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INTERPRETATION OF CULTURE & SUSCEPTIBILITY REPORTS

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Antimicrobial stewardship programs typically recommend culture and susceptibility testing to guide clinicians in choosing optimal antimicrobial therapy; however, the majority of antimicrobial selections are made empirically,[1,2] rather than based on test results from individual patients. Antimicrobial selection guided by culture and susceptibility testing is conducted mostly for chronic or recurrent infections.[3,4]

Culture and susceptibility reports are often underused by veterinary practitioners because of a number of limitations, including cost and the time delay between sampling and results.[4] Even after results are obtained, clinicians may lack the information necessary to interpret the reports in a meaningful way.

Culture & Susceptibility Reports

A culture and susceptibility report from a microbiology laboratory identifies the bacterial pathogen and lists antimicrobials labeled with an S, R, or I, designating ***S**usceptible*, ***R**esistant,* or ***I**ntermediate*, respectively.[5] These labels indicate the likelihood of a clinical response to antimicrobial treatment. Categories are determined by clinical *breakpoints* (ie, values that express whether specific bacterial pathogens will respond to certain antimicrobials), which are determined for specific antimicrobial/bacteria combinations based on the minimum inhibitory concentration (MIC) and the designation S, R, or I that corresponds to a specific MIC value (see ***Determining Breakpoints***). MIC values are based on populations of the specific bacteria, the pharmacodynamic data for a specific species, and evidence from clinical use in patients treated with that antimicrobial.[6] The clinical use is specific to the dose regimen (ie, dose, route of administration, frequency of administration) and disease. If any aspect of the regimen is altered (eg, the drug is administered orally instead of by injection), the predictive values of the breakpoints are no longer reliable.

Established Breakpoints

The Clinical Laboratory Standards Institute (CLSI) sets the standards for conducting and interpreting veterinary antimicrobial susceptibility tests.[7] Breakpoints have been set only for a limited number of antimicrobial/bacteria combinations in veterinary species. If veterinary breakpoints are not available, breakpoints derived from human data are often provided on the report; this practice, however, is controversial, with some veterinary microbiologists stating that interpretation from nonveterinary breakpoints should not be performed or should only be performed with extreme caution.[8,9] The CLSI recommends that microbiology laboratories should inform clinicians of the breakpoint source (ie, human or veterinary), but such designations rarely appear on culture and susceptibility reports. Thus, the report must be used in conjunction with knowledge of the pharmacokinetics and pharmacodynamics of the antimicrobial and the pathophysiology of the disease to determine if a specific drug is a reasonable treatment option (see ***Breakpoint Sources & Resistance***).[10]

Diagnostic laboratories independently choose which bacterial isolates and which antimicrobial susceptibilities to report. Although laboratories recommend reporting only isolates that are clinically relevant, as

DETERMINING BREAKPOINTS[5-6]

- **Breakpoint**: The specific concentration of an antimicrobial that defines susceptibility or resistance
- **MIC**: The lowest concentration of an antimicrobial required to inhibit the growth of specific bacteria
  - **MIC less than local drug concentration**: Associated with a high likelihood of therapeutic success, therefore susceptible (S)
  - **MIC equal to local drug concentration**: Associated with an uncertain effect; might be effective if concentrated at the site of infection or if the dose is increased, therefore intermediate (I)
  - **MIC greater than local drug concentration**: Associated with a high likelihood of therapeutic failure, therefore resistant (R)

reporting clinically irrelevant isolates can lead to unnecessary antimicrobial use, this would require oversight by a veterinary microbiologist with an adequate clinical background[1]; however, not all laboratories have the services of such specialists. It is also recommended that laboratories practice *selective reporting* (ie, all determined susceptibilities are not automatically reported), which helps prevent clinicians from choosing antimicrobials for cases in which they are not appropriate.[1] For example, the susceptibility of an *Escherichia coli* isolate to nitrofurantoin should only be reported for isolates from an uncomplicated UTI, as UTI is the only clinical situation in which nitrofurantoin is an effective treatment. Susceptibilities for last resort drugs important in human medicine (eg, vancomycin, imipenem) should not be routinely reported.

Resistance & Susceptibility

It is important to recognize intrinsic resistance when interpreting culture and susceptibility reports.[11] There are certain antimicrobial/bacteria combinations for which resistance should be assumed (eg, enterococci and cephalosporins). Some pathogens are intrinsically resistant to most major categories of antimicrobials. For example, *Pseudomonas aeruginosa* is a common secondary invader in cases of chronic otitis externa in dogs. Therefore, it is common to see resistance reported to all antimicrobials except aminoglycosides, fluoroquinolones, and antipseudomonal penicillins (eg, piperacillin). As another example, methicillin-resistant staphylococci should be reported as resistant to all penicillins and cephalosporins and imipenem; even if in vitro test results indicate susceptibility, the laboratory should report the result as resistant if there is a known intrinsic resistance. Results reported as susceptible should be questioned, as they are most likely the result of an identification or susceptibility testing error, indicating potential problems with the laboratory's adherence to standard guidelines.

Unexpected resistance results (eg, penicillin-resistant streptococci) should also be identified and investigated (see ***Breakpoint Sources & Resistance***). Although such results might be due to the emergence of antimicrobial resistance, it is more commonly the result of laboratory error.[8,12]

Rather than listing drugs in alphabetical order, it is preferable for the reporting laboratory to list drugs in groups according to class and in order of appropriate first-line, second-line, and third-line treatment choices to support prudent antimicrobial use. Cross-resistance often occurs within classes of antimicrobials and may be more difficult for the clinician to visualize if drugs are listed in alphabetical order. This order may also prevent practitioners from simply choosing the first drug labeled "S" for therapy.

See next page for references.

BREAKPOINT SOURCES & RESISTANCE

To view a table outlining breakpoint sources for and resistance to common antimicrobials, visit **cliniciansbrief.com/interpretation-culture-susceptibility-reports**

CLSI = Clinical Laboratory Standards Institute
MIC = minimum inhibitory concentration

References

1. Weese JS, Giguère S, Guardabassi L, et al. ACVIM consensus statement on therapeutic antimicrobial use in animals and antimicrobial resistance. *J Vet Intern Med*. 2015;29(2):487-498.
2. AVMA Task Force for Antimicrobial Stewardship in Companion Animal Practice. Antimicrobial stewardship in companion animal practice. *J Am Vet Med Assoc*. 2015;246(3):287-288.
3. Hardefeldt LY, Holloway S, Trott DJ, et al. Antimicrobial prescribing in dogs and cats in Australia: results of the Australasian Infectious Disease Advisory Panel Survey. *J Vet Intern Med*. 2017;31(4):1100-1107.
4. Fowler H, Davis MA, Perkins A, et al. A survey of veterinary antimicrobial prescribing practices, Washington State 2015. *Vet Rec*. 2016;179:651.
5. Silley P. Susceptibility testing methods, resistance and breakpoints: what do these terms really mean? *Rev Sci Tech*. 2012;31(1):33-41.
6. MacGowan AP, Wise R. Establishing MIC breakpoints and the interpretation of in vitro susceptibility tests. *J Antimicrob Chemother*. 2001;48(Suppl 1):17-28.
7. Clinical and Laboratory Standards Institute. Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals. CLSI supplement VET01S. 3rd ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2015:28(8).
8. Rubin JE. Antimicrobial susceptibility testing methods and interpretation of results. In: Giguère S, Prescott JF, Dowling PM, eds. *Antimicrobial Therapy in Veterinary Medicine*. 5th ed. Ames, IA: Wiley Blackwell; 2013:11-20.
9. Hnot ML, Cole LK, Lorch G, et al. Evaluation of canine-specific minocycline and doxycycline susceptibility breakpoints for meticillin-resistant *Staphylococcus pseudintermedius* isolates from dogs. *Vet Dermatol*. 2015;26(5):334-338.
10. Lubbers B. Using individual animal susceptibility test results in bovine practice. *Vet Clin North Am Food Anim Pract*. 2015;31(1):163-174, vii.
11. Leclercq R, Cantón R, Brown DF, et al. EUCAST expert rules in antimicrobial susceptibility testing. *Clin Microbiol Infect*. 2013;19(2):141-160.
12. Livermore DM, Winstanley TG, Shannon KP. Interpretative reading: recognizing the unusual and inferring resistance mechanisms from resistance phenotypes. *J Antimicrob Chemother*. 2001;48(Suppl 1):87-102.
13. Weese JS, Blondeau JM, Boothe D, et al. Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats: antimicrobial guidelines working group of the international society for companion animal infectious diseases. *Vet Med Int*. 2011;2011:263768.
14. Lee JH, Bae IK, Lee SH. New definitions of extended-spectrum β-lactamase conferring worldwide emerging antibiotic resistance. *Med Res Rev*. 2012;32(1):216-232.
15. Hillier A, Lloyd DH, Weese JS, et al. Guidelines for the diagnosis and antimicrobial therapy of canine superficial bacterial folliculitis (Antimicrobial Guidelines Working Group of the International Society for Companion Animal Infectious Diseases). *Vet Dermatol*. 2014;25(3):163-175.
16. Wu MT, Burnham CA, Westblade LF, et al. Evaluation of oxacillin and cefoxitin disk and MIC breakpoints for prediction of methicillin resistance in human and veterinary isolates of *Staphylococcus intermedius* group. *J Clin Microbiol*. 2016;54(3):535-542.
17. Livermore DM, Brown DF. Detection of β-lactamase-mediated resistance. *J Antimicrob Chemother*. 2001;48(Suppl 1):59-64.
18. Rubin JE, Pitout JD. Extended-spectrum β-lactamase, carbapenemase and AmpC producing Enterobacteriaceae in companion animals. *Vet Microbiol*. 2014;170(1-2):10-18.
19. Rubin JE, Ball KR, Chirino-Trejo M. Antimicrobial susceptibility of *Staphylococcus aureus* and *Staphylococcus pseudintermedius* isolated from various animals. *Can Vet J*. 2011;52(2):153-157.
20. Priyantha R, Gaunt MC, Rubin JE. Antimicrobial susceptibility of *Staphylococcus pseudintermedius* colonizing healthy dogs in Saskatoon, Canada. *Can Vet J*. 2016;57(1):65-69.
21. Thungrat K, Price SB, Carpenter DM, Boothe DM. Antimicrobial susceptibility patterns of clinical *Escherichia coli* isolates from dogs and cats in the United States: January 2008 through January 2013. *Vet Microbiol*. 2015;179(3-4):287-295.
22. Schink AK, Kadlec K, Hauschild T, et al. Susceptibility of canine and feline bacterial pathogens to pradofloxacin and comparison with other fluoroquinolones approved for companion animals. *Vet Microbiol*. 2013;162:119-126.
23. Durante-Mangoni E, Grammatikos A, Utili R, Falagas ME. Do we still need the aminoglycosides? *Int J Antimicrob Agents*. 2009;33(3):201-205.
24. Maaland M, Guardabassi L. In vitro antimicrobial activity of nitrofurantoin against *Escherichia coli* and *Staphylococcus pseudintermedius* isolated from dogs and cats. *Vet Microbiol*. 2011;151(3-4):396-399.
25. De Lucia M, Bardagi M, Fabbri E, et al. Rifampicin treatment of canine pyoderma due to multidrug-resistant meticillin-resistant staphylococci: a retrospective study of 32 cases. *Vet Dermatol*. 2017;28(2):171-e36.

Suggested Reading

Weese JS. Correct use of antimicrobial therapy. *Clinician's Brief*. 2016;14(7):91-94. https://www.cliniciansbrief.com/article/correct-use-antimicrobial-therapy.