

MINIMIZING ANTIMICROBIAL RESISTANCE PART II: INTERPRETING CULTURE AND SUSCEPTIBILITY DATA

Dawn Merton Boothe, DVM, MS, PhD, DACVIM, DACVCP
Auburn University, AL USA boothdm@auburn.edu

Introduction

For all infections, but particularly complicated infections, or in patients at risk for therapeutic failure or developing resistance, antimicrobial decision making should be guided by the three D's: **de-escalate** antimicrobial use, **design** a proper dosing regimen, and **decontaminate** such that the spread of infection is minimized. This session will focus on the design of the dosing regimen. Once the decision to treat with systemic antimicrobials is made, the design of the dosing regimen includes not only selecting the best drug to target the infecting pathogen, but designing the most effective dosing regimen that minimizes emergent resistance. Among the most effective tools to support design of the dosing regimen is culture and susceptibility data. Clearly, patient data is most useful, but population culture and susceptibility data can support empirical therapeutic decision making. Identification of the infecting organism most appropriately should be based on appropriately collected cultures with (ideally) tube dilution susceptibility testing to allow assessment of "how" susceptible the isolate is, in general, to other drugs, but specifically to the drug of choice, such that a dosing regimen can be designed for the bug in the patient. Basing antimicrobial selection on C&S data does not guarantee success, just as failing to use C&S as a basis for selection (or selecting a drug characterized by "R" on the data) does not guarantee failure. Further, there are many pitfalls to C&S testing, including mis or over interpretation.

1. The data is only as good as sample collection, handling and testing. Just as absence of growth does not indicate absence of infection, isolation of an organism is not necessarily evidence of infection, nor even if infection is present, does the isolated organism represent the infecting organism. One of the biggest challenges is making sure that the cultured organism is the pathogen causing harm to the patient. Pure, vibrant (meaning special media was not needed to coax the growth of the organism) of a large number of colonies are indicators of infection. The isolation of three or more different organisms (including more than one strain of the same organism) may indicate contamination and reculture should be considered. As such, the method of sample collection is critical and must minimize contamination while optimizing pathogen growth. Clearly, (properly collected) culture of an organism from a tissue that is normally sterile indicates infection. Organisms that do not make sense (eg, *Bacillus*; an anaerobe from the urinary tract, etc) might indicate questionable data. For urine, cystocentesis. For tissues, as convenient as swabs can be, they increase the risk of contamination with commensals if the site is not properly prepared, are inhibitory to microbe growth, and organisms in the depth of the swab may not be cultured. They also preclude colony counts which otherwise not only help confirm pathogenicity, but give an indication of extent of growth, which in turn, should impact the dosing regimen (more bugs=more drug molecules. The extent of growth should be strongly considered when deciding to treat. Generally, clinical signs of infection may require, depending on the site, $>10^6$ CFU/ml (or g tissue). For C&S purposes, quantitative cultures can be helpful: the urinary tract is not considered infected until $>10^5$ CFU/ml are present whereas only $>10^3$ is indicative of infection in the respiratory tract. Another reason that samples must be handled properly is exemplified with UTI: with an *E. coli* doubling time as short as 20 minutes, a small colony count indicative of no infection can rapidly become a high colony count ($>10^5$ CFU/ml) indicative of infection. Use of "urinary" paddles might be considered for samples that are being shipped in order to increase accuracy of identification and numbers. Laboratories may also indicate "heavy, moderate or light" growth; isolates with the greatest amount growth might be targeted if all cannot be. Regarding the laboratory, no mandated accreditation process assures the quality of

the data. A *veterinary* microbiologist should be available to answer questions; *veterinary* interpretive criteria (breakpoints) generated by the Clinical Laboratory Standards Institute (CLSI) must be followed. A call to the diagnostic lab might be prudent before marked financial commitment is put into treating an organism that is not causing infection.

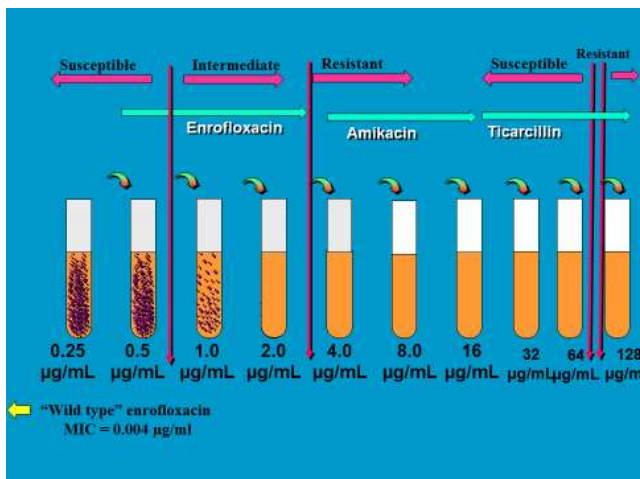
2. To wait or not to wait? Frequently, antimicrobial therapy is begun before cultures are collected. This is particularly true and appropriate in critical patients or in patients for which clinical signs are evident and are detracting from quality of life (patient or parent). However, should therapy begin and the choice prove to be wrong once C&S data is received, the original C&S data collected before the drug was begun may no longer be relevant to the patient. The use of the drug may change the pattern of resistance versus susceptibility, or may result in higher MIC (see mutant prevention concentration). If the patient has responded, no change is indicated. If not, a reculture may be indicated at that time, if possible. Certainly, dosing regimens with the appropriate drug should take into account the possibility that some level of resistance has developed toward the indicated drug.

3. In vitro to In vivo: Some of the Pitfalls. The C&S procedures themselves are fraught with potential errors. For practices that provide in-house susceptibility testing, care must be taken to follow guidelines established and published by (or comparable to) the Clinical and Laboratory Standards Institute (CLSI) or comparable standard-setting agency. Materials, including interpretive standards, should be validated by the appropriate agency. As such, in-house susceptibility testing should be considered with caution. Minor changes in pH, temperature, humidity, etc can profoundly affect results. Personnel should be trained specifically in culture techniques and hospitals that provide this service (as do diagnostic labs) should maintain well designed and adequately collected quality control data to validate their procedures (CLSI indicates control organisms). Pitfalls of susceptibility testing also reflect the drugs selected for testing. Not all companies are interested in

establishing interpretive criteria and as such, not all drugs are available for testing. Because automated systems can not accommodate and laboratories (nor clients) can not afford to test all potential drugs used to treat an infection, one drug often is tested as a model for other drugs in the class. For example, cephalothin models first generation cephalosporins, even though it is no longer used clinically. Note that it does not represent cefazolin well, the latter being more effective toward Gram negative (especially *E coli*) isolates. No single cephalosporin can represent 2nd or beyond generations. Enrofloxacin often represents the fluoroquinolones. In general, cross resistance can be expected among the FQs, although differences in potency do exist (for example, ciprofloxacin is more potent toward *Pseudomonas* or *E coli*, but less to Gram positives compared to enrofloxacin). Culture does not take into account active metabolites of some drugs (eg, enrofloxacin converted to ciprofloxacin). Note that if an organism is R to any FQ, FQ should be used only cautiously even if another is “S”. Amikacin is often more effective than gentamicin toward many organisms, but less effective toward *Staphylococcus* sp. (hence both are often on a report). Note that CLSI interpretive criteria are generated for specific species, and often for specific organisms and specific infections. Human laboratories will use human interpretive criteria, which often are not relevant to animals (eg., ciprofloxacin). Ciprofloxacin (CIP) oral bioavailability in dogs is 30 to 40% of that in humans, and despite its increased potency compared to enrofloxacin (ENR) toward Gram negative organisms, its potential efficacy

E coli UTI	Week 1		Week 4	
Amikacin	≤2	S	≤2	S
Amoxi-Clav	≤8	S	≥32	R
Ampicillin	≥32	R	≥32	R
Carbenicillin	≥512	R	≥512	R
Cephalothin	8	I	≥32	R
Ceftiofur	≤1	S	≥8	R
Chloramph	≥32	R	≥32	R
Ciprofloxacin	≤0.5	S	≥4	R
Enrofloxacin	≤0.25	S	≥4	R
Gentamicin	≤0.5	S	1	I
Nitrofurantoin	≤32	S	≤32	S
Piperacillin	≥256	R	≥256	R
Tetracycline	≤1	S	≥16	R
Ticarcillin	≥256	R	≥256	R
Tobramycin	≤0.5	S	≤0.5	S
Trim-Sulfa	10	S	≥320	R

Culture and susceptibility from a 3 year Weimeraner with recurrent UTI. The second result was collected 2 weeks after 14 days



(MIC_{BP}) is equivalent to or less for many organisms. Susceptibility data also does not take into account active metabolites, again exemplified by ENR, which is metabolized to

CIP: both C_{max} and area under the curve (AUC) of bioactivity of ENR may increase up to 50% or more by CIP; as such, C&S data may underestimate efficacy. MIC_{BP} generally are based on the highest labeled dose (eg. 20 mg/kg for enrofloxacin, 13 mg/kg q 8 hrs for amoxicillin for canine UTI), but higher doses might be safely administered for many antibiotics. If recommended doses change, the manufacturer should provide CLSI with updated pharmacokinetic information so that interpretive criteria may change. One of the disadvantages of current susceptibility testing is that the concentrations tested are close to the MIC_{BP} and thus, does not allow identification of isolates that are very susceptible (that is, MIC are far away from the MIC_{BP}). A final concern relates to the 3rd and 4th generation (extended spectrum) cephalosporins: they are susceptible to extended spectrum beta-lactamase (ESBL) that tend to be induced *in vivo* but often missed *in vitro*. If CLSI guidelines are followed, resistance to cefpodoxime indicates ESBL being produced, If CLSI guidelines are not followed, therapeutic failure may occur. Carbapenems and clavulanic acid (eg, amoxicillin-clavulanic acid) generally are not susceptible to these enzymes.

BRIDGING PHARMACODYNAMIC (PD) AND PHARMACOKINETIC (PK) DATA

Agar gel diffusion data, which is the only data available for organisms that do not grow rapidly enough, only provides a “yes” (S) or “no” (R) (and sometimes “maybe” [I]) which is helpful, but not nearly as much as tube dilution data. An example of population data is the 2016 Cumulative Antimicrobial Susceptible Report which is a simple yes vs no for agar gel and tube dilution data (the number of isolates tested is in the first column; the percent of those isolates susceptible to each drug is in the appropriate cell). On the other hand, although tube dilution data does provide S, I, or R information, along with quantitative data (the MIC, or Minimum , Inhibitory Concentration), it is difficult to interpret. Simplistically, the MIC

Table 1. CLSI interpretive criteria for selected drugs (*criteria established for animals for specific conditions)

Drug	MIC BP	
	S	R
*Amikacin	≤ 16	≥ 64
Amoxicillin	≤ 25 ¹	≥ 0.5
	≤ 16 ²	≥ 32
*Amoxicillin with clavulanic acid	≤ 4/2 ¹	≥ 8/4
*Ampicillin ⁴	≤ 8/4 ²	≥ 32/16
	≤ 25 ¹	≥ 0.5
	≤ 8 ²	≥ 32
Azithromycin	≤ 4	≥ 8
Carbencillin	≤ 16	≥ 64
*Cefazolin	≤ 8	≥ 32
Cefotaxime	≤ 8	≥ 64
Cefoxitin	≤ 8	≥ 32
Cefpodoxime	≤ 2	≥ 8
Ceftazidime	≤ 2	≥ 32
*Ceftiofur	≤ 2	≥ 8
Ceftizoxime	≤ 2	≥ 32
Ceftriaxone	≤ 2	≥ 64
Cefuroxime	≤ 8	≥ 32
Cephalexin	≤ 8	≥ 32
*Cephalothin	≤ 8	≥ 32
*Chloramphenicol	≤ 8	≥ 32
Ciprofloxacin (≤ 1	≥ 8
Clarithromycin	≤ 8	≥ 32
*Clindamycin	≤ 0.5	≥ 4
*Difloxacin	≤ 0.5	≥ 4
Doxycy, line	≤ 4	≥ 16
*Enrofloxacin	≤ 0.5	≥ 4
Erythromycin	≤ 0.5	≥ 4
	≤ 0.25	≥ 1
Florfenicol	≤ 2	≥ 8
Gentamicin*	≤ 4	≥ 16
*Imipenem/cilastin	≤ 4	≥ 16
Kanamycin*	≤ 16	≥ 64
Lincomycin	≤ 0.5	≥ 4
Marbofloxacin	≤ 1	≥ 4
Meropenem	≤ 8	≥ 32
Metronidazole	≤ 8	≥ 32
Nitrofurantoin	≤ 32	≥ 128
*Orbafloxacin	≤ 1	≥ 8
*Oxacillin	≤ 2	≥ 4
Penicillin G	≤ 8 ¹	≥ 16
	≤ 0.12 ²	≥ 0.25
Piperacillin	≤ 16 ²	≥ 128
	≤ 64 ¹	≥ 128
*Rifampin	≤ 1	≥ 4
Sulfadiazine	≤ 2	≥ 4
*Tetracycline	≤ 4	≥ 16
*Ticarcillin	≤ 64 ³	≥ 128
	≤ 16 ⁴	≥ 128
*Ticarcillin with clavulanic acid	≤ 64/2 ³	≥ 128/2
	≤ 16/2 ⁴	≥ 128/2
*Trimethoprim/ Sulfamethoxazole	≤ 2/38	≥ 4/76
	≤ 0.5/9.5	≥ 32
*Vancomycin	≤ 4	≥ 32

indicates “what is needed” in the patient to facilitate antimicrobial efficacy. Care must be taken with this simplistic approach: susceptibility data is generated from in vitro methodologies, yet it is applied to in vivo (and abnormal) conditions. Note that population susceptibility data can be helpful with empirical selection of antimicrobials (see below).

Pharmacodynamic (Microbiological) data: what you need. In contrast to disk diffusion, tube dilution methods involve inoculation of a series of test tubes with a standard number of organisms. The test tubes contain increasing concentrations of the drug of interest in two-fold dilutions whose range varies with the drug, reflecting concentrations achieved in the patient for that drug at the recommended dose. Following a standard time, the tubes are evaluated for detectable growth. The test tube that contains the lowest concentration of drug and no visible growth contains the minimum amount of drug necessary to inhibit (not kill) the growth of the organism cultured from the patient (the MIC). Ideally, this concentration must be achieved at the site of infection. Adaptation to computerized/automated systems allow much more accurate testing in short time periods. For either method of susceptibility testing, simplistically, the likelihood of a drug being effective in the patient is based on whether or not the recommended dose on the label is likely to generate plasma drug concentrations (PDC) that equal or surpass the MIC of the infecting organism. Diagnostic laboratories indicate the likelihood of susceptibility by the “SIR” letter. It also must be handled properly: with a doubling time as short as 20 minutes, a small colony count indicative of no infection can rapidly become a high colony count (>10⁵ CFU/ml) indicative of infection. Understanding the basis of that designation will facilitate antimicrobial selection. The SIR designation reflects whether or not the MIC of the infecting organism is less than (“S”), close or equal to (“I”) or greater than (“R”) the breakpoint MIC (MIC_{BP}) of the drug. CLSI determines the breakpoint, based in part, on peak plasma drug concentrations (C_{max}) of the drug (population data). Because dose and C_{max} varies for each drug (eg, at 20 mg/kg, C_{max} of enrofloxacin is 4 mcg/ml; at 22 mg/kg, C_{max} of amikacin is 65 mcg/ml), the concentrations of drugs tested by the laboratory vary, and the breakpoint will also vary. Thus, one should not compare an MIC for

enrofloxacin (eg, 0.25 mcg/ml) to an MIC for amikacin (eg, 4 mcg/ml) and assume the former is better. Rather, “how far” that MIC is from the C_{max} determines how susceptible the isolate is to each drug. Note also that the range of each drug tested is very narrow, leading to “≤” on reports. For example, for the culture report below and amikacin, ≤ 4 means no growth occurred in the test tube containing 8 mcg/ml, which was the lowest concentration tested by the lab, so the MIC must be lower than



2016 Cumulative Antimicrobial Susceptibility Report Canine Isolates

PERCENT SUSCEPTIBLE
(No. ISOLATES TESTED) *

	No. of Isolates	Amikacin	Amoxicillin/CA	Ampicillin	Cefepime	Ceftiofur	Chloramphenicol	Clindamycin	Doxycycline	Enrofloxacin	Erythromycin	Gentamicin	Marsilofloxacin	Nitrofurantoin	Quacilin + 2% NaCl	Flucanil	Rifampin	Tetracycline	Trimethoprim/Sulfa
Enterobacteriaceae	88		100 (19)				93			40 (67)	8 (13)		34 (67)	100 (56)	100 (58)	12 (42)	55 (64)		
Enterococcus faecium	24		29 (7)				96			0 (17)	0 (17)		0 (17)	29 (7)	24 (21)	27 (15)	16 (22)		
Escherichia coli	241	92 (263)	56 (258)	51 (251)	71 (241)	70 (246)	56			76 (260)		92 (260)	81 (260)	96 (174)				81 (250)	82 (257)
Klebsiella pneumoniae	40	100 (36)	50 (37)	0 (37)	72 (39)	69 (39)	95			81 (39)		95 (39)	80 (39)	12 (24)				85 (39)	75 (39)
Proteus mirabilis	85	100 (54)	80 (56)	71 (56)	86 (56)	88 (56)	63			95 (56)		96 (56)	9 (56)					0 (56)	84 (56)
Pseudomonas aeruginosa	53	84 (67)								31 (67)		94 (67)	81 (67)						
Staphylococcus aureus	19	94 (16)	36 (18)		60 (15)	53 (15)	94 (13)	85 (13)		67 (18)	50 (14)	95 (14)	72 (18)	100 (5)	55 (15)	27 (15)	88 (13)	84 (17)	94 (17)
Staphylococcus intermedius [§]	265	96 (244)	52 (227)		84 (185)	84 (222)	27 (252)	55 (188)		59 (229)	49 (217)	55 (254)	62 (236)	100 (39)	44 (216)	13 (216)	89 (238)	52 (250)	58 (236)
Group G Beta Staphylococci	71	2 (67)	100 (56)	92 (56)			100 (170)	58 (67)	76 (75)	57 (61)	91	46 (71)	78 (59)					100 (58)	

* Number in parentheses represent actual number tested if different from total.
 § Represents what is presently known as S. aureus group and includes S. aureus, S. pseudintermedius, and S. saprophyticus.

8 or ≤ 4 mcg/ml, (the next lowest concentration). The isolate is susceptible. An MIC of $> X$ is accompanied by an “R” because the organism was not susceptible to the highest concentration tested. CLSI updates MIC_{BP} (generally yearly) particularly as new data is provided regarding organism susceptibility. Increasing resistance to organisms may lead to changes in the MIC_{BP} such as has recently occurred for amoxicillin and doxycycline. For older antibiotics approved decades ago, originally labeled doses may be inappropriate for all except very sensitive organisms. Again, a good laboratory will follow CLSI guidelines.

Not all “S’s” are alike. The selection of an antimicrobial should be based on the likelihood that therapeutic (effective) concentrations will be achieved at the tissue site. What is needed for therapeutic efficacy for infections is determined largely by the susceptibility (pharmacodynamic data) of the organism. If you have a C&S from your patient with MIC, the MIC for the drug of interest is how much you need. (For populations of microbes, the MIC₉₀ provides an indication of what is needed.) Efficacy

Table 2. Selected Pharmacokinetic Data for Antimicrobials

Drug	HL	Dose	Route	C _{max}
	hr	mg/kg		mcg/ml
Amikacin (C)	1	20	IV	55
Amoxicillin (T)	1	12.5	PO	4.5-6
Amoxi-clav (T)	1-1.5	12.5	PO	4.5-6
Ampicillin (T)+A29	0.5-1.5	30	PO	10
Cefotaxime	0.8	50	IV,IM	41
Cefpodoxime	5.6	5	PO	8.2
Ceftazidime (T) ^{5nd}	0.82	30	SC	42
Cephalexin (T) ^{1st}	1.3-2.5	20	PO	20
Chloramphenicol (T)	1.2-2.7	20	PO	23
Ciprofloxacin (C)	5.3	20	PO	2.8
Doxycycline (T)	4.6	2.5	PO	3
Enrofloxacin (C)	4.1	20	PO	4.2
Gentamicin (C)	1	10	IV	28
Imipenem/cilastin (T)	1	5	IM	13
Marbofloxacin (C)	11	2	PO	1.4
Orbifloxacin (C)	5	2.5	PO	2
Sulfadimethoxine (T)	13	55	PO	67
Tetracycline (T)	10	13.75	IV	7
Ticarcillin (T)	1	40	IV	80
Ticar-clav (T)	1	40	IV	80

C=concentration dependent

T=time dependent

E. coli UTI	Week 1		C _{max} :MIC
Amikacin	≤ 2	S	>32
Amoxi-Clav	≤ 8	S	< 1
Ampicillin	> 0.5	R	
Carbenicillin	> 512	R	
Cephalothin	8	I	2.5
Ceftiofur	≤ 1	S	NA
Chloramph	≥ 32	R	
Ciprofloxacin	≤ 0.5	S	> 5
Enrofloxacin	≤ 0.25	S	> 17
Gentamicin	≤ 0.5	S	> 56
Nitrofurantoin	≤ 32	S	NA
Piperacillin	≥ 256	R	
Tetracycline	≤ 1	S	> 7
Ticarcillin	> 256	R	
Tobramycin	≤ 0.5	S	NA
Trim-Sulfa	10	S	6.7

of an antibiotic is most likely to occur when the pharmacodynamic data is coupled with what is achieved in the patient. For the clinician seeking to improve antimicrobial efficacy, the further the MIC of the infecting organism is from the C_{max} (or MIC_{BP}) of the drug, the more likely effective concentrations will be reached at the site of infection. If a number of drugs are designated as “S”, the selection of which “S” is best might be narrowed by focusing on those drugs for which the MIC is furthest from the MIC_{BP} or C_{max}. The most susceptible, lowest tier drug should be selected.

Just because a drug is “S” does not mean that resistance is not developing. This is probably one of the most important points to understand. The “S” on a culture report indicates that CLSI anticipates that if the **dose used for breakpoint determination** is used in the patient, therapeutic success is more likely. As indicated above, the further the MIC is from the C_{max}, the more likely this is to be true. However, an isolate may have developed some level of resistance. This is demonstrated in the culture report above: resistance to ticarcillin, an extended spectrum penicillin has emerged in this *E. coli* yet it remains

susceptible to amoxicillin-clavulanic acid, indicating it is producing beta-lactamases. An isolate that has not resistance to enrofloxacin (“wild type) would have an MIC approximating 0.004 mcg/ml; an isolate with an MIC of 0.25 to 0.5 mcg/ml has already undergone 1 to 2 steps of mutations (in topoisomerases) yet is still considered “Susceptible”. Unfortunately, most C&S methods do not test very low below the breakpoint (the limitation is in the number of wells that can be tested using commercial test kits) and as such, how low the MIC actually is often cannot be determined. **Bottom line: Selecting a drug: patient data:** Compare the MIC (what is needed) to the peak drug concentration achieved at the recommended (or modified) dose: the higher the C_{max} is compared to the MIC, the greater the chance of therapeutic success and the less the chance of resistance. Once the “best” drugs are identified based on C&S, then the list can be narrowed down based on other factors. The same approach can be used for population data. Note that for the data above, when the MIC is compared to the C_{max} for those “S” drugs, the following can be decided: the organism is most susceptible to the aminoglycosides and of them, gentamicin; followed by the fluorinated quinolones, with enro (at **20 mg/kg**) being “more effective” compared to ciprofloxacin. Amoxi has a ratio of less than 1, even though it is “S”. Why? Because amoxicillin is only tested now for *E. coli* when infecting the urinary tract (effective concentrations to treat soft tissue infections can not be achieved, let alone maintained for amoxi with or without clavulanic acid, or ampicillin). This points out that for some drugs, CLSI does have different breakpoints for different tissues, particularly those that are effective only in urine (nitrofurantoin is another example).

Population data: Population data can be used for empirical antimicrobial selection. For example, using an antibiogram which indicates the proportion of isolates resistant vs susceptible to a drug. Similarly, the Target® Antimicrobial Handbook indicates not only the most likely organisms cultured (but not necessarily pathogenic) from selected sites, but also provides a “scoring” system of susceptibility. For antibiograms (see Auburn University Canine Cumulative Antimicrobial Susceptibility Report) drugs to which >75% or more of isolates are susceptible might be wiser selections. A patient that has not been previously exposed to antimicrobials is more likely to be represented by the “susceptible” isolates whereas an “at risk” patient (eg, previously exposed to antimicrobials, immunosuppressed) may be better represented by the resistant proportion. Likewise, package inserts for newer antimicrobials include susceptibility data (MIC) and as such, can guide not only the selection of a drug, but the design of a dosing regimen. The MIC data represents isolates of the same organism collected from many different patients. A population distribution (which should be robust, ideally 100 or more isolates) found on a label may include: 1. the range of MIC for susceptible organisms; 2. the mode of MIC (the most frequently cited MIC); 3. or the MIC₅₀ and the MIC₉₀. The data are population statistics; the latter two reflect, respectively, the MIC below which 50% and 90% of the isolates (by genus and species) are inhibited (not killed). However, the MIC₅₀ and MIC₉₀ should be based on a large number of microorganisms to assure accurate sample representation of the population (ideally >300). Organisms with MIC₉₀ that are low are more susceptible than organisms with higher MIC₉₀; organisms whose MIC₉₀ is approaching the C_{max} of the drug (also on a package insert) prudently should not be treated with that drug. See also concentration and time dependency. An example of population MIC data is demonstrated from a fluorinated quinolone package insert. Those organisms most susceptible to the drug have the lowest MIC whereas organisms with higher MIC are less likely to respond.

Infection is (usually) in the tissue, not the blood. A reminder that C&S data is based on **plasma** not tissue concentrations. Further, other considerations must be made when basing drug selection and doses on the MIC. The MIC is the key, not the sole consideration. Design of dosing regimens are equally important to drug selection.



Cumulative Antimicrobial Susceptibility Report Feline Isolates from January 2015 to December 2016

PERCENT SUSCEPTIBLE
(No. ISOLATES TESTED) ^a

	No. of Isolates	Amikacin	Amoxicillin/CA	Ampicillin	Cefepodoxime	Ceftiofur	Cefovecin	Chloramphenicol	Clindamycin	Enrofloxacin	Erythromycin	Gentamicin	Marbofloxacin	Nitrofurantoin	Oxacillin	Penicillin	Rifampin	Tetracycline	Trimethoprim/Sulfa
<i>Enterococcus faecalis</i>	30		100 (8)	100 (17)				93		47	12 (17)		40	100 (12)		100 (17)	15 (13)	38 (24)	
<i>Enterococcus faecium</i>	6		17					100		0	0 (4)		0	0 (1)			0 (3)	20 (5)	
<i>Escherichia coli</i>	54	100	44 (52)	35	77 (53)	77 (52)	77 (52)	79 (53)		75 (53)		87 (52)	79 (53)	100 (37)				72 (50)	82 (51)
<i>Klebsiella pneumoniae</i>	4	100	0	0	0	0	0	100		0		0	0					75	0
<i>Pseudomonas aeruginosa</i>	14	71								36		76	71						
<i>Staphylococcus aureus</i>	8	100 (7)	43 (7)		50 (6)		50	100	75	88	75	88	88		50	12	100	86 (7)	100
<i>Staphylococcus intermedius</i> ^b	7	100	71				71	100	57	71	57	71	71		71	14	100	57	71
Group G Beta Streptococci	9	0 (8)	100 (8)	100 (8)				89	50 (8)	75 (8)	56	67	88 (8)				100 (8)		100 (8)

a. Numbers in parentheses represent actual number tested if different from total.

b. Represents what is presently known as *S. intermedius* group and includes *S. intermedius*, *S. pseudintermedius*, and *S. delphini*.