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The Frequency and Clinical Implications of Bacteriuria in Chronically Paralyzed Dogs

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Background: Paralysis is a known risk factor for urinary tract infections (UTI), sepsis, and death in paralyzed people, but there are no data available on diagnostic criteria for UTI versus bacteriuria, their frequency, or clinical implications in chronically paralyzed dogs.

Hypothesis/Objectives: That chronically paralyzed dogs suffer frequent bacteriuria causing reduced duration of survival. We documented the frequency of bacteriuria, associated clinical signs, and survival rate in chronically paralyzed dogs.

Animals: Forty-seven client-owned dogs paralyzed with no pelvic limb pain perception for >3 months and at least one urine culture (UC) performed.

Methods: Retrospective, observational study. Medical records of dogs meeting inclusion criteria were reviewed for results of UC, urinalysis, and clinical signs. Outcome was compared between dogs with and without bacteriuria.

Results: Thirty-five of 47 dogs had at least 1 positive UC, and 13 had recurrent bacteriuria. Rectal temperature and urinalysis results were extracted from records. Fever was present at time of UC in 5 of 68 observations, 2 with and 3 without bacteriuria. Pyuria was significantly associated with positive cultures ($P < 0.001$), cloudiness was not ($P = 0.076$). Survival data in 35 dogs (8 dead) showed no association between bacteriuria and survival ($P = 0.69$).

Conclusions and Clinical Importance: Bacteriuria is common in paralyzed dogs but does not cause fever; diagnostic criteria of UTI are unclear. We did not detect an association of bacteriuria with survival, but this needs further confirmation.

Key words: Canine; Incontinence; Spinal cord injury; Urinary tract infection.

Spinal cord injury (SCI) increases the risk of urinary tract infections (UTIs) in both people[1–7] and dogs[8–12] due to impairment of the storage and voiding function of the lower urinary tract. Failure to effectively clear bacteriuria because of infrequent and incomplete urine voiding, as well as introduction of bacteria through indwelling or intermittent catheterization, contribute to development of UTI in these dogs.[1–3,5–10] The overall incidence of UTI is 0.68 episodes per 100 patients per day in chronically paralyzed people.[2] Appropriate diagnosis and treatment of these infections are important as they increase the risk of pyelonephritis, negatively impact quality of life, and interfere with rehabilitation.[1–3,8] Furthermore, UTI is an important cause of septicemia, one of the major contributors to increased mortality in spinal cord-injured patients.[5,8,13–15]

Abbreviations:

CFU	colony-forming unit
E. coli	*Escherichia coli*
hpf	high-power field
IVDH	intervertebral disk herniation
SCI	spinal cord injury
UTI	urinary tract infection

However, this clinical picture is complicated by the frequency of asymptomatic bacteriuria. This is considered a common finding among people with SCI and is not an indication for antimicrobial treatment because it could give rise to antibiotic-resistant infections.[6,7] The diagnostic criteria that differentiate UTI from asymptomatic bacteriuria in spinal cord-injured people are not standardized, but commonly include the presence of bacteriuria over a certain threshold of colony numbers (>10^5 CFU/mL) with one or more signs and symptoms including fever, pyuria, pain over kidneys and bladder, new onset of incontinence, increased spasticity, autonomic dysreflexia, increased use of catheters, cloudy urine with foul smell, hematuria, lethargy and malaise, and change in difficulty in voiding urine.[1,3–7,13,16,17] Diagnostic work up includes urinalysis, aerobic culture, and sensitivity testing.

While there are published data on the frequency of UTI in dogs recovering from acute SCI,[9–12] there are no data on the frequency with which such infections occur in chronically paralyzed dogs. Differentiating subclinical bacteriuria from clinical UTI in these neurologically compromised dogs has also not been investigated. Current guidelines for diagnosing dogs with UTI include occurrence of inappropriate urination, dysuria, hematuria, stranguria, pollakiuria, malodorous urine, and significant bacteriuria (>10^5 CFU/mL) determined by quantitative urine culture.[18,19] This approach to

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diagnosis is however challenging in a spinal cord-injured dog with dysfunctional micturition, diminished sensory perception, and no ability to report clinical signs. There is no standardized set of guidelines defining the clinical signs suggestive of UTI and entailing treatment and management in dogs with chronic SCI.

The purpose of this retrospective study was to determine the frequency of bacteriuria in chronically paralyzed dogs, to define the organisms involved, and to describe the range of clinical signs observed in these dogs as well as overall survival. A secondary aim was to investigate the frequency of clinical signs suggestive of UTI in this population. We hypothesized that survival rates would be higher in paralyzed dogs without a history of bacteriuria.

Materials and Methods

Case selection criteria

Medical records of dogs with chronic paraplegia evaluated by the canine SCI program at NC State College of Veterinary Medicine for participation in clinical trials between November 1999 and November 2016 were reviewed. Inclusion criteria were as follows: history of acute, severe thoracolumbar SCI more than 3 months previously; failure to recover pain perception or ambulation; at least one documented urine culture.

Criteria for diagnosis of UTI

The medical literature was reviewed to generate a list of criteria suggestive of UTI in people with SCI. The resulting criteria were examined and those for which there were reliable data recorded for participating dogs were identified for further examination. Nine papers reporting guidelines for diagnosis of urinary tract infection in paralyzed people were identified.[1,3–7,13,16,17] Recommendations varied (Table S1) but in all, UTI was recognized as bacteriuria $>10^5$ CFU/mL and was associated with fever. A range of additional signs was considered consistent with UTI. Among these, the signs that could be extracted from medical records for the majority of the dogs were pyuria, urine cloudiness and foul smell, and body temperature to indicate the presence of fever.

Data collection

Data extracted from each dog's medical record were as follows: age (at the onset of paraplegia, at presentation, and at the time of euthanasia or death if applicable), sex, breed, weight, duration of paraplegia at time of writing or when died, initial cause of paraplegia, history of surgery, and, if dead, cause of death and time from paralysis until death. Urine samples were routinely taken by cystocentesis if performed at the author's institution. Method of collection was not available for cultures performed by general practitioners. Data collected on urine cultures and urinalysis included number of cultures per dog, number of cultures with bacterial growth of $>10^5$ CFU/mL (based on the criteria of UTI established from the human literature), number of dogs with at least 1 positive culture, number of dogs with recurrent positive cultures (defined as 3 or more positive cultures during a 12-month period including refractory infections, reinfections, and relapses), identity of organisms, number of positive cultures for each organism, number of cultures with antibiotic-resistant organisms (defined as Gram-negative isolates resistant to both aminoglycosides and fluoroquinolones, *Staphylococcal sp*. resistant to oxacillin, and *Enterococcus* and *streptococcal sp*. resistant to penicillin), number of dogs with antibiotic-resistant infections, the presence of pyuria (defined as >5 WBCs per high-power field of urine), cloudiness and foul odor in cultured urine samples, and rectal temperature at the time of obtaining each cultured sample. Fever was determined as body temperature higher than 102.5°F. Cloudiness was either reported in the urinalysis by a clinical pathologist or recorded during urine sample submission for culture by the person collecting the specimen. The presence of foul-smelling urine was extracted from history and physical examination findings in each dog's discharge or from the sample submission form.

Statistical analysis

Summary data were prepared and reported as median and range, mean and standard deviation, or proportion depending on data type and distribution. The association of clinical signs (fever, pyuria, and cloudy urine yes or no) with positive culture results was examined. The following variables were compared between dogs with at least one positive culture, dogs with no positive cultures, and dogs with recurrent positive cultures: sex, age at onset of paralysis, duration of paralysis, number of cultures per dog, and survival (alive, yes or no). Categorical data were evaluated by construction of a contingency table and chi-square analysis. Fisher exact test was used where indicated by low sample size. Continuous data were evaluated by a Wilcoxon rank sum test. P values <0.05 were considered significant.

Results

Study cohort

Medical records from 58 dogs were reviewed. Eleven dogs did not have any urine cultures recorded and were therefore excluded despite meeting the first 2 inclusion criteria. Forty-seven dogs with chronic paraplegia due to an acute, severe thoracolumbar SCI at least 3 months previously that did not recover pain perception and independent ambulation and had at least one bacterial urine culture and sensitivity testing in their records were identified. There were 23 females (49%) and 24 (51%) males. The main cause of paraplegia was intervertebral disk herniation (IVDH) (38/47; 80.85%). Seven cases of paraplegia were due to vertebral fracture and/or luxation (15%), and 2 cases were of unknown cause (4%). All dogs were being managed routinely by manual expression of their bladder by their owners.

Thirty-five dogs (35/47, 75%) had at least one positive urine culture, 13 of which were considered recurrent (13/47, 28%), whereas 12 dogs (12/47, 26%) had no growth on any of the urine cultures. Full details of the signalment of these dogs are provided in Table 1. The breeds of dogs with bacteriuria included Dachshund (9), Mixed Breed Dog (3), French Bulldog (3), Labrador Retriever (3), American Cocker Spaniel (2), Schnauzer (2), Poodle (2), American Staffordshire Terrier (2), Bichon Frise (1), Shih Tzu (1), Pug (1), Australian Cattle Dog (1), Dogue de Bordeaux (1), German Shepherd Dog (1), Doberman Pinscher (1), American Bulldog (1), and Weimaraner (1). The breeds of dogs with negative cultures included Dachshund (8), Mixed Breed Dog (2), Bichon Frise (1), and Pembroke Welsh Corgi (1).

Table 1. Summary data for dogs divided into groups according to urine culture results.

	Dogs with negative urine cultures N = 12	Dogs with positive urine culture[a] N = 35	Dogs with recurrent positive cultures[b] N = 13
Age at the onset of paraplegia (years)	4.41 ± 1.83	4.02 ± 2.16	3.53 ± 1.5
Duration of paraplegia (years)	5.42 ± 1.9	5.07 ± 2.8	6.36 ± 3.13
Sex	3 F	20 F (2/20 intact)	7 F (1/7 intact)
	9 M (2/9 intact)	15 M (2/15 intact)	6 M (1/6 intact)
Weight	8.74 ± 3.5 kg	11.4 kg (range 4–40.08 kg)	9.3 kg (range 5.3–40.08 kg)
Number of euthanized dogs	2/7	6/28	3/11
	28.57%	21.42%	27.27%
Duration of postparalysis survival in euthanized dogs	N = 2; 64, 74 months	N = 6; 12, 50, 52, 92, 99, 144 months	N = 3; 52, 99, 144 months
Number of dogs with antibiotic-resistant isolates	–	7/35	6/13
		20%	46.15%
Number of cultures per dog	3 (1–6)	3 (1–28)	10 (4–28)

[a]This column represents all the dogs that had at least 1 positive culture.
[b]This column represents the subset of dogs that met the criteria for recurrent positive urine culture.

Bacterial culture results

Two hundred and fifty-one cultures were performed, with a median of 3 and a range of 1–28 cultures per dog. Two hundred and eighteen of the 251 cultures were performed for the 35 dogs that had at least one positive culture result and the remaining 33 cultures were performed for the 12 dogs that had only negative cultures (Table 1).

Of the 251 cultures recorded, 110 of 251 (43.8%) were considered negative (8 of these cultures had $<10^5$ CFU/mL). The majority of positive cultures grew *E. coli*; however, cultures growing multiple organisms were also common, and 14 different organisms were represented overall (Table 2). Fourteen of 141 of the positive cultures grew antibiotic-resistant organisms where *E. coli* was the prominent organism accounting for 10/14 (71%) of resistant infections. Thirteen of 14 (93%) of the resistant infections occurred in dogs with recurrent UTIs.

Table 2. Distribution of bacterial isolates from 141 positive urine cultures in 35 dogs with 1 or more positive urine cultures.

Organism	Number of positive cultures
Escherichia coli	49 (34.8%)
Polymicrobial	22 (15.6%)
Enterococcus spp	17 (12.1%)
Staphylococcus spp	12 (8.5%)
Proteus spp	11 (7.8%)
Klebsiella spp	11 (7.8%)
Enterobacter spp	5 (3.5%)
Pseudomonas spp	5 (3.5%)
Beta-hemolytic Streptococci	3 (2.1%)
Citrobacter spp	2 (1.4%)
Corynebacterium-like organisms	1 (0.7%)
Pantoea agglomerans	1 (0.7%)
Salmonella spp	1 (0.7%)
Globicatella sanguinis	1 (0.7%)
Total	141

Clinical signs of UTI in dogs

Rectal temperature was recorded 68 times when submitting a urine culture (out of 251), 35 times with a negative, and 33 times with a positive culture result (Table 3). The body temperature exceeded the reference range in 3 of 35 negative and 2 of 33 dogs with positive cultures. Organisms isolated from the 2 positive cultures were *Proteus mirabilis* and *Enterococcus faecium* (polymicrobial) and *Globicatella sanguinis*. There was no significant difference between positive and negative cultures and occurrence of fever ($P = 0.08$).

A urinalysis was performed for 98 of the urine cultures (Table 3). There was no growth in 44/98 of these cultures. Pyuria was documented 40 times, 35 in dogs with positive cultures (Table 4). The presence of pyuria was significantly associated with positive cultures ($P < 0.001$) when the results of all 98 cultures accompanied by a urinalysis were compared. One hundred and forty-one of 251 samples collected for urine cultures had a report of cloudiness (Table 3), 71 of which showed no growth. There were 19 urine specimens that yielded in *E. coli* with a concurrent observation on cloudiness. Of these, 17 (17/19 90%) were cloudy, but there was no significant difference in presence of cloudiness between the positive and negative cultures considered as a whole ($P = 0.076$).

Table 3. Signs and symptoms recorded with urine cultures.

	Culture results	
Signs	Positive cultures	Negative cultures
Fever	2/33	3/35
Pyuria	35/54	5/44[a]
Cloudiness	60/70	46/71
Foul odor	38[b]	6

[a]1 of the 5 "negative" cultures with pyuria had bacterial growth of $<10^5$ CFU/mL.
[b]Presence of foul odor was recorded but absence was not.

A report of malodorous urine was present either in the history, physical examination or while submitting samples for culture in 44 of 251 urine samples (Table 3). Thirty-eight of these samples yielded bacterial growth. The pathogens isolated were as follows: *E. coli* (19/38 50%), polymicrobial (7/38 18%), *Klebsiella spp.* (3/38 8%), *Staphylococcus spp.* and *Proteus spp.* (2/38 5%), *Enterococcus spp.*, *Enterobacter spp.*, *Pseudomonas spp.*, *Pantoea agglomerans,* and *Corynebacterium spp.* (each 1/38 3%). Recording of foul odor was not standard in the medical record. The absence of information on urine odor could therefore have meant there was no foul odor or simply that this variable had not been assessed. As such, statistical analysis of the association between foul odor and urine culture results was not attempted.

Survival

Survival data were available on total of 35 dogs at the time of writing, 28 of which had at least one positive culture (Table 1). Eight of these 35 dogs had died (7 by euthanasia). Reason for euthanasia could not be established in 3 of these dogs. Reasons in the remaining dogs included chronic kidney disease due to congenital hydronephrosis and hydroureter (n = 1), cancer (n = 1), multisystem failure due to advanced age (n = 1), inability to express bladder (n = 1), and cervical disk disease (n = 1). There was no difference in survival of these 35 dogs between those with and without bacteriuria ($P = 0.69$) or with or without recurrent bacteriuria ($P = 0.68$). There were too few dogs (8) that were dead to perform statistical analysis on the effect of bacteriuria or recurrent bacteriuria on duration of survival (Table 1).

Table 4. Details of white blood cell counts as related to culture results.

Culture results	N with pyuria/N cultures with UA	WBC counts/mL: N
Negative: no growth	4/43	40–50: 1 <15: 3
Negative $<10^5$ CFU/mL	1/1	5–10: 1
Escherichia coli	10/13	>50: 4 20–50: 2 5–10: 4
Polymicrobial	4/8	>50: 3 15–20: 1
Enterococcus spp	4/8	10–15: 1 5–10: 3
Staphylococcus spp	2/5	>50: 2
Proteus spp	2/4	>50: 2
Klebsiella spp	3/4	>50:1 30–40: 1 5–10:1
Enterobacter spp	4/4	20–50: 3 5–10: 1
Pseudomonas spp	3/3	>50: 1 5–10: 2
Beta-hemolytic Streptococci	2/0	NA
Citrobacter spp	1/1	>50: 1
Corynebacterium-like organisms	1/1	40–50: 1
Pantoea agglomerans	0	NA
Salmonella spp	1/1	10–25:1
Globicatella sanguinis	0	NA

N, number; CFU, colony-forming units; Spp, species; NA, not applicable.

Risk assessment

While there were 3 females that did not have bacteriuria, compared with 9 males, there was no significant difference in frequency of bacteriuria ($P = 0.055$) or recurrent bacteriuria between female and male dogs ($P = 0.68$). Also, the age at the onset of paraplegia and duration of paraplegia did not influence the frequency of bacteriuria ($P = 0.57$) or recurrent bacteriuria ($P = 0.86$).

Discussion

In this study, we found that 35 of 47 (75%) chronically paraplegic dogs experienced at least 1 episode of bacteriuria based on quantitative aerobic culture results ($>10^5$ CFU/mL) with 13 of these 35 dogs suffering recurrent episodes of bacteriuria. *E. coli* was the most common cause. Clinical signs associated with bacteriuria were inconsistently recorded, but pyuria was highly associated with presence of bacteriuria. By contrast, fever was an unusual finding.

Unlike previous studies that mainly focused on the incidence of UTI in the postoperative period and during the acute phase of SCI,[9–12] our cases were dogs that were in the chronic phase (more than three months after injury). This population of dogs is unable to void urine effectively, and the resulting urine retention predisposes them to bacteriuria.[18] This predisposition was such that male dogs suffered bacteriuria as frequently as female dogs, over-riding the effect of the well-established risk factor of sex for UTI.[9,18]

The frequency of bacteriuria was high in this study with 75% of dogs that underwent a urine culture having at least one positive culture. There are limited data on the frequency of bacteriuria in this particular population. In one study on owner attitudes to managing paralyzed dogs, nearly 60% of owners reported UTIs (defined as bloody urine) were not a problem and approximately 35% of owners reported them as "very infrequent" (fewer than 1 a month), but there were no clinicopathologic data to substantiate this further.[20] In our study, a single organism was grown in 84% of all positive cultures. As with previous studies in both people and dogs,[2,7,8,10–12,16,18] *E. coli* was the major organism isolated from urine samples with 34.75% of all positive cultures. Overall *E.coli*, multiple organisms, *Enterococcus spp.*, *Staphylococcus spp.*, *Klebsiella spp.*, and *Proteus spp.* were responsible for 86.5% of all infections. Antibiotic-resistant infections were mainly caused by enteric bacteria, 71.4% of which were *E. coli.*

Determining whether bacteriuria is a clinical infection or a clinically insignificant finding is a key step in

deciding whether antibiotic treatment is warranted.[6,7] Current definition of UTI is in a state of flux, however, most would agree on presence of one or more clinical signs with a bacterial growth of $>10^5$ CFU/mL. According to medical literature, diagnosis of UTI in chronically paraplegic people relies heavily on signs and symptoms that accompany each episode of positive urine culture.[7,16] Symptoms cannot be self-reported by dogs, and as such, owners become surrogates for their pets, reporting their clinical signs. The symptoms and signs used to determine the presence of a UTI in paraplegic people are not standardized and vary between studies.[7] Many include patient reported pain, lethargy or malaise, and incontinence, but clinical signs such as fever, foul odor, and pyuria are all considered important.[1,3–7,13,17] The clinical signs associated with UTI are particularly challenging for owners to recognize in a paraplegic animal, but relevant information could potentially be generated. Review of our records showed that while many important facts may have been elicited by questioning, these were infrequently recorded, and indeed, to limit cost, urinalyses were not consistently performed. The presence of pyuria may be important in determining the clinical significance of an infection and so ideally should be performed at the time of culture. Many owners simply brought their dog to their vet for a cystocentesis with no attempt by the veterinary office to perform a physical exam or obtain a detailed urinary history. As such, we have generated a form with a series of questions and observations to be completed whenever a urine culture is performed (Data S1) with the intent to identify the clinical signs associated with bacteriuria and ultimately to develop a clinical tool that guides treatment decisions.

Despite the consensus of medical literature on fever as a prominent sign of UTI in people with chronic paraplegia,[1–7] in this study, a body temperature above the reference range was recorded in only 5 of 68 dogs with cultures performed, 3 times in dogs with negative cultures, and twice in dogs with positive cultures performed concurrently. While body temperature was recorded in only approximately ¼ of the cultures performed, the lack of fever could either indicate that fever is rare in dogs with clinical UTIs consistent with fever being classified as a sign of pyelonephritis in dogs and not UTI[21,22] or that presence of a clinical UTI is extremely uncommon. While cloudiness appeared to be present with negative cultures as well as positive ones, pyuria was found to be significantly correlated with positive cultures ($P < 0.001$). One explanation for this could be that cloudiness can also be the result of crystals, bacteria, mucus, lipid, and contaminating materials in urine rather than being solely the result of bacteria and blood cells in urine.[23] The presence of foul odor was not consistently recorded, and the lack of mention of this variable did not necessarily imply it was not present. We therefore did not evaluate this variable statistically in relation to presence of bacteriuria.

Clinical signs such as autonomic dysreflexia have not been appreciated in paralyzed dogs. Signs such as lethargy, new onset of incontinence, spasticity and pain or a sense of unease especially during bladder expression could theoretically be reported by the owners but were not reliably solicited or recorded in records of these dogs.

In spite of our initial hypothesis that survival rate would be lower in paralyzed dogs with bacteriuria compared with those without bacteriuria, there was no significant difference in survival times between the two groups. One dog was euthanized because of chronic kidney disease, but this dog happened to have a congenital anomaly of its urinary tract. None of the other dogs euthanized or died due to pyelonephritis or septicemia. This is in contrast to the fact that UTI is one the major causes of septicemia in paralyzed people[14,15] and although the rates of UTI-related deaths have significantly decreased during the past decades,[2] it still serves as one of the more important causes of death in people with chronic SCI (9%).[15] The number of dogs for which we had survival data was limited to 35, and only 8 of these dogs were deceased and so the lack of significance may simply reflect the small amount of data. Our findings therefore need to be confirmed in a larger cohort of chronically paralyzed dogs followed prospectively for an adequate period of time to assess survival.

According to human medical literature, subclinical bacteriuria is not an indication for antibiotic treatment.[16] Details of treatment and progression of infections over time were not evaluated for this study given the retrospective nature of the study, the frequency with which owners pursued treatment at their local veterinarian and the difficulty of obtaining full medical records in these cases. However, it is notable that it is standard practice to treat positive cultures with $>10^5$ CFU/mL bacteria at the participating institution based on results of culture and specificity testing. It is possible that this approach prevented the occurrence of septicemia and pyelonephritis although it may also have increased the frequency of resistant infections. A prospective study evaluating the frequency of bacteriuria, soliciting a full urinary history at each urine culture, and evaluating the effectiveness of antibiotic treatment would determine the frequency of UTI and the most appropriate guidelines for treatment.

This study was limited by its retrospective nature. In particular, a lack of adequate information on each dog (history, body temperature, result of urinalysis) with each urine culture limited the conclusions that could be drawn. Some dogs could potentially have many more positive urine cultures with a more informative set of clinical signs, but either their records were unavailable or the owners opted for empirical treatment of bacteriuria episodes with their veterinarian. Moreover, some dogs were lost to follow-up which limited the survival data. In addition, we decided to include only dogs that had undergone at least one documented urine culture for which results were available to document the frequency of bacteriuria, but this meant that there was bias toward dogs with bacteriuria and the data on prevalence of bacteriuria are likely an overestimate for the whole population.

Our findings regarding the range of clinical signs associated with UTI suggest that clinical signs and symptoms used to establish a diagnosis of UTI in paraplegic people might not be relevant to dogs, whereas other clinical signs including lethargy, increase in frequency of catheterization or manual expression, discomfort in being manually expressed, and spasticity should be evaluated prospectively to develop appropriate parameters for management of dogs that are chronically paralyzed.

In conclusion, bacteriuria and recurrent bacteriuria are a common complication in paralyzed dogs, suggesting routine monitoring would be beneficial. Obtaining a thorough history and performing a complete physical examination as well as urinalysis and urine culture is warranted in these dogs. The indications for antibiotic treatment of bacteriuria in this population of dogs need further investigation.

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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.

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Supporting Information

Additional Supporting Information may be found online in the supporting information tab for this article:

Table S1. Signs and symptoms suggestive of UTI in SCI people derived from medical literature.

Data S1. Urinary Tract Health Information in Paralyzed Dogs.