Cefepime, a fourth-generation, extended-spectrum cephalosporin, is often used to treat Enterobacteriaceae infections (1). Concentrations of cefepime above the MIC of the infecting organism for at least 60% to 70% of the dosing interval are recommended to obtain maximal bactericidal effects (2, 3). Doses of 1 to 2 g every 12 h may not achieve adequate concentrations to treat infections when the MIC is 4 μg/ml or greater (1, 2). Earlier this year, the Clinical Laboratory and Standards Institute (CLSI) adapted the MIC breakpoints for cefepime against Enterobacteriaceae based upon several studies demonstrating clinical failure for MICs of 4 to 8 μg/ml. This MIC range is now considered “susceptible dose dependent” (SDD), suggesting that dosing regimens higher than those needed for isolates with lower drug MICs should be employed (4). These alternative dosing strategies may also be of benefit for infections due to Pseudomonas aeruginosa, which does not currently have an SDD interpretive category.

We reviewed all Enterobacteriaceae-positive cultures and P. aeruginosa-positive cultures at a tertiary medical center located in urban Detroit from January 2010 to December 2013. Isolates were included according to CLSI standards for antibiograms (5). The objectives were to identify the proportion of isolates with MICs of 4 to 8 μg/ml and to characterize the cefepime dosing strategies used prior to the CLSI recommendation. All MICs were determined using Vitek 2. The MIC distribution was characterized by organism, location, culture site, and year the culture was collected. Cefepime utilization was described in defined doses (DDDs) per 1,000 patient days.

In total, 9,396 isolates were included: 8,809 (94%) Enterobacteriaceae and 587 (6%) P. aeruginosa isolates. Of the Enterobacteriaceae isolates, 1,045 (12%) were extended-spectrum β-lactamase (ESBL) producers. The emergency department (ED) had 5,184/9,396 (55%) isolates cultured, 2,479 (26%) isolates were from non-intensive care units (ICU), 866 (9%) were from medical intensive care units (MICU), and 867 (9%) were from surgical intensive care units (SICU). Only 407/9,396 (4%) isolates had an MIC of 4 to 8 μg/ml; 236/407 (58%) were Enterobacteriaceae. The proportions of Enterobacteriaceae and P. aeruginosa isolates with an MIC of 4 μg/ml numerically decreased over the study period, while those with an MIC of 8 μg/ml numerically increased. Statistically significant trends for 2010 to 2013 can be seen in P. aeruginosa isolates with an MIC of ≤1 μg/ml (4.1% versus 11.8%, P = 0.01), P. aeruginosa isolates with an MIC of ≤1 μg/ml (11.5% versus 4.4%, P = 0.01), Enterobacteriaceae isolates with an MIC of ≤1 μg/ml (86.9% versus 89.2%, P = 0.02), Enterobacteriaceae isolates with an MIC of 4 μg/ml (2.4% versus 1.2%, P < 0.001), and Enterobacteriaceae isolates with an MIC of 32 μg/ml (1% versus 0.3%, P < 0.001). Additional MIC trends can be seen in Fig. 1. Examining the 236 Enterobacteriaceae isolates with an MIC of 4 to 8 μg/ml, 88 (37%) isolates were from the ED, 77 (33%) isolates from non-ICU, and 44 (19%) isolates from any ICU. The most common culture sites were urine (81%), lower respiratory tract (9%), skin/wound (4%), and blood (4%). Annual cefepime utilization rates were 882 DDDs per 1,000 patient days in 2010; 955 DDDs per 1,000 patient days in 2011; 962 DDDs per 1,000 patient days in 2012; and 925 DDDs per 1,000 patient days in 2013. The most common cefepime dose used was 2 g every 8 h regardless of organism MIC.

![Cefepime MIC distribution by year.](https://example.com/cefpime-mic-distribution.png)

---

**Citation**


Accepted manuscript posted online 15 December 2014

Address correspondence to Susan L. Davis, sldavis@wayne.edu.

Copyright © 2015, American Society for Microbiology. All Rights Reserved.

doi:10.1128/AAC.04491-14
This evaluation demonstrated that despite significant cefepime exposure in the population, the *Enterobacteriaceae* and *P. aeruginosa* cefepime MIC distributions have not demonstrated clinically significant changes. The change in CLSI reporting of *Enterobacteriaceae* isolates to SDD had a small (3%) impact on previously isolated *Enterobacteriaceae* bacteria. The future impact of this breakpoint change remains to be seen; however, optimal dosing should be utilized in treating patients infected with organisms within this SDD category.

**REFERENCES**