26}\) Depending on the geographic region, 25% to 51% of CA-MRSA isolates tested are D-zone test positive, suggesting that clindamycin therapy would be ineffective via a ribosomally mediated mechanism.\(^\text{19,21}\) In addition, approximately 70% of CA-MRSA isolates for the last 6 months of the study were resistant to erythromycin, suggesting that the prevalence of CA-MRSA with \(erm\) genes among our population may be high; however, this was not directly measured by the diffusion disk test.\(^\text{25}\) Although there is 0.0% resistance to linezolid, vancomycin, and rifampin in an outpatient setting, these are unreasonable choices for antibiotic therapy because of their administration route, cost, and availability.

A similar retrospective analysis was performed between June 1994 and May 1997 on pediatric skin infections from the same outpatient dermatology clinic in Miami.\(^\text{27}\) In that study, \(S\) aureus was isolated from 36% of nares cultures (\(n = 118\)) and from 47% of skin cultures (\(n = 131\)). Of 42 \(S\) aureus nares cultures, 79% were resistant to penicillin, 31% to erythromycin, 10% to cloxacillin and cephalothin, and 8% to tetracycline. Although the study did not analyze cultures based on MRSA or MSSA, a general observation comparing these data with our data is that \(S\) aureus is now more resistant to erythromycin and tetracycline. Data suggest that antibiograms may improve empirical therapy decision making by increasing knowledge of local outpatient prevalence of antibiotic resistance.\(^\text{1}\)

Our study has several limitations. The morphology of cutaneous MRSA infection is variable, and common areas for involvement include the legs, knees, thighs, feet, and buttocks.\(^\text{28}\) This study did not measure the incidence ormorphology of MRSA-related and MSSA-related skin infections at these anatomic locations, and this measurement would have been relevant to report. The study also did not record the type of skin infection (eg, impetigo, folliculitis, furunculosis, cellulitis, etc). Because this was a retrospective study, we were also unable to look at the genotypes. Regardless of which genotype was most prevalent in the Miami setting, the choice of the empirical antibiotic would be unchanged. One variable that may have affected the results is the fact that cultures were sent to 2 separate laboratories. A possibility exists that the laboratories may have slightly different methods in measuring sensitivities to antibiotics, which by itself should not have grossly altered the sensitivities reported. The number of cases sent to one of the laboratories was so small that this probably did not significantly influence the results. The antibiogram result for ciprofloxacin was not reported in 2010 for MRSA and MSSA, which may have affected the trend in antibiotic sensitivity. Unfortunately, the exact age of most of the patients was unknown because of database limitations of the laboratories performing the sensitivity tests. The findings in this population of dermatology clinic patients in Miami may not be generalizable to other regions or clinical settings. This study should be repeated with additional data within the next few years to observe if the trend is the same or is changing.

In conclusion, it is important for physicians to obtain cultures of infected sites before administering an antibiotic and to tailor therapy to antibiogram results as soon as possible to appropriately treat a MRSA or MSSA infection. Notably, in vitro susceptibility testing does not necessarily predict in vivo efficacy of an antibiotic, and physicians should alter therapy only if there is no clinical improvement.

Accepted for Publication: March 10, 2012.
Published Online: January 16, 2013. doi:10.1001/jamadermatol.2013.2424
Correspondence: Michael P. McLeod, MS, Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, 1475 12th Ave NW, Ste 2175, Miami, FL 33136 (mpmcleod@med.miami.edu).

Author Contributions: Drs Zabielski, Aber, Izakovic, and Schachner and Mr McLeod had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Aber, Izakovic, and Schachner. Ac-
obtained fund-

Drafting of the manuscript: Zabielinski, McLeod, Aber, Izakovic, and Schachner. Critical revision of the manuscript for important intellectual content: Zabielinski, McLeod, Aber, Izakovic, and Schachner. Statistical analysis: McLeod. Study supervision: Aber, Izakovic, and Schachner. Obtained funding: None.

Conflict of Interest Disclosures: None reported.

Additional Contributions: Christina Jacomino and Jacquelyn Salazar provided administrative, technical, and material support.

REFERENCES

17. Diamantis ML, Ortega-Loayza AG, Morrell DS. Update on the characterization of Staphylococcus aureus skin infections in a pediatric dermatology tertiary care outpatient facility: antibiotic susceptibility patterns and decreased methi-

©2013 American Medical Association. All rights reserved.