Article

Antimicrobial resistance and prevalence of canine uropathogens at the Western College of Veterinary Medicine Veterinary Teaching Hospital, 2002–2007

Katherine R. Ball, Joseph E. Rubin, M. Chirino-Trejo, Patricia M. Dowling

Abstract — Between January 2002 and June 2007, uropathogens were isolated from 473 of 1557 canine urine samples submitted to Prairie Diagnostic Services from the Western College of Veterinary Medicine Veterinary Teaching Hospital. Culture and susceptibility results were analyzed, retrospectively, to estimate the prevalence of common bacterial uropathogens in dogs with urinary tract infections and to identify changes in antimicrobial resistance. The most common pathogens identified were *Escherichia coli, Staphylococcus intermedius, Enterococcus* spp., and *Proteus* spp. Antimicrobial resistance increased during the study period, particularly among recurrent *E. coli* isolates. Using the formula to help select rational antimicrobial therapy (FRAT), bacterial isolates were most likely to be susceptible to gentamicin, fluoroquinolones, amoxicillin-clavulanic acid, and groups 4 and 5 (third generation) cephalosporins.

Résumé — Résistance aux antimicrobiens et prévalence des pathogènes urinaires canins à l'hôpital d'enseignement vétérinaire du Western College of Veterinary Medicine. Entre janvier 2002 et juin 2007, des pathogènes urinaires ont été isolés de 473 des 1557 échantillons d'urine de chiens soumis au Prairie Diagnostic Services du Western College of Veterinary Medicine Veterinary Teaching Hospital. Les résultats des cultures et des susceptibilités ont été analysés rétrospectivement afin d'estimer la prévalence des bactéries uropathogènes courantes du chien atteint d'infection du tractus urinaire et d'identifier des modifications de la résistance aux antimicrobiens. Les pathogènes identifiés les plus courants étaient *Escherichia coli, Staphylococcus intermedius, Enterococcus* spp. et *Proteus* spp. La résistance aux antimicrobiens a augmenté au cours de la période d'étude, particulièrement parmi les isolats d'*E. coli* récurrents. Selon une formule visant à aider à choisir une thérapie antimicrobienne rationnelle (FTAR), les isolats bactériens avaient plus de chances d'être susceptibles à la gentamycine, aux fluoroquinolones, à l'amoxicilline-acide clavulanique et aux céphalosporines de groupes 4 et 5 (3ième génération).

(Traduit par Docteur André Blouin)

Can Vet J 2008;49:985–990

Introduction

Bacterial urinary tract infection (UTI) is one of the most commonly diagnosed infectious diseases in canine practice and affects approximately 14% of dogs presented for veterinary care (1). Uropathogenic strains of *Escherichia coli* are the most common cause of UTIs in both humans and dogs, and strains of this species are often abundant in the gastrointestinal tract at the time of infection (2,3). In contrast to most intestinal strains of *E. coli,* uropathogenic strains possess virulence factors which facilitate survival and persistence in the urinary tract (3). The risk of UTI recurrence is increased when highly pathogenic bacteria or underlying problems (such as, anatomic abnormalities, neoplasia, diabetes mellitus) are present (4,5). Microbiological culture and susceptibility testing is the cornerstone of UTI diagnosis and the results are used by veterinarians to select antimicrobial therapy (6). Susceptibility results from specific populations are used to select empirical therapy and to monitor trends in antimicrobial resistance (5,7). Antimicrobial resistance in uropathogens complicates therapy in dogs and is also a public health concern because these pathogens may be zoonotic (2,8,9).

The epidemiology of human uropathogens varies significantly by region and care setting (10). Given the many other similarities between human and canine UTIs, there is likely regional and population-specific variation in the epidemiology of canine uropathogens (8,9). The prevalence of fluoroquinolone resistance in canine uropathogens is increasing in the United States,

Department of Veterinary Biomedical Sciences (Ball, Dowling), Department of Veterinary Microbiology (Rubin, Chirino-Trejo), Western College of Veterinary Medicine, University of Saskatchewan, 52 Campus Drive, Saskatoon, Saskatchewan S7N 5B4.

Address all correspondence to Dr. Katherine R. Ball; e-mail: katherine.ball@usask.ca

Drs. Katherine R. Ball and Joseph E. Rubin were supported by Interprovincial Graduate Student Fellowships.

but only limited information is available about antimicrobial resistance trends in Canadian isolates (11,12).

Multi-drug resistance was observed in canine urinary isolates from an intensive care unit at the Ontario Veterinary College teaching hospital (13); however, the population of that study may not be representative of the general population of dogs in other areas, such as western Canada. The objectives of this study were to estimate the prevalence of uropathogens in dogs with urinary tract infections at the Western College of Veterinary Medicine Veterinary Teaching Hospital (WCVM-VTH), to apply the formula to help select rational antimicrobial therapy (FRAT) developed by Blondeau and Tillotson (7), and to identify changes in antimicrobial resistance among canine uropathogens over a 5-year period,

Materials and methods

Bacterial isolates

Records were obtained from Prairie Diagnostic Services (PDS) for all canine urine samples that had been submitted by the WCVM-VTH between January 2002 and June 2007 for culture and susceptibility testing. During this period, urine samples were plated on Columbia agar supplemented with 5% sheep blood and on MacConkey agar (Becton Dickinson and Company, Sparks, Maryland, USA) upon receipt. Each plate was divided in half such that each sample could be applied twice (1 μL and 10 μL) for quantitative analysis. Blood agar plates were incubated with 5% CO_2 while MacConkey agar plates were incubated aerobically. All samples were incubated at 37°C for 18 to 24 h until adequate growth was present. Identification was based on colony type and morphology, Gram staining characteristics, and standard biochemical tests. Antimicrobial susceptibility was determined by the Kirby-Bauer disk diffusion method. Zones of growth inhibition were interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Anaerobic cultures were performed when hematuria was evident or if requested by the attending veterinarian.

Statistical analysis

Statistical analysis was performed using a commercial statistical software package (SPSS 12.0 for Windows, SPSS, Chicago, Illinois, USA). The mean was taken from the ages recorded from all submissions for each dog to produce a single measure of age. Numbers of antimicrobials to which isolates were resistant were compared with the Kruskal-Wallis test, with alpha set to 0.05. Post-hoc analysis was performed by the Mann-Whitney U-test with Bonferroni's correction. Recurrent isolates were excluded from all analyses except for recurrent *E. coli* isolates, which were analyzed separately. Analyses of the number of antimicrobials to which isolates were resistant included results reported for amoxicillin-clavulanic acid, ampicillin, cephalothin, ceftiofur, chloramphenicol, clindamycin, enrofloxacin, gentamicin, tetracycline, and trimethoprim-sulfamethoxazole. Change in resistance to individual antimicrobial drugs over time was evaluated using simple logistic regression with year as a continuous variable. The relationship between sex, age, and resistance to individual antimicrobial drugs was evaluated by logistic regression with backward stepwise variable entry and evaluation by likelihood ratio. The same approach was used to examine the relationship between sex, age, and mixed infections (defined as more than 1 species isolated from 1 urine sample) and the relationship between sex, age, resistance, and recurrent infection.

Table 1. Isolates from canine urine samples submitted by WCVM-VTH for culture and susceptibility testing, 2002–2007

Organism	Percent of positive cultures — overall results (%)	Percent of positive cultures — single organism infections (%)	Percent of positive cultures — mixed infections (%)
E. coli	51.1	55.6	30.0
S. intermedius	16.5	17.1	13.3
Enterococcus spp.	10.2	6.7	26.7
Proteus spp.	5.9	6.9	1.1
Streptococcus spp.	4.6	4.2	6.7
Staphylococcus spp.	3.8	3.2	6.7
Minor species[a]	3.1	2.3	6.7
Enterobacter spp.	1.7	0.9	5.6
Pseudomonas spp.	1.3	1.4	1.1
Klebsiella spp.	1.1	1.2	1.1
Fungal species	0.4	0.5	0.0
Anaerobic bacteria	0.2	0.0	1.1

[a] Minor species included *Acinetobacter* spp., *Bacillus* spp., *Bacteroides* spp., *Citrobacter* spp., *Clostridium* spp., *Corynebacterium* spp., *Lactobacillus* spp., *Morganella morganii,* and *Pasteurella multocida*

Table 2. Bacteria isolated from dogs with recurrent urinary tract infections

Species	Percent of recurrent infections *(n)*
E. coli	63.6% (35)
S. intermedius	14.5% (8)
Enterococcus spp.	5.5% (3)
Proteus spp.	5.5% (3)
Other species	10.9% (6)

n — number of dogs

The impact factors for individual antimicrobial drugs were calculated using susceptibility data for *E. coli, Enterococcus* spp., *Staphylococcus intermedius, Streptococcus canis, Proteus* spp., *Staphylococcus* spp., *Streptococcus* spp., *Enterobacter* spp., *Pseudomonas* spp., and *Klebsiella pneumoniae* isolates and the formula to help select rational antimicrobial therapy (FRAT, Equation 1) (7).

$$F_S = \sum_{i=1}^{n} P_{Pathogen\ (i)} \times S_{Antimicrobial} \times 100$$

The impact factor is F_S, $P_{Pathogen\ (i)}$ is the prevalence of pathogen *i*, and $S_{Antimicrobial}$ is the proportion of pathogen *i* isolates susceptible to the antimicrobial in question. Anaerobes, fungal species, and bacterial isolates of minor species (prevalence $< 3.1\%$) were excluded from this consideration, as susceptibility data were available for only a small proportion of these isolates. To allow comparison of impact factors between years, prevalence values used in the equation were calculated after exclusion of fungal species and minor bacterial isolates.

Results

Samples

Between January 2002 and June 2007, 1557 urine samples from 1149 dogs were submitted to PDS by the WCVM-VTH

Table 3. Mean (standard error) number of antimicrobials to which bacterial isolates from canine urine samples were resistant, by year

Species	2002	2003	2004	2005	2006	2007
All isolates	1.68 (0.20)	1.49 (0.16)	2.12 (0.23)	1.74 (0.18)	2.04 (0.18)	2.74 (0.35)
All *E. coli*	1.45 (0.18)	1.37 (0.16)	1.67 (0.21)	1.74 (0.24)	1.55 (0.20)	2.09 (0.43)
E. coli (recurrent)[a]	1.71 (0.56)	1.15 (0.15)	1.64 (0.36)	1.83 (0.65)	2.08 (0.61)	4.00 (1.01)
E. coli (single positive culture)	1.36 (0.17)	1.50 (0.24)	1.67 (0.26)	1.73 (0.26)	1.36 (0.17)	1.05 (0.08)
S. intermedius	1.00 (0.32)	0.95 (0.27)	0.88 (0.45)	0.64 (0.15)	1.00 (0.22)	1.20 (0.49)
Enterococcus spp.	2.17 (0.48)	3.14 (0.99)	5.29 (0.97)	2.86 (0.59)	3.41 (0.45)	5.43 (0.30)
Proteus spp.	3.20 (0.20)	3.00 (0.82)	3.33 (0.33)	3.75 (0.48)	3.55 (0.43)	4.25 (1.25)

[a] Denotes significant change in resistance during the study period ($P < 0.05$) based on analysis by Kruskal-Wallis test

Table 4. Antimicrobial impact factors calculated using FRAT for the 10 most prevalent bacterial species isolated from canine urine samples submitted from the WCVM-VTH

Drug	Impact factor 2002	Impact factor 2007	Cumulative impact factor[a]
Gentamicin	96.4	89.1	93.3
Enrofloxacin	92.8	87.2	91.1
Amoxicillin-clavulanic acid	87.5	81.8	90.1
Ceftiofur	89.6	74.4	89.1
Chloramphenicol	89.1	85.4	87.8
Trimethoprim-sulfamethoxazole	79.8	85.4	86.7
Tetracycline	67.3	70.9	73.8
Ampicillin	68.4	65.4	71.6
Cephalothin	65.5	45.5	62.2
Clindamycin	30.9	16.4	24.8

[a] Includes prevalence and resistance data from all years (2002–2007)

for culture and susceptibility testing. Of these samples, 1 to 14 were submitted from each dog, with a median of 1 submission per dog. The mean age of the dogs ranged from 2 mo to 18.7 y, with a median of 8 y; age was not reported for 1.13% of the dogs. Urine samples were submitted from 492 spayed females (42.8%), 157 intact females (13.7%), 347 castrated males (30.2%), and 153 intact males (13.3%).

Microbial isolates

A positive bacterial culture was obtained from 473 samples from 361 dogs. Of these samples, 4 (0.85%) yielded 3 different bacterial species, 39 samples (8.25%) yielded 2 species, and the remainder yielded a single bacterial species. The prevalence of bacterial species differed between mixed infections and cases where the pathogen was isolated in pure culture (Table 1). There was no significant association between mixed infections, age, and sex. One hundred and twelve isolates were from cases where the same bacterial species was cultured on more than 1 occasion (referred to as recurrent pathogens). *Escherichia coli* was the most common recurrent pathogen, followed by *S. intermedius, Enterococcus* spp., and *Proteus* spp. (Table 2). *Escherichia coli* was isolated more than once from 17.3% of all cases where it had ever been isolated. This recurrence rate was higher than the rates observed for *S. intermedius* (10.5%), *Enterococcus* spp. (6.7%), and *Proteus* spp. (10.7%). There was no significant association between recurrent infection by *E. coli, S. intermedius, Enterococcus* spp., or *Proteus* spp. and age or sex.

The number of antimicrobials to which recurrent *E. coli* isolates were resistant increased significantly during the study period ($P = 0.010$), specifically between 2003 and 2007 ($P < 0.001$). There was no significant change in the number of antimicrobials to which nonrecurrent *E. coli, Enterococcus* spp., *S. intermedius,* and *Proteus* spp. isolates were resistant (Table 3). Gentamicin, enrofloxacin (indicator for veterinary fluoroquinolones), amoxicillin-clavulanic acid, and ceftiofur (indicator for groups 4 and 5 cephalosporins, also classified as 3rd generation) had the highest cumulative antimicrobial impact factors, reflecting the high frequency of in vitro susceptibility to these drugs among the bacterial isolates (Table 4). Antimicrobial impact factors decreased for all antimicrobials between 2002 and 2007 except for tetracycline and trimethoprim-sulfamethoxazole, in which the impact factors increased (Table 4).

Of the 267 *E. coli* isolates, 73 (27.3 %) were from dogs with recurrent *E. coli* infections (defined here as more than one positive *E. coli* culture result during the study period). Recurrence among *E. coli* was associated with resistance to increasing numbers of antimicrobials [odds ratio (OR) 1.22, 95% confidence interval (CI) 1.03–1.45]. There was no significant association of recurrence and antimicrobial resistance for *S. intermedius, Enterococcus* spp., and *Proteus* spp. There was no significant effect of sex on the number of antimicrobials to which nonrecurrent *E. coli, S. intermedius, Enterococcus* spp., and *Proteus* spp. isolates were resistant. Resistance to cephalothin, indicating resistance to group 1 and group 2 (first generation) cephalosporins, increased among nonrecurrent *Enterococcus* spp. (Table 5). Among *S. intermedius,* resistance to ampicillin increased over the study period (Table 5). Resistance to cephalothin, chloramphenicol, and gentamicin increased among recurrent *E. coli* isolates (Table 5). Resistance to cephalothin decreased among nonrecurrent *E. coli* (Table 5). There was no significant increase in resistance to any individual antimicrobial drug among *Proteus* spp. isolates. Recurrent *E. coli* isolates were more likely to be resistant to chloramphenicol (OR = 6.65; 95% CI = 1.96–22.54) and gentamicin (OR = 4.59; 95% CI = 1.05–20.07) than isolates from dogs with a single *E. coli* isolate. *Escherichia coli* isolates that were resistant to gentamicin were resistant to between 5 and 10 antimicrobials, and those that were resistant to trimethoprim-sulfamethoxazole were resistant to between 3 and 10 antimicrobials. Chloramphenicol-resistant *E. coli* were resistant to between 3 and 10 antimicrobials.

Discussion

Escherichia coli, Staphylococcus spp., *Proteus* spp., *Klebsiella* spp., and *Enterococcus* spp., have been reported as the most common canine uropathogens, composing 44.1%, 11.6%, 9.3%, 9.1%, and 8.0% of microbial isolates, respectively (14). Other

Table 5. Odds ratios (95% confidence intervals) for increasing resistance to individual antimicrobials by year

Pathogen	Amoxicillin-clavulanic acid	Ampicillin	Ceftiofur	Cephalothin	Chloramphenicol	Clindamycin	Enrofloxacin	Gentamicin	Tetracycline	Trimethoprim-sulfamethoxazole
All nonrecurrent isolates	1.08 (0.83–1.39)	1.10 (0.95–1.26)	1.25 (0.98–1.591)	1.03 (0.87–1.20)	1.14 (0.88–1.49)	1.11 (0.97–1.27)	1.07 (0.80–1.42)	1.14 (0.83–1.56)	0.91 (0.79–1.05)	0.91 (0.79–1.05)
E. coli (nonrecurrent)	0.73 (0.42–1.25)	1.00 (0.77–1.27)	NR	0.75[a] (0.57–0.98)	0.83 (0.44–1.57)	R	0.96 (0.47–1.96)	0.84 (0.41–1.74)	0.79 (0.56–1.10)	0.78 (0.56–1.10)
E. coli (recurrent)	NR	1.82[a] (1.19–2.79)	NR	1.71[a] (1.15–2.56)	1.83[a] (1.10–3.03)	R	NR	3.91[a] (1.09–14.01)	1.311 (0.87–1.98)	1.311 (0.87–1.98)
Enterococcus spp.	1.48 (0.66–3.32)	1.94 (0.82–4.58)	1.25 (0.86–1.84)	1.55[a] (1.03–2.34)	0.95 (0.47–1.93)	1.18 (0.70–1.997)	1.02 (0.66–1.58)	0.92 (0.53–1.61)	0.77 (0.53–1.13)	0.77 (0.53–1.13)
Proteus spp.	5.73 (0.38–85.78)	1.50 (0.60–3.76)	NR	5.73 (0.38–85.78)	1.38 (0.77–2.47)	R	NR	NR	0.53 (0.07–3.80)	0.53 (0.07–3.80)
S. intermedius	NR	1.38[a] (1.02–1.87)	NR	NR	NR	0.84 (0.34–2.10)	NR	NR	0.71 (0.49–1.04)	0.71 (0.49–1.04)

Recurrent isolates were excluded from analysis except where stated
NR — cases where too few resistant organisms were observed to allow analysis ($< 1/y$)
R — cases where too few nonresistant organisms were observed to allow analysis ($< 1/y$)
[a] A statistically significant change in resistance with year modeled as a continuous variable

studies have had similar results for *E. coli* and *Staphylococcus* spp. prevalence, but for *Proteus* spp. the prevalence fluctuates between 18% and 35.2% (15–18). The differences in prevalence between our study and previous reports are likely attributable to the WCVM-VTH being a predominantly primary care hospital. Compared to referral cases, primary care cases are less likely to have been treated on multiple occasions, producing different selection pressures for uropathogens. A primary care caseload likely includes a smaller proportion of cases with secondary UTIs such as catheter-associated infections compared with a referral caseload. The nature of the caseload may also partially account for the lower frequency of mixed infections in our study compared with previous reports (14). Additionally, geographical factors may contribute to the differences in the prevalence of bacterial uropathogens (10). Unlike findings in a previous study where mixed infections were more common in females, there was no significant association between sex and prevalence of mixed infections in our study population (14).

Isolation of the same bacterial species on more than 1 occasion can result from re-infection (2 infections separated by a period where the pathogen is eradicated from the urinary tract) or persistent infection (where the pathogen is not eradicated). Although these processes were indistinguishable from each other in this study, *E. coli* is over-represented in cases where multiple positive cultures revealed the same organism. Genetic analysis would allow distinction to be made between persistence and re-infection.

Uropathogenic *E. coli* possess multiple adaptations for survival and persistence in the urinary tract. These adaptations facilitate their invasion into transitional epithelial cells, where they can either enter a latent state within membrane-bound vesicles or reproduce and establish biofilm-like intracellular bacterial communities free within the cytoplasm (19,20). Bacteria later emerge from the intracellular communities and, by assuming a filamentous form, can bridge between epithelial cells without entering the urine (21,22). Some of the intracellular bacteria also emerge from the epithelial cells into the urine (21,22). The normal host defense of exfoliating infected epithelial cells disseminates *E. coli* in the environment and exposes deeper layers of tissue for invasion by bacteria in the urine (23). Neutrophil recruitment disrupts the integrity of the epithelium, which may also contribute to deeper penetration of the infection (23). While these mechanisms for survival in the urinary tract have been studied extensively in mouse models of human disease, their role in canine *E. coli* UTIs remains unclear. However, there is remarkable genetic similarity between uropathogenic *E. coli* isolated from humans and dogs (3). Because uropathogenic *E. coli* can survive and multiply within epithelial cells, urine samples can produce negative culture results despite ongoing infection, and infection can persist despite the presence of bactericidal concentrations of antimicrobial drugs in urine (21,24). Therefore, therapeutic efficacy likely depends on achieving appropriate antimicrobial concentrations within the uroepithelium.

With the exception of decreased resistance to group 1 and group 2 (first generation) cephalosporins among nonrecurrent *E. coli,* antimicrobial resistance increased over the study period. While fluoroquinolone resistance increased among *E. coli* isolates

in a previous study, no change was observed in the present study (based on resistance to enrofloxacin) (12). Gentamicin and chloramphenicol are not commonly used to treat bacterial UTIs in dogs so the increased resistance of recurrent *E. coli* to these antimicrobials is likely attributable to co-selection, as these isolates were resistant to multiple antimicrobials (data not shown). Co-selection for antimicrobial resistance may be facilitated by the presence of class 1 integrons. These genetic elements facilitate the uptake and maintenance of gene cassettes coding for antimicrobial resistance (25,26). Co-selection of antimicrobial resistance occurs when multiple gene cassettes are included in the integron, such that exposure to any drug to which the bacterium is resistant selects for all resistance genes present (25). Class 1 integrons containing chloramphenicol and gentamicin resistance genes have been reported in uropathogenic and other *E. coli* strains isolated from humans and animals (27–30). Further study is needed to determine the role of class 1 integrons in disseminating antimicrobial resistance in canine uropathogenic *E. coli* isolates.

Laboratory culture and susceptibility results are often used for monitoring antimicrobial resistance, but there is inherent bias to this approach (31). Samples tend to be submitted from animals with more severe clinical signs. In some cases, urine may not be submitted for culture and susceptibility testing until initial antimicrobial therapy (based on urinalysis results and Gram staining) has failed. This case selection bias may overestimate antimicrobial resistance. However, case selection bias is counterbalanced by the limited sensitivity of disk diffusion testing to changes in resistance. Because the results are reported as categorical data, changes are observed at only one breakpoint representing the transition between "intermediate" and "resistant" (permitting classification as "not resistant" and "resistant"). Consequently, shifts in minimum inhibitory concentrations are not apparent unless they occur around the breakpoint.

Prudent use of antimicrobials is an important step in reducing the emergence of antimicrobial resistance. In the context of canine UTIs, prudent use includes considering likely pathogens and their susceptibility patterns when choosing empirical treatment. Antimicrobial impact factors calculated using FRAT reflect the probability that a pathogen randomly selected from the study population is susceptible to a particular antimicrobial on disk diffusion testing. Based on these factors, canine UTIs are likely to be susceptible to a number of antimicrobials. However, the antimicrobial impact factors should not be used alone to select empirical therapy. The impact factors are based on in vitro susceptibility data, which does not necessarily reflect clinical efficacy for antimicrobials that achieve substantially higher concentrations in urine than what is evaluated in vitro or in cases involving intracellular infection. In the present study, gentamicin, enrofloxacin and amoxicillin-clavulanic acid had cumulative impact factors between 90 and 94. Small differences in impact factors are likely of little clinical significance, so other factors including pharmacokinetics, antimicrobial use strategies to reduce the emergence of resistance, drug safety profile, cost and convenience of administration must be considered when choosing empirical therapy. However, impact factors decreased between 2002 and 2007 for all antimicrobials except tetracycline and trimethoprim-sulfamethoxazole, consistent with increasing prevalence of antimicrobial resistance. Culture and susceptibility testing for individual cases remains the best instrument for guiding treatment decisions, especially for recurrent infections.

Increasing antimicrobial resistance is a growing concern in both human and veterinary medicine. Because pathogens isolated from recurrent infections are more resistant and resistance is increasing over time, appropriate management of recurrent infections is critical to control antimicrobial resistance. Underlying anatomic or metabolic problems should be identified and addressed whenever possible. Novel treatment strategies should address the virulence mechanisms of uropathogenic *E. coli* which facilitate persistent infection.

Authors contributions

Dr. Ball conducted the literature review, performed the statistical analysis, and wrote the initial manuscript. Dr. Rubin assisted in writing the Materials and Methods section and contributed to the Discussion. Dr. Dowling provided the initial ideas for this project and assisted with interpretation of results, and assisted with manuscript editing. Dr. Chirino-Trejo assised with interpretation of results.

Acknowledgments

The authors thank Brian Chelack and Prairie Diagnostic Services for providing culture and susceptibility data. CVJ

References

1. Ling GV. Therapeutic strategies involving antimicrobial treatment of the canine urinary tract. J Am Vet Med Assoc 1984;185:1162–1164.
2. Low DA, Braaten BA, Ling GV, Johnson DL, Ruby AL. Isolation and comparison of *Escherichia coli* strains from canine and human patients with urinary tract infections. Infect Immun 1988;56:2601–2609.
3. Johnson JR, Kaster N, Kuskowski MA, Ling GV. Identification of urovirulence traits in *Escherichia coli* by comparison of urinary and rectal *E. coli* isolates from dogs with urinary tract infection. J Clin Microbiol 2003;41:337–345.
4. Drazenovich N, Ling GV, Foley J. Molecular investigation of *Escherichia coli* strains associated with apparently persistent urinary tract infection in dogs. J Vet Intern Med 2004;18:301–306.
5. Seguin MA, Vaden SL, Altier C, Stone E, Levine JF. Persistent urinary tract infections and reinfections in 100 dogs (1989–1999). J Vet Intern Med 2003;17:622–631.
6. Bartges JW. Diagnosis of urinary tract infections. Vet Clin North Am Small Anim Pract 2004;34:923–933.
7. Blondeau JM, Tillotson GS. Formula to help select rational antimicrobial therapy (FRAT): Its application to community- and hospital-acquired urinary tract infections. Int J Antimicrob Agents 1999;12:145–150.
8. Johnson JR, Clabots C. Sharing of virulent *Escherichia coli* clones among household members of a woman with acute cystitis. Clin Infect Dis 2006;43:E101–E108. Epub 2006 Oct 10.
9. Kurazono H, Nakano M, Yamamoto S, et al. Distribution of the usp gene in uropathogenic *Escherichia coli* isolated from companion animals and correlation with serotypes and size-variations of the pathogenicity island. Microbiol Immunol 2003;47:797–802.
10. Zhanel GG, Hisanaga TL, Laing NM, et al. Antibiotic resistance in outpatient urinary isolates: Final results from the North American Urinary Tract Infection Collaborative Alliance (NAUTICA). Int J Antimicrob Agents 2005;26:380–388.
11. Cooke CL, Singer RS, Jang SS, Hirsh DC. Enrofloxacin resistance in *Escherichia coli* isolated from dogs with urinary tract infections. J Am Vet Med Assoc 2002;220:190–192.
12. Cohn LA, Gary AT, Fales WH, Madsen RW. Trends in fluoroquinolone resistance of bacteria isolated from canine urinary tracts. J Vet Diagn Invest 2003;15:338–343.
13. Ogeer-Gyles J, Mathews K, Weese JS, Prescott JF, Boerlin P. Evaluation of catheter-associated urinary tract infections and multi-drug-resistant

Escherichia coli isolates from the urine of dogs with indwelling urinary catheters. J Am Vet Med Assoc 2006;229:1584–1590.
14. Ling GV, Norris CR, Franti CE, et al. Interrelations of organism prevalence, specimen collection method, and host age, sex, and breed among 8,354 canine urinary tract infections (1969–1995). J Vet Intern Med 2001;15:341–347.
15. Féria CP, Correia JD, Machado J, Vidal R, Gonçalves J. Urinary tract infection in dogs. Analysis of 419 urocultures carried out in Portugal. Adv Exp Med Biol 2000;485:301–304.
16. Bush BM. A review of the aetiology and consequences of urinary tract infections in the dog. Br Vet J 1976;132:632–641.
17. Wooley RE, Blue JL. Quantitative and bacteriological studies of urine specimens from canine and feline urinary tract infections. J Clin Microbiol 1976;4:326–329.
18. Wierup M. Bacteriological examination of urine specimens from non-catheterized and catheterized dogs with symptoms of urinary tract infection. Nord Vet Med 1978;30:318–323.
19. Kau AL, Hunstad DA, Hultgren SJ. Interaction of uropathogenic *Escherichia coli* with host uroepithelium. Curr Opin Microbiol 2005;8:54–59.
20. Garofalo CK, Hooton TM, Martin SM, et al. *Escherichia coli* from urine of female patients with urinary tract infections is competent for intracellular bacterial community formation. Infect Immun 2007;75: 52–60.
21. Mulvey MA, Schilling JD, Hultgren SJ. Establishment of a persistent *Escherichia coli* reservoir during the acute phase of a bladder infection. Infect Immun 2001;69:4572–4579.
22. Justice SS, Hung C, Theriot JA, et al. Differentiation and developmental pathways of uropathogenic *Escherichia coli* in urinary tract pathogenesis. Proc Natl Acad Sci U S A 2004;101:1333–1338.
23. Bower JM, Eto DS, Mulvey MA. Covert operations of uropathogenic *Escherichia coli* within the urinary tract. Traffic 2005;6:18–31.
24. Schilling JD, Lorenz RG, Hultgren SJ. Effect of trimethoprim-sulfamethoxazole on recurrent bacteriuria and bacterial persistence in mice infected with uropathogenic *Escherichia coli.* Infect Immun 2002;70:7042–7049.
25. Ploy MC, Lambert T, Couty JP, Denis F. Integrons: An antibiotic resistance gene capture and expression system. Clin Chem Lab Med 2000;38:483–487.
26. Solberg OD, Ajiboye RM, Riley LW. Origin of class 1 and 2 integrons and gene cassettes in a population-based sample of uropathogenic *Escherichia coli.* J Clin Microbiol 2006;44:1347–1351.
27. Cocchi S, Grasselli E, Gutacker M, Benagli C, Convert M, Piffaretti JC. Distribution and characterization of integrons in *Escherichia coli* strains of animal and human origin. Fems Immunol Med Microbiol 2007;50: 126–132.
28. Martinez-Freijo P, Fluit AC, Schmitz FJ, Grek VSC, Verhoef J, Jones ME. Class I integrons in Gram-negative isolates from different European hospitals and association with decreased susceptibility to multiple antibiotic compounds. J Antimicrob Chemothe 1998;42:689–696.
29. Kim TE, Jeong YW, Cho SH, Kim SJ, Kwon HJ. Chronological study of antibiotic resistances and their relevant genes in Korean avian pathogenic *Escherichia coli* isolates. J Clin Microbiol 2007;45:3309–3315.
30. Du XD, Shen ZQ, Wu BB, Xia SC, Shen JZ. Characterization of class 1 integrons-mediated antibiotic resistance among calf pathogenic *Escherichia coli.* FEMS Microbiol Lett 2005;245:295–298.
31. Hillier S, Bell J, Heginbothom M, et al. When do general practitioners request urine specimens for microbiology analysis? The applicability of antibiotic resistance surveillance based on routinely collected data. J Antimicrob Chemother 2006;58:1303–1306.