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VETPATH LABORATORY SERVICES

MIC – WHAT ARE THEY AND HOW CAN THEY BENEFIT MY PRACTICE?

What is the MIC?

MIC refers to the minimum inhibitory concentration of an antimicrobial. The MIC (usually expressed in mg/L or µg/mL) is the lowest concentration of an antimicrobial required to inhibit the growth of a microorganism.

How are MICs determined?

Once a pathogen is isolated in pure culture, MICs can be determined by using broth or agar dilution methods. In these methods known concentrations of the antimicrobial are diluted in a series of liquid or solid media and a known concentration of the organism is inoculated. Following appropriate incubation, growth is assessed and the lowest concentration in which no visible growth is recorded is referred to as the MIC. Standards on how the techniques are to be performed are published by the Clinical Laboratory Standards Institute (CLSI) which importantly includes resistant (R), intermediate (I) and susceptible (S) breakpoints and MIC ranges for control organisms to make sure testing is always accurately performed. Both broth and agar dilution methods are labour intensive and thus costly, however the advent of the VITEK® 2 clinical diagnostics system from bioMérieux provides both rapid biochemical identification of diagnostic isolates and automated MIC testing for a range of antimicrobials. Vetpath Laboratory Services can provide MIC testing to its veterinary clientele.

How is MIC testing different from conventional disk diffusion testing?

MIC testing is a QUANTITATIVE technique that yields a concentration for the antimicrobial which can be compared against clinically established susceptible, intermediate and resistant breakpoints (Table 1), whereas disk diffusion testing is a QUALITATIVE technique, with the isolate classified as susceptible, intermediate or resistant based on the size of a zone of inhibition surrounding an antimicrobial impregnated disc placed on top of a lawn culture of the organism.

SUSCEPTIBLE indicates a strong likelihood of successful treatment of the infection (based on plasma concentrations) when the antimicrobial is administered at the recommended dose rate. RESISTANT indicates a strong likelihood of antimicrobial treatment failure due to resistance mechanisms present in the bacteria or inadequate drug concentrations in the patient.

Vetpath Laboratory Services welcomes feedback on all aspects of our service from couriers to lab results. Please feel free to contact us at **9259 3666** or email **enquiries@vetpath.com.au**

Is MIC testing better than conventional disc diffusion testing?

Whilst the two techniques operate on the same principle, MIC testing allows for more precisely targeted therapy and dose rates. For example, in the case of a *Pseudomonas* ear infection, a disc diffusion test may only classify the isolate as resistant to enrofloxacin.

However, with MIC testing, even though the isolate may still be in the resistant category, its MIC could range all the way from 4μg/mL to >128 μg/mL. Concentrations higher than 4μg/mL are definitely achievable with most topical treatments containing enrofloxacin, meaning that the infection could still be adequately treated if the isolate had an MIC of 4-16 μg/mL and possibly higher, but treatment would not be recommended if the MIC was >64 μg/mL.

MIC testing can also be used to more precisely determine effective dose rates for urinary tract infections (particularly in the case of amoxicillin-clavulanate which concentrates in urine), though it still must be remembered that in complicated cystitis cases involving penetration of the mucosa, it is far more important to achieve adequate tissue concentrations rather than high urine concentrations for therapeutic success. The inserts accompanying most veterinary antimicrobials provide information on serum concentrations achieved following the recommended dose.

One of the applications the Australian Infectious Diseases Advisory Panel would like to develop is a MIC calculator as a smart phone app. Enter the antimicrobial MIC for the organism and it will calculate a dose rate and determine if it is within the recommended dose range.

Should MICs be interpreted differently for concentration vs time-dependent antimicrobials?

Concentration-dependent antimicrobials such as fluoroquinolones (FQs) and aminoglycosides require the maximum serum concentration (C_{max}) following dosing to remain above the MIC. The remaining time-dependent antimicrobials (such as the beta-lactams) require serum concentration to remains above the MIC for 60-80% of the time between dosing intervals. Additionally for the FQs, the C_{max} should also remain above the mutant preventing concentration for the organism, the concentration of the antimicrobial that prevents spontaneous mutations. In veterinary practice this supports the use of the high end of the recommended dose rate.

(Nuke 'em before they mutate!!).

Table 1: CLSI Minimum inhibitor concentration breakpoints for some common antimicrobials used in veterinary practice

Antimicrobial	Susceptible (μg/ml)	Resistant (μg/ml)
Ampicillin	< 0.25	> 0.5
Amoxicillin/Clavulanate	< 0.25 / 0.12	> 1 / 0.5
Cephalothin	<2	>8
Chloramphenicol	<8	>32
Clindamycin	<0.5	>4
Enrofloxacin	<0.5	>4
Marbofloxacin	<1	>4