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Antimicrobial susceptibility patterns of clinical *Escherichia coli* isolates from dogs and cats in the United States: January 2008 through January 2013

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ABSTRACT

Escherichia coli is among the most common bacterial pathogens in dogs and cats. The lack of a national monitoring program limits evidence-based empirical antimicrobial choices in the United States. This study describes antimicrobial susceptibility patterns for presumed clinical *E. coli* isolates from dogs ($n=2392$) or cats ($n=780$) collected from six geographic regions in the United States between May 2008 and January 2013. Minimum inhibitory concentrations (MIC) were determined for 17 drugs representing 6 drug classes. Urinary tract isolates were most common (71%). Population MIC distributions were generally bimodal with the second mode above the resistant breakpoint for all drugs except gentamicin, amikacin, and meropenem. The MIC_{90} exceeded the susceptible breakpoint for ampicillin, amoxicillin–clavulanic acid, cephalothin (surrogate drug for cephalexin), and doxycycline but was below the susceptible breakpoint for all others. None of isolates was susceptible or resistant to all drug tested; 46% were resistant to 1 or 2 antimicrobial categories, and 52% to more than three categories. The resistance percentages were as follows: doxycycline (100%), cephalothin (98%) > ampicillin (48%) > amoxicillin–clavulanic acid (40%) > ticarcillin–clavulanic acid (18%) > cefpodoxime (13%), cefotaxime (12%), cefoxitin (11%), cefazolin (11%), enrofloxacin (10%), chloramphenicol (9.6%) > ciprofloxacin (9.2%), ceftazidime (8.7%), trimethoprim–sulfamethoxazole (7.9%), gentamicin (7.9%) > meropenem (1.5%), amikacin (0.7%) ($P<0.05$). Resistance to ampicillin and amoxicillin–clavulanic acid was greatest in the South-Central region ($P<0.05$). *E. coli* resistance may preclude empirical treatment with doxycycline, cephalexin, ampicillin, or amoxicillin–clavulanic acid. Based on susceptibility patterns, trimethoprim–sulfonamides may be the preferred empirical oral treatment.

1. Introduction

Antimicrobial resistance contributes to therapeutic failure, increased patient morbidity and mortality, and health care costs (Cosgrove, 2006). To date, national surveillance programs exist for the monitoring of emerging antimicrobial resistance in human beings and food animals (Anderson et al., 2003); similar programs have not been implemented for companion animals in the United States. However, surveillance programs do exist in Sweden (SVARM, 2011) and Norway (NORM/NORM-VET, 2012). Limited data has been collected in Veterinary Teaching Hospitals, although applicability of data may not be relevant to the general veterinary population (Morris et al., 2006). Population- based surveys in human medicine have proven vital for quantifying emergence of antimicrobial resistance, thus contributing to evidence-based healthcare planning, and evaluation of therapeutic failure (Paul et al., 2010).

Escherichia coli is a reasonable sentinel microbe for investigation of current trends in antimicrobial resistance in pets because of its ubiquitous environmental presence, its importance in disease, and the ease by which it develops antimicrobial resistance (Miller et al., 2004). Several mechanisms of antimicrobial resistance are regulated by the expression of specific genes (Boerlin and White, 2013). *E. coli* in particular is able to transfer resistance genes between microorganisms (Winokur et al., 2001). Preemptive surveillance of canine and feline clinical *E. coli* isolates would

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facilitate empirical antimicrobial treatment as well as provide a foundation for the study of potential risk factors associated with the emergence of multi-drug resistant *E. coli* across the country.

The purposes of this study are to describe the current patterns of antimicrobial susceptibility and resistance for feline and canine clinical *E. coli* isolates in the United States, and to characterize demographic and clinical features with associated *E. coli* antimicrobial resistance. Descriptors include extent (proportions), level (minimum inhibitory concentration [MIC] statistics), and type (non-multi versus multi drug) of resistance. Further, the purpose of this study is to identify factors that could predict the risk of resistance in such clinical isolates.

2. Materials and methods

2.1. Source of isolates

Isolates ($n = 3172$) of *E. coli* were provided by a private veterinary diagnostic laboratory (VDL) to the clinical pharmacology laboratory (CPL) at Auburn University. Samples had been submitted to the VDL from January 2008 through January 2013 by veterinary practitioners after collection from dogs or cats with presumed naturally-occurring infection. Although susceptibility testing had been performed by the CDL prior to submission to the CPL, this data was not available to the study investigators.

2.2. Sample collection and susceptibility testing

On receipt, each isolate was prepared for susceptibility testing using procedures, as followed by the Clinical Laboratory Standards Institute (CLSI, 2013), using 96 well custom-made plates (TREK Diagnostic Systems, Cleveland, OH). Samples were confirmed to be *E. coli* and tested for contamination with other bacteria by culture on CHROMagar™ Orientation (BD Diagnostic Systems, Sparks, MD). Contaminated samples were excluded. Susceptibility testing was performed using 17 antimicrobials representing 6 drug classes and classified into 12 antimicrobial categories based on the type of resistance: penicillins: ampicillin (AMP, also serving as a surrogate for amoxicillin); penicillins + β-lactam inhibitors: amoxicillin–clavulanic acid (AMC, also serving as the surrogate for

Table 1
MICs (μg/ml) statistics for all *E. coli* isolates and each of 17 antimicrobial agents.

Drug	Conc. range tested (μg/mL)	Breakpoint MIC (μg/mL)		Mode	MIC_{50}	MIC_{75}	MIC_{90}	GE mean	Percentages of MIC ratio (MIC:R-MIC_{BP})	
		Susceptible	Resistant						1–8	≥8
Penicillins										
AMP	0.25–256	≤8[b]	n/a	2	4	128	>256[π]	10.1	5	47[*]
Penicillins + β-lacatamase inhibitors										
AMC	0.12–1024	≤8/4[b]	n/a	4	4	8	32	5.2	19[#]	34[*]
Antipseudomonal + β-lacatamase inhibitors										
TIM[a]	0.25–512	≤16/2	≥128/2	2	2	8	64	4.75	18[#]	8
Non-extended spectrum cephalosporins (1st generation and 2nd generation cephalosporins)										
CEP	0.5–1024	≤2	n/a	8	8	16	512[π]	16.9	49[*]	51[*]
CEF (n=318)	0.5–1024	≤2	n/a	2	2	4	128[π]	4.63	N/A	N/A
Extended-spectrum cephalosporins (3rd generation and 4th generation cephalosporins)										
CAZ[a]	0.06–128	≤4	≥16	0.25	0.12	0.25	2	0.3	6	3
CPD	0.06–256	≤2	≥8	0.5	0.5	1	32	1.1	8	12[#]
CTX[a]	0.06–64	≤1	≥64	≤0.06	≤0.06	1	4	0.3	7	3
Cephamycin										
FOX[a]	0.5–1024	≤8	≥4	2	2	4	16	3.7	13	9
Carbapenem										
MEM[a]	0.06–15	≤1	≥4	≤0.03	≤0.03	≤0.25	≤0.5	0.07	1	1
Tetracyclines										
DOX	0.25–128	≤0.12	≥0.5	2	2	2	16	1.9	12	9
Phenicols										
CHL[a]	0.5–512	≤8	≥32	4	8	8	8	6.7	57[*]	6
Fluoroquinolones										
CIP[a] (n=2939)	0.008–64	≤1	≥4	0.015	0.015	0.03	0.5	0.04	1	9
ENR	0.008–128	≤0.5	≥4	0.03	0.03	0.06	1	0.06	3	11[#]
Aminoglycosides										
GEN	0.25–128	≤2	≥8	0.5	0.5	1	2	0.75	7	5
AMK[c] (n=1622)	0.12–128	≤16	≥32	2	2	4	8	1.39	0.4	n/a
Sulfonamides										
SXT[a]	0.015–128	≤2	≥8	≤0.06	≤0.06	≤0.06	0.25	0.09	1	8

The proportions of low-level (ratio of MIC to R-MIC_{BP} less than 8 fold) or high-level (ratio of MIC to R-MIC_{BP} more than 8-fold) resistance were significantly higher than those among other drugs with $^{*}P<0.01$ and $^{\#}P<0.05$. [π]The isolates which the ratio of MIC_{90}:R-MIC_{BP} were above 8 fold represented expressing high-level resistance.
Abbreviations: amikacin (AMK); amoxicillin–clavulanic acid (AMC); ampicillin (AMP); ticarcillin–clavulanic acid (TIM); cefotaxime (CTX); cefoxitin (FOX); cefpodoxime (CPD); ceftazidime (CAZ); cefazolin (CEF); cephalothin (CEP); chloramphenicol (CHL); doxycycline (DOX); enrofloxacin (ENR); ciprofloxacin (CIP); gentamicin (GEN); meropenem (MEM) and trimethoprim–sulfamethoxazole (SXT).

[a] Breakpoints were not veterinary-specific followed to human approved CLSI.

[b] Breakpoint MICs were valid for urinary tract infections only; for other infections the breakpoint MIC is 0.25 (μg/ml).

[c] Breakpoint MIC are anticipated to be adjusted, and the impact such adjusted will have on percent susceptible.