

Relationship of Body Weight to Maintenance Cyclosporine A Dose in Canine Atopic Dermatitis

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ABSTRACT

Cyclosporine A (CsA) is a commonly prescribed and effective therapy for canine atopic dermatitis. The purpose of this study was to investigate the potential relationship between patient body weight and CsA dosing. Seventy-seven cases of canine atopic dermatitis managed between 2000 and 2011 were evaluated retrospectively. Duration of CsA therapy was at least 16 wk. Groups analyzed included the study population as a whole, those treated with only CsA, and those treated with both CsA and metoclopramide. The division between small and large dogs was set at 15 kg. Descriptive analysis, two-way analysis of variance, Pearson correlations, and a Student *t* test were used to analyze data. There were no significant differences between CsA dose and body weight regardless of method of analysis. Concurrent corticosteroid use, other medication use, and pruritus score were also analyzed over the study period. There was a significant decrease in CsA dose, corticosteroid dose, medication score, and pruritus score between the time points for all patients, but no significant relationship between those changes and body weight. These study findings suggest that differential CsA dosing is not warranted based on body weight.

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Introduction

Cyclosporine A^a (CsA) is a lipophilic cyclic polypeptide with immunomodulatory properties, made from extracts of the fungal species *Beauveria nivea*. CsA acts primarily through the inhibition of calcineurin, which subsequently blocks the transcription of cytokines such as interleukin-2 and prevents the activation of T lymphocytes. In addition, CsA exerts its immunomodulatory effect in the skin by inhibiting mast cell and eosinophil function as well as inhibiting cytokine secretion. CsA also acts to reduce the number of Langerhans cells in the skin, thereby inhibiting their function as antigen presenting cells and preventing tumor necrosis factor-mediated, immunoglobulin E and mast cell-directed inflammatory cell infiltration into sites of inflammation.^{1–3}

Initial pilot studies as well as randomized, double-blind, case-controlled studies have established a 5 mg/kg dose for daily CsA administration in the atopic dog.^{4,5} In a double-blind randomized

controlled trial involving atopic dogs, that dose was found to be superior to a 2.5 mg/kg/day dose in reducing pruritus and signs of atopic dermatitis.⁶ At the 5 mg/kg/day dose, randomized controlled trials demonstrated a significant reduction in atopy-induced pruritus by 4–6 wk after the start of treatment. In approximately 40–50% of atopic dogs, dosing could be reduced by at least 50% within 8–12 wk.^{3,5,7,8}

There has been a clinical impression that smaller dogs require higher dosages of CsA than larger dogs require to achieve the same degree of atopy control. A single study from human medicine suggests that in children, larger oral doses of CsA are required for immunosuppression, attributed mainly to a smaller absorptive surface area in a shorter intestine.⁹ There are no known veterinary studies addressing this issue in the veterinary literature.

In dogs, the bioavailability of CsA formulated into a micro-emulsion has been reported to be approximately 35%.^{10,11} CsA

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CsA cyclosporine A

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bioavailability is additionally affected by other drugs that, like CsA, use the cytochrome P450 metabolic pathway. Although ketoconazole has been most commonly used to slow CsA metabolism and subsequently reduce CsA doses, numerous studies have sought to identify additional substances that may offer similar dose-sparing effects.^{12–14} In humans, concurrent metoclopramide use resulted in an approximately 30% increase in CsA bioavailability.¹⁵ That data has been used by some in veterinary medicine to empirically reduce the dose of CsA by one-third in patients concurrently treated with CsA. However, a recent canine study has demonstrated that CsA metabolism is not inhibited by concurrent administration of metoclopramide.¹⁶

The purpose of this retrospective study was to investigate whether patient body weight affected the ultimate dose of CsA used in the management of canine atopy. We hypothesize that smaller dogs would require higher dosages of CsA to achieve the same degree of atopy control as larger dogs.

Materials and Methods

The database of the Colorado State University Veterinary Teaching Hospital was searched for canine patients diagnosed with atopic dermatitis and receiving CsA between 2000 and 2011. A primary diagnosis of atopic dermatitis was based on clinical signs and history, restrictive diet trial, intradermal testing, and/or serum allergy testing. Patients had to have received continuous treatment with CsA for a minimum of 16 wk and be presented for re-evaluation between 16 wk and 24 wk following initiation of CsA treatment. Patients receiving either generic CsA or those with a diagnosis of concurrent sebaceous adenitis, perianal fistulas, sterile pyogranulomatous dermatitis, demodicosis, or uncontrolled systemic disease were excluded. Patients receiving concurrent ketoconazole were not included in the study given the well established, but variable nature, of the dose-sparing interaction between ketoconazole and CsA.^{12,13} Concurrent metoclopramide administration was permitted based on a recent study that showed no effect of metoclopramide on concurrent CsA pharmacokinetics.¹⁶ Patients that had received allergen-specific immunotherapy injections for a minimum of 1 yr, hypothyroid patients that had received therapy and were stabilized for a minimum of 6 mo, patients with a confirmed food allergy who were maintained on a consistent diet during the study period, and patients with either localized or generalized demodicosis that had resolved prior to starting CsA were included.

Patient data were collected at two time points; day 0 (i.e., the hospital visit during which the CsA was started) and again during a second hospital visit 16–24 wk after the initiation of CsA therapy. The 16–24 wk range was established because not every patient had

a re-evaluation visit at exactly the 16 wk point. The following information was extracted from each clinical record at each of these two visits: age at the start of CsA therapy, breed, sex, body weight, CsA dose (mg/kg/day), concurrent medications, and pruritus score.

CsA was routinely dosed *q* 24 hr initially following the general convention of an initial 5 mg/kg/day dose (although this may have varied due to limitations in capsule size or other factors). Dose reductions over time were achieved by reducing the dose frequency (commonly to *q* 48 hr dosing) and/or reducing the amount of CsA received with each oral dose (commonly to the next smallest capsule size available). The decision as to the timing of and manner by which a particular patient's dose was changed was made based on clinical evaluation of patient progress and status at the time of the evaluation. For patients no longer receiving CsA on a daily basis at the 16–24 wk time point, a mg/kg/day dose was calculated using their total weekly CsA dose divided by 7 days.

Medications the patient was currently receiving were recorded on day 0 and 16–24 wk time points. The patient could have been receiving medication for any length of time prior to the appointment. A medication scoring system (**Table 1**) was devised based on a previous scoring system.¹⁷ That system was intended to represent the type of medication a patient was receiving at a given time point relative to the medication's potential antipruritic effects. Relative antipruritic effect was determined based on the previously established scoring system and clinical judgment. A total medication score was calculated for each patient at each time point. Using the scoring system, a medication score could be as low as 0 but had no upper limit. Corticosteroid doses were recorded as mg/kg of oral prednisone, with all other types of steroids being converted to their equivalent prednisone dose to account for variability in corticosteroid potencies.¹⁸

A pruritus score was obtained at each visit using a subjective scoring system used routinely by the members of the hospital's dermatology service between 2000 and 2011. The client presenting the patient was asked at each hospital visit to verbally rate their pet's current level of pruritus on a scale from 0 to 10, with 0 being nonpruritic and 10 being the most severe pruritus their animal had ever experienced.

Initially, data from all patients meeting the inclusion criteria was analyzed. The patient population was then split into groups for further analysis. The entire patient population was divided into two groups: those that received metoclopramide and those that did not receive metoclopramide. The entire patient population was then divided into two groups based on body weight. Those weighing < 15 kg in group A and those weighing > 15 kg in group B. The weight division was based on a common break point applied in

TABLE 1**Description of the Medication Scoring System**

Medication*	Score (points)
None	0
Topical therapy (unlimited number), including nonsteroid-containing shampoos, conditioners, lotions, sprays, etc.	5
Topical corticosteroid therapy (points/item), including steroid-containing shampoos, conditioners, lotions, sprays, etc.	5
Fatty acid supplementation	5
Corticosteroid-containing ear medication	5
Topical tacrolimus	10
Antihistamines	10
Antibiotics	20
Glucocorticoids < 0.2 mg/kg/day	10
Glucocorticoids 0.2 to < .5 mg/kg/day	20
Glucocorticoids 0.5 to < 1 mg/kg/day	30
Glucocorticoids ≥ 1 mg/kg/day	40

*Medications were assigned points relative to their clinically relevant antipruritic benefit. Glucocorticoid doses were either based on or converted to the relative potency of prednisone administered *per os*.

various canine studies over the past decade.^{19–22} Those body weight groups were then each split into patients that received metoclopramide (groups A1 and B1) and those that did not receive metoclopramide (groups A2 and B2).

Statistical Analysis

All analyses were performed using statistical software^b. Descriptive statistics and frequency counts were performed. Simple Pearson correlations were performed between CsA dose, corticosteroid dose, medication score, and pruritus scores (at each time point and with the change between time points) with body weight (in kg) for all dogs and for dogs by metoclopramide use separately. Simple Pearson correlations adjusted for metoclopramide use were performed between CsA dose, corticosteroid dose, medication score, and pruritus score and body weight (in kg). CsA dose, corticosteroid dose, medication score, and pruritus score were compared between weight categories (group A, < 15 kg; group B, > 15 kg) at each time point (day 0 and 16–24 wk) using a Student *t* test. The folded form *F* statistic was used to test if variances were equal between groups. If unequal, then the Satterthwaite approximation for degrees of freedom for the student *t* test was used. A two-factor analysis of variance was used to compare CsA dose, corticosteroid dose, medication score, and pruritus score simultaneously between both weight categories and metoclopramide use, including a weight category by metoclopramide use interaction. Comparisons of CsA dose, corticosteroid dose, medication score, and pruritus score between time points were made using

a paired *t* test. All hypothesis tests were two-sided, and the significance level was $P = .05$.

Results

Initial database search revealed 222 atopic canine patients that had received CsA during the search period. Of those, 77 met the study criteria. Patients were not included most commonly for either concurrent ketoconazole use or lack of follow-up.

There were 47 female patients (43 spayed) and 30 male patients (29 castrated). Mean body weight was 15.6 kg (range, 2.1–47.2 kg), and mean age was 6.1 yr (range, 1.3–15.1 yr). The most common breeds were mixed-breed dogs ($n = 8$), cocker spaniels ($n = 5$), pugs ($n = 5$), Boston terriers ($n = 3$), golden retrievers ($n = 3$), dachshunds ($n = 3$), Yorkshire terriers ($n = 3$), toy fox terriers ($n = 3$), and Scottish terriers ($n = 3$). There were two each of the following breeds: beagles, Silky terriers, bichon frises, English setters, Australian shepherds, West Highland white terriers, Jack Russell terriers, German shepherd dogs, and Chihuahuas. There was one Welsh corgi, blue heeler, Alaskan malamute, Cairn terrier, Swedish Vallhound, shih tzu, Shetland sheepdog, basset hound, Norfolk terrier, English bulldog, boxer, Welsh terrier, bull terrier, keeshond, Cavalier King Charles spaniel, Australian heeler, Bernese mountain dog, and Maltese.

When body weight was considered as a continuous variable for all patients, the mean initial CsA dose was 4.7 mg/kg/day (range, 2.1–6.8 mg/kg/day). There was a significant negative correlation between body weight and initial CsA dose ($r = -.32$; $P = .0045$). The mean 16–24 wk CsA dose was 3.7 mg/kg/day (range, 0.5–6.7 mg/kg/day). There was a mean 0.94 mg/kg/day decrease (range, –4.7 mg/kg/day to 2.58 mg/kg/day) in CsA dose from day 0 to the 16–24 wk time point ($P < .0001$).

The mean initial medication score was 19 (range, 0–60), and the mean 16–24 wk medication score was 9 (range, 0–40). There was a mean 10 point decrease in medication score from day 0 to the 16–24 wk time point ($P < .0001$), which ranged from a 55 point decrease to a 25 point increase.

On the initial day of presentation, 23 patients (30% of the entire study population) had been receiving corticosteroids. Corticosteroids used included prednisone, prednisolone, and methyprednisolone. All corticosteroids were administered orally. The corticosteroid dose was converted to mg/kg/day of prednisolone prior to analysis to account for the varying potencies of different corticosteroids being used. The mean initial corticosteroid dose was 0.11 mg/kg/day (range, 0.04–1.25 mg/kg/day). Nine patients (12% of the entire study population) were receiving corticosteroids at the 16–24 wk time point, seven of which had also initially received corticosteroids. The mean 16–24 wk corticosteroid

dose was 0.03 mg/kg/day (range, 0.025–0.77 mg/kg/day). There was a mean 0.08 mg/kg/day decrease in corticosteroid dose from day 0 to the 16–24 wk time point ($P = .0115$).

The mean initial pruritus score (on a scale from 0 to 10) was 6 (range, 0–10), and the mean 16–24 wk pruritus score was 3 (range, 0–9). There was a mean three point decrease in pruritus score from day 0 to the 16–24 wk time point ($P < .0001$), which ranged from a 9 point decrease to a 4.5 point increase (Table 2).

Of the 77 patients included in the study, 20 (26%) received metoclopramide during the study period (Table 3). The mean metoclopramide dose for those patients was 8.63 mg (0.37 mg/kg/day). When the 20 patients receiving concurrent metoclopramide were considered alone, mean initial CsA dose was 4.42 mg/kg (range, 2.59–5.96 mg/kg) and mean 16–24 wk CsA dose was 3.57 mg/kg (range, 0.53–6.15 mg/kg). There were no significant differences in the day 0 or 16–24 wk CsA dose, pruritus score, medication score, or corticosteroid dose between patients receiving metoclopramide and those that did not. When the 20 patients receiving metoclopramide were excluded from the analysis, the previous negative correlation between weight and initial CsA dose was no longer present ($r = -.09$; $P = .5053$).

When the 57 patients not receiving concurrent metoclopramide were considered alone, mean initial CsA dose was 4.8 mg/kg (range, 3.2–6.8 mg/kg) and mean 16–24 wk CsA dose was 3.9 mg/kg (range, 0.98–6.7 mg/kg). There was a mean 1.03 mg/kg/day decrease in CsA dose between the day 0 and the 16–24 wk time point ($P < .0001$). Neither the mean decrease nor the day 0 and 16–24 wk CSA doses were significantly different than when all patients were considered.

There were no significant differences in CsA dose, steroid dose, medication score, or pruritus score between weight groups A and B or between weight groups and metoclopramide categories (groups A1 and B1 and groups A2 and B2).

Fourteen patients had an increased mg/kg CsA dose at the 16–24 wk time point compared with day 0. Eight of the 14 had an increased mg dose of CsA at the 16–24 wk time point. Half of those eight cases were dogs that had received metoclopramide on day 0. The other 4 dogs had not received metoclopramide at any time during the study period. Six patients had an increased mg/kg dose due to a weight change from day 0 to the 16–24 wk time point, but no change in the mg dose of CsA. Nine of the 14 cases were < 15 kg and 5 were > 15 kg. Of the patients with an increased mg and mg/kg dose (i.e., a true dosage increase), 5 of 8 dogs were < 15 kg and 3 of 8 dogs were > 15 kg.

Discussion

This retrospective study evaluated the potential relationship between patient body weight and CsA dosing. The rationale for the study was based on a clinical impression that smaller dogs appeared to require more and larger dogs less than the standard 5 mg/kg/day CsA dose to achieve desired clinical improvement. If such were the case, there would potentially be a rationale for placing smaller dogs on a higher CsA dosage at the onset of therapy with the hope of achieving a more rapid onset of benefit in a higher percentage of dogs. Conversely, larger dogs could potentially be started on smaller dosages, primarily because of the substantial cost of CsA therapy. However, the results of this study would suggest that differential dosing of CsA based on body weight is not warranted as

TABLE 2

Study Results

	All subjects (n = 77)			Group A (n = 44)			Group B (n = 33)		
	Mean	SD	Range	Mean	SD	Range	Mean	SD	Range
CsA dose on day 0*	4.66	.93	2.14–6.76	4.81	.8	2.75–6.76	4.47	1.07	2.14–5.96
CsA dose at 16–24 wk*	3.73	1.54	.53–6.69	3.91	1.64	.98–6.69	3.48	1.39	.53–6.4
Medication score on day 0†	19.42	15.81	0–60	19.32	16.12	0–60	19.55	15.63	0–50
Medication score at 16–24 wk†	9.08	9.79	0–40	7.95	7.34	0–30	10.61	12.3	0–40
Pruritus score on day 0‡	5.93	2.63	0–10	6.1	2.71	0–10	5.7	2.56	1–10
Pruritus score at 16–24 wk‡	2.72	1.82	0–9	2.59	1.84	0–8	2.89	1.81	.5–9
Corticosteroid dose on day 0 (n = 23)**	.11	.25	.04–1.25	.12	.28	.04–1.25	.1	.2	.04–.75
Corticosteroid dose at 16–24 wk (n = 9)**	.03	.12	.03–.77	.01	.05	.03–.26	.06	.18	.03–.77

*CsA dose in mg/kg/day

†Medication score on a scale from 0 to no upper limit

‡Pruritus score on a scale from 0 to 10

**Corticosteroid dose in mg/kg/day. All steroids were converted to mg of prednisolone. CsA, cyclosporine A; SD, standard deviation.

TABLE 3

CsA Dose for Patients With and Without Concurrent Metoclopramide

	Entire study population (n = 77)	Patients receiving concurrent metoclopramide (n = 20)	Patients not receiving concurrent metoclopramide (n = 57)
CsA dose on day 0*	4.66 ± .93 (2.14–6.76)	4.42 ± .26 (2.59–5.96)	4.83 ± .67 (3.22–6.76)
CsA dose at 16–24 wk*	3.73 ± 1.54 (0.53–6.69)	3.57 ± 1.5 (0.53–6.15)	3.89 ± 1.52 (0.98–6.69)

*CsA doses were given as mg/kg/day ± standard deviation (range).
CsA, cyclosporine A.

there was no significant difference in ultimate CsA dose between larger and smaller dogs.

Those findings were consistent when data from the entire patient population was analyzed for correlation between CsA dose and body weight, regardless of whether metoclopramide was used concurrently. There was also no significant difference when the comparison was based on dividing the population into two groups (large versus small dogs). The body weight used in the study to establish a cut-off point between large and small dogs was 15 kg. That cut-off point has been used in a number of other studies.^{19–22} That was also the mean body weight of the study population (15.6 kg), which further supported the use of 15 kg as a division point for the study group. Had body condition scores been available for the study population, that score may have provided a more objective and informative means to evaluate and compare the study population. Patients receiving metoclopramide were accepted into the study in light of recent data that showed that metoclopramide does not affect concurrent CsA bioavailability. Findings were consistent when data from the entire population was analyzed for correlation between CsA dose and body weight, regardless of concurrent metoclopramide use.

Medication score, concurrent corticosteroid dose, and pruritus score were also assessed to help determine additional factors that may have played a role in the dose of CsA a patient received at any time point. Change in CsA dose, medication score, concurrent corticosteroid dose, and pruritus score did not differ at any time point, regardless of how the overall study population was divided or when only the 57 patients who did not receive metoclopramide were considered.

There were several limitations to this study that were largely related to its retrospective nature. Those included the prevalent use of concurrent ketoconazole in larger dogs in the initial study population as well as the common use of multiple concurrent medications during the study period. The most frequent reason for case exclusion in the initial study population was the concurrent use of ketoconazole. Ketoconazole was most commonly used in larger dogs for its dose and cost-sparing effects. That may have

affected the ultimate results in that a greater number of larger dogs may have been excluded from the study for that reason. As numerous studies have shown unpredictable variability in the effect of ketoconazole on CsA bioavailability, there was no uniform way to include those cases given the retrospective nature of the study.^{12–14}

Concurrent corticosteroids and other medications may have affected pruritus and, therefore, ultimate CsA doses. It would have been ideal to evaluate patients who were only on CsA therapy. However, as the majority of our patients presented with a chronic, recurrent history of primary and secondary signs of atopic dermatitis (i.e., erythema, pruritus, pyoderma, otitis externa, etc.) it was common for those patients to have been receiving multiple therapies at the initial visits and throughout the study. To allow patients receiving additional medications (such as corticosteroids, antihistamines, and topical therapies) to be included in the study, a medication scoring system was created. This medication score was a modification of a previously reported medication scoring system.¹⁷ Scores were assigned based on the known and/or expected degree of clinical, antipruritic effect associated with any given therapy. The assignment of a score allowed for the subsequent more objective analysis of the effects that medications may have had on pruritus and CsA doses. There was no correlation between medication scores and body weight and no significant difference between medication scores when the patients were divided by weight or metoclopramide use at either time point or from time point to time point. Given the value that various medications were assigned within the medication scoring scheme, the decrease in medication score between time points could represent the discontinuation of either antipruritic or antibiotic therapies. That would be expected as secondary infections related to atopy were controlled and a greater control of allergic flares was achieved with CsA use. However, the retrospective nature of this study precluded a more definitive explanation for the decrease in medication scores noted.

There was also no significant association between corticosteroid dose and body weight at each time point. Although most patients did not receive corticosteroids in conjunction with the CsA, those that did (12% of the total study population by 16–24 wk) required doses

below an anti-inflammatory level ($<0.5\text{--}1\text{mg/kg/day}$) following the first mo of CsA therapy. Interestingly, none of the patients with the highest pruritus scores at 16–24 wk were receiving corticosteroids at that time, although that may have represented patients for whom adjunctive corticosteroid therapy should have been considered, patients that could not tolerate corticosteroid therapy, or clients who were not interested in using corticosteroids.

Pruritus scoring in this study was little more than a subjective means of quantifying patient progress. The method of generating the score was not standardized. The retrospective nature and time frame of this study prevented use of one of the more recently developed visual analog canine pruritus severity scales.²³ Even when achieved in the latter fashion, pruritus scores are prone to problems. Different clients (spouses, other family members) may present the patient from appointment to appointment or the perception of pruritus level may not necessarily translate directly to what is observed clinically. Interestingly, the overall decrease in pruritus as assessed by the owners was only 3 points (33%) from baseline day 0 to the 16–24 wk time point. A 33% decrease in pruritus is lower than that previously reported with CsA use and could wither represent a limitation of this type of scoring system or lower clinical efficacy of this product within the study population as compared with previous reports.^{3,24} Alternatively, as the number of patients receiving corticosteroids just prior to, but not overlapping with the day 0 initiation of CsA therapy was not recorded, recent corticosteroid use prior to the study period may have also contributed to initially lower pruritus scores. Subsequent glucocorticoid discontinuation and possible escalation of pruritus may have then served to reduce the perceived effect of the CsA.

Ideally, the authors would have evaluated the study findings in conjunction with body condition scoring. However, that data were not available for every case, and in those cases where it was available, the protocol for generating the score was not standardized. It has been suggested that in humans, obesity may affect CsA pharmacokinetics and that CsA may be more effectively dosed based on ideal rather than actual body weight.²⁵ Had body condition scoring been standardized and available for each case, that would have allowed for a more objective method of determining if obesity, rather than just body weight, had any effect on CsA dosages.

There was a negative correlation between weight and initial CsA dose at day 0 when patients receiving metoclopramide were included in the analysis. Patients receiving metoclopramide were accepted in to the study based on recent data that showed no effect of metoclopramide on CsA pharmacokinetics. However, during the earlier phases of the study period, some dogs were initially prescribed less than the routine 5 mg/kg dose of CsA, based on previous studies in humans demonstrating increased CsA

bioavailability with concurrent metoclopramide administration.^{15,16} That likely accounts for the negative correlation between weight and initial CsA dose at day 0 because that finding was not present when patients receiving metoclopramide were removed from the analysis. Although some of the initial clinical dosing decisions were made on the assumption that there would be some dose-sparing effect of the metoclopramide when all patients were considered, insufficient clinical response at any time point resulted in CsA doses being adjusted as needed. That was likely reflected in the 4 of 14 metoclopramide treated cases that had an increased CsA dose at the 16–24 wk time point. The lack of a correlation between CsA dose and weight at the 16–24 wk time point for the group receiving metoclopramide, compared with the negative correlation at the day 0 time point, is attributed to such dose changes. Regardless, there was no significant difference in CsA dose from day 0 to the 16–24 wk time points when all study patients, only those concurrently receiving metoclopramide, or only those who did not receive metoclopramide were considered.

The factors assessed in this study (CsA dose, pruritus score, medication score, and corticosteroid dose) were all chosen to help allow for more objective evaluation of the study population within the confines of a retrospective study. It would have been ideal to have body condition scores and visual analog pruritus scores at each time point to better assess the question. It would have also been ideal to exclude all those patients using any concurrent medications with a known antipruritic or antimicrobial effect. A prospective study would allow for greater control over those concurrent and confounding factors. In addition, a prospective study could allow greater numbers of truly large or small patients to be enrolled, which could identify differences not seen in this study.

Conclusion

In this retrospective study, smaller dogs did not require higher maintenance doses of CsA than larger dogs. Those findings suggest that differential CsA dosing is not warranted based on body weight. Until a controlled, prospective study is undertaken to more definitively investigate this factor, the current dosing regimen is supported, regardless of body weight. ■

FOOTNOTES

^a Atopica; Novartis, East Hanover, NJ

^b SAS version 9.2; SAS Institute Inc., Cary, NC

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