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Risk factors for enterococcal bacteriuria in dogs: A retrospective study

Michael W. Wood[1] | Adam Lepold[2] | Dahlia Tesfamichael[3] | Michael R. Lasarev[4]

[1]Department of Medical Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin

[2]School of Veterinary Medicine, University of Wisconsin-Madison, Madison, Wisconsin

[3]College of Letters and Science, University of Wisconsin-Madison, Madison, Wisconsin

[4]Department of Biostatistics and Medical Informatics, School of Medicine and Public Health, University of Wisconsin-Madison, Madison, Wisconsin

Correspondence
Michael W. Wood, School of Veterinary Medicine, University of Wisconsin-Madison, 2015 Linden Drive, Madison, WI53706.
Email: mwood5@wisc.edu

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Abstract

Background: In humans, *Enterococcus* spp. urinary tract infections (UTI) are commonly associated with urinary catheter-induced urothelial inflammation but this is not the case in dogs.

Hypothesis/Objectives: To identify risk factors predisposing dogs to enterococcal bacteriuria.

Animals: Seventy dogs with *Enterococcus* spp. bacteriuria (case) and 70 dogs with *Enterococcus coli* bacteriuria (control).

Methods: A single center retrospective case-control study with subjects and controls identified by a medical records search for *Enterococcus* spp. (subject) or *E coli* (control) bacteriuria from January 1, 2014 to December 31, 2017. Cases and controls were balanced with respect to average age and weight. Binary logistic regression was used to estimate and test whether the odds of having *Enterococcus* spp. bacteriuria (instead of *E coli*) were associated with the presence of any given characteristic.

Results: A history of recurrent bacteriuria was significantly more common in *Enterococcus* spp. cases than in *E coli* controls (odds ratio [OR]: 2.07; 95% confidence interval [CI]: 1.04-4.16, P = .04). Comorbidities associated with the presence of *Enterococcus* spp. bacteriuria included lower urinary tract (LUT) anatomic abnormalities (OR: 2.94; 95% CI: 1.17-8.10, P = .02), urolithiasis (P = .01), and the presence of LUT neoplasia (P = .04). Small frequencies (n = 12 and n = 6, respectively) compromise our ability to precisely estimate the genuine OR for the latter 2 characteristics.

Conclusions and Clinical Importance: If the identified risk factors promote *Enterococcus* spp. colonization in dogs via induced LUT inflammation similar to people then *Enterococcus* spp. bacteriuria could be a sentinel for underlying LUT inflammation.

KEYWORDS

cystitis, *Enterococcus faecalis*, *Enterococcus faecium*, urinary tract infection

1 | INTRODUCTION

Gram-positive enterococci are commensal microbiota of the mammalian gastrointestinal tract. Despite generally exhibiting low virulence,

Abbreviations: cfu, colony forming units; CI, confidence interval; *E. coli*, *Escherichia coli*; *E. faecalis*, *Enterococcus faecalis*; *E. faecium*, *Enterococcus faecium*; LUT, lower urinary tract; OR, odds ratio; UTI, urinary tract infection.

enterococci have high pathogenic potential as they are capable of growing in hypertonic, hypotonic, acidic, alkaline, aerobic, and facultative anaerobic environments permitting colonization of the bile, blood and urine of dogs.[1-4] Once an enterococcal infection is present additional bacterial adaptations make eradication difficult. By means of inherent and acquired traits this bacterial genus rapidly acquires multidrug antimicrobial resistance making *Enterococcus* spp. pathogens increasing in importance in human and veterinary medicine.[5,6] In people, *Enterococcus* spp. are the third most common cause of nosocomial infections and the second most common cause of complicated urinary tract infections (UTI).[5,7] In dogs, *Enterococcus* spp. are the fourth to fifth most common bacteriuria isolate. Of dogs with *Enterococcus* spp. bacteriuria, nearly 50% display signs of lower urinary tract (LUT) disease consistent with clinical UTI.[1,8,9]

In humans, *Enterococcus* spp. UTIs are commonly urinary catheter-associated, secondary to catheter induced urothelial injury and a subsequent local inflammatory response.[10,11] Unlike humans, routine urinary catheterization is uncommon in dogs and a rare cause of recurrent *Enterococcus* spp. UTI.[12] However, the prevalence of *Enterococcus* spp. in dogs with recurrent UTI (17%-25%) is double the prevalence in all UTI in dogs (8.8%-11.3%).[6,9,12-14] These data can be interpreted to suggest that in dogs risk factors other than catheterization create an environment favorable for *Enterococcus* spp. colonization.

Enterococcal UTI in dogs is associated with comorbidities including neurologic dysfunction, endocrinopathies, incontinence, corticosteroid administration, urolithiasis, neoplasia, LUT anatomic abnormalities, chronic kidney disease, and urinary catheterization.[1] To date, there is a lack of case control studies that identify risk factors for the development of *Enterococcus* spp. bacteriuria in dogs.

The purpose of this study was to identify risk factors predisposing dogs to enterococcal bacteriuria by comparing clinical and pathological variables between dogs presenting with *Enterococcus* spp. and *Escherichia coli* (*E coli*) bacteriuria. Given the association between urinary catheter-induced inflammation and enterococcal UTI in humans, we hypothesized that conditions such as urolithiasis and neoplasia that disrupt the urothelium would also be identified as risk factors for enterococcal bacteriuria in dogs.

2 | MATERIALS AND METHODS

2.1 | Study design and population

This was a single center retrospective case-control study with cases and controls selected so the 2 groups would be balanced with respect to average age and weight. Subjects were identified upon review of the University of Wisconsin-Madison Veterinary Teaching Hospital Microbiology Service urine culture records from January 1, 2014 to December 31, 2017, as permitted by the hospital board. Case subjects were dogs with significant *Enterococcus* spp. bacterial growth from urine samples while control subjects were dogs with significant *E coli* growth. *Enterococcus coli* was chosen as the control organism given that it is the most common cause of significant bacteriuria in dogs.[8] Significant bacterial growth was defined as individual bacterial species colony forming units (cfu) >100 000 cfu/mL for midstream free catch urine samples, >10 000 cfu/mL for urinary catheter acquired samples and >100 cfu/mL for cystocentesis collected samples.[15] Only information from the most recent episode of *Enterococcus* spp./*E coli* bacteriuria was recorded for dogs with multiple positive urine cultures.

2.2 | Study variables

Demographic data collected from the medical record for each subject included age, weight, sex, and breed. Clinical data collected included the presence/absence of urinary symptoms (stranguria, pollakiuria, dysuria, and gross hematuria), recurrent bacteriuria defined as ≥2 documented bacteriuria episodes in the last 6 months or ≥3 documented bacteriuria episodes in the last year, and antibiotic use in the last 30 days. Comorbidity data collected from the medical record included the presence/absence of diabetes mellitus, hyperadrenocorticism, renal azotemia, urolithiasis, urinary incontinence, LUT neoplasia, neurogenic ataxia, orthopedic ataxia, LUT anatomic abnormalities including a recessed vulva, vestibulovaginal remnant, and ectopic ureters, corticosteroid or immunosuppressive medication administration at the time of urine collection, and a history of urinary catheterization in the last 30 days. Clinical pathology variables recorded included urine specific gravity, the presence/absence of proteinuria or hematuria as identified via urine dipstick analysis, and the presence/absence of ≥1-3 per high power field of white blood cells or epithelial cells via urine sediment analysis. Microbiology variables recorded included the number of bacterial species isolated and the number of antibiotic classes to which the bacteria had resistance. Antibiotic classes included penicillin, cephalosporin, fluoroquinolone, aminoglycoside, carbapenem, and other (such as nitrofurantoin). Isolates were identified using biochemical identification methods and/or a commercial identification system (Vitek 2, BioMérieux Inc, Durham, North Carolina). A commercial system was also used to determine each isolate's antibiotic minimal inhibitory concentrations (Sensititre, TREK Diagnostic Systems, Cleveland, Ohio) and interpreted based on the Clinical and Laboratory Standards Institute guidelines for antimicrobial susceptibility.[16-18]

2.3 | Statistical methods

Categorical characteristics of interest were summarized through frequencies and percentages for cases and controls, while continuous variables were summarized through means and SD. Binary logistic regression was used to estimate and test whether the odds of having *Enterococcus* spp. bacteriuria (instead of *E coli*) were associated with the presence of any given characteristic. Significance was assessed using a likelihood ratio test from the logistic regression model, and odds ratios (ORs) found by inverting the test. Preliminary power

TABLE 1 Frequency and percent occurrence of various characteristics in dogs with *Enterococcus* or *Escherichia coli* UTI. The *P*-value given assesses overall significance (via likelihood ratio test) of the characteristic among levels of a given categorical factor; estimated odds ratios (Est. OR) show increase (or decrease) in the odds associated with *Enterococcus* infection for each level of a given factor relative to the indicated reference level, or relative to the geometric mean of the odds (GM odds) for factors with several levels where a definitive reference would otherwise be arbitrary

Characteristic, n (%)	*P*-value	Case (n = 70)	Control (n = 70)	Est. OR	95% CI
Weight (kg)	.59				
GM odds = 1.038:1					
(4,10]		17 (24.3)	19 (27.1)	0.862	0.483, 1.531
(10,20]		16 (22.9)	10 (14.3)	1.542	0.809, 3.029
(20,30]		17 (24.3)	21 (30.0)	0.780	0.440, 1.371
(30,80]		20 (28.6)	20 (28.6)	0.964	0.552, 1.681
Sex	.23				
GM odds = 0.700:1					
Male/intact		3 (4.3)	6 (8.6)	0.715	0.212, 2.071
Female/intact		6 (8.6)	11 (15.7)	0.780	0.317, 1.829
Female/spayed		54 (77.1)	43 (61.4)	1.795	1.020, 3.250
Male/neutered		7 (10.0)	10 (14.3)	1.000	0.420, 2.334
Other bacteria detected	.24				
0		39 (55.7)	46 (65.7)	Ref	
1		27 (38.6)	23 (32.9)	1.385	0.688, 2.807
2		4 (5.7)	1 (1.4)	4.718	0.664, 94.30
Resistance pattern	.33				
No resistance		20 (28.6)	28 (40.0)	Ref	
Resistant to 1 class		19 (27.1)	21 (30.0)	1.267	0.544, 2.966
Resistant to 2 classes		12 (17.1)	9 (12.9)	1.867	0.666, 5.396
Resistant to 3+ classes		19 (27.1)	12 (17.1)	2.217	0.891, 5.694
Infection type	.04				
New infection		26 (39.4)	39 (57.4)	Ref	
Recurrent		40 (60.6)	29 (42.6)	2.070	1.040, 4.160
Clinical signs of LUTD	.21				
No		30 (44.8)	24 (34.3)	Ref	
Yes		37 (55.2)	46 (65.7)	0.640	0.320, 1.280
Antibiotic Tx within 30d before presentation	.18				
No		44 (63.8)	52 (74.3)	Ref	
Yes		25 (36.2)	18 (25.7)	1.640	0.800, 3.430
History of urinary catheterization	.23				
No		56 (84.8)	64 (91.4)	Ref	
Yes		10 (15.2)	6 (8.6)	1.900	0.660, 5.910
Diabetes mellitus	.70				
No		67 (95.7)	66 (94.3)	Ref	
Yes		3 (4.3)	4 (5.7)	0.740	0.140, 3.470
Hyperadrenocorticism	1.00				
No		65 (92.9)	65 (92.9)	Ref	
Yes		5 (7.1)	5 (7.1)	1.000	0.270, 3.750
Steroid treatment	.03				
No		64 (91.4)	55 (78.6)	Ref	
Yes		6 (8.6)	15 (21.4)	0.340	0.120, 0.910

(Continues)

TABLE 1 (Continued)

Characteristic, n (%)	*P*-value	Case (n = 70)	Control (n = 70)	Est. OR	95% CI
Immunosuppressive Tx	.44				
No		54 (77.1)	50 (71.4)	Ref	
Yes		16 (22.9)	20 (28.6)	0.740	0.340, 1.580
Kidney disease	.77				
No		63 (90.0)	64 (91.4)	Ref	
Yes		7 (10.0)	6 (8.6)	1.190	0.370, 3.870
Uroliths	.01				
No		54 (81.8)	68 (97.1)	Ref	
Yes		12 (18.2)	2 (2.9)	7.560	1.950, 49.89
Urinary incontinence	.20				
No		41 (61.2)	50 (71.4)	Ref	
Yes		26 (38.8)	20 (28.6)	1.590	0.780, 3.270
LUT neoplasia	.04				
No		63 (91.3)	69 (98.6)	Ref	
Yes		6 (8.7)	1 (1.4)	6.570	1.080, 125.9
Ataxia neurologic	.32				
No		47 (68.1)	53 (75.7)	Ref	
Yes		22 (31.9)	17 (24.3)	1.460	0.700, 3.100
Ataxia orthopedic	.44				
No		58 (84.1)	62 (88.6)	Ref	
Yes		11 (15.9)	8 (11.4)	1.470	0.560, 4.040
Noted LUT anatomic abnormalities	.02				
No		52 (75.4)	63 (90.0)	Ref	
Yes		17 (24.6)	7 (10.0)	2.940	1.170, 8.110
USG category	.04				
GM odds = 1.381:1					
(1.000, 1.015]		10 (20.4)	20 (36.4)	0.362	0.143, 0.785
(1.015, 1.030]		21 (42.9)	26 (47.3)	0.585	0.246, 1.175
(1.030, 1.045]		12 (24.5)	8 (14.5)	1.086	0.413, 2.605
(1.045, +++]		6 (12.2)	1 (1.8)	4.345	1.104, 40.05
Proteinuria	.12				
No		19 (39.6)	30 (54.5)	Ref	
Yes		29 (60.4)	25 (45.5)	1.830	0.840, 4.060
Hematuria (on dipstick)	.61				
No		27 (55.1)	33 (60.0)	Ref	
Yes		22 (44.9)	22 (40.0)	1.220	0.560, 2.680
Pyuria (on sediment)	.02				
No		22 (46.8)	14 (25.5)	Ref	
Yes		25 (53.2)	41 (74.5)	0.390	0.170, 0.880
Epithelial cells (on sediment)	.61				
No		16 (34.0)	21 (38.9)	Ref	
Yes		31 (66.0)	33 (61.1)	1.230	0.550, 2.810

Abbreviations: LUT, lower urinary tract; LUTD, lower urinary tract disease; Ref, reference value; tx, treatment.

analysis revealed that n = 70 per group would yield at least 80% power (at the 0.05 level) to detect genuine ORs of 3.25 or more when prevalence is between 13% and 68%. All analyses were performed using R v. 3.5.1 (R Core Team. R: A Language and Environment for Statistical Computing. Vienna, Austria: R Foundation for Statistical Computing; 2018).

3 | RESULTS

A total of 126 cases of *Enterococcus* bacteriuria were identified during the study period with 83 being unique dogs. Of these 83 cases, 13 did not meet the definition of significant *Enterococcus* spp. bacterial growth leaving 70 *Enterococcus* spp. bacteriuria cases. Of these cases, 43 were *Enterococcus faecalis*, 14 *Enterococcus faecium*, and 13 genus unspecified *Enterococcus*. An equal number of controls (n = 70) were chosen from 509 cases of *E coli* bacteriuria identified during the same time period. Cases and controls were chosen to be similar overall with respect to age (first priority) and weight (secondary concern). The difference in mean age between cases (9.0 ± 3.9 years) and controls (9.1 ± 4.1 years) was 0.9% of the average SD, while the difference in mean weight between the 2 groups was 4.3% of the average SD (24.1 ± 15.6 and 23.4 ± 14.4 kg for cases and controls, respectively). The urine collection method was not a characteristic used to balance cases and controls. However, 33 case and 34 control urine samples were collected by cystocentesis, 29 case and 32 control samples by free catch urine sampling, and 8 case and 4 control urine samples were collected by transurethral catheterization. All *E coli* controls had >100 000 cfu/mL of bacteria detected regardless of the urine collection method. In the *Enterococcus* spp. group all urine samples had >100 000 cfu/mL of bacteria detected, with the exception of 3 cystocentesis samples with 50 000 cfu/mL, 1 transurethral catheter collected sample with 10 000 cfu/mL, and 1 cystocentesis sample with 1000 cfu/mL of enterococci detected. Frequency and relative frequency of various characteristics of interest within each group are summarized in Table 1 and might deviate from n = 70 due to missing values or if certain laboratory tests were available/performed on a subset of animals.

Demographically the distribution of sex in combination with spaying/neutering did not differ significantly ($P = 0.23$) between cases and controls, though spayed females did show increased odds of *Enterococcus* spp. bacteriuria relative to the typical odds of this type of bacteriuria in the cohort (OR: 1.80; 95% confidence interval [CI]: 1.02-3.25). Clinically, a history of recurrent bacteriuria was significantly more common in *Enterococcus* spp. cases than in *E coli* controls (OR: 2.07; 95% CI: 1.04-4.16, $P = 0.04$).

Comorbidities most commonly associated with the presence of *Enterococcus* spp. bacteriuria included LUT anatomic abnormalities (OR: 2.94; 95% CI: 1.17-8.10, $P = 0.02$). Both uroliths and presence of LUT neoplasia were also each separately associated with greater odds of being a case ($P = 0.01$ and $P = 0.04$, respectively), though small frequencies (n = 12 and n = 6 respectively) compromise our ability to precisely estimate the genuine OR for those 2 characteristics.

Clinicopathologic data revealed that highly concentrated urine (USG > 1.045) demonstrated greater odds (OR: 4.34; 95% CI: 1.10-40.1) of being a case while hyposthenuria and isosthenuria together were associated with 63.8% (95% CI: 21.5-85.7%) lower odds of *Enterococcus* spp. bacteriuria. Detection of pyuria on urine sediment exam also was less likely to be associated with *Enterococcus* spp. bacteriuria when compared to *E coli* (OR: 0.39; 95% CI: 0.17-0.88). Overall 55.2% of enterococcal cases presented with LUT signs of stranguria, pollakiuria, dysuria, or gross hematuria. These findings, along with the other comparators of interest, appear in Table 1.

4 | DISCUSSION

A history of recurrent bacteriuria and multiple comorbidities including LUT abnormalities, uroliths, and LUT neoplasia were correlated with an increased risk of *Enterococcus* spp. bacteriuria in dogs in this study. Similar to previous veterinary reports, in this study *E faecium* and *E faecalis* were the predominant enterococci identified with 61% of all cases being *E faecalis* spp.[1,19] Given the low total number of cases, we were unable to compare comorbidity and clinicopathologic data of different enterococci species. Despite this shortcoming, the prevalence of *E faecalis* is of note because this species of enterococci contain more virulence genes and express higher levels of antibiotic resistance than other *Enterococcus* spp.[20-23]

Despite high levels of resistance, enterococci were once thought to be nonpathogenic bacteria. This mindset has changed in human medicine as enterococci have a 57% isolation rate from hospitalized patients and have been identified as the second most common cause of UTI and the third most common cause of bacteremia.[24] In companion, animals *Enterococcus* spp. infections have been linked to UTI, pyonephrosis, endocarditis, and cholangitis.[2,3,25] In our study, virulence was not directly assessed, however, 55.2% of enterococcal cases presented with LUT signs of stranguria, pollakiuria, dysuria, or gross hematuria suggesting cystitis. In addition, 60.6% of enterococcal cases were associated with recurrent bacteriuria. Although this study did not differentiate bacteriuria and UTI, in dogs with recurrent *Enterococcus* spp. infections this combination of virulence and developing antimicrobial resistance might create a long-term management problem.

Optimal management of recurrent infections includes identifying and correcting the underlying abnormality permitting bacterial colonization. In 75% of dogs with recurrent UTI, the defect allowing bacterial recolonization cannot be effectively managed or identified forcing clinicians to treat with repeated antibiotic therapy.[12,26-29] In our study, recurrent bacteriuria was identified as a risk factor for *Enterococcus* spp. bacteriuria. This correlation could indicate a cause/effect relationship. If enterococci and recurrent bacteriuria are correlated, knowing this could facilitate identification of a defect promoting colonization that can be corrected.

Our study did not assess enterococcal bacteriuria causation, however, mouse models have demonstrated that both a local inflammatory response and proteinuria are necessary for enterococcal growth and colonization of the urinary bladder.[30,31] Similarly in people with urinary catheter-induced proteinuria and inflammation, the incidence of enterococcal UTI increases from 5% to 15%-30%.[11,32,33] These data suggest that enterococcal colonization occurs secondarily to urinary tract injury. In dogs, *Enterococcus* spp. infections account for only 6% to 8% of all UTI but increases to 17% to 25% of recurrent UTI.[8,12,13,34] In veterinary medicine, urinary catheterization is much less common than in people. However, recurrent bacteriuria,

urolithiasis, and/or urinary tract neoplasia were identified as *Enterococcus* spp. bacteriuria risk factors in this study and are potential alternate mechanisms to create urinary bladder inflammation and proteinuria. If this is true, then there might be a similar biological mechanism behind the genesis of *Enterococcus* spp. bacteriuria the human and dog.

The identified risk factor from our study that on the surface would not primarily be associated with inflammation and proteinuria is the presence of LUT anatomic abnormalities. A similar study of risk factors for *E faecalis* infection in humans also identified structural abnormalities of the urinary tract as a risk factor for bacteriuria with an OR: 2.634; 95% CI: 1.294-5.362; P = .008.[35] One hypothesis to explain these findings is that LUT abnormalities predispose an individual to UTI and thereby secondarily are a risk factor for *Enterococcus* spp. bacteriuria.[36] Similar logic might also help to explain why in this and earlier studies spayed female dogs appear to be at increased risk of developing *Enterococcus* spp. bacteriuria (OR: 1.795; 95% CI: 1.020-3.250).[8] Given that female dogs are diagnosed with UTI at a greater than 2:1 ratio when compared to males, with spayed female dogs having the highest overall risk, enterococcal bacteriuria might be occurring secondary to prior infection.[37]

Despite the above associations, an argument against inflammation and proteinuria being necessary cofactors for enterococcal bacteriuria in dogs is that neither proteinuria nor pyuria were identified as risk factors for *Enterococcus* spp. bacteriuria in our study. These factors were respectively identified in 60.4% and 53.2% of cases and 44.5% and 74.5% of controls. This seemingly confounding finding could indicate an unaccounted for bias within our data since only bacteriuria was recorded and not clinical UTI. Another explanation is that *Enterococcus* spp. bacteriuria in dogs occurs via an alternate mechanism. However, importantly in people and mice it is not the presence of urinary albumin, measured as protein on urinalysis, and pyuria, measured on urine sediment exam, that is necessary for enterococcal colonization but rather fibrinogen protein and the inflammatory mediators IL-6 and IL-1β.[30,38,39] In our study, the concentration of these proteins and inflammatory mediators were not assessed.

The primary limitation of this study is the low number of dogs with certain comorbidities. This restricted our ability to calculate genuine ORs for some variables. In addition, the retrospective design and hence reliance on medical records did limit data collection for some dogs with incomplete medical records. Finally, this study assessed enterococcal bacteriuria risk development. It is possible that enterococcal UTI is associated with different risk factors.

This study associated recurrent bacteriuria, LUT abnormalities, uroliths, and LUT neoplasia with increased *Enterococcus* spp. bacteriuria risk in dogs. It is unclear whether these risk factors increase urinary inflammation and fibrinogen similar in effect to urinary catheterization in humans.

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CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

ORCID

Michael W. Wood https://orcid.org/0000-0002-6142-4769

REFERENCES

1. KuKanich KS, Lubbers BV. Review of enterococci isolated from canine and feline urine specimens from 2006 to 2011. *J Am Anim Hosp Assoc*. 2015;51:148-154.
2. Harrison JL, Turek BJ, Brown DC, Bradley C, Callahan Clark J. Cholangitis and cholangiohepatitis in dogs: a descriptive study of 54 cases based on histopathologic diagnosis (2004-2014). *J Vet Intern Med*. 2018;32:172-180.
3. Semedo-Lemsaddek T, Tavares M, Sao Braz B, et al. Enterococcal infective endocarditis following periodontal disease in dogs. *PLoS One*. 2016;11:e0146860.
4. Fisher K, Phillips C. The ecology, epidemiology and virulence of *Enterococcus*. *Microbiology (Reading, England)*. 2009;155:1749-1757.
5. Arias CA, Murray BE. The rise of the *Enterococcus*: beyond vancomycin resistance. *Nat Rev Microbiol*. 2012;10:266-278.
6. Hall JL, Holmes MA, Baines SJ. Prevalence and antimicrobial resistance of canine urinary tract pathogens. *Vet Rec*. 2013;173:549.
7. Poh CH, Oh HM, Tan AL. Epidemiology and clinical outcome of enterococcal bacteraemia in an acute care hospital. *J Infect*. 2006;52:383-386.
8. 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.
9. McMeekin CH, Hill KE, Gibson IR, Bridges JP, Benschop J. Antimicrobial resistance patterns of bacteria isolated from canine urinary samples submitted to a New Zealand veterinary diagnostic laboratory between 2005-2012. *N Z Vet J*. 2017;65:99-104.
10. Ortega M, Marco F, Soriano A, et al. Epidemiology and prognostic determinants of bacteraemic catheter-acquired urinary tract infection in a single institution from 1991 to 2010. *J Infect*. 2013;67:282-287.
11. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. *Nat Rev Microbiol*. 2015;13:269-284.
12. 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.
13. Wong C, Epstein SE, Westropp JL. Antimicrobial susceptibility patterns in urinary tract infections in dogs (2010-2013). *J Vet Intern Med*. 2015;29:1045-1052.
14. Ball KR, Rubin JE, Chirino-Trejo M, et al. Antimicrobial resistance and prevalence of canine uropathogens at the Western College of

Veterinary Medicine Veterinary Teaching Hospital, 2002-2007. *Can Vet J-Rev Vet Can*. 2008;49:985-990.
15. Osborne CA, Lees GE. Diagnostic urine culture. In: Osborne CA, Finco DR, eds. *Canine and Feline Nephrology and Urology*. 1st ed. Media, PA: Williams and Wilkins; 1995:206-210.
16. Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated from Animals; Approved Standard. CLSI document VET01–A4*. 4th ed. Wayne, PA: Clinical and Laboratory Standards Institute; 2013a.
17. Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Disk and Dilution Susceptibility Tests for Bacteria Isolated from Animals. CLSI Document VET01–S2*. Wayne, PA: Clinical and Laboratory Standards Institute; 2013b.
18. Clinical and Laboratory Standards Institute. *Performance Standards for Antimicrobial Susceptibility Testing. CLSI Document M100–23*. Wayne, PA: Clinical and Laboratory Standards Institute; 2013c.
19. Jackson CR, Fedorka-Cray PJ, Davis JA, Barrett JB, Frye JG. Prevalence, species distribution and antimicrobial resistance of enterococci isolated from dogs and cats in the United States. *J Appl Microbiol*. 2009;107:1269-1278.
20. Kubasova I, Strompfova V, Laukova A. Safety assessment of commensal enterococci from dogs. *Folia Microbiol*. 2017;62:491-498.
21. Iseppi R, Messi P, Anacarso I, et al. Antimicrobial resistance and virulence traits in *Enterococcus* strains isolated from dogs and cats. *New Microbiol*. 2015;38:369-378.
22. Boyar Y, Aslantaş Ö, Türkyılmaz S. Antimicrobial resistance and virulence characteristics in *Enterococcus* isolates from dogs. *Kafkas Univ Vet Fak Derg*. 2017;23:655-660.
23. Montgomerie JZ, Kalmanson GM, Guze LB. Virulence of enterococci in experimental pyelonephritis. *Urol Res*. 1977;5:99-102.
24. Mutnick AH, Biedenbach DJ, Jones RN. Geographic variations and trends in antimicrobial resistance among Enterococcus faecalis and *Enterococcus faecium* in the SENTRY Antimicrobial Surveillance Program (1997-2000). *Diag Microbiol Infect Dis*. 2003;46:63-68.
25. Cray M, Berent AC, Weisse CW, Bagley D. Treatment of pyonephrosis with a subcutaneous ureteral bypass device in four cats. *J Am Vet Med Assoc*. 2018;252:744-753.
26. Gibson JS, Morton JM, Cobbold RN, Sidjabat HE, Filippich LJ, Trott DJ. Multidrug-resistant *E-coli* and Enterobacter extraintestinal infection in 37 dogs. *J Vet Intern Med*. 2008;22:844-850.
27. Sidjabat HE, Townsend KM, Lorentzen M, et al. Emergence and spread of two distinct clonal groups of multidrug-resistant *Escherichia coli* in a veterinary teaching hospital in Australia. *J Med Microbiol*. 2006;55:1125-1134.
28. 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.
29. Senior DF. Management of urinary tract infections. In: Elliott J, Grauer G, eds. *BSAVA Manual of Canine and Feline Nephrology and Urology*. Gloucester, UK: British Small Animal Veterinary Association; 2007:282-289.
30. Guiton PS, Hannan TJ, Ford B, Caparon MG, Hultgren SJ. *Enterococcus faecalis* overcomes foreign body-mediated inflammation to establish urinary tract infections. *Infect Immun*. 2013;81:329-339.
31. Kau AL, Martin SM, Lyon W, Hayes E, Caparon MG, Hultgren SJ. *Enterococcus faecalis* tropism for the kidneys in the urinary tract of C57BL/6J mice. *Infect Immun*. 2005;73:2461-2468.
32. Maki DG, Tambyah PA. Engineering out the risk for infection with urinary catheters. *Emerg Infect Dis*. 2001;7:342-347.
33. Jarvis WR, Martone WJ. Predominant pathogens in hospital infections. *J Antimicrob Chemother*. 1992;29(Suppl A):19-24.
34. Criel D, Steenbergen J, Stalpaert M. Prevalence and antimicrobial susceptibility of canine uropathogens in Northern Belgium: a retrospective study (2010 to 2012). *J Small Anim Pract*. 2015;56:73.
35. Kajihara T, Nakamura S, Iwanaga N, et al. Clinical characteristics and risk factors of enterococcal infections in Nagasaki, Japan: a retrospective study. *BMC Infect Dis*. 2015;15:426.
36. Burdick S, Berent AC, Weisse C, Langston C. Endoscopic-guided laser ablation of vestibulovaginal septal remnants in dogs: 36 cases (2007-2011). *J Am Vet Med Assoc*. 2014;244:944-949.
37. Brloznik M, Sterk K, Zdovc I. Prevalence and resistance patterns of canine uropathogens in regard to concurrent diseases. *Berl Munch Tierarztl*. 2016;129:340-350.
38. Tambyah PA, Maki DG. The relationship between pyuria and infection in patients with indwelling urinary catheters: a prospective study of 761 patients. *Arch Intern Med*. 2000;160:673-677.
39. Shaikh N, Shope TR, Hoberman A, Vigliotti A, Kurs-Lasky M, Martin JM. Association between uropathogen and pyuria. *Pediatrics*. 2016;138:e20160087.

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