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Associations Between Atopic Dermatitis and Anxiety, Aggression, and Fear-Based Behaviors in Dogs

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ABSTRACT

The goal of this study was to determine if anxiety, aggression, and fear-related behaviors are more common in pruritic dogs with atopic dermatitis than nonpruritic, healthy dogs. One hundred forty-one pruritic dogs >1 yr of age with a clinical diagnosis of atopic dermatitis and a >3 mo history of pruritus were recruited. Dog owners completed a behavioral survey (canine behavioral assessment and research questionnaire) and a pruritus scale (pruritus visual analog scale). Pruritic, atopic dogs showed significant increases in fear- and anxiety-related behaviors as well as aggression compared with a large control group of healthy dogs. Stranger-directed aggression, owner-directed aggression, familiar-dog aggression, dog-directed fear, nonsocial fear, touch sensitivity, excitability, and attention-seeking behaviors were all increased in the study group. Trainability was decreased in the study group. Chronically pruritic dogs experience fear and anxiety and are more likely to display aggression. This is an important welfare issue for these animals. Early recognition of the behavioral derangements that can be associated with chronic pruritic skin disease could allow early intervention with a multidisciplinary approach for these patients, thus improving patient and owner quality of life and long-term treatment outcomes. (*J Am Anim Hosp Assoc* 2022; 58:161–167. DOI 10.5326/JAAHA-MS-7210)

Introduction

In veterinary medicine, behavioral disorders and atopic dermatitis (AD) are chronic disease conditions that are complex, recurrent, and often incurable. These conditions can be frustrating to treat for both the pet owner and the practitioner. Both require frequent follow-up with modifications to the treatment plan, typically for the life of the animal. These diseases and their long-term treatments can have a significant negative effect on both owner and patient quality of life (QOL).^{1,2} When both behavioral issues and chronic pruritic skin disease coexist in the same patient, treatment can become even more complex, and failure to address both diseases could lead to suboptimal outcomes.

Studies have demonstrated that caring for a dog with AD can have a negative effect on caretaker QOL.² In addition to their own decrease in QOL, 73% of owners of atopic dogs perceived that their dog's disease negatively influenced the animal's QOL.³ In a similar study, owners stated that "behavioral or mood changes" (unspecified) were the areas most affected by their dog's disease.² Recurrent clinical signs of AD may cause pet owners to seek opinions from multiple practitioners, disrupting continuity of care for the pet and leading to increased frustration and financial expenditure for the owner. This may ultimately delay diagnosis and treatment, leading to animal suffering. This process can lead to breakdown of the human-animal bond and subsequent relinquishment or euthanasia.

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AD (atopic dermatitis); C-BARQ (Canine Behavioral Assessment and Research Questionnaire); PVAS (pruritus visual analog scale); QOL (quality of life)

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A similar situation occurs with long-standing behavior problems. Anxiety, fear, and aggression are the most common reasons pet owners seek consultation with veterinary behaviorists.⁴⁻⁶ The combination of dermatologic and behavior issues could cause serious detriment to the animal's welfare and damage the human-animal bond.

In human dermatology, it is well documented that chronic pruritus is associated with increased stress and anxiety. Increased stress and anxiety can exacerbate itch, which then worsens anxiety, creating a perpetuating cycle.⁷ The itch-anxiety cycle exists concurrently with the itch-scratch cycle, wherein scratching directly causes skin damage and worsening of the disease state, thereby perpetuating itch.⁸

A 2008 study showed no association between pruritus and behavioral disorders such as aggression and anxiety in a population of pet dogs.⁹ No distinction was made among causes and durations of pruritus (acute versus chronic), which could have different effects on behavioral problems. A dog pruritic from a flea infestation may be temporarily more irritable but would likely not have the same long-term behavioral changes (increased reactivity, aggression, touch sensitivity) as a dog experiencing years of moderate to severe pruritus due to AD.

We hypothesized dogs with chronic, moderate to severe pruritus due to AD would show increased anxiety- and fear-based behaviors, increased aggression, and increased sensitivity to handling compared with healthy, nonpruritic dogs.

Materials and Methods

The study design was reviewed by the institutional review board at the University of Missouri and was exempt from institutional review board oversight.

Study Population

Dogs were enrolled in the study if they were diagnosed with AD by a veterinarian and were >1 yr of age. Dogs could be any breed. The majority of cases were collected at the dermatology clinic at the University of Missouri Veterinary Health Center Wentzville, with additional cases supplied by the behavior clinic at the university. Additional cases were gathered through an internet survey (Google form developed for this study) that was supplied to other veterinary dermatology and behavior specialty clinics and some general practice clinics. Most respondents were located in the United States and Canada, with a smaller number from European, South American, and Asian countries. A total of 141 dogs diagnosed with AD were enrolled.

Diagnosis of AD

Patient medical records and history forms were evaluated for signs of AD. Inclusion criteria were as follows: pruritus lasting longer than

3 mo or seasonally recurrent, chronic or chronic-relapsing dermatitis, and a typical distribution of pruritus and skin lesions (facial, digital, ventral).¹⁰ To eliminate other causes of chronic, recurrent pruritus, mainly food allergy and ectoparasites, all dogs enrolled were being administered routine parasiticides to prevent fleas and other ectoparasites, and had completed an elimination dietary trial with no improvement, had distinctly seasonal signs, or had a combination of food and environmental sensitivity as part of the broader current working definition of AD.¹¹

Control Population

The control population was drawn from the Canine Behavioral Assessment and Research Questionnaire (C-BARQ) database to reflect the average behavior of a large number of healthy adult dogs. At the time of writing, 57,455 pet dogs are represented in the database. Dogs with any reported medical condition and dogs younger than 1 yr were excluded, leaving 43,328 dogs. The oldest dog was 17 yr, and the average age was 4.3 yr. There were 20,801 female dogs (48%) and 22,527 male dogs (51.9%). There were 11,077 mixed-breed dogs (25.5%), 3,760 Labrador and golden retrievers (8.6%), 1,941 German shepherd dogs (4.5%), 1,703 pit bulls and their mixes (3.9%), 535 cocker spaniels (English and American, 1.2%), 406 bulldogs (French, English, American, Olde English, 0.9%), 300 shih tzu (0.7%), and 125 West Highland white terriers (0.2%).

Of the 43,328 dogs in the control group, only 2,278 (4.6%) were described as having "serious" behavioral concerns, with 33,497 (77%) reporting "no problems" or "only minor problems," indicating that the majority of dogs behaved "normally" according to their owners and their completion of the C-BARQ was not necessarily motivated by a perceived behavior problem.

Survey Administration

In-clinic respondents were owners of dogs presented for consultation for chronic pruritus secondary to AD. Dogs were determined to have a likely diagnosis of AD after initial history, exam, and diagnostics were performed as described above. Clients were given a brief description of the study and consented to fill out the forms. Clients were asked to rank their dog's pruritus level using the pruritus visual analog scale (PVAS).^{12,13} If the patient had recently been started on antipruritic treatment, the owner was asked to report the dog's pruritus score prior to starting treatment to provide a more accurate average level of pruritus. Owners were then asked to complete a paper copy of the C-BARQ.¹⁴ The dog's age, breed, and survey responses were then entered manually into the C-BARQ website by the primary investigator (<https://vetapps.vet.upenn.edu/cbarq/>). PVAS scores for this group were collected in an electronic spreadsheet.³

Online respondents (outside clinic) were directed to a Google form, which asked for the dog's age, breed, duration of signs, and the PVAS. The Google form then directed these respondents to follow the link provided to the C-BARQ website to complete the questionnaire.

The 14 main behavioral categories or factors of the C-BARQ survey are defined as follows:

1. Stranger-directed aggression: threatening or hostile responses to strangers approaching or invading the dog's or owner's personal space, territory, or home range.
2. Owner-directed aggression: threatening or hostile responses to the owner or other members of the household when challenged, man-handled, stared at, or stepped over or when approached while in possession of food or objects.
3. Dog-directed aggression: threatening or hostile responses when approached by unfamiliar dogs.
4. Dog rivalry (familiar dog aggression): threatening or hostile responses to other familiar dogs in the same household.
5. Stranger-directed fear: fearful or wary responses when approached by strangers.
6. Nonsocial fear: fearful or wary responses to sudden or loud noises, traffic, and unfamiliar objects and situations, including noise/thunderstorm phobia.
7. Dog-directed fear: fearful or wary responses when approached by unfamiliar dogs.
8. Separation-related problems: vocalizing and/or destructiveness when separated from the owner, often accompanied or preceded by behavioral and autonomic signs of anxiety including restlessness, loss of appetite, trembling, and excessive salivation.
9. Attachment and attention-seeking: maintaining close proximity to the owner or other members of the household, soliciting affection or attention, and displaying agitation when the owner gives attention to third parties.
10. Trainability: willingness to attend to the owner, obey simple commands, learn quickly, fetch objects, respond positively to correction, and ignore distracting stimuli.
11. Chasing: chasing cats, birds, and/or other small animals, given the opportunity.
12. Excitability: displaying strong reactions to potentially exciting or arousing events, such as going for walks or car trips, doorbells, arrival of visitors, and the owner arriving home; has difficulty settling down after such events.
13. Touch sensitivity: fearful or wary responses to potentially painful procedures, including bathing, grooming, nail-clipping, and veterinary examinations.
14. Energy level: energetic, "always on the go," and/or playful.

These categories or factors were extracted originally by factor analysis^{14,15} and consist of 100 questionnaire items that ask respondents to use a series of 5-point, ordinal rating scales (from 0 to 4) to indicate their dogs' typical responses to a variety of everyday situations during the recent past. The scales rate either the severity (aggression, fear, and excitability factors, with 0 indicating no sign of the behavior and 4 indicating a severe form of the behavior) or frequency (all remaining factors and miscellaneous items, with 0 indicating "never" and 4 indicating "always") of the behaviors.

Responses are averaged to give the dog an overall score for each category. Each category score is then compared with the population average, and the dog is given a score of green (close to the average and/or unlikely to pose a problem), yellow (a somewhat higher or less desirable score than average; the behavior may pose a minor problem), orange (an even less desirable score that corresponds to a moderate behavior problem), or red (score is far from average and likely to cause a significant problem, depending on the behavior).

Dog names, demographic data, and PVAS scores from the Google form were downloaded and added to the existing spreadsheet containing the same information from in-clinic respondents.

Statistical Analysis

The C-BARQ scores of the pruritic dogs and the control dogs were analyzed with statistical software^b. Scores for each C-BARQ factor were tested for normality and distributions were not normal. The data were analyzed with the nonparametric Wilcoxon signed ranks test and the Mann-Whitney *U* test to compare the median scores of the two groups. Each of the 14 main factors of the C-BARQ was evaluated. Results were considered significant with *P* values of $\leq .05$.

The mean pruritus score was calculated for the study dogs to determine how pruritic this population was overall. The pruritus scores and duration of pruritus were not compared with the behavioral scores in this analysis.

Results

Eighty-six surveys (C-BARQ and PVAS) were initially completed in person, on paper, at the dermatology clinic. No client who was asked to complete the survey declined. Two surveys from this group were later eliminated when it was determined the dog had a different dermatologic diagnosis.

One hundred forty-five additional responses were gathered through the online form. Seventy-nine were excluded because they did not complete the C-BARQ. Of those that completed the online form and the C-BARQ, three were eliminated because the dog was <1 yr of age, five were eliminated because the dog was not given routine parasiticides, and an additional three were eliminated because the duration of itching was <3 mo. Of an initial 231 responses, 141 were included in statistical analysis.

The most common type of dog evaluated in this study were mixed-breed dogs (28, 19.8%), followed by "pit bulls"/"pit bull-type dogs" (16, 11.3%), bulldogs (French, English, and American, 12, 8.5%), Labrador retrievers (10, 7%), shih tzu (7, 5%), golden retrievers (6, 4.2%), schnauzers (6, 4.2%), hound mixes (6, 4.3%), West Highland white terriers (4, 2.8%), boxers (3, 2%), Australian cattle dogs (2, 1.4%), cocker spaniels (2, 1.4%), Cavalier King Charles spaniels

(2, 1.4%), chow chows (2, 1.4%), Great Danes (2, 1.4%), Jack Russell terriers (2, 1.4%), and Maltese–shih tzu crosses (2, 1.4%). There were single individuals of the following breeds: basset hound, Belgian Malinois, bull terrier, dachshund, English setter, flat-coated retriever, toy fox terrier, wire fox terrier, Japanese chin, Labradoodle, Maltese, miniature pinscher, Patterdale terrier, Plott hound, Andalusian hound, Pomeranian, poodle (toy), pug, Spinone Italiano, vizsla, and Weimaraner. The youngest dog was 1 yr and the oldest was 14 yr, with an average age of 5.5 yr. There were 72 female (51%) and 69 male (48.9%) dogs. Spay/neuter status was not reported for most dogs.

Study dogs had moderate to severe pruritus, with an average pruritus score of 6.8/10. One hundred sixteen respondents gave a duration of itching, which ranged from 3 mo to 14 yr, with an average of 4 yr.

The scores for 9 of the 14 C-BARQ factors were found to be statistically significantly different in the study dogs compared with the control group. The following variables in the pruritic dogs were found to be increased (more severe, less desirable scores) when compared with the control dogs: stranger-directed aggression, owner-directed aggression, familiar dog aggression, dog-directed fear, nonsocial fear, touch sensitivity, excitability, and attention-seeking behaviors (Table 1). The pruritic dogs had a significantly lower (worse) trainability score than the control dogs.

The sample size differed among some variables because some owners did not complete all questions, mostly in relation to the dog-dog interaction questions (they do not own more than one dog or encounter other dogs) or because they had never observed their dog in that scenario (the nonsocial fear category).

The following variables were not significantly different compared with the control dogs: dog-directed aggression, stranger-directed fear, separation-related problems, chasing, and energy.

Discussion

This is the first study to demonstrate that dogs who experience chronic moderate to severe pruritus due to AD exhibit significant increases in anxiety- and fear-based behaviors as well as overall reactivity (aggression, excessive excitability) compared with a large population of healthy dogs. These results are comparable to the anxiety, stress, and overall irritability that are often reported by humans with pruritic skin diseases.^{7,16} In human dermatology, chronic pruritic skin disease can worsen stress and anxiety. In turn, stress and anxiety can exacerbate pruritus.⁷ Although causation cannot be determined in this study, the data show an association between moderate to severe pruritus and the presence of behavioral changes. This was a preliminary study with a relatively small sample size, but the results suggest that dogs with chronic pruritus and AD may be more likely

TABLE 1

Summary Data for Each C-BARQ Factor

C-BARQ Variable	Control Mean	Control Standard Deviation	Sample Mean	Sample Standard Deviation	Z Test Statistic	P Value	Number of Control Dogs	Number of Pruritic Dogs
Trainability	2.63	0.64	2.494	0.567	3.001	.0027	42,995	136
Stranger-directed aggression	0.630	0.710	0.730	0.719	-2.585	.0097	42,088	140
Owner-directed aggression	0.155	0.384	0.241	0.478	-3.686	.0002	42,890	141
Dog-directed aggression	1.034	1.049	1.179	1.083	-1.770	.0767	41,209	129
Familiar dog aggression	0.533	0.749	0.747	0.928	-2.627	.0086	35,808	107
Dog-directed fear	0.791	0.900	0.94	0.975	-2.111	.0347	41,210	135
Stranger-directed fear	0.680	0.947	0.736	0.942	-0.808	.419	42,468	138
Nonsocial fear	0.827	0.760	1.03	0.793	-3.405	.0007	42,379	138
Separation-related problems	0.616	0.649	0.773	0.814	-1.875	.0608	42,846	140
Touch sensitivity	0.796	0.793	1.12	0.857	-4.910	.0000	41,786	140
Excitability	2.115	0.824	2.33	0.823	-2.975	.0029	42,610	141
Attention seeking	2.082	0.807	2.33	0.860	-3.530	.0004	42,728	141
Energy	2.072	1.054	1.982	1.020	1.119	.2630	43,116	141
Chasing	2.118	1.109	2.153	1.075	-0.525	.5993	41,417	139

Bold values are statistically significant.

C-BARQ, Canine Behavioral Assessment and Research Questionnaire.

to exhibit problematic behaviors and may be at greater risk for developing behavioral disorders.

Although it is known that anxiety and depression are common sequelae to many pruritic skin diseases in humans,¹⁷ this mental state is harder to prove in animals. A study performed on mice demonstrated that experimental induction of AD skin lesions led to increased anxiety and depressive-like behaviors.¹⁸ Another mouse study demonstrated that specific neurons in the amygdala are activated by pruritogens, and experimental activation of those neurons caused anxiety behaviors.¹⁹ Itch sensation directly led to anxiety behaviors in these mice. Many of the same neurons activated by pruritogens were also activated by pain stimuli, and Sanders et al. hypothesized that overlap of pain and itch signaling results in convergence to a general “aversive” signal, which in turn promotes anxiety and avoidance behaviors. Patients with AD can develop anxiety; this has been documented in humans and mice. It is reasonable to expect that this process occurs in other species and seems likely to occur in dogs.

A recent study evaluated the behavior of atopic and nonatopic Labrador and golden retrievers in the United Kingdom as a subset of the Itchy Dog Project.²⁰ The authors hypothesized that dogs with AD would have more “anxious” personality types and would have higher scores for categories reflecting fear and anxiety.²¹ The data did not show an increase in fear behaviors or aggression but found increased frequency of other behaviors that may have an anxiety component (mounting, restlessness, leash-pulling, attention-seeking).²¹ In contrast, our study found increases in anxiety- and fear-related behaviors and aggression.

Dogs with severe nonsocial fear and separation-related issues have previously been reported to have an increased frequency and severity of unspecified skin disorders.¹ Our results concur: pruritic dogs exhibited more nonsocial fear. Another review of medical conditions associated with behavioral problems showed increased incidence of behavioral problems in dogs with neurologic diseases such as epilepsy and brain tumors; endocrine or metabolic diseases; and pain-related conditions.^{22,23} Although dermatologic conditions were not mentioned specifically, the signaling overlap of pain and pruritus, especially in the amygdala as shown in the mouse model, could cause pruritic animals to display similar physiologic and behavioral changes as animals experiencing pain.^{19,22,24,25} Any animal presenting with a change in behavior should be evaluated for an underlying medical problem.⁶

AD leads to long-term pruritus and discomfort. The dogs in the present study demonstrated a much greater sensitivity to touch than control dogs. These dogs may be prone to overreact to basic handling when their skin is itchy and painful, or they may have enduring touch sensitivity.^{24–26} Chronic pruritus and associated nervous

system sensitization in humans frequently leads to *alloknesis* (itch induced by light touch) and *hyperknesis* (excessive itch in response to a mild itch stimulus).²⁷ It is reasonable to expect this also occurs in dogs. A seemingly innocuous touch may be perceived as aversive by the animal. Topical treatments such as bathing and applying sprays/ointments are an important part of successful management of atopic dogs, and a dog with an aversion to handling could be difficult for owners to treat. If practitioners are aware that touch sensitivity may be a concern for these patients, they could implement desensitization and counterconditioning techniques, pain medications, anxiolytics, or a combination of the above, benefitting dog and owner.

Dogs in this study also scored above average in the category of “excitability.” These dogs tend to become overaroused by average stimuli and have difficulty recovering to baseline after the inciting event. Studies in humans have described autonomic nervous system dysfunction in subjects with moderate to severe AD. These individuals demonstrated chronic sympathetic overactivation as well as sympathetic overresponse to the sensation of itch and the act of scratching compared with nonatopic controls.^{28,29} Similar nervous system overactivation could be occurring in canine patients. With higher scores across the categories of aggression, fear, and excitability, these dogs could be described as overall more reactive to a wide range of stimuli than their nonpruritic counterparts.

There are several potentially confounding variables that could have influenced our results. Cases enrolled at referral clinics, either dermatology or behavior, may be more severely affected by their disease conditions, thus resulting in greater severity of behavioral problems. Dogs in this study averaged a pruritus score of 6.8/10, which is moderate to severe itching that interrupts normal activities. There are many atopic dogs not this severely pruritic. Ranking pruritus level would be useful in any future studies.

Case selection in the clinic was predominately determined by the primary investigator; cases may have been more likely to be enrolled if the owner mentioned behavioral concerns or if the patient displayed anxiety at the clinic, despite deliberate effort to enroll patients without bias. Additionally, current therapies for the pruritic dogs, such as oral corticosteroids, could have altered the dog’s behavior, so separating dogs into treatment groups in future studies could be helpful to elucidate possible treatment-related behavioral effects.

Owner assessments of their dog’s behavior are necessarily subjective and therefore potentially susceptible to unconscious biases. Owners may intentionally or unconsciously skew answers for behaviors they may find embarrassing, such as aggression or house soiling, leading to falsely lower incidences of problem behaviors. Owners may also have difficulty interpreting their dog’s reaction to certain situations and may not be able to correctly interpret or notice subtle signs of anxiety and fear.

In the control group, it was owner-reported whether the dog had any medical issues, and any dog with a reported medical issue was excluded from this analysis. It is possible that some dogs in the control group were experiencing pruritus or fit a clinical description of AD but the dog owner was unaware or had not received a diagnosis from a veterinarian. Given the large size of the control group, this would be unlikely to significantly affect the analysis.

Other studies have correlated the severity of the pruritus to the severity of behavioral abnormalities²¹; this would be difficult with these data because almost all dogs experienced moderate to severe pruritus (PVAS score of 5 or higher). To include a wider spectrum of atopic dogs, patients could be recruited through primary care clinics. This would capture a variety of clinical presentations of AD. With mildly affected atopic dogs represented in the study population, a behavioral comparison between less pruritic and more pruritic dogs could be performed to determine if severity of atopic disease correlates with severity of behavioral disorders.

Our study results did not concur with the behavioral findings of the Itchy Dog Project. There are potentially several reasons for this disparity. One difference is the study population. Patients in the present study are likely to be more severely affected by their skin disease because the majority were recruited directly from a veterinary dermatologist's caseload. Those in the Itchy Dog Project were recruited through social media and kennel club advertising, with owners self-reporting their dog's diagnosis of AD. Increased severity of skin disease likely correlates with increased severity of behavioral abnormalities; more studies are needed to support this correlation. Results may also be influenced by breed-specific gene pools and temperaments. Focusing on two similar breeds without a representation of the wide variety of dogs that can be affected by AD may have skewed the behavioral results in the study by Harvey et al.

Thirty-seven different purebreeds were represented in the current study, with the distribution of breeds skewing toward breeds commonly affected with AD (pit bulls, bulldogs, and Labrador retrievers being the most common).³⁰ Breed composition differed between the control and test groups. The largest group in both control and study dogs were mixed-breed dogs. The study dogs were 19.8% mixed-breed dogs and 11.3% "pit bull-type" dogs, whereas the control dogs were 25.5% mixed-breed dogs and only 3.9% pit bull-type dogs. Given that pit bull type indicates a wide range of phenotypes versus a specific breed in this context, many pit bull-type dogs could also have been categorized as mixed-breed dogs; consequently, this distinction is likely insignificant here. If all pit bull-type dogs were recategorized as mixed-breed dogs, then 31.1% of pruritic dogs and 29.4% of control dogs were mixed-breed dogs, respectively—a similar percentage. To truly make a distinction between pit bull-type dogs and other dogs, this group of dogs would

require a specific definition. The study group did have a much higher percentage of all bulldogs (8.5% versus 0.9% of the control group); therefore, the temperament of these types of dogs could have affected the results of the analysis. Future studies would benefit from a larger sample size, which could also allow for breed- and age-matched controls.

As with all cross-sectional studies, causation cannot be determined, but important correlations and relationships should be considered. Recently, several longitudinal cohort studies have examined risk factors for the development of AD in specific breeds; it would be enlightening to include behavioral evaluations in those studies to determine when problem behaviors may begin in relation to the onset of clinical signs of AD.

Conclusion

Chronically pruritic dogs experience anxiety. More attention needs to be given to behavioral medicine and emotional welfare in our veterinary patients. The long-term negative effects of chronic stress and anxiety on disease and patient QOL are increasingly recognized in human medicine and are starting to be acknowledged in veterinary medicine. The veterinary team must be proactive not only in identifying anxious pets but also in owner education. The development of a protocol for owners to evaluate the behavior of their itchy pet could help practitioners and owners recognize problems early. Prompt medical intervention in AD is critical to modulate the disease process before permanent immunological changes and skin damage occur; similarly, timely intervention can alter behavior before it becomes established and affects neural pathways. Prompt implementation of a multidisciplinary treatment plan for atopic dogs, including treatment of behavioral disorders, could help reduce patient fear and anxiety, which could facilitate less stressful care and ultimately improve patient and caregiver QOL. ■

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FOOTNOTES

- ^a Microsoft Excel; Microsoft Corporation, Redmond, Washington
- ^b Stata IC 13.1 statistical software; StataCorp LLC, College Station, Texas

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