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Laboratory News

VOL. 37, NO. 10 - AUGUST 8, 2014

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UPCOMING CHANGES IN GRAM NEGATIVE CEPHALOSPORIN AND CARBAPENEM SUSCEPTIBILITY TEST REPORTING

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Effective August 11, 2014, Marshfield Labs will implement the current Clinical and Laboratory Standards Institute (CLSI) interpretive criteria (i.e., 'breakpoints') of antimicrobial susceptibility testing (AST) for the following beta-lactam antimicrobial agents as applied to the *Enterobacteriaceae*[1] group of bacteria: ceftazidime, ceftriaxone, cefepime, imipenem, and meropenem. In all cases, the revised breakpoints were lowered to better predict clinical outcomes without the need for supplemental AST procedures.

Important points related to the new breakpoints are:

- The presence of extended spectrum beta lactamase (ESBL) enzyme in *E. coli*, *Klebsiella*, and *Proteus* will no longer be routinely pursued and explicitly reported.
- Similarly, the mechanisms behind carbapenem non-susceptibility (e.g., KPC, NDM, VIM, and others) will not be routinely identified.
- ESBL-positive strains of *E. coli* and *Klebsiella* spp. will no longer be automatically reported as resistant to all penicillins and cephalosporins; instead, only those agents that test resistant will be reported as such.
- Tests for ESBL and carbapenemase enzymes will still be available following doctoral microbiologist consult.

BACKGROUND

For many years, clinical microbiology laboratories strove to identify ESBLs and other resistance mechanisms in the *Enterobacteriaceae*

[1] The bacterial family *Enterobacteriaceae* is comprised of *Citrobacter, Enterobacter, Escherichia, Klebsiella, Proteus, Serratia*, and related genera.

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with an array of supplemental AST methods. More recently, carbapenemase-producing *Enterobacteriaceae* have gained national attention. At the same time, it has become increasingly apparent that the various combinations and permutations of resistance mechanisms in the *Enterobacteriaceae* group make the supplemental AST methods needed to detect them difficult to perform, and results when reported (e.g., 'ESBL' or 'KPC') of questionable relevance to the clinician.

Beginning in 2010, the CLSI began publishing revised breakpoints for aztreonam and a number of parenteral cephalosporins and carbapenems including cefazolin, ceftriaxone, ceftazidime, cefepime, doripenem, ertapenem, imipenem and meropenem when tested against the *Enterobacteriaceae.* (Oral cephalosporins and penicillins were unaffected.) Clinical outcomes data as well as Monte Carlo simulation and other pharmacokinetic/pharmacodynamic modelling were used to set the new breakpoints. In all cases, the minimum inhibitory concentration (MIC) breakpoints for 'Susceptible', 'Intermediate', and 'Resistant' for these drugs were reduced by 2-3 twofold dilutions. The intent of the lowered breakpoints is to detect clinically relevant resistance without having to resort to supplemental AST. **An important consequence of this change is that all penicillins and cephalosporins will no longer be automatically reported as resistant when resistance to only one or several agents in this group is identified. Instead, only those antimicrobial agent(s) that test resistant will be reported as 'Resistant'**. Relatedly, isolates of *E. coli* and *Klebsiella* will no longer be designated as ESBL-positive. An example of this change in reporting may be seen in Table 1 for an *E. coli* strain carrying the CTX-M ESBL. (Altered interpretations are highlighted.)

Table 1

Drug	Old Breakpoints	New Breakpoints
Amoxicillin/Clavulanate	S	S
Ampicillin	R	R
Cefazolin	R	R
Ceftazidime	R	S
Ceftriaxone	R	R
Cefepime	R	S
Imipenem	S	S
Meropenem	S	S

REFERENCES

- CLSI. Performance standards for antimicrobial susceptibility testing: 24th informational supplement. M100-S24. 2014. Clinical and Laboratory Standards Institute. Wayne PA.
- Dudley, M.N., P.G. Ambrose, S.M. Bhavnani *et al*. Background and rationale for revised Clinical and Laboratory Standards Institute interpretive criteria (breakpoints) for *Enterobacteriaceae* and *Pseudomonas aeruginosa*: I. Cephalosporins and aztreonam. 2013. Clin. Infect. Dis. 56:1301.

ORDERING INFORMATION

No changes in ordering at this time.

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