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Escherichia coli and *Enterococcus faecalis* are identified as the most frequently isolated bacteria associated with urinary tract infections in pet rabbits

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Objective
To describe the clinical features of urinary tract infections in pet rabbits, identify the bacterial species involved and their antimicrobial susceptibility profiles, and investigate risk factors.

Methods
In this retrospective multicentric observational study, data were retrieved from the medical records of 3 veterinary centers located in the Greater Paris region, France, between 2009 and 2025. Inclusion criteria consisted of all rabbits presented for consultation in which a urine culture had been carried out. Signalment and clinical data were analyzed for statistical associations with urine culture results (positive vs negative). Antimicrobial susceptibility profiles were retrieved.

Results
79 rabbits underwent urine bacterial culture. Overall, 34.2% (27 of 79) of rabbits had a positive urine culture, of which 59.3% (16 of 27) were female and 84.6% (22 of 26) had urinary sludge, 9.1% (2 of 22) urolithiasis, 33.3% (8 of 24) consistent ultrasonographic signs of pyelonephritis, and 71.4% (15 of 21) bacteria on urine microscopic examination. Most urine samples were collected by cystocentesis (94.8% [73 of 77]). The presence of bacteria on urine microscopic examination was the only statistically significant parameter associated with urinary tract infection, with a sensitivity of 71% (95% CI, 60% to 82%) and specificity of 90% (95% CI, 82% to 98%) when compared to culture results. In 74.1% (20 of 27) of cases, a single species of bacteria was isolated, with a total of 36 different isolates. The most common bacteria were *Escherichia coli* (27.8% [10 of 36]), *Enterococcus faecalis* (19.4% [7 of 36]), and *Staphylococcus* spp (11.1% [4 of 36]). Resistance was reported for azithromycin (66.2% [15 of 20]), penicillin (57.9% [13 of 19]), sulfonamides-trimethoprim (31.4% [11 of 35]), enrofloxacin (17.9% [5 of 28]), and ceftiofur (17.1% [6 of 35]). Overall, 52.8% (19 of 36) of bacteria were multidrug resistant.

Conclusions
Frequent resistance to empirically used antibiotics was observed. As no risk factors could be identified, larger-scale studies are needed.

Clinical Relevance
Bacterial isolation is common, and urine culture should be encouraged to adjust therapy in accordance with antimicrobial stewardship practices.

Keywords: rabbits, urinary tract infection, risk factor, *Escherichia coli*, multidrug-resistant bacteria

A urinary tract infection (UTI) can affect any part of the urinary tract, including the kidneys, ureters, bladder, and urethra. In dogs and cats, UTIs are specifically classified as bacterial cystitis (sporadic or recurrent), pyelonephritis, or subclinical bacteriuria.[1]

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Urinary tract infections in pet rabbits are mentioned in the veterinary literature,[2–4] but detailed characterization remains limited, with distinction only between bacterial cystitis and pyelonephritis. Clinical signs of bacterial cystitis may overlap with those of urinary sludge or urolithiasis, 2 frequent urinary disorders in pet rabbits.[2–4] Pyelonephritis is an infection of the renal parenchyma that can occur from either bacterial hematogenous spread or ascending urinary infection. Rabbits suffering from pyelonephritis may present with pyrexia, renal pain, and renal failure.[4]

Diagnosis of UTI is made on the basis of compatible clinical signs and positive urine bacterial culture. Antimicrobial susceptibility testing is crucial to adjust antimicrobial therapy in cases of resistance.[1] The bacteria reported in cases of UTI in rabbits include *Enterococcus* spp, *Staphylococcus* spp, *Escherichia* spp, *Streptococcus* spp, *Enterobacter* spp, *Proteus* spp, *Klebsiella* spp, *Acinetobacter* spp, *Burkholderia* spp, *Stenotrophomonas* spp, or *Rothia* spp.[5,6] *Pasteurella multocida* and *Staphylococcus* spp have been described as frequent etiologies of pyelonephritis.[2,3]

Escherichia coli is the most commonly isolated bacteria in dogs and cats with UTI.[7–12] Multiple risk factors for UTI have been identified in dogs and cats, including female sex, increased age, functional or anatomic abnormality of the lower urinary tract, presence of urolithiasis, prior urogenital surgeries, and recent use of antibiotics.[7,9,13]

In guinea pigs, female sex is also a risk factor for UTI.[14] In this species, single or mixed infection by *Corynebacterium* spp, *Streptococcus* spp, *Pasteurella* spp, *Staphylococcus* spp, *Pseudomonas* spp, and *E coli* has been reported.[14,15]

It has been hypothesized that incomplete voiding and excess urine sludge may predispose rabbits to developing bacterial cystitis by damaging the bladder urothelium.[2,16] It has also been hypothesized that cystitis may be associated with urolithiasis, either as a cause or consequence.[2,16]

Exotic animal–based textbooks[2–4] and databases (PubMed, ScienceDirect, and Google Scholar) were searched with the keywords *urinary tract infection*, *pyelonephritis*, *cystitis*, and *rabbit* on May 1, 2025.

One study[17] described 2 rabbits with polypoid cystitis and a concurrent UTI due to *Proteus* spp and *Enterococcus* spp, respectively. Another study[18] reported a rabbit with a renal abscess due to *E coli*, diagnosed by PCR after nephrectomy, but urine culture was not performed. This rabbit also had a concurrent renal infection caused by *Encephalitozoon cuniculi*, diagnosed by immunohistochemistry.[18]

Urinary tract infections in rabbits are mentioned in various retrospective studies, 2 on the profile of bacterial infections in rabbits in Spain[5] and Romania[6] and another on diseases classified by body system, with diagnosis obtained mainly by necropsy, cytology, or biopsy. In the latter, infectious nephritis was diagnosed in 8.4% (22 of 262) of pet rabbits, including 16 *E cuniculi* and 6 bacterial nephritis, and cystitis in 5.3% (14 of 262), with only a single case of bacterial cystitis (*Enterobacter* spp).[19] Two other retrospective studies[20,21] of conditions grouped by body systems did not show occurrence of UTI. Beyond these, no research studies were found with a detailed description of clinical and paraclinical characteristics or evaluation of risk factors of UTI in pet rabbits.

The objectives of the present study were to (1) describe the clinical and paraclinical characteristics of UTI in rabbits; (2) provide evidence on etiology and antibiotic susceptibility testing of urinary bacteria in rabbits; and (3) investigate potential risk factors for UTI in rabbits and describe the outcome. We hypothesized that female rabbits would be more prone to developing UTI than males and that positive urine culture would be associated with the presence of urinary sludge or urolithiasis.

Methods

Study design and inclusion criteria

This retrospective multicentric observational study involved the veterinary teaching hospital of l'École Nationale Vétérinaire d'Alfort (ENVA) and 2 private veterinary hospitals: Centre Hospitalier Vétérinaire (CHV) Frégis Evidensia (Gentilly) and CHV AniCura Advetia (Vélizy-Villacoublay). All 3 centers, located in the Greater Paris region, provide primary and referral care.

Data were retrieved from the medical records with the use of the software specific to each center (Sirius [ENVA], Vetup [CHV Frégis Evidensia], or AssistoVet [CHV AniCura Advetia]) and over different periods (between January 1, 2009, and February 1, 2025 [ENVA]; between January 1, 2015, and February 1, 2025 [CHV Frégis Evidensia]; or between January 1, 2020, and February 1, 2025 [CHV AniCura Advetia]).

The inclusion criteria were all rabbits for which a urine culture had been carried out. These rabbits were brought in for consultation due to urinary or nonurinary signs, and a urine culture was performed. Any rabbits that did not undergo a urine bacterial culture or whose results were not recorded in the medical file were excluded from the study. Databases were searched with the keywords *rabbit* AND *urine culture*. Two groups were formed. The negative-culture group included all rabbits with a negative urine culture. The positive-culture group included all rabbits with a positive urine culture, considered diagnostic for UTI. Rabbits with multiple positive cultures were counted once at the first positive result. If a rabbit had a negative culture followed by a positive culture, it was assigned to the UTI group and the prior negative culture was recorded in the medical history.

Data extracted

For each case, the following were recorded: signalment (age, sex, and breed [lop-eared or erect-eared rabbits]), body weight, and body condition score (thin, ideal, or overweight). Dietary information included the presence of fresh green vegetables, use of calcium-rich hay (ie, hay with a calcium content exceeding 1% of dry matter), water source (bowl or bottle), and presence of a salt lick. Husbandry details covered group or single housing, living conditions (caged, partially free-roaming, or fully free-roaming), and whether a specific litter box was provided. Presenting complaints were noted, distinguishing between urinary and nonurinary concerns. Medical history included antibiotic use during the previous 30 days, precedent urinary episodes, and previous urogenital surgeries other than neutering. Clinical signs and physical examination findings were recorded, including micturition signs (hematuria, stranguria, pollakiuria, or thick urine), inappropriate urination, soiled perineum, urinary incontinence, polyuria-polydipsia, loss of appetite, reduced fecal output, and rectal temperature. Concurrent diseases

were documented, including digestive, respiratory, cardiocirculatory, integumentary, ophthalmic, neurological, musculoskeletal, endocrine, reproductive, or neoplastic conditions. Abdominal radiographic and ultrasound findings included urinary sludge, urolithiasis and its location, urinary bladder wall thickening, and ultrasonographic features compatible with pyelonephritis. Blood chemistry parameters (urea, creatinine, and total calcium) and *E cuniculi* serological status (immunoglobulin M and immunoglobulin G) were recorded. Finally, urine data included the collection method (urethral catheterization or cystocentesis), microscopic examination findings (presence of crystals, RBCs, WBCs, and bacteria), and urine culture results (number of cultures performed per rabbit, positive or negative status, cultured bacterial species, and antibiotic susceptibility testing).

Management (hospitalization, antibiotic treatment, NSAIDs, or fluid therapy) and outcome data were retrieved. The outcome was classified as recovery, recurrence, persistence, death, or euthanasia.

Urine samples and laboratory methods

Urine was collected via ultrasound-guided cystocentesis or urethral catheterization into urine tubes (Vacutainer; Becton, Dickinson and Co) containing boric acid, sodium borate, and sodium formate, or into ESwab tubes (Copan Diagnostics Inc). Urine cultures performed on Vacutainer urine tubes provided a quantitative assessment, whereas cultures performed on ESwab tubes provided only a semiquantitative assessment. Each center submitted to its affiliated laboratory: Biopôle (ENVA), Anydiag (CHV Frégis Evidensia), and LABO NAC & CO (CHV AniCura Advetia). Samples for LABO NAC & CO were road transported and cultured within 48 hours of collection, and samples processed on-site (Biopôle and Anydiag) were cultured within 24 hours.

Cultures were incubated aerobically for 24 to 72 hours on trypticase soy agar (Biopôle), Clarity UTI agar (Anydiag) or Columbia agar with 5% sheep blood, and CNA agar for gram-positive bacteria or McConkey agar for gram-negative bacteria (LABO NAC & CO). LABO NAC & CO additionally performed anaerobic culture on Schaedler agar. Cultures were incubated at 37 °C. Bacteria were identified with the use of matrix-assisted laser desorption ionization–time of flight mass spectrometry.

Antimicrobial susceptibility testing to antibiotics of different classes (β-lactams, aminoglycosides, macrolides, lincosamides, tetracyclines, amphenicols, quinolones, sulfonamides-trimethoprim, polypeptides, and nitrofurans) was performed with the disk diffusion method in accordance with laboratory protocols and Normes Françaises et Européennes standards (NF U47-107). Results were interpreted as susceptible, intermediate, or resistant according to the guidelines of the Comité de l'Antibiogramme de la Société Française de Microbiologie (CA-SFM) established in 2013 and the latest version of the veterinary CA-SFM established in 2023. Multidrug-resistant (MDR) bacteria were defined as nonsusceptible to at least 1 agent in ≥ 3 antimicrobial classes.[22]

Standardization of data collection

To enhance data collection reliability, all data extraction was performed by a single operator (AP) on February 27, 2025. Medical records were systematically completed by clinicians for each consultation, but some data may have been missing. To minimize subjective ultrasound interpretation by operators, particularly for the assessment of pyelonephritis, several ultrasonographic features were relied on (pyelectasia, proximal ureter dilation, decreased corticomedullary distinction, increased or decreased renal size, and renal hyperechogenicity[23,24]). Each urinalysis and urine culture was performed by trained laboratory staff, and a detailed report was produced. Despite different transportation and culture methods, the 3 laboratories followed French national guidelines for interpreting antimicrobial susceptibility testing. As the quantitative assessment of the bacterial isolates was heterogenous between the 3 laboratories, this parameter was excluded from the study.

Statistical analysis

Normality of continuous variables was assessed with the Shapiro-Wilk test. Continuous variables were summarized as mean ± SD.

Given the small number of cases, associations between the different retrieved clinical variables and culture status were tested with univariate analysis followed by the Holm-Bonferroni correction for multiple comparisons. Associations between continuous variables and culture status were tested with binary logistic regression. Linearity was verified with the Box-Tidwell transformation, checking for outliers (any standardized residuals exceeding 2.5 times the SD in absolute value). Associations between ordinal variables and culture status were tested with the Cochran-Armitage test. Associations between categorical variables and culture status were tested with the χ^2 test when there were sufficient case numbers or Fisher exact test otherwise. Effect size was assessed by calculating the ϕ coefficient or Freeman θ coefficient for the categorical variables. The value of the coefficient was used to interpret the effect size as small (> 0.1), medium (> 0.3), or large (> 0.5). For continuous variables, ORs and their 95% CIs were provided. Parameters for which data were missing for > 50% of individuals or for which there were < 5 occurrences for one of the options were excluded from the statistical analysis.

All analyses were conducted in SPSS Statistics (version 26; IBM Corp). The significance level was set at .05.

The presence of bacteria on urine microscopic examination was compared to bacterial urine culture and regarded as the gold-standard test, and sensitivity, specificity, positive predictive value, and negative predictive value were calculated.

Results

Seventy-nine rabbits met the inclusion criteria: 27 in the UTI-positive group (16 from ENVA, 5 from CHV Frégis Evidensia, and 6 from CHV AniCura Advetia) and 52 in the negative-culture group (21 from ENVA, 24 from CHV Frégis Evidensia, and 7 from CHV AniCura Advetia).

Univariate analysis

Due to insufficient available data, several variables were excluded from the statistical analysis: presence of calcium-rich hay (10 of 79), source of water (25 of 79), presence of a specific litter box (31 of 79), *Encephalitozoon cuniculi* serological status (26 of 79), blood total calcium value (27 of 79), method of urine collection (77 of 79), and presence of a salt lick (54 of 79; **Supplementary Table S1**).

Most urine samples were collected by cystocentesis. Only 4 rabbits had their urine collected by urethral catheterization and were part of the UTI group.

The presence of bacteria on urine microscopic examination was the only variable that was statistically significantly different between the UTI group and the negative-culture group ($P < .001$ before correction, and $P < .001$ after Holm-Bonferroni correction; **Table 1**). In the UTI group, 15 of 21 rabbits (71.4%) had bacteria on urine microscopic examination, whereas in the negative-culture group, 4 of 39 rabbits (10.3%) did. The presence of bacteria on urine microscopic examination was compared to bacterial urine culture, regarded as the gold-standard test, and showed a sensitivity of 71% (95% CI, 60% to 82%), specificity of 90% (95% CI, 82% to 98%), positive predictive value of 79% (95% CI, 69% to 89%), and negative predictive value of 85% (95% CI, 76% to 94%).

Several variables approached statistical significance before Holm-Bonferroni correction. Effect size was of medium magnitude for urinary bladder wall thickening and the presence of WBCs on urine microscopic examination (Table 1).

Loss of appetite and reduced fecal output were reported in 12 of 27 (44.4%) and 9 of 27 rabbits (33.3%) in the UTI group, respectively, and in 28 of 52 (53.8%) and 17 of 52 rabbits (32.7%) in the negative-culture

Table 1— Selective results of the univariate analysis of variables as potential risk factors for urinary tract infections in 27 rabbits with positive culture and 52 rabbits with negative culture by use of binary logistic regression, the χ^2 or Cochran-Armitage test, and the Holm-Bonferroni correction for multiple comparisons. Effect size was assessed by calculating the ϕ coefficient for the categorical variables and providing the OR and its 95% CI for the continuous variables.

	Positive-culture group		Negative-culture group		Effect size			
	n	% or mean ± SD	n	% or mean ± SD	OR (95% CI)	ϕ	*P* value	*P* value after Holm-Bonferroni correction
Age (y; n = 78)	26	5.61 ± 2.26	52	4.80 ± 2.38	1.16 (0.95–1.42)	—	.16	1
Weight (kg; n = 79)	27	1.64 ± 0.66	52	1.81 ± 0.59	0.61 (0.26–1.42)	—	.25	1
Rectal temperature (°C; n = 63)	21	37.6 ± 1.64	42	38.1 ± 1.13	0.66 (0.42–1.06)	—	.08	1
Sex (n = 79)	27		52		—	0.2	.078	1
Female	16	59.3	20	38.5				
Male	11	40.7	32	61.5				
Breed (n = 79)	27		52		—	–0.23	.004	1
Erect-eared rabbit	25	92.6	38	73.1				
Lop-eared rabbit	2	7.4	14	26.9				
Precedent urinary episodes (n = 79)	27		52		—	0.26	.023	.759
No	14	51.9	40	76.9				
Yes	13	48.1	12	23.1				
Precedent urogenital surgeries other than neutering (n = 79)	27		52		—	0.25	.043	1
No	22	81.5	50	96.2				
Yes	5	18.5	2	3.8				
Urinary sludge (n = 77)	26		51		—	0.24	.033	1
No	4	15.4	20	39.2				
Yes	22	84.6	31	60.8				
Urolithiasis (n = 73)	22		51		—	–0.27	.021	.714
No	20	90.9	33	64.7				
Yes	2	9.1	18	35.3				
Urinary bladder wall thickening (n = 71)	24		47		—	0.35	.003	.105
No	12	50.0	39	83.0				
Yes	12	50.0	8	17.0				
Presence of RBCs in urine (n = 56)	19		36		—	–0.27	.075	1
No	18	94.7	26	72.2				
Yes	1	5.3	10	27.8				
Presence of WBCs in urine (n = 56)	19		36		—	0.35	.023	.736
No	12	63.2	33	91.7				
Yes	7	36.8	3	8.3				
Presence of bacteria in urine (n = 60)	21		39		—	0.63	< .001	< .001
No	6	28.6	35	89.7				
Yes	15	71.4	4	10.3				

— = Not applicable.

group, respectively. In the UTI group, 5 of 27 rabbits (18.5%) presented only with loss of appetite and reduced fecal output and did not show urinary clinical signs. Complete results of the univariate analysis are presented in **Supplementary Table S2**. No statistically significant differences were observed after Holm-Bonferroni correction between the UTI group and the negative-culture group for the other studied parameters, including loss of appetite and reduced fecal output.

Bacterial culture results and antimicrobial susceptibility testing

In the negative-culture group, 47 of 52 rabbits (90.4%) had 1 negative urine culture; 4 of 52 rabbits (7.7%) had 2 negative urine cultures separated by 131, 153, 160, and 616 days; and 1 of 52 rabbits (1.9%) had 3 negative urine cultures (with the second and third at 7 and 47 days after the first, respectively).

Of the 27 rabbits with a positive urine bacterial culture from the UTI group, 36 bacteria were isolated. *Escherichia coli* was the most common (27.8% [10 of 36]), followed by *Enterococcus faecalis* (19.4% [7 of 36]), *Staphylococcus* spp (11.1% [4 of 36]), and *Enterobacter* spp (8.3% [3 of 36]; **Table 2**).

Table 2—Distribution of bacterial species cultured in the urine of rabbits with urinary tract infection. A total of 36 bacteria were isolated from 27 rabbits. The bacteria are separated into gram-negative and gram-positive species.

Bacterial species	n	%
Gram-positive species		
Enterococcus faecalis	7	19.4
Staphylococcus spp	4	11.1
Aerococcus viridans	2	5.6
Unspecified species of gram-positive cocci	2	5.6
Jeotgalicoccus halotolerans	1	2.8
Trueperella pyogenes	1	2.8
Gram-negative species		
Escherichia coli	10	27.8
Enterobacter spp	3	8.3
Klebsiella pneumoniae	2	5.6
Acinetobacter baumannii	1	2.8
Chryseomonas indologenes	1	2.8
Mannheimia caviae	1	2.8
Serratia marcescens	1	2.8

Single infections (74.1% [20 of 27]) predominated over mixed infections (25.9% [7 of 27]). Among the rabbits from which urine was collected by urethral catheterization, 1 had a single infection by *E faecalis* and 3 had mixed infections. These 3 mixed infections consisted of *E coli* and *E faecalis*; *Aerococcus viridans*, *E faecalis*, and *Jeotgalicoccus halotolerans*; and *A viridans*, *E coli*, and *Staphylococcus xylosus*, respectively. The other 4 mixed infections were reported in rabbits that had their urine collected by cystocentesis and consisted of 2 unspecified species of Gram-positive cocci, *E coli* and *E faecalis* (2 rabbits) and *Chryseomonas indologenes* and *Staphylococcus cohnii*.

Antimicrobial susceptibility testing results are summarized in **Table 3**. Regarding the *E coli* isolates tested, 100% (2 of 2) showed resistance to penicillin (natural resistance), 80% (4 of 5) to azithromycin, 33.3% (3 of 9) to sulfonamides-trimethoprim, 22.2% (2 of 9) to ceftiofur, 14.3% (1 of 7) to enrofloxacin, 11.1% (1 of 9) to chloramphenicol, 10% (1 of 10) to gentamicin, and 10% (1 of 10) to marbofloxacin. Overall, 66.2% (15 of 20) of bacteria isolates were resistant to azithromycin, 57.9% (13 of 19) to penicillin, 31.4% (11 of 35) to sulfonamides-trimethoprim, 22.2% (8 of 36) to marbofloxacin, 19.2% (5 of 26) to chloramphenicol, 17.9% (5 of 28) to enrofloxacin, 17.1% (6 of 35) to ceftiofur, and 8.3% (3 of 36) to gentamicin. Complete results of the antimicrobial susceptibility testing are presented in **Supplementary Table S3**.

Overall, 52.8% (19 of 36) of bacteria were MDR, particularly 50% of *E coli* and *Staphylococcus* spp isolates, 85.7% of *E faecalis* isolates, and 66.7% of *Enterobacter* spp isolates **(Supplementary Table S4)**.

Presumptive pyelonephritis

Of the rabbits in the negative-culture group, 43.5% (20 of 46) had ultrasonographic findings consistent with pyelonephritis. Pyelectasia was reported in 80% (16 of 20) of cases, proximal ureter dilation in 50% (10 of 20), decreased corticomedullary distinction in 35% (7 of 20), increased renal size in 30% (6 of 20), decreased renal size in 5% (1 of 20), and renal hyperechogenicity in 65% (13 of 20). Bilateral involvement was noted in 80% (16 of 20) of cases. Of the rabbits in the positive-culture group, 34.8% (8 of 23) had consistent ultrasonographic signs

Table 3—Results of susceptibility of isolated bacteria to antimicrobials used from positive-culture urine samples of rabbits by disk diffusion method following the Normes Françaises et Européennes standards (NF U47-107) and the guidelines of the Comité de l'Antibiogramme de la Société Française de Microbiologie (CA-SFM) 2013 and the veterinary CA-SFM 2023.

	E coli **(n = 10)**			***E faecalis*** **(n = 7)**			***Staphylococcus*** **spp (n = 4)**			**Other (n = 15)**			**Total (n = 36)**		
	n (S%)	**n (I%)**	**n (R%)**	**n (S%)**	**n (I%)**	**n (R%)**	**n (S%)**	**n (I%)**	**n (R%)**	**n (S%)**	**n (I%)**	**n (R%)**	**n (S%)**	**n (I%)**	**n (R%)**
Penicillin	0 (0)	0 (0)	2 (100)	1 (25)	0 (0)	3 (75)	2 (50)	0 (0)	2 (50)	3 (33.3)	2 (22.2)	4 (44.4)	6 (31.6)	2 (10.5)	11 (57.9)
Ceftiofur	7 (77.8)	0 (0)	2 (22.2)	2 (28.6)	3 (42.9)	2 (28.6)	3 (75)	0 (0)	1 (25)	14 (93.3)	0 (0)	1 (6.7)	26 (74.3)	3 (8.6)	6 (17.1)
Gentamicin	9 (90)	0 (0)	1 (10)	6 (85.7)	1 (14.3)	0 (0)	3 (75)	0 (0)	1 (25)	13 (86.7)	1 (6.7)	1 (6.7)	31 (86.1)	2 (5.6)	3 (8.3)
Azithromycin	0 (0)	1 (20)	4 (80)	0 (0)	1 (33)	2 (66.7)	1 (33.3)	0 (0)	2 (66.7)	3 (27.3)	1 (9.1)	7 (63.6)	4 (18.2)	3 (13.6)	15 (66.2)
Tetracycline	4 (80)	0 (0)	1 (20)	1 (25)	0 (0)	3 (75)	1 (50)	0 (0)	1 (50)	5 (83.3)	0 (0)	1 (16.7)	11 (64.7)	0 (0)	6 (35.3)
Chloramphenicol	8 (88.9)	0 (0)	1 (11.1)	3 (60)	0 (0)	2 (40)	2 (66.7)	0 (0)	1 (33)	8 (88.9)	0 (0)	1 (11.1)	21 (80.8)	0 (0)	5 (19.2)
Enrofloxacin	6 (85.7)	0 (0)	1 (14.3)	3 (42.9)	3 (42.9)	1 (14.3)	3 (75)	0 (0)	1 (25)	7 (70)	1 (10)	2 (20)	19 (67.9)	4 (14.3)	5 (17.9)
Marbofloxacin	9 (90)	0 (0)	1 (10)	2 (28.6)	3 (42.9)	2 (28.6)	3 (75)	0 (0)	1 (25)	10 (66.7)	1 (6.7)	4 (26.7)	24 (66.7)	4 (11.1)	8 (22.2)
Sulfonamides-trimethoprim	6 (66.7)	0 (0)	3 (33)	6 (85.7)	0 (0)	1 (14.3)	3 (75)	0 (0)	1 (25)	8 (53.3)	1 (6.7)	6 (40.0)	23 (65.7)	1 (2.9)	11 (31.4)

I% = Percentage of isolates with intermediate resistance to the antimicrobial. R% = Percentage of isolates resistant to the antimicrobial. S% = Percentage of isolates susceptible to the antimicrobial.

of pyelonephritis. Pyelectasia was reported in 87.5% (7 of 8) of cases, proximal ureter dilation in 37.5% (3 of 8), decreased corticomedullary distinction in 75% (6 of 8), increased renal size in 37.5% (3 of 8), and renal hyperechogenicity in 75% (6 of 8). Bilateral involvement was noted in 62.5% (5 of 8) of cases. The presence of consistent ultrasonographic signs of pyelonephritis was not significantly different between the 2 groups (Supplementary Table S2). No pyelocentesis was performed in any of the rabbits. Among the 8 rabbits with ultrasonographic signs of pyelonephritis in the UTI group, 10 bacterial isolates were identified. *Staphylococcus* spp and *E coli* were isolated in 2 of 10 cases each, followed by *C indologenes*, *Enterobacter hormaechei*, *E faecalis*, *Klebsiella pneumoniae*, *Mannheimia caviae*, and *Serratia marcescens* (1 of 10 each).

Treatment and outcome

Among the rabbits in the negative-culture group, 36 of 52 (69.2%) were hospitalized and 16 of 52 (30.8%) were managed as outpatients. In this group, urogenital diseases included urolithiasis, urinary sludge, acute kidney injury, chronic kidney disease, presumptive encephalitozoonosis, inflammation of the urogenital tract (cystitis, ureteritis, urethritis, vaginitis, and vulvitis), presumptive pyelonephritis, renal mass, and iatrogenic ligation of the ureter.

Of the rabbits in the UTI group, 22 of 27 (81.5%) were hospitalized and 5 of 27 (18.5%) received care at home. Twenty-five of 27 rabbits (92.6%) were given antibiotics, 18 of 27 (66.7%) were given meloxicam as an NSAID, and 20 of 27 (74.1%) received fluid therapy. The choice of antibiotics was made empirically while awaiting the results of urine culture. Antimicrobial therapy was adjusted in case of resistance on the basis of bacterial culture and antimicrobial susceptibility profiles once they became available. Most of the rabbits (68% [17 of 25]) received a single antibiotic, and 8 of 25 (32%) received dual-antibiotic therapy. Sulfonamides-trimethoprim (42.4% [14 of 33]) were the most commonly used antibiotics, followed by marbofloxacin (21.2% [7 of 33]), doxycycline (12.1% [4 of 33]), chloramphenicol (9.1% [3 of 33]), azithromycin (6.1% [2 of 33]), enrofloxacin (3.0% [1 of 33]), ceftiofur (3.0% [1 of 33]), and metronidazole (3.0% [1 of 33]). Two of 27 rabbits (7.4%) did not receive antibiotics: one died shortly after discharge and the other was lost to follow-up.

In the group of rabbits with negative urine culture, 19.2% (10 of 52) had their conditions fully resolved, 40.4% (21 of 52) presented with recurrence or persistence of their conditions, 17.3% (9 of 52) died, 9.6% (5 of 52) were euthanized, and 13.5% (7 of 52) were lost to follow-up.

Regarding the outcome in the UTI group, 4 of 27 rabbits (14.8%) died within 2 days after diagnosis (3 had consistent ultrasonographic signs of pyelonephritis), 1 of 27 (3.7%) was euthanized and had presented consistent ultrasonographic signs of pyelonephritis, 8 of 27 (29.6%) were lost to follow-up after the initial consultation or before knowing whether the UTI had been resolved (3 had consistent ultrasonographic signs of pyelonephritis), 8 of 27 (29.6%) were cured at the last consultation for which information was available (2 had consistent ultrasonographic signs of pyelonephritis), 3 of 27 (11.1%) were cured temporarily and presented a recurrence, and 3 (11.1%) had a persistent UTI. The 3 rabbits with persistent UTI presented with chronic cystitis: 1 rabbit had hyperplastic cystitis confirmed by postmortem histopathological examination and multiple positive urinary cultures with different bacteria isolated later, 1 had polypoid lesions observed during cystoscopy and multiple positive urinary cultures with the same and a different bacteria isolated later, and 1 had membranes in the urinary bladder described sonographically and multiple positive urinary cultures with the same bacteria isolated 9 months after the initial diagnosis. Of the 3 rabbits that experienced recurrence, 2 showed urinary signs, but had a second negative urine culture, and 1 had a second positive urine culture, but with different bacterial isolates.

Discussion

The present study described the characteristics of UTI in rabbits, investigated potential risk factors, and provided information on etiology and antimicrobial susceptibility of urinary bacteria. Most of the rabbits with UTI were presented to consultation with urinary complaints (59.3% [16 of 27]), including inappropriate location of urination (37.0% [10 of 27]), micturition signs (29.6% [8 of 27]), urinary incontinence (14.8% [4 of 27]), soiled perineum (14.8% [4 of 27]), and polyuria-polydipsia (11.1% [3 of 27]). Loss of appetite (44.4% [12 of 27]) and decreased fecal output (33.3% [9 of 27]) were also frequent, with 18.5% (5 of 27) of rabbits with UTI showing only these signs without urinary concerns. Clinical presentation did not reliably distinguish UTI from other urinary conditions such as urolithiasis, urinary sludge, acute kidney failure, or chronic kidney disease, as group differences were not significant.

Escherichia coli was the most commonly isolated pathogen (27.8% [10 of 36]), followed by *E faecalis* (19.4% [7 of 36]) and *Staphylococcus* spp (11.1% [4 of 36]). These results diverge from those of a study[5] in which *Enterococcus* spp were the most common bacteria in the urinary tract of rabbits, followed by *Staphylococcus* spp and *E coli*. *Staphylococcus* spp (3 of 9) were the most commonly isolated pathogen in rabbits with consistent ultrasonographic signs of pyelonephritis, which is consistent with data provided in textbooks.[2,3] *Pasteurella multocida* is also cited as a frequent cause of pyelonephritis in rabbits; however, neither our study nor a study by Fernández et al[5] found *P multocida*. Several factors may explain this discrepancy, including geographical variation in bacterial populations or methodological differences in urine sampling and culture. It is difficult to assess the reliability of these statements in textbooks, as no original research articles were cited. However, in our study, no pyelocentesis was performed on any of the rabbits from either the negative- or positive-culture group. This could have led to false-negative results, particularly in rabbits included in the negative-culture group with ultrasonographic findings consistent with

pyelonephritis but with a negative cystocentesis culture. The predominance of *E coli* in rabbits from this study is consistent with findings in dogs and cats, in which *E coli* is the most common bacteria. Large-scale surveys from the UK, Chile, and the US identified *E coli* in approximately 49.7% to 58.0% of cats and 42.6% to 55.6% of dogs.[7–12] These results suggest that ascending bacterial infections from enteric microorganisms (such as *E coli* or *Enterococcus* spp) may be a major route in rabbits, as in dogs and cats.[13]

Identified risk factors of UTI in cats and dogs include female sex, advanced age, poor body condition score or obesity, prior urogenital surgery, functional or anatomic abnormality of the lower urinary tract, presence of urolithiasis, urinary incontinence, recent use of antibiotics, immunosuppression, or chronic kidney disease.[7,9,13,25] Statistical analysis identified the presence of bacteria on urine microscopic examination as the only statistically significant parameter associated with positive urine culture. Our initial hypotheses assuming an association between UTI and female sex as well as the presence of urinary sludge and urolithiasis were not validated. The absence of other identified risk factors in rabbits may indicate species differences with dogs and cats, but it is more likely explained by the small population sample and limited statistical power of the present study. Several other variables approached statistical significance before Holm-Bonferroni correction (female sex, erect-eared rabbits, precedent urinary episodes, precedent urogenital surgeries other than neutering, body condition score, urinary bladder wall thickening, urinary sludge, and presence of WBCs on urine microscopic examination). In particular, urinary bladder wall thickening and the presence of WBCs on urine microscopic examination had a medium effect size. These parameters could be interpreted as false-negative results and could be the subject of future studies to investigate their role as possible factors associated with UTI.

We found a relatively good agreement between the detection of bacteria in microscopic examination and urine culture results, with satisfactory sensitivity (71%; 95% CI, 60% to 82%) and specificity (90%; 95% CI, 82% to 98%). These results were in accordance with those for dogs, in which a sensitivity of 64.1% (95% CI, 47.2% to 78.3%) and specificity of 98.1% (95% CI, 95.0% to 99.4%) were found.[26] This finding suggested that the presence of bacteria in microscopic examination of urine could be used as a screening tool for UTI in rabbits, especially in practices where access to urine culture is limited or in situations where owners have limited financial resources.

A major concern was the high prevalence of MDR bacteria (52.8% [19 of 36]). Studies of dogs and cats with UTIs reported MDR bacteria rates between 24.6% and 31.5%.[8,10,12] In Spain, antimicrobial resistance profiles of overall bacterial infection in pet rabbits were investigated and revealed high rates of MDR bacteria (eg, 48% of *E coli* isolates were MDR).[5] In Romania, another similar study[6] of rabbits reported an overall proportion of 49% of MDR bacteria. These findings pose therapeutic challenges, given that the choice of antibiotics that can be administered enterally is already limited in rabbits because of the digestive toxicity of certain antibiotics (β-lactams and aminosides). Cystocentesis and urine culture should be the cornerstones of UTI diagnosis in order to determine an appropriate antibiotic treatment, as recommended by the International Society for Companion Animal Infectious Diseases guidelines.[1] Antimicrobial stewardship is paramount to limit the risk of developing antibiotic resistance in the future. On the basis of our study, sulfonamides-trimethoprim may represent a good first-line antibiotic, as bacterial resistance is one of the lowest (31.4%) among tested antibiotics. Fluoroquinolones may also represent a good choice in countries where their prescription is not restricted. On the other hand, treating subclinical bacteriuria (defined as the presence of bacteria in urine culture in the absence of clinical urinary signs) with antibiotics is not recommended according to the latest guidelines.[1,13] However, the study of subclinical bacteriuria is limited in pet rabbits, and the prevalence is not known. One study[27] found 40% of subclinical bacteriuria in a population of 100 laboratory rabbits. Bacterial culture was performed on urine samples collected under optimal hygienic conditions and revealed the presence of *Klebsiella aerogenes*, *Staphylococcus epidermidis*, *Staphylococcus pyogenes*, *Pseudomonas aeruginosa*, *Streptococcus* spp, and *Proteus mirabilis*.[27] Metagenomics sequencing, which is already used to characterize the rabbit ear microbiome,[28] could similarly provide insights into the urinary microbiome of healthy rabbits.

The limitations of our study must be acknowledged. First, the inclusion method only took into account rabbits for which a urine culture was performed and included only sick rabbits that were brought in for consultation, with or without urinary signs, introducing a selection bias. The negative-culture group did not consist of healthy rabbits that could have been considered as controls for the statistical analysis of risk factors. In addition, false-negative cases could have been included in the negative-culture group, as it is possible for a rabbit with a UTI to have a negative urine culture. Incomplete medical records were inherent to the retrospective design of the study, resulting in missing data and the exclusion of some variables from the statistical analysis. Two rabbits did not receive antibiotics, but the reason was unclear and it was difficult to determine whether the records were incomplete. Furthermore, it was not possible to determine from the medical records whether the empirical antibiotic was prescribed before or after the urine samples were sent for culture. Urine culture being performed after the start of empirical antimicrobial treatment in some cases could have led to false-negative results that were included in the negative-culture group. Nonstandardized urine collection introduced possible bias, as all 4 catheterized rabbits yielded positive cultures, raising the possibility of contamination. Transportation and time to culture were also not standardized across the 3 centers, possibly creating biases in the culture results. In particular, samples from CHV AniCura

Advetia were transported within 48 hours (compared to 24 hours at the other centers), as there was no in-house laboratory. Moreover, the relatively small sample size, particularly in the UTI group, restricted the power of the statistical analysis to detect potential risk factors. We lack a clear classification of UTI in pet rabbits compared to dogs and cats. Presumptive diagnosis of pyelonephritis was supported by concurrent ultrasonographic findings and positive urine culture in our study, but no pyelocentesis was performed in any of the rabbits (with either positive or negative cystocentesis culture). As ultrasound images of obstructive ureteral urolithiasis may resemble those of pyelonephritis, it would have been relevant to perform pyelocentesis. Adopting International Society for Companion Animal Infectious Diseases terminology could initially help to distinguish between sporadic cystitis, recurrent cystitis, pyelonephritis, and subclinical bacteriuria,[1] in addition to urethritis and ureteritis, and guide future treatment decisions.

In conclusion, to our knowledge, this retrospective multicentric study was the first to provide a clinical and paraclinical description of UTI in pet rabbits. It highlights the presence of bacteria on urine microscopic examination as the only statistically significant result of our study that could serve as a screening test for UTI, the predominance of *E coli*, and a high proportion of MDR bacteria. Our study population only included pet rabbits in the Greater Paris region, France, from centers with both general and referral activities. Further studies, ideally prospective in design and with larger cohorts, with a standardized protocol would help to clarify risk factors of UTI in rabbits.

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Supplementary Materials

Supplementary materials are posted online at the journal website: avmajournals.avma.org.