Antimicrobial Stewardship News
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Antibiogram Updates 2019

Introduction

In an era of increasing antimicrobial resistance, local antibiograms provide essential data to guide empiric treatment choices. Each year, the Clinical and Laboratory Standards Institute (CLSI) makes updates to interpretive criteria. The 2019 update includes important revisions to the fluoroquinolone (FQ) MIC breakpoints for Enterobacteriaceae and *Pseudomonas aeruginosa*.[1] This newsletter discusses these recent changes and provides helpful reminders for developing antibiograms in community hospitals.

Updated Fluoroquinolone Breakpoints:

In February 2019, the CLSI published updated fluoroquinolone breakpoints for Enterobacteriaceae and *P. aeruginosa*.[1] These changes were based on a thorough review of recent *in vitro*, pharmacokinetic and pharmacodynamic, and clinical studies. The review concluded that the target AUC:MIC for ciprofloxacin and levofloxacin could not be met with traditional dosing regimens in many hospitalized patients using the previous breakpoints. Thus, the CLSI announced lower breakpoints (Tables 1 and 2). These new breakpoints increase the likelihood of pharmacodynamic target attainment with approved dosing regimens.

Using 2019 Breakpoints, Gram-negatives will be categorized as FQ-resistant more frequently.

Table 1. Past vs 2019 Enterobacteriaceae MIC Breakpoints

	Ciprofloxacin			Levofloxacin		
	S	**I**	**R**	**S**	**I**	**R**
Previous Breakpoints	≤ 1	2	≥ 4	≤ 2	4	≥ 8
2019 Breakpoints	≤ 0.25	0.5	≥ 1	≤ 0.5	1	≥ 2

S, susceptible; I, intermediate; R, resistant
Ciprofloxacin dose: 400mg IV or 500mg PO every 12 hours
Levofloxacin dose: 750mg IV or PO every 24 hours

Table 2. Past vs 2019 *P. aeruginosa* MIC Breakpoints

	Ciprofloxacin			Levofloxacin		
	S	**I**	**R**	**S**	**I**	**R**
Previous Breakpoints	≤ 1	2	≥ 4	≤ 2	4	≥ 8
2019 Breakpoints	≤ 0.5	1	≥ 2	≤ 1	2	≥ 4

Ciprofloxacin dose: 400mg IV every 8 hours
Levofloxacin dose: 750mg IV or PO every 24 hours

DASON recommends implementing new 2019 breakpoints as soon as feasible.

Due to regulatory approval processes, it may take some time for commercially available testing platforms to be updated to 2019 breakpoints. It will be important to work closely with the microbiology laboratory to know when the new breakpoints are implemented as more non-susceptible isolates will be reported. We anticipate that this change will be very noticeable to front-line providers, who will need education about this change.

Antibiogram Best Practices

Reporting Frequency – In general, DASON recommends disseminating facility-wide antibiograms on an annual basis using a minimum of a year of data. More frequent reporting periods often result in too few isolates to provide meaningful data. Some situations may warrant more frequent antibiograms: when large changes in susceptibility are observed or if there is a large number of isolates.[1] In order to differentiate new antibiograms from previous versions, consider printing on an alternative paper color.

Minimum Number of Isolates – The CLSI standard for the minimum number of diagnostic isolates to include in an antibiogram is 30.[2] If this threshold is difficult to obtain for an important organism, consider combining data from similar facilities within the geographic region or extending the reporting period.[2,3] Either of these methods is desired over reporting fewer than the

minimum threshold of 30 isolates where one resistant organism can greatly influence results.

Unit-specific Antibiograms – Unit-specific antibiograms can be particularly helpful to clinicians, especially in the setting of selecting empiric therapy for hospital-onset infections. DASON supports development of ICU-specific antibiograms and encourages hospitals with limited isolates to report two years of data. Other hospital units to consider include the Emergency Department and Long-term Care, if applicable.

Source-specific Antibiograms – Antibiograms are often separated based on the source of the sample. For example, urine versus non-urine (e.g., blood, respiratory, tissue, wound, and CSF). Separating urine from non-urine sources is beneficial because certain antimicrobials are approved for urinary tract infections only (e.g., nitrofurantoin) and should not be routinely reported against non-urine pathogens. In addition, cefazolin can be listed as a surrogate agent for oral cephalosporins, such as cephalexin, for urine sources only. DASON recommends reporting isolates from urine sources separately, if feasible.

Combination Antibiograms – Combination antibiograms are used to identify antimicrobial combinations that would provide the greatest empiric activity against targeted pathogens in order to inform treatment decisions. An example combination antibiogram is shown below. Table 3 reports susceptibility to agents frequently used in combination regimens for *P. aeruginosa* isolates that are resistant to cefepime.

Table 3. Percent Susceptible if Resistant to Cefepime

If Resistant to Cefepime:	*P. aeruginosa* (n=25)
Ciprofloxacin	28%
Levofloxacin	32%
Amikacin	76%
Tobramycin	88%

As shown in Table 3, the fluoroquinolones had limited activity against cefepime-resistant *P. aeruginosa* isolates. Therefore, empiric combination regimens including fluoroquinolones would not be beneficial and may put the patient at risk of adverse events.

How to Identify Reporting Errors – Antimicrobial susceptibility reporting errors can arise from a number of different issues including errors in tiered reporting structure and testing platform software, to name a few. In general, we encourage stewards to be suspicious of susceptibility rates that seem too good to be true. For example, if *E. coli* or *P. aeruginosa* is 100% susceptible to piperacillin-tazobactam, it might indicate that some data (e.g., non-susceptible isolates) are not coming across from the susceptibility testing platform. Additionally, if there are large discrepancies between susceptibility rates for gentamicin and tobramycin, it might indicate that there is an issue with the tiered reporting structure for those two agents. We encourage all stewards to investigate scenarios such as these and reach out to DASON staff for more information. In addition, we encourage routine review by other members of the antimicrobial stewardship committee and front-line clinicians prior to publication.

Leveraging Your Antibiogram for Stewardship Success – Carefully consider the agents reported on your antibiogram. Since the main purpose of an antibiogram is to drive empiric therapy selection, agents intended for use only in rare and/or targeted indications can be omitted. For example, DASON hospitals trying to limit ertapenem use to cases of multidrug-resistant Gram-negative infections have omitted reporting ertapenem on the annual antibiogram. Similarly, tigecycline and quinupristin/dalfopristin are rarely reported on antibiograms.

Looking for More Information?

The CLSI now publishes annual guidance on susceptibility testing with free public access. The document is called the M100, and can be accessed following this link. To access this document, be sure to select "Click here to use guest access" in the top right of the screen.

Take Home Points:

- DASON encourages hospitals to implement the new fluoroquinolone breakpoints as recommended by the CLSI once commercially available testing platforms are updated.
- DASON encourages all hospitals to develop and disseminate a facility-specific antibiogram each year as described in the Best Practices section.
- It is critical for stewards to identify and investigate reporting errors when susceptibility rates seem too good to be true.

References:

1. CLSI. Fluoroquinolone Breakpoints for Enterobacteriaceae and Pseudomonas aeruginosa. 1st ed. CLSI rationale document MR02. Wayne, PA: Clinical and Laboratory Standards Institute; 2019.
2. Hindler JF, Stelling J. Analysis and presentation of cumulative antibiograms: a new consensus guideline from the Clinical and Laboratory Standards Institute. *Clin Infect Dis.* 2007;44(6):867-873.
3. Hostler CJ, Moehring RW, Ashley ESD, et al. Feasibility and Value of Developing a Regional Antibiogram for Community Hospitals. *Infect Control Hosp Epidemiol.* 2018;39(6):718-722.