

Standard Article

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Hypothermia in Uremic Dogs and Cats

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Background: The prevalence of uremic hypothermia (UH) and the effects of improving uremia on body temperature have not been determined in veterinary patients.

Objectives: To determine the prevalence of UH and correlations between uremia and body temperature in patients undergoing intermittent hemodialysis (IHD).

Animals: Uremic dogs (n = 122) and cats (n = 79) treated by IHD at the Bobst Hospital of the Animal Medical Center from 1997 to 2013.

Methods: Retrospective review of medical records.

Results: The prevalence of hypothermia was 38% in azotemic cats and 20.5% in azotemic dogs. Statistically significant temperature differences were observed between uremic and nonuremic dogs (nonuremic: mean, 100.8°F; range, 91.2–109.5°F; uremic: mean, 99.9°F; range, 95.6–103.8°F; $P < .0001$) and cats (nonuremic: mean, 100.6°F; range, 94.0–103.8°F; uremic: mean, 99.3°F; range, 92.3–103.4°F; $P < .0001$). In dog dialysis patients, significant models included (1) timing (pre-dialysis versus post-dialysis) with weight class (small [$P < .0001$], medium [$P = .016$], and large breed [$P = .033$] dogs), (2) timing with serum creatinine concentration ($P = .021$), and (3) timing with BUN concentration ($P < .0001$). In cat dialysis patients, there was a significant interaction between timing and weight as a categorical variable (<5 kg and ≥ 5 kg).

Conclusions and Clinical Importance: Uremic hypothermia appears to be a clinical phenomenon that occurs in cats and dogs. Uremic patients are hypothermic compared to ill nonuremic patients and body temperatures increase when uremia is corrected with IHD in dogs and in cats > 5 kg. In cats, UH seems to be a more prevalent phenomenon driven by uremia. Uremic hypothermia does occur in dogs, but body weight is a more important predictor of body temperature.

Key words: Body temperature; Blood urea nitrogen; Creatinine; Uremia; Uremic hypothermia.

The concept of azotemic patients having lower body temperatures has long been recognized in human and veterinary medicine. Although the pathophysiology remains unclear, the notion of uremic hypothermia (UH) dates as far back as the 18th century when experimental uremia first led to hypothermia.^{1,a} In 1961, UH was documented in human dialysis patients with an increase in temperature after correction of uremia and in dogs after urea injections and bilateral ureteral ligation.^b In 1970, a letter to the editor of *New England Journal of Medicine* reignited interest in UH.²

Over the next 2 decades, research focused on UH pathophysiology. A 1971 study concluded that hypermagnesemia did not play an important role.³ Later, a 1987 study hypothesized that UH is secondary to a reduction in metabolic rate and concluded that the

Abbreviations:

UH	uremic hypothermia
AKI	acute kidney injury
IHD	intermittent hemodialysis
ICU	intensive care unit
BUN	blood urea nitrogen
ANOVA	analysis of variance
ANCOVA	analysis of covariance
LS	least squares

direct action of toxic substances at the cellular level was the cause. This study was unable to show the effect of specific toxins.⁴ A 1981 study investigating endogenous cryogens excreted by the kidneys concluded that dialysis of urinary cryogens led to increased body temperature.⁵ In 1985, another study failed to confirm the hypothesis that cyanate was responsible for hypothermia in anephric rabbits.⁶ Later, a 1991 editorial attempted to explain UH at a cellular level, describing the decreased transmembrane chemical potential resulting from an accumulation of uremic toxins, which leads to decreased heat production.⁷ Even after decades of research, the pathophysiology of UH remains unclear.

The role of the kidneys in thermoregulation is documented in the literature. The kidneys contribute $> 10\%$ of total body heat as a consequence of their highly aerobic metabolism.⁸ One study documented that 23% of pre-dialysis human chronic kidney failure patients were hypothermic.⁹ Other authors have reiterated the role of the kidneys in thermogenesis when nephrectomized rabbits exhibited lower core temperatures and lower heat tolerance than did controls.^{10,11} More recently, subtotal renal ablation induced sympathetic nervous system stimulation in brown adipose tissue, mobilizing fat for thermoregulation.^{12,13}

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The concept of UH is mentioned in veterinary textbooks, but to our knowledge, there are no studies that document a correlation between uremia and hypothermia in clinical veterinary patients. Furthermore, no veterinary studies document temperatures in the uremic and posturemic phases. Two recent studies regarding acute kidney injury (AKI) in cats have shown that cats with AKI commonly present hypothermic and that body temperature is a prognostic indicator.^{14,15} There is also a trend toward longer hospital stays in hypothermic cats with urethral obstruction.¹⁶ It has, thus, become increasingly important to continue investigating UH.

This study aims to determine the prevalence of UH in uremic patients and to elucidate correlations between uremia and body temperature in patients undergoing intermittent hemodialysis (IHD). We hypothesized that (1) azotemic dogs and cats are hypothermic on presentation and (2) uremic hypothermia in dogs and cats would resolve as azotemia is controlled with IHD.

Materials and Methods

Case Selection

A retrospective review of the medical records of uremic dogs and cats treated by IHD at the Bobst Hospital of the Animal Medical Center from 1997 to 2013 was performed. Animals with a history of chronic end-stage kidney disease or nonuremic disease as the indication for IHD were excluded. If the medical record was not available for review, the case was excluded. A rectal temperature obtained on admission into the intensive care unit (ICU) and before anesthesia was required for inclusion into Part 1. A rectal temperature obtained before and after each IHD treatment was required for the treatment to be included in Part 2. The first IHD treatment for each patient was excluded because the majority of patients were recovering from anesthesia for dialysis catheter placement at the start of the first dialysis treatment. Dialysis treatments were performed using an intermittent hemodialysis delivery system with the dialysate temperature set at 37.6°C (99.7°F) for all treatments.^c Any treatments performed using other dialysis delivery systems were excluded. If anesthesia was performed within 6 hours before an IHD treatment, that treatment was excluded from further analysis to avoid including anesthesia-induced changes in body temperature in our analysis. A circulating water heating pad was placed under all patients for each treatment; additional external heating (blankets, circulating hot air) were used at the discretion of the clinician. Their use was not routinely recorded.

To identify control animals, records of patients in the ICU at the Bobst Hospital of the Animal Medical Center from August 2012 to August 2013 were reviewed. Patients were excluded from the control group if they had an increased blood urea nitrogen (BUN) concentration, serum creatinine concentration, or both, based on the laboratory reference range. A control group was chosen from the nonazotemic ICU group to match uremic patients with respect to species, sex, and age group (<7 years, 7–12 years, and >12 years). The ratio of control cases to IHD cases was 2 : 1 for dogs. Because of the lower number of cat admissions and higher percentage of cats excluded because of increased BUN or serum creatinine concentration, only 1 control cat was identified for each feline case.

Medical Records Review

Data retrieved from the medical records of the uremic patients included signalment (species, age, sex, and weight), rectal temperature on initial presentation, rectal temperature before and after each IHD treatment, and BUN and serum creatinine concentrations before and after each IHD treatment. Data retrieved from the medical records of the nonazotemic ICU control patients included signalment (species, age, sex, and weight), rectal temperature on initial presentation, BUN concentration, and serum creatinine concentration.

Renal variables were analyzed at an on-site IDEXX^d laboratory at the Bobst Hospital of the Animal Medical Center. Several different chemistry analyzers were used over the study period with the first in operation before 2007, the second from 2007 to 2012, and the latest since 2012.^{e,f,g} The current normal reference ranges for cats are serum creatinine concentration, 0.9–2.5 mg/dL and BUN concentration, 16–37 mg/dL, where the normal ranges for dogs are serum creatinine concentration, 0.5–1.5 mg/dL and BUN concentration, 9–31 mg/dL.

Data Analysis

The error residuals of temperature were analyzed by the Kolmogorov-Smirnoff test ($P < .05$) and passed for descriptive and multivariate models. Weight was analyzed as both a continuous and categorical variable. Dogs were categorized into 4 weight classes to represent small (<10 kg), medium (10–25.9 kg), large (26–40.9 kg), and giant (≥ 41 kg) breeds. Cats were categorized in 2 weight classes (cats <5 kg and cats ≥ 5 kg).

Statistical Methods

Part 1: Uremic and Nonuremic Cases. Univariate and multivariate models were developed for the analysis of variance (ANOVA) and analysis of covariance (ANCOVA) to determine whether the mean temperatures were different between the uremic and nonuremic patient populations (case type). Multivariate models also included interactions between case type (uremic versus control) and additional covariates.

Part 2: Intermittent Hemodialysis in Uremic Patients. To determine if the phenomenon of uremic hypothermia resolved with the correction of uremia, the mean temperatures of the dog and cat populations were evaluated before and after each dialysis treatment. This was done by univariate analysis and with interaction terms of additional covariates including age, weight (both as a continuous and a categorical variable), BUN concentration, and serum creatinine concentration. Univariate and multivariate repeated-measures ANOVA and ANCOVA models were built with subject nested within replication to determine whether the mean temperature was different between pre-dialysis and post-dialysis (timing). The covariance structure was assigned as compound symmetry. The multivariate models incorporated additional covariates as interaction terms to determine whether the behavior of the covariate was the same between the 2 times measured. Least squares means generated by the models were evaluated by a Dunnett's adjustment. All analyses were considered significant at $P \leq .05$ using SAS 9.3.^h Nonsignificant results were not reported.

Results

Part 1: Uremic and Nonuremic Cases

There were 122 dogs in the uremic group (53 spayed females, 2 intact females, 45 castrated males, and 22 intact males) and 244 dogs in the nonuremic group (88

spayed females, 19 intact females, 109 castrated males, and 28 intact males). The median age of uremic dogs was 7.4 years (range, 0.2–14.6 years) and the median age of nonuremic dogs was 7.0 years (range, 0.2–14.8 years; $P = .81$). The median weight of uremic dogs was 21.3 kg (range, 3.0–57.4 kg) and the median weight of the nonuremic dogs was 10.6 kg (range, 0.7–80.5 kg; $P < .001$). On presentation, the prevalence of hypothermia (rectal temperature $<99^{\circ}\text{F}$) in azotemic dogs was 20.5%, whereas the prevalence of hypothermia in nonuremic dogs was 13.5% ($P = .085$).

There were 79 cats in both the uremic (36 spayed females, 41 castrated males, and 2 intact males) and nonuremic (37 spayed females, 4 intact females, 36 castrated males, and 2 intact males) groups. The median age of uremic cats was 7.8 years (range, 0.6–15.9 years), and the median age of nonuremic cats was 9.0 years (range, 0.5–15.7 years; $P = .46$). The median weight of uremic cats was 5.0 kg (range, 2.3–12.0 kg), and the median weight of nonuremic cats was 4.2 kg (range, 1.46–8.8 kg; $P = .0027$). The prevalence of hypothermia in azotemic cats was 38%, whereas the prevalence of hypothermia in nonuremic cats was 12.7% ($P = .0003$).

In both the dog and cat populations, statistically significant mean temperature differences were observed between uremic and nonuremic populations in univariate analyses (Fig 1). The mean temperature of nonuremic dogs was significantly higher than that of uremic dogs (nonuremic dogs: mean, 100.8°F ; range, 91.2 – 109.5°F ; uremic dogs: mean, 99.9°F ; range, 95.6 – 103.8°F ; $P < .0001$). This was also true of the cat population, where the mean temperature of nonuremic cats was significantly higher than that of uremic cats (nonuremic cats: mean, 100.6°F ; 94.0 – 103.8°F ; uremic cats: mean, 99.3°F ; range, 92.3 – 103.4°F ; $P < .0001$).

Within the dog model, results were mixed as additional covariates (BUN concentration, serum creatinine concentration, weight as both a continuous and categorical variable) were introduced into the model in the presence of case type (uremic versus nonuremic). The mean temperature of nonuremic dogs remained significantly higher than that of uremic dogs ($P < .0001$) when modeled separately in the presence of age, sex, and weight as a continuous variable, but nonsignificant when measured in the presence of BUN concentration ($P = .84$). In the multivariate dog model, when case type was analyzed in the presence of both BUN concentration and weight, both case type ($P = .26$) and BUN ($P = .17$) were nonsignificant, whereas weight remained significant ($P = .002$). The multivariate dog model suggested that the mean temperature of nonuremic cases was significantly higher ($P < .0001$) than that of uremic cases in the presence of weight ($P = .002$), where for every 1 unit increase in weight the temperature increased by 0.024°F .

Within the cat model, results showed a similar pattern. The mean temperature of nonuremic cats was significantly higher than that of uremic cats ($P < .0001$) when analyzed separately in the presence of age, sex, and weight as a continuous variable, but nonsignificant in the presence of BUN concentration ($P = .56$). In the

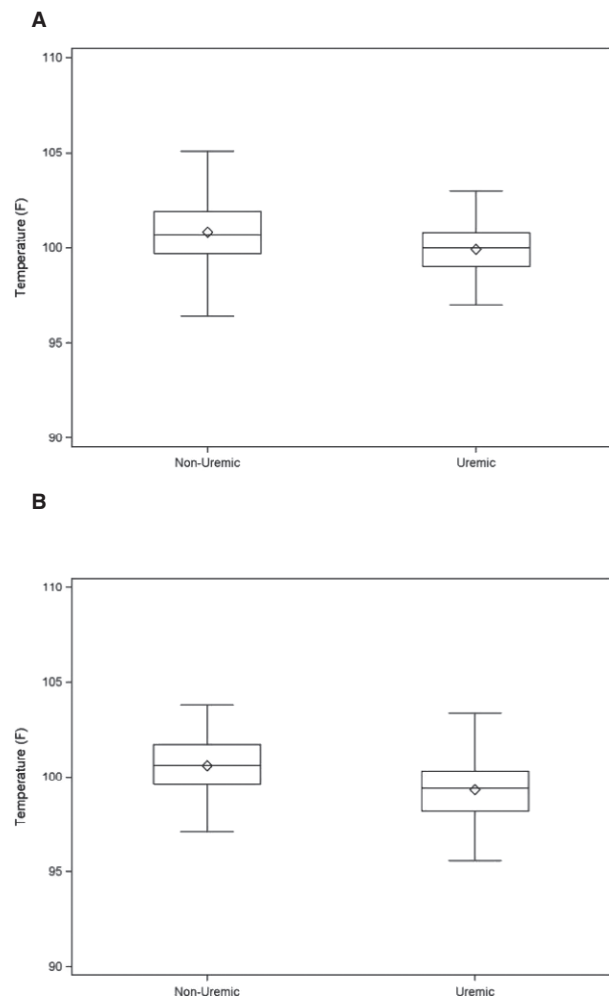


Fig 1. Boxplots demonstrating body temperature in the cases (uremic) and controls (nonuremic) of the dog (A) and cat (B) populations in Part 1. In both dogs and cats, there was a statistically significant mean temperature difference between uremic and nonuremic populations in univariate analyses.

multivariate cat model, when case type was analyzed in the presence of both BUN concentration and weight, both case type ($P = .74$) and weight ($P = .14$) remained nonsignificant, whereas BUN concentration remained significant ($P = .0058$). Interaction models between case type and the aforementioned covariates were nonsignificant.

Part 2: Intermittent Hemodialysis in Uremic Patients

The final analysis included 122 uremic dogs undergoing 667 dialysis treatments (using 100HGⁱ [n = 7], 400HG^h [n = 39], 500HG^h [n = 148], F3^j [n = 65], F4ⁱ [n = 167], F40ⁱ [n = 6], F5ⁱ [n = 14], F8ⁱ [n = 130], Revaclear^h [13], Revaclear Max^h [77], and not recorded [n = 1] dialyzers) and 79 uremic cats undergoing 274 dialysis treatments (using 100HG^h [n = 96] and F3ⁱ [n = 178] dialyzers). In the dog population, the least squares (LS) mean temperature after dialysis (101.0°F) was significantly higher than the LS mean temperature before dialysis (100.7°F) in the univariate analysis

($P < .0001$). This was not true of the cat population in univariate analysis, where the LS mean temperature after dialysis (100.7°F, $P = .41$) was not significantly higher than the LS mean temperature before dialysis (100.6°F).

More patients started with a temperature above the dialysate temperature of 99.7°F than below (Table 1). Of these, 54% of the dogs and 42% of the cats had an increase in temperature at the end of treatment.

Significant multivariate models for the uremic dog population included interactions of timing (ie, pre-dialysis versus post-dialysis) with weight class, timing with serum creatinine concentration, and timing with change in BUN concentration. A single significant multivariate model was demonstrated in the uremic cat population, namely the interaction between timing and weight class. These 4 significant interaction models for the uremic dog and cat populations are described as follows:

First, several statistically and clinically significant pairwise differences were observed between timing (pre-dialysis versus post-dialysis) and weight class in the uremic dog population (Table 2). These included the interactions between timing and body weight in the small ($P < .0001$), medium ($P = .016$), and large ($P = .033$) breed dogs. The comparison between timing and weight in the giant breed weight class was not significant ($P = .32$).

Second, the interaction term of timing by serum creatinine concentration was significant in the uremic dog population ($P = .021$; Fig 2). When examining this group of dogs pre-dialysis, temperatures remained relatively static regardless of the degree of increase in serum creatinine concentration. This is in contrast to the dogs post-dialysis, in which there was a moderate downward slope of temperature with increasing serum creatinine concentration. Specifically, for every 1 unit increase in serum creatinine concentration, temperature decreased by 0.05°F.

Third, the interaction term of timing by difference in BUN concentration from pre-dialysis to post-dialysis was significant ($P < .0001$) in the uremic dog population in that a greater decrease in BUN concentration was associated with a greater increase in temperature. Specifically, for every 1 unit decrease in BUN concentration, temperature increased by 0.0067°F.

Lastly, in the uremic cat population, statistical significance was demonstrated when weight was treated as a categorical variable with 2 groups (cats < 5 kg and cats ≥ 5 kg) (Table 3). For cats < 5 kg, mean body temperature decreased after dialysis, but the change was not significant (pre-dialysis, 100.5°F; post-dialysis, 100.4°F; $P = .50$). For cats ≥ 5 kg, mean body temperatures increased significantly after dialysis (pre-dialysis, 100.7°F; post-dialysis, 101.0°F; $P = .0099$). The highest mean body temperature was identified in cats > 5 kg post-dialysis. The mean temperature of this group was significantly higher than the mean temperature of cats pre-dialysis < 5 kg ($P = .023$) and pre-dialysis ≥ 5 kg ($P = .01$).

Table 1. Relationship between dialysate temperature and changes in body temperature (°F) following IHD.

Temperature (T) Parameters	Dogs		Cats	
	Starting T		Starting T	
	<99.7°F	>99.7°F	<99.7°F	>99.7°F
Increase in T (#)	96	278	54	79
Decrease in T (#)	6	238	12	110
Mean starting T	98.9°F	101.0°F	98.7°F	101.3°F
Mean post T	100.3°F	101.2°F	99.8°F	101.0°F
P	<.001	.002	<.001	.002

T, temperature (°F); #, number of subjects.

Table 2. Relationship between weight (categorical), timing (pre-dialysis versus post-dialysis), and body temperature (°F) in the uremic dog population.

Weight Class (N Measurements)	Temperature (°F)			SE
	Pre-dialysis	Post-dialysis	P	
Small breed (84)	100.09	100.84	<.0001	0.1135
Medium breed (140)	100.55	100.93	.016	0.0879
Large breed (302)	100.89	101.13	.033	0.0599
Giant breed (141)	100.88	101.10	.32	0.0876

SE, standard error; small breed, dogs less than 10 kg; medium breed, dogs 10–25.9 kg; large breed, dogs 26–40.9 kg; giant breed, dogs greater than or equal to 41 kg.

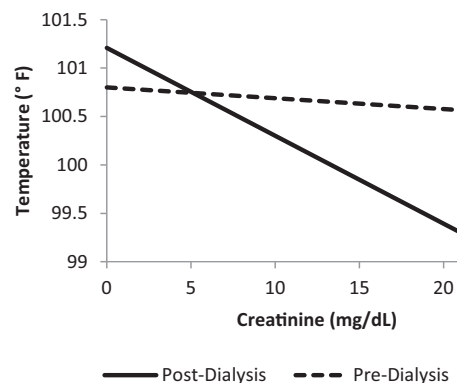


Fig 2. Relationship between serum creatinine concentration (mg/dL) and body temperature (°F) in dogs shown pre-dialysis and post-dialysis. The interaction term of timing by serum creatinine concentration was significant in the uremic dog population ($P = .021$). For dogs post-dialysis, temperature decreased by 0.05°F for every 1 unit increase in serum creatinine concentration.

Discussion

Results from our study suggest that UH occurs in uremic cats and dogs. Within the uremic cat population, the prevalence of hypothermia (38%) was significantly higher and the mean temperature significantly lower (99.3°F) as compared with the nonuremic cat population. Within the uremic dog population, the prevalence of hypothermia (20.5%) was not significantly higher,

Table 3. Relationship between weight (categorical), timing (pre-dialysis versus post-dialysis), and body temperature (°F) in the uremic cat population.

Weight Class (N Measurements)	Temperature (°F)		<i>P</i> *	SE
	Pre-dialysis	Post-dialysis		
<5 kg (140)	100.52	100.37	.0496	0.114
>5 kg (147)	100.66	100.98	.0010	0.114

SE, standard error.

*<5 kg pre versus >5 kg post, *P* = .0226.

but the mean temperature (99.9°F) was significantly lower as compared with the nonuremic dog population. Hypothermia was mitigated in dogs and in cats >5 kg with improvement in uremia after IHD. In the uremic dog population, UH is more correlated with body weight than BUN or serum creatinine concentrations. This was different from the uremic cat population, in which UH seemed primarily to be a consequence of uremia.

The concept of uremic patients having lower body temperatures has resurfaced many times in the human literature over the past 6 decades.^{7,17,18,k} The prevalence of uremic hypothermia in human dialysis patients is variable, with studies citing rates as low as 9% and as high as 73%.^{9,18,19,h} The clinical relevance of uremic hypothermia also has been investigated. A 2012 study focused on the relationship between body temperature and outcome in chronic dialysis patients, ultimately concluding that the best survival occurred in patients with the higher body temperatures at baseline and stable body temperatures throughout follow-up.¹⁷ Despite decades of attention, the specific etiology underlying uremic hypothermia remains only partially elucidated. Hypometabolism at the cellular level secondary to the effects of uremic toxins is one of the main proposed mechanisms.³⁻⁶

Uremic hypothermia also is addressed in the veterinary literature, albeit less directly. A retrospective study evaluating rectal temperatures of male cats with urethral obstruction found that BUN and serum creatinine concentrations were significantly higher in the hypothermic group.¹⁶ Another study investigating prognostic factors for cats with AKI found lower body temperature to be a useful predictor of death.¹⁴ In another study of cats with AKI treated by hemodialysis, the prevalence of hypothermia was high at 64%, making hypothermia one of the most common abnormalities detected on physical examination.¹⁵

Part 1: Uremic and Nonuremic cases

In our study, uremic dogs and cats had significantly lower body temperatures than did control patients with nonuremic illness. The prevalence of hypothermia was significantly higher in azotemic cats (38%) compared with nonazotemic cats (12.7%), although this did not hold true for dogs. Therefore, azotemia should be considered in hypothermic cats when renal laboratory test results are not immediately available.

In the dog model, weight was the major driver of body temperature within the uremic dog population, as opposed to BUN or serum creatinine concentrations. This may indicate that although uremic hypothermia exists in the dog population, body weight actually is a more important factor in maintaining normothermia. Conversely, this finding also may support the idea that hypothermia may be more generally related to critical illness in dogs, as opposed to uremia specifically. These hypotheses are supported by the lack of significant difference in the prevalence of hypothermia in uremic (20.5%) versus nonuremic (13.5%) dogs. In the uremic dog population, body temperature increased by 0.024°F for every 1 kg increase in body weight. Therefore, although uremic hypothermia may exist at the cellular level, body weight may be able to counteract this phenomenon by allowing dogs to retain body heat in the presence of uremia.

In the cat model, of the variables investigated, BUN concentration had the most significant impact on body temperature. This finding emphasizes the idea that uremic hypothermia exists in cats. The effects of uremia on body temperature may be more evident in cats because of their small body size and limited variability in body size, both of which permit a substantial amount of heat to be lost at the body surface, allowing uremia to decrease body temperature.

Part 2: Intermittent Hemodialysis in Uremic Patients

In the dog population undergoing IHD, body temperature increased post-dialysis both with a greater magnitude of decrease in BUN concentration and with lower post-dialysis serum creatinine concentration. This increase in temperature could be due to removal of uremic toxins or endogenous cryogens, but it is also possible that dialysis warmed some patients. The dialysate temperature was warmer than the starting body temperature for 16% of dogs. It is not surprising that exposure to the warmer dialysate would increase patient temperature. However, in dogs, the post-dialysis temperature of these patients was 100.3°F, which is 0.6°F higher than dialysate temperature, suggesting that factors other than passive warming by dialysate were operative. In patients starting with a temperature above that of dialysate, a decrease in temperature at the end of treatment could be explained by passive cooling. However, 54% of dogs starting above dialysis temperature had an increase in temperature at the end of treatment, despite the cooling effects of exposure to the relatively cooler dialysate. Dialysate temperature can be adjusted on modern dialysis machines, and increasing the dialysate temperature for hypothermic patients may further assist in correcting hypothermia. Because temperature is not correlated with serum creatinine concentration pre-dialysis, it is unlikely that creatinine is the major mediator of hypothermia. However, a molecule or uremic toxin comparable in size and charge that is cleared by IHD similarly to creatinine could explain these findings. The correction of hypothermia post-dialysis held especially true when dogs were categorized into clinically relevant weight categories. These

findings again support the idea that although uremic hypothermia exists in the dog population, the major determinant of body temperature in uremic dogs actually is body weight. Possible explanations for this phenomenon include the possibility that dogs may be better able to retain body heat because of differences in adipose tissue metabolism, mechanical insulation properties, or larger surface area for absorbing ambient heat.

In the cat population undergoing IHD, only cats ≥ 5 kg had increases in their body temperature after dialysis (mean increase in body temperature of 0.32°F). Cats < 5 kg actually had lower body temperatures post-dialysis (mean decrease in body temperature of 0.15°F). Although statistically significant, these relatively small changes in body temperature may not be clinically relevant. The dialysate temperature was warmer than the starting body temperature for 24% of cats. In those cats, post-dialysis temperature increased by 1.1°F, with the mean post-dialysis temperature of 99.8°F being similar to dialysate temperature. The majority (58%) of cats who were treated with a dialysate temperature cooler than body temperature had a decrease in temperature at the end of treatment. We suspect that smaller cats are more likely to lose body heat during dialysis despite standard efforts to conserve heat. Furthermore, smaller cats will have a larger proportion of their blood in the extracorporeal circuit and slow transit time through the circuit exposes the blood to ambient room temperature for a longer time. Thus, small body size may mask the effects of correcting azotemia on uremic hypothermia. Increasing the dialysate temperature may be especially beneficial in preserving heat in the cat population.

Despite the modest amount of previous research regarding the etiology of UH, the etiology remains unclear.³⁻⁷ Small molecules that are removed easily by dialysis may be involved in the pathogenesis of UH given our findings. Disproportionate changes in concentrations of various solutes may also affect temperature regulation because neither middle molecules (eg, cytokines, $\beta 2$ microglobulin, cyanocobalamin) nor large molecules (most hormones) are effectively removed by the hemophane dialyzers used in approximately 1/3 of the dialysis treatments in this study.

There are several limitations of our study. First is the retrospective nature of the investigation, which may have limited the detection of clinically relevant variables involved in UH. Although the uremic and nonuremic groups were well matched based on age and sex, the nonuremic dog and cat groups had lower median body weights compared with the uremic groups. This was expected because dogs and cats < 2.5 kg were less likely to be dialyzed. Despite the finding that temperature increased with weight, the smaller control patients overall had higher median temperature rather than lower temperature. Thus, the lack of matched weights between the groups does not appear to explain our findings. In future studies, these issues can be avoided by weight matching controls. Furthermore, the nature of the study design was such that controls for both dogs and cats were obtained from the 2012–2013 patient population,

which may have introduced some bias (differences in disease types, severity, or both) due to the limited time period of control enrollment. In addition, it is possible that patients with mild kidney disease were included in the ill nonuremic group because substantial renal function is lost before azotemia develops. This would likely underestimate the prevalence of UH. Lastly, factors confounding body temperature may be present in all stages before (concurrent illness, environmental factors), during (ambient temperature, external heating mechanisms, standard dialysate temperature of 99.7°F, percentage of the blood in the extracorporeal circuit), and after (patient warming mechanisms) dialysis.

In conclusion, UH appears to be a clinical phenomenon that occurs in both cats and dogs. Uremic patients are hypothermic as compared to ill nonuremic patients and body temperatures increase when uremia is corrected by IHD in dogs and in cats > 5 kg. In cats, UH seems to be a more prevalent phenomenon that is associated with uremia. Uremic hypothermia does occur in dogs, but body weight is a more important predictor of body temperature than is uremia. Therefore, hypothermia may increase the initial suspicion of uremia before renal function test results are available and hypothermia also may reflect the severity of uremia. In the future, larger prospective studies are indicated for further investigation into the specific etiology, possible confounding factors, clinical relevance, prognostic utility, and outcome of patients with UH.

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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.

Footnotes

- ^a Bourneville. Études cliniques et thermométriques sur les maladies du système nerveux. Paris, 1873
 - ^b Berner LB and Rhodes FG. Effect of urea on body temperature. Renal Laboratory, Children's Hospital of Washington DC. 1961
 - ^c Gambro Century System 3 and Gambro Phoenix, Gambro Baxter, Lakewood, CO
 - ^d IDEXX Reference Laboratory at the Animal Medical Center, New York, NY
 - ^e Roche Hitachi 911, Roche Diagnostics, Indianapolis, IN
 - ^f Olympus AU 400, Olympus Corporation, Tokyo, Japan
 - ^g Beckman Coulter AU680, Beckman Coulter, Brea, CA
 - ^h SAS Institute Inc, Cary, NC
 - ⁱ COBE Gambro, Lakewood, CO
 - ^j Fresenius, Bad Homburg, Germany
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