**Five-Year Trend of Antimicrobial Susceptibility Rates and Daptomycin Activity among Staphylococcus aureus Isolates Collected in Latin American Medical Centers (2005-2009)

**D.J. BIEDENBACH, RN JONES, HS SADER**
JMI Laboratories, North Liberty, IA, USA.

---

**ABSTRACT**

Background: Daptomycin is lipopeptide with a unique mechanism of action and rapid bactericidal activity against Gram-positive cocci. Daptomycin is approved for the treatment of Gram-positive pathogen associated with community-acquired and hospital-onset infections. Staphylococcus aureus (SA)-associated bacteremia and endocarditis in the United States, Europe and other Latin American countries. In vitro activity of daptomycin and comparator agents was evaluated against clinical isolates of SA collected in five Latin American countries over five years.

**Methods:** 6,301 SA isolates were collected in 10 medical centers located in Argentina, Brazil, Chile, Colombia and Mexico. Antibiotic susceptibility was tested against oxacillin-resistant (MRSA) and –susceptible (MSSA) S. aureus. MICs were determined by the microdilution method in 96-well plates using defined Mueller-Hinton broth adjusted Mueller-Hinton broth supplemented to 50 mL of calcium for daptomycin tests.

**Results:** The overall oxacillin resistance (MRSA) rate in Latin America was 41.1% and varied from 32.1% in Brazil, 39.0% in Mexico, 51.7% in Chile and 51.9% in Argentina. During the period studied, overall MRSA rates increased from 34.7 to 48.4%. Major increases were observed in Chile (36.2 to 57.6%) and Mexico (29.7 to 62.6%; Figure 1).

**Conclusions:** Daptomycin was highly active against MRSA (MIC90 ≤ 0.06 µg/mL; 100% susceptible), and was less active against MSSA (MIC90 ≤ 2 µg/mL; only one doubling dilution above the susceptible breakpoint) isolated from a patient with SSSI in Mexico in 2008.

---

**INTRODUCTION**

Gram-positive bacteria are very common and important pathogens causing serious infections in the hospital environment. Staphylococcus aureus, coagulase-negative staphylococci (CoNS) and enterococci are among the five most frequently isolated pathogens from nosocomial bloodstream infections (BSIs). These three pathogens are responsible for approximately 49% of BSIs cases in Latin American medical centers evaluated by the ENTRAYA Antimicrobial Surveillance Program.

Daptomycin is a lipopeptide with a unique mechanism of action and rapid bactericidal activity against Gram-positive cocci. United States Food and Drug Administration (USA-FDA) approved daptomycin for the treatment of nosocomial pneumonia, Staphylococcus aureus (SA)-associated bacteremia and endocarditis at a dose of 6 mg/kg every 24 hours, and for comparison in an animal model of Staphylococcus aureus (SA)-associated bacteremia using a dose of 4 mg/kg every 24. Daptomycin is also approved for the same indications in various European and Latin American countries. In the present study, we evaluated the antimicrobial activity and comparator agents tested against clinical isolates of S. aureus collected in four Latin American countries over five years.

**MATERIALS AND METHODS**

Bacterial isolates: As part of a worldwide Daptomycin Surveillance Program, 6,031 S. aureus isolates were collected in 10 medical centers located in Argentina (1,075 isolates from two medical centers), Brazil (2,637 isolates from four medical centers), Chile (1,345 isolates from two medical centers) and Mexico (1,345 isolates from two medical centers). Isolates were consecutively collected from prevalent sources of infection, including BSIs (42%), SSIs (28.6%) and others, and a common surveillance design. All organisms isolated from documented human infections and only one isolate per patient infection episode was included in the study. The isolates were identified locally and forwarded to a central monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA) for confirmation of species identity, when necessary, and reference susceptibility testing.

Susceptibility test methods: Daptomycin and comparator agents were tested by the Clinical and Laboratory Standards Institute (CLSI) broth microdilution methods in validated microtiter plate panels manufactured by TREK Diagnostic Systems (TREK, Westlake, OH), and Mueller-Hinton broth adjusted to contain physiological levels of calcium (50 mg/L). CLSI interpretive criteria were used to categorize the isolates as susceptible, intermediate and resistant. A daptomycin susceptibility breakpoint of ≤1 µg/mL was applied as recommended by the CLSI and the USA-FDA. The following quality control (QC) organisms were concurrently tested: S. aureus ATCC 29213, Enterococcus faecalis ATCC 29212 and Staphylococcus pneumoniae ATCC 49619. All QC results were within published ranges.

**RESULTS**

- Daptomycin was very active against 6,031 S. aureus isolates tested (MIC90, 0.250/0.5 µg/mL; ≥99.9% susceptible; Tables 1 and 2). Only one strain showed a non-susceptible daptomycin MIC value; an oxacillin-susceptible S. aureus with a daptomycin MIC of 2 µg/mL (only one doubling dilution above the susceptible breakpoint) isolated from a patient with SSSI in Mexico in 2008.

- The overall oxacillin resistance (MRSA) rate in Latin America was 41.1% and varied from 32.1% in Brazil, 39.0% in Mexico, 51.7% in Chile and 51.9% in Argentina.

- During the period studied, overall MRSA rates increased from 34.7 to 48.4%. Major increases were observed in Chile (36.2 to 57.6%) and Mexico (29.7 to 62.6%; Figure 1).

- Daptomycin was highly active against MRSA (MIC90 ≤ 0.06 µg/mL; 100% susceptible), and was less active against MSSA (MIC90 ≤ 2 µg/mL; only one doubling dilution above the susceptible breakpoint) isolated from a patient with SSSI in Mexico in 2008.

**Conclusions:** Daptomycin was extremely rare and observed in only one of 197,000 isolates of S. aureus collected in Latin American medical centers.

---

**Table 1: Antimicrobial activity of daptomycin and comparator agents tested against isolates of Staphylococcus aureus from Latin American medical centers.**

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>50%</th>
<th>90%</th>
<th>Range</th>
<th>%S / %R a</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin (1,075)</td>
<td>0.25</td>
<td>2.0</td>
<td>&gt;99.9 / 0.1</td>
<td>100.0 / 0.0</td>
</tr>
<tr>
<td>Oxacillin (1,075)</td>
<td>&gt;2</td>
<td>&gt;8</td>
<td>71.6 / 27.2</td>
<td>61.7 / 38.3</td>
</tr>
<tr>
<td>Teicoplanin (1,075)</td>
<td>&gt;2</td>
<td>&gt;8</td>
<td>98.5 / 1.5</td>
<td>99.2 / 0.8</td>
</tr>
<tr>
<td>Gentamicin (1,075)</td>
<td>&gt;2</td>
<td>&gt;8</td>
<td>9.5 / 90.5</td>
<td>2.0 / 98.0</td>
</tr>
<tr>
<td>Ampicillin (1,075)</td>
<td>&gt;2</td>
<td>&gt;8</td>
<td>99.9 / 0.1</td>
<td>100.0 / 0.0</td>
</tr>
<tr>
<td>Ciprofloxacin (1,075)</td>
<td>&gt;2</td>
<td>&gt;8</td>
<td>99.9 / 0.1</td>
<td>100.0 / 0.0</td>
</tr>
<tr>
<td>Trimethoprim/sulfamethoxazole (1,075)</td>
<td>&gt;2</td>
<td>&gt;8</td>
<td>99.9 / 0.1</td>
<td>100.0 / 0.0</td>
</tr>
<tr>
<td>Gentamicin (1,075)</td>
<td>&gt;2</td>
<td>&gt;8</td>
<td>99.9 / 0.1</td>
<td>100.0 / 0.0</td>
</tr>
<tr>
<td>Teicoplanin (1,075)</td>
<td>&gt;2</td>
<td>&gt;8</td>
<td>99.9 / 0.1</td>
<td>100.0 / 0.0</td>
</tr>
</tbody>
</table>

**REFERENCES**