

A Retrospective Study Regarding the Treatment of Lupoid Onychodystrophy in 30 Dogs and Literature Review

The treatment records of 30 dogs with lupoid onychodystrophy were evaluated retrospectively. Dogs were treated with fatty acid supplementation (n=18), doxycycline and niacinamide (n=12), tetracycline and niacinamide (n=10), pentoxifylline (n=6), prednisolone (n=5), azathioprine (n=1), clofazimine (n=1), or with combinations thereof. An excellent response was seen in almost half of the patients treated with tetra- or doxycycline in combination with niacinamide. Six of the dogs were maintained successfully on fatty acid supplementation. Spontaneous remissions and recurrences made evaluation of success rates difficult and emphasized the varied and often unclear etiology and natural course of the syndrome. *J Am Anim Hosp Assoc* 2003;39:139–150.

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Introduction

Onychodystrophy or onychodysplasia (i.e., abnormal claw formation), onychomalacia (i.e., soft claws), onychoschizia (i.e., splitting or lamination of the claws), onychorrhhexis (i.e., spontaneous splitting of the claws), and onychomadesis (i.e., sloughing of claws) may be due to a variety of diseases. Trauma, bacterial and fungal infections, immune-mediated diseases (e.g., pemphigus, systemic lupus erythematosus, cold agglutinin disease, drug eruption, vasculitis, and a lupus-like syndrome), and neoplasia have all been suggested as possible etiologies. Much of this information was anecdotal.¹⁻³ More recently, a number of retrospective⁴⁻⁶ and prospective studies^{7,8} have attempted to define canine claw disease in more detail. A clinical syndrome termed lupoid onychodystrophy appears to be more commonly encountered.⁵ This syndrome seems to have multiple possible causes,⁷ and a number of treatment modalities have been reported.^{5,6,9,10} The purpose of this retrospective study was to evaluate the efficacy of various therapeutic options in 30 dogs with lupoid onychodystrophy.

Materials and Methods

The records of 30 dogs with lupoid onychodystrophy diagnosed by history, clinical examination, and histopathological changes were reviewed for this study. Data was recruited from the Veterinary Teaching Hospital of the Colorado State University; the Animal Skin and Allergy Clinic, a private referral practice in Melbourne, Australia; and Denver Veterinary Specialists, a private referral practice in Denver, Colorado. The initial presenting complaints for all dogs were onychomadesis, onychodystrophy, and onychoschizia affecting multiple claws on all four feet. Biopsies were obtained by onychectomy or by a recently described procedure of onychobiopsy without onychectomy¹¹ and revealed the features previously described for lupoid onychodystrophy.^{5,7} All but four biopsies were reviewed by one of the authors (Mueller). The other four biopsies were reviewed by a dermatopathology service in California.^a In many dogs, complete blood counts (n=28), serum biochemical profiles (n=22),

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antinuclear antibody testing (n=21), total thyroxine (T₄) concentrations (n=18; both for screening and to assess control in those diagnosed with preexisting hypothyroidism), cytopathology of claw fold discharge (n=16), fungal (n=16) and bacterial cultures (n=15), and elimination diets (n=8) complemented the diagnostic evaluation. Signalment and concurrent diagnosed diseases were recorded.

Dogs underwent a variety of therapeutic trials [Table 1]. Tetracycline^b and niacinamide^c were both given, at 250 mg q 8 hours (if the dog was <15 kg body weight) or 500 mg q 8 hours (if the dog was >15 kg body weight). If this therapy led to a good or excellent response, tapering of therapy to q 12 hours and then to q 24 hours was attempted. In a number of patients, doxycycline^d was used instead of tetracycline at a dose of 5 to 10 mg/kg body weight, q 24 hours, as once-daily administration was preferred by the owners. Essential fatty acid supplementation consisted of one of three commercial supplements. Product 1^e was used in case nos. 2-4, 6, 8, 9, and 12-15 at a dose of 1 mL per 3 to 5 kg body weight, q 24 hours; product 2^f was used in case nos. 18 through 22 at a dose of 1 capsule per 10 to 15 kg body weight, q 12 hours; and product 3^g was used in case nos. 27, 28, and 30 at a dose of 1 capsule per 7 to 15 kg body weight, q 24 hours. Contents of the fatty acid supplementations are listed in Table 2. Pentoxifylline^h was used at approximately 10 mg/kg body weight, q 8 to 12 hours, and clofazimineⁱ was used at 2 mg/kg body weight, q 24 hours. Prednisolone^j was initially used at 1 mg/kg body weight, q 24 hours, and azathioprine^k was initially used at 2 mg/kg body weight, q 24 hours; these drugs were then tapered until half of the initial dose was given every other day. Each therapy was administered for at least 8 weeks. In some dogs, a combination of several different drugs was administered concurrently, and if the combination was effective, one drug at a time was subsequently discontinued to achieve optimal treatment outcome with minimal drug therapy and to identify the most effective treatment. Antibiotics administered for secondary bacterial infections included clavulanic acid/amoxicillin^l at 12.5 to 15 mg/kg body weight, q 8 to 12 hours, and cephalexin^m at 25 to 30 mg/kg

body weight, q 24 hours for 3 to 6 weeks. Adverse effects of all therapies were recorded.

When potential adverse reactions to food or drug reactions caused by food preservatives or additives were evaluated, a home-cooked elimination diet was fed, consisting of a novel protein and a novel carbohydrate source fed exclusively for at least 6 to 8 weeks.

The response to treatment was described as excellent, good, partial, or poor. An excellent response was defined as complete regrowth of normal claws; a good response was defined as complete resolution of pain, onycholysis, and onychomadesis, but with continued abnormal claw morphology. Continuing onychomalacia and onychodystrophy with reduced but occasional episodes of onycholysis and onychomadesis constituted a partial response. Dogs with a poor response showed no substantial improvement.

Results

Of the 30 dogs reviewed for this study, eight were castrated males, seven were intact males, four were intact females, and 11 were spayed females. Average body weight was 22.8 kg, with a range of 6 to 50 kg. A number of breeds were represented. Those breeds with more than one dog affected were Labrador retrievers (n=4), German shepherd dogs (n=4), miniature schnauzers (n=3), greyhounds (n=2), and West Highland white terriers (n=2). The mean age of onset was 5.2 years, with a range from 1 year to 12 years of age. The results of various treatments in individual patients are outlined in Table 1, and a summary of the drug efficacy is shown in Figure 1.

Tetracycline and Niacinamide

A combination of tetracycline and niacinamide was used in 10 dogs, with an excellent response in four dogs (case nos. 16, 20-22), a good response in two dogs (case nos. 25, 26), a partial response in two dogs (case nos. 17, 27), and a poor response in two dogs (case nos. 18, 19). Of the four dogs with an excellent response, the treatment of one (case no. 21) was changed to fatty acid supplementation after 8 weeks, and the dog remained in remission on that treatment.

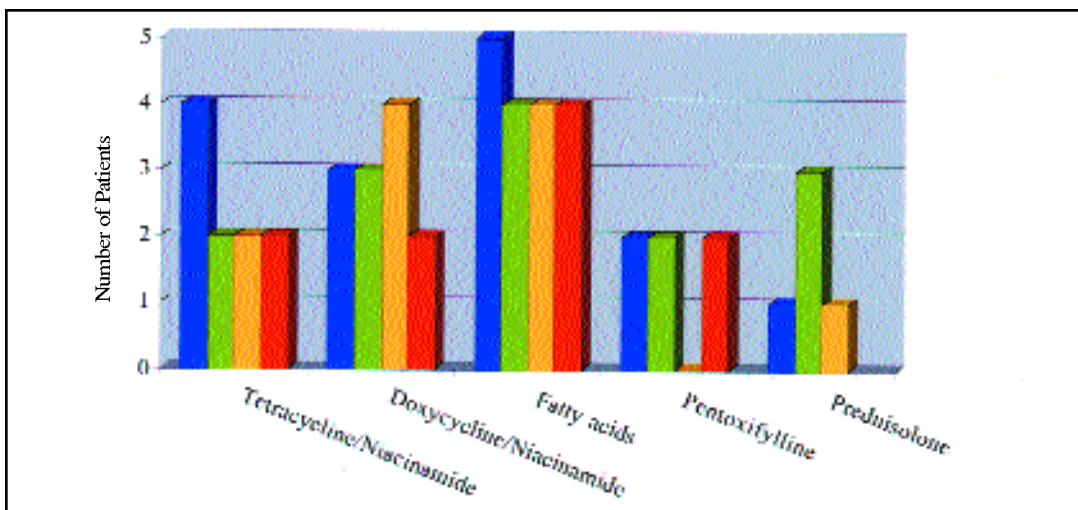


Figure 1—Efficacy of medications used in the treatment of canine lupoid onychodystrophy. Note that drugs were given in combination to some patients, and response was attributed equally to each drug.

Table 1
Efficacy of Various Treatments in 30 Dogs With Lupoid Onychodystrophy

Case No.	Signalment*	Duration of Disease Prior to Treatment	Initial Treatment	Response†	Further Treatment	Response†	Further Treatment	Response†
1	2-yr, M Cavalier King Charles spaniel	5 mos	Clavulanic acid/amoxicillin	Excellent	No further treatment needed for 2 yrs			
2	6-yr, M German shepherd dog	3 mos	Doxycycline/niacinamide	Good	Added fatty acid ^e	Same	Fatty acids ^e /niacinamide	Partial; deterioration was treated twice with a course of doxycycline during 2-yr follow-up period
3	1-yr, MC Silky terrier	1 mo	Clavulanic acid/amoxicillin	Excellent for 6 mos, then recurrence	Flea control and fatty acid ^e	Excellent for 18 mos		
4	2-yr, FS Doberman pinscher	1 mo	Elimination diet, fatty acid ^e	Good	"Preservative-free" dog food only	Recurrence after trauma 6 mos later	Elimination diet/fatty acid ^e	Good for 30 mos
5	7-yr, M miniature poodle	2 mos	Doxycycline/niacinamide	Partial	Elimination diet/niacinamide	Excellent, relapse 2 mos after discontinuation of niacinamide and food rechallenge	Lost to follow-up	
6	1-yr, F bearded collie	3 mos	Doxycycline/niacinamide	Partial	Doxycycline/niacinamide/fatty acid ^e	Same	Maintained on fatty acids ^e alone	Same for 2 yrs
7	6-yr, MC Rhodesian ridgeback	3 wks	Doxycycline/niacinamide/diet	Excellent	Rechallenge with normal food	Complete remission with no further treatment	Lost to follow-up	
8	6-yr, FS German shepherd dog	Unknown	Doxycycline/niacinamide	Good	Doxycycline/niacinamide/fatty acid ^e	Deterioration	Pentoxifylline	Excellent for 6 mos

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Table 1 (cont'd)
Efficacy of Various Treatments in 30 Dogs With Lupoid Onychodystrophy

Case No.	Signalment*	Duration of Disease Prior to Treatment	Initial Treatment	Response†	Further Treatment	Response†	Further Treatment	Response†
9	6-yr, F terrier mixed-breed dog	1 mo	Doxycycline/niacinamide/fatty acids ^e	Excellent	Fatty acids ^e alone	Same for 18 mos		
10	1-yr, FS Dalmatian mixed-breed dog	1 mo	Doxycycline/niacinamide/diet	Poor	Pentoxifylline	Same	Clofazimine	Excellent for 6 mos
11	6-yr, MC terrier mixed-breed dog	2 mos	Doxycycline/niacinamide/diet	Partial	Prednisolone, immunotherapy	Excellent for 6 mos	Lost to follow-up	
12	4-yr, M miniature schnauzer	1 yr	Doxycycline/niacinamide/fatty acids ^e	Poor	Elimination diet	Excellent, no recurrence with dietary rechallenge		
13	8-yr, M German shepherd dog	3 wks	Fatty acids ^e	Partial	Doxycycline/niacinamide	Same, complete remission after cessation of drugs	Recurrence 6 mos later, pentoxifylline	Excellent
14	6-yr, FS Labrador retriever	1 mo	Doxycycline/niacinamide/fatty acids ^e	Partial	Doxycycline/prednisolone/fatty acids ^e	Same, lost to follow-up		
15	12-yr, F West Highland white terrier	1 mo	Doxycycline/niacinamide/fatty acids ^e for 5 days	Excellent	Tapered to q 24 hrs	Same, lost to follow-up		
16	4-yr, MC Labrador retriever	2 mos	Tetracycline/niacinamide	Excellent	Tapered to q 12 hrs	Same for 5 yrs		
17	7-yr, F West Highland white terrier	3 mos	Tetracycline/niacinamide	Partial	Lost to follow-up			
18	6-yr, M miniature schnauzer	10 mos	Tetracycline/niacinamide/fatty acids ^f	Poor	Pentoxifylline	Same	Prednisolone	Good for 8 mos

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Table 1 (cont'd)
Efficacy of Various Treatments in 30 Dogs With Lupoid Onychodystrophy

Case No.	Signalment*	Duration of Disease Prior to Treatment	Initial Treatment	Response†	Further Treatment	Response†	Further Treatment	Response†
19	8-yr, FS miniature schnauzer	1 yr	Tetracycline/niacinamide/fatty acids†	Poor	Pentoxifylline	Good, lost to follow-up		
20	10-yr, MC mixed-breed dog	6 wks	Tetracycline/niacinamide/fatty acids†	Excellent	No treatment for 2 yrs			
21	2-yr, FS Labrador retriever	6 wks	Tetracycline/niacinamide	Excellent	Switch to fatty acids†	Same for 2 yrs		
22	3-yr, FS schipperke	4 mos	Tetracycline/niacinamide/fatty acids†	Excellent	Tetracycline/niacinamide tapered to q 24 hrs	Same for 6 mos		
23	10-yr, FS mixed-breed dog	4 mos	Doxycycline	Good for 8 mos	Recurrence 4 wks after cessation of therapy			
24	10-yr, MC mixed-breed dog	2 mos	Cephalexin	Excellent	No further treatment for 2 yrs			
25	1-yr, M Akita	4 mos	Tetracycline/niacinamide	Good	Tapered to q 12 hrs	Recurrence	q 8 hrs	Good for 3 yrs
26	2-yr, MC golden retriever	1 mo	Tetracycline/niacinamide	Good				
27	6-yr, MC greyhound	1 mo	Tetracycline/niacinamide/fatty acids§	Partial for 10 mos				
28	1-yr, FS Labrador retriever	1 wk	Prednisolone, fatty acids§	Good	Maintained on fatty acids§	Same for 18 mos		
29	6-yr, FS German shepherd dog	6 wks	Azathioprine, pentoxifylline	Good	Pentoxifylline	Same for 5 mos		
30	7-yr, FS greyhound	1 mo	Prednisolone, Fatty acids§	Good	Therapy discontinued	Same for 2 yrs		

* M=male; MC=male castrated; FS=female spayed; F=female
† See **Materials and Methods** section for response grading definitions; Same=the same response as recorded with previous therapy

Table 2

Fatty Acid Supplementations Used in the Treatment of 30 Dogs With Lupoid Onychodystrophy

Active Ingredients	Product 1 ^e	Product 2 ^f	Product 3 ^g	Product 4 ⁿ
Linoleic acid	70 mg/mL	386 mg/capsule		247.2 mg/capsule
-linoleic acid		112 mg/capsule		30.8 mg/capsule
Eicosapentaenoic acid	112.5 mg/mL	75.6 mg/capsule	250 mg/capsule	9.8 mg/capsule
Docosahexaenoic acid	75 mg/mL	16.8 mg/capsule	167 mg/capsule	6.5 mg/capsule
Other	1 mg/mL tocopheryl acetate	75 IU vitamin E		Vitamins E (13 IU), A, B ₁ , B ₂ , B ₃ , B ₆ , B ₁₂ , C, D, E, biotin, folic acid, pantothenic acid

In two dogs, therapy was tapered to *q* 12 hours (case no. 16) and *q* 24 hours (case no. 22) within 8 months of starting medication, and the dogs remained in remission. In the last dog (case no. 20), therapy was discontinued after 2 months, with no further evidence of onychodystrophy. One dog with good response (case no. 25) showed a recurrence of clinical signs upon tapering to *q* 12 hours; he subsequently recovered and was maintained on tetracycline and niacinamide *q* 8 hours for 3 years. The two dogs with poor responses concurrently received fatty acid supplementation.

Doxycycline and Niacinamide

Doxycycline was combined with niacinamide in 12 dogs. An excellent response was seen in three dogs (case nos. 7, 9, 15), a good response was seen in two dogs (case nos. 2, 8), a partial response was seen in five dogs (case nos. 5, 6, 11, 13, 14), and a poor response was seen in two dogs (case nos. 10, 12). In one of the excellent responders (case no. 15), niacinamide was tapered to *q* 24 hours drug administration, and the dog was maintained in remission with this regimen. In case nos. 7 and 9, the drugs were administered concurrently with either an elimination diet (case no. 7) or fatty acid supplementation (case no. 9). The dog on the concurrent elimination diet (case no. 7) was challenged with his original diet after cessation of the doxycycline and niacinamide, and he maintained complete remission. In case no. 9, doxycycline and niacinamide were discontinued after 8 weeks, and the dog continued to receive fatty acid supplementation only. Remission was maintained on that treatment. This dog subsequently developed pruritic skin disease without claw involvement 18 months later while still on fatty acid supplementation. In two dogs (case nos. 2, 8) with good responses, fatty acids were added to achieve further improvement. One of these dogs (case no. 2) was maintained on fatty acids and niacinamide (*q* 24 hours), while the other (case no. 8) deteriorated after 4 months of combination therapy and was later

controlled on pentoxifylline as the sole therapy for 6 months before being lost to follow-up. Of the five partially responding dogs (case nos. 5, 6, 11, 13, 14), one (case no. 6) did not improve further with added fatty acid supplementation, but was actually maintained on the latter alone for more than 2 years to the owner's satisfaction. Case no. 5 improved further when the dog was placed on an elimination diet and niacinamide and doxycycline was discontinued. This dog relapsed again 2 months after both diet and niacinamide were discontinued. One dog (case no. 13) with a partial response grew back normal claws during winter (after medications had been discontinued) and relapsed 6 months later. Doxycycline was used alone with a good response in one dog (case no. 23). Clinical signs recurred 4 weeks after doxycycline was discontinued.

Fatty Acid Supplementation

Fatty acid supplementation was used as a single initial therapy in only one dog (case no. 13) with a partial response. In 10 dogs, fatty acids were administered in combination with doxy- or tetracycline and niacinamide. Three of these dogs (case nos. 9, 20, 22) had excellent responses. Clinical signs did not recur after cessation of the fatty acid supplementation in one dog (case no. 22), which was then maintained on tetracycline and niacinamide. Resolution was maintained in one dog (case no. 20) after all medications were discontinued. Case no. 9 was successfully maintained on exclusive therapy with fatty acids after doxycycline and niacinamide were discontinued. Three dogs on combination therapy (case nos. 6, 14, 27) showed a partial response. In the four remaining dogs (case nos. 8, 12, 18, 19), response was poor. In three dogs, fatty acid supplementation was added to the therapeutic protocol because of the less than excellent response to other medications. In two of these dogs (case nos. 2, 6), no further improvement could be detected. The third dog deteriorated (case no. 8). Four

dogs (case nos. 6, 9, 21, 28) that had responded initially to other drugs (one partial, one good, and two excellent responses) received exclusive maintenance therapy with fatty acids. The same level of clinical improvement was maintained in all cases. One dog (case no. 2) initially responded well to a combination of doxycycline and niacinamide and was then maintained on fatty acid therapy and niacinamide daily to the owner's satisfaction, although the response to that treatment was only partial, and two courses of doxycycline were needed to control recurrences in the 2-year follow-up period. One dog (case no. 4) responded to fatty acid supplementation in conjunction with an elimination diet, but she relapsed upon food rechallenge. Clinical signs resolved again on the diet and stayed in remission for 6 months with a commercial, preservative-free dog food without fatty acid supplementation. After apparently traumatizing one claw, clinical signs recurred and responded again to a strict elimination diet and fatty acid supplementation. Case no. 15 discontinued fatty acid therapy after 5 days and was not included in the discussion of efficacy for that reason.

Antibiotics

Eighteen of the 30 dogs underwent initial treatment with antibiotics for bacterial infections based on the results of cytology, bacterial cultures, or both. Fifteen of these dogs improved only partially with treatment, although cytopathology and clinical examination after antibiotic therapy revealed no evidence of ongoing infection. Antibiotic treatments of these dogs are not included in Table 1 and the **Discussion**, as the infections were considered secondary. Three dogs responded to a 6-week course of only clavulanic acid/amoxicillin (case nos. 1, 3) or cephalexin therapy (case no. 24), respectively. Two of these dogs (case nos. 1, 24) were followed for 2 years with no further treatment or recurrence of clinical signs. One of these dogs (case no. 1) was 1 year old when initially presented; the other (case no. 24) was hypothyroid and had been maintained on the same dose (*q* 12 hours) of levothyroxine supplementation before, during, and after the occurrence of claw disease. When the dog was presented for claw disease, a post-pill T_4 concentration was in the upper reference range. The third dog (case no. 3) was in remission for 6 months and then showed a recurrence of the claw disease with concurrent cutaneous signs of flea allergy dermatitis. All clinical signs resolved with flea control and fatty acid supplementation.

Pentoxifylline

Pentoxifylline was used in six dogs, with an excellent response in two dogs (case nos. 8, 13) and a good response in two dogs (case nos. 19, 29). The remaining two dogs (case nos. 10, 18) showed no improvement. One of the dogs with an excellent response (case no. 8) had previously not responded to treatment with doxycycline and niacinamide and fatty acids for 4 months and then underwent spontaneous remission for 6 months. When clinical signs recurred, she responded rapidly to pentoxifylline.

Prednisolone

Prednisolone was used in five dogs. It was used alone (case no. 18) or in combination with fatty acid supplementation (case nos. 28, 30), allergen-specific immunotherapy (case no. 11), and doxycycline and fatty acids (case no. 14), respectively. In three of these dogs (case nos. 11, 14, 18), prior protocols had failed to improve their claw disease. In case no. 14, no further improvement was noted. Two dogs showed a good (case no. 18) and excellent (case no. 11) response, respectively; the other two dogs (case nos. 28, 30) showed a good initial response to prednisolone and fatty acid supplementation and did not deteriorate after the prednisolone (case no. 28) or all medications (case no. 30) were discontinued.

Other Drugs

Clofazimine was administered to one dog (case no. 10) with an excellent response, but a recurrence of the claw disease with additional clinical signs compatible with atopic dermatitis occurred after 6 months while the dog was still on treatment. Azathioprine was used in combination with pentoxifylline in one dog (case no. 29), with a good response. It was discontinued, and the dog was kept on pentoxifylline only, with the same good response.

Concurrent Diseases

Concurrent diseases included hypothyroidism (case nos. 8, 11, 16, 24, 25), atopic dermatitis (case nos. 9, 10, 11, 25), ear margin dermatitis (case nos. 18, 19), chondrodystrophy (case no. 20), demodicosis (case no. 8), food adverse reaction (case no. 4), flea allergic dermatitis (case no. 3), and hip dysplasia (case no. 11). Many of the concurrent diseases were present before the onset of claw disease, and dogs had either been treated successfully and were cured (demodicosis), were on successful maintenance therapy based on laboratory testing and other clinical signs (hypothyroidism), or were not treated for the concurrent disease at the time of claw disease (hip dysplasia). The dog (case no. 20) with osteoarthritis of one elbow was treated concurrently with carprofen. Clinical signs of atopic dermatitis, flea allergy dermatitis, ear margin dermatitis, and food adverse reaction either occurred at the initial onset of claw disease or 2 to 18 months later.

Adverse Effects of Therapy

Adverse effects of therapy were noted in four dogs. Case no. 15 became flatulent with fatty acid supplementation. The flatulence improved once therapy was discontinued. Case nos. 28 and 29 developed vomiting after 1 week on prednisolone, and vomiting and diarrhea after 1 month on azathioprine, respectively, and they recovered after cessation of these therapies. Ataxia and a head tilt were observed with case no. 14, which was given prednisolone, doxycycline, and fatty acid supplementation concurrently. The clinical signs abated when therapy was discontinued, and the dog was subsequently lost to follow-up.

Discussion

Canine claw disease and particularly lupoid onychodystrophy have been the focus of recent attention.^{5-7,9-13} In this study, various medications for the treatment of lupoid onychodystrophy were evaluated. Patients did not all receive the same drugs in the same sequence, which is an inherent problem with retrospective studies. In addition, combinations of several medications were given concurrently in a number of patients, which rendered evaluation of efficacy more difficult. However, as a large number of patients were included, the information was considered valuable for the small animal practitioner.

Fatty Acid Supplementation

In the first report dedicated to this syndrome, Scott *et al.* indicated a complete response to a commercial fatty acid product^f at a dose of 1 capsule per 9 kg body weight, *q* 24 hours.⁵ Further evidence for the efficacy of fatty acid supplementation was presented by Bergvall,⁹ who treated five dogs with lupoid onychodystrophy with a different commercial fatty acid supplement.ⁿ Bergvall's patients initially received 1 to 2 capsules per 10 kg body weight, *q* 24 hours. After remission was achieved, the dogs received a slightly higher dose of fatty acids without the added minerals and vitamins.^o All five dogs responded to treatment and were maintained in remission on fatty acids only. In each of the above-mentioned studies, fatty acid treatment was discontinued in two dogs, and the disease recurred. Upon readministration of the supplement, clinical signs again subsided.

In another case report, treatment with the same commercial fatty acid supplementationⁿ used in Bergvall's study did not improve the patient during 1 year of therapy.¹⁰ The dog's claws were then carefully cut and trimmed every 2 weeks, and the clinical signs subsided over the next months. No other management or environmental changes could be detected. The dog was followed for 2 years without recurrence.

A more recent retrospective study by Auxilia *et al.* evaluated the treatments of six dogs with lupoid onychodystrophy.⁶ Three of these dogs were treated with the commercial fatty acid supplementation^o also used in Bergvall's report. One of these dogs responded well, one partially, and one dog did not respond at all, and evaluation criteria were similar to the criteria used in this study. Tetracycline and niacinamide were administered at 500 mg *q* 8 hours each, in four dogs (two of which had undergone fatty acid supplementation with partial and no response). The dog that failed fatty acid therapy also showed a lack of response to tetracycline and niacinamide and later did not improve on prednisolone at 1 mg/kg body weight *q* 12 hours. The other patient previously treated with fatty acids responded well to the combination of tetracycline and niacinamide. A good and a partial response were seen in the other two dogs. In the last dog of this report, therapy with azathioprine and prednisolone at immunosuppressive doses led to a good response.

The findings in the authors' study with regard to treatment with fatty acids are less straightforward than initial reports evaluating this therapy.^{5,9} Very few dogs were

treated with fatty acids alone, and responses could have been due to concurrent therapies. The incidence of positive responses in this study did not equal some previous observations, wherein success approached 100%.^{5,9} Only one dog was treated with fatty acids as an initial sole therapy and had a partial response. Fatty acids were used in 18 dogs. They were administered in conjunction with other drugs in 12 dogs, were added to already existing protocols in three dogs, and were utilized as maintenance therapies following responses to other drugs in four dogs. In three of 12 dogs started on combination therapies, overall responses were poor. Two dogs showed only a partial response. Three dogs from the group with excellent responses and one with a good response failed to deteriorate after fatty acids were discontinued, suggesting that they were not critical for maintaining response. In three dogs, where fatty acids were added to the regimen to enhance response, no benefit was seen, and one dog actually deteriorated. Although continued responses were seen in the four dogs in which fatty acids were used as maintenance therapy, the efficacy of therapy could not be ascertained, because treatment was not stopped in any individual. Based on the findings in this study, fatty acids may be useful in treating dogs with lupoid onychodystrophy and particularly in keeping dogs in remission after a more aggressive initial therapy, but the success rates observed by Scott *et al.*⁵ and Bergvall⁹ could not be duplicated.

There are several possible explanations for observed variations in response to fatty acids between studies. Response to fatty acids may depend on the underlying etiology. Different primary diseases can result in the development of lupoid onychodystrophy.⁷ Response to fatty acid therapy may partially depend on genetic makeup, which may have also differed among the various studies. Genetic predispositions for dogs with lupoid onychodystrophy have been suggested based on the increased incidence of the disease in certain breeds such as the German shepherd dog.^{7,8} In Bergvall's report, three of the five dogs were schnauzers.⁹ Miniature schnauzers, German shepherd dogs, and Labrador retrievers appeared to be over represented in the authors' study, but numbers were not compared with hospital populations. Fatty acid intake is also known to vary substantially with diet. Dietary intake was not controlled in any of these studies. This may also have contributed to varying results. It is unlikely that the vitamins A, D, and E present in one of the supplements contributed to the effects of fatty acid supplementation. None of the dogs in Bergvall's report showed recurrence of clinical signs when switched to a vitamin-free supplement.⁹ Two of the three fatty acid preparations used in the authors' study contained vitamin E. All dogs with a poor response to fatty acids received supplements containing vitamin E. Products 1 and 3 contained a much higher amount of omega-3 fatty acids and a much lower amount of omega-6 fatty acids than the other fatty acid supplementations, but there did not seem to be a difference in response between products in this study, suggesting that the type of fatty acid supplementation was not critical to treatment outcome.

Tetracycline/Doxycycline and Niacinamide

Tetracycline and niacinamide have been reported to be effective in the treatment of immune-mediated disease in humans and dogs. Tetracycline alone¹⁴ or in combination with niacinamide¹⁵ has been reported to be an effective treatment for bullous pemphigoid and cicatricial pemphigoid in humans. This drug combination has been reported as a well-tolerated treatment option for immune-mediated canine skin disorders, such as discoid lupus erythematosus,¹⁶ sterile pyogranulomatous disease,¹⁷ and pemphigus foliaceus.¹⁶ Recently, it has been mentioned as a useful treatment for canine lupoid onychodystrophy.^{2,6} Doxycycline is a semisynthetic tetracycline that is well absorbed when given with or without food, with a half-life of approximately 12 hours in the dog.¹⁸ Thus, it may conveniently be given *q* 12 or 24 hours compared to the *q* 8 hours administration recommended for tetracycline. Doxycycline also affects the immune system.¹⁹ Responses to tetracycline or doxycycline and niacinamide were excellent or good in almost half of the patients treated. These success rates are comparable to the ones reported by Auxilia *et al.*, wherein two of four dogs showed a good response, one showed a partial response, and one showed a poor response.⁶ Typically, tapering of tetracycline and niacinamide to *q* 12 hours or even *q* 24 hours administration was possible in dogs that were treated long term with this combination of drugs in the authors' study. In case no. 25, however, clinical signs resolved on *q* 8 hours administration, only to recur when the drugs were reduced to *q* 12 hours. This dog improved again once the frequency of administration was increased to *q* 8 hours. Based on the findings of this study, both doxycycline and tetracycline in combination with niacinamide are useful combinations in the treatment of canine lupoid onychodystrophy. The above data would suggest that tetracycline and doxycycline are relatively equipotent in treating lupoid onychodystrophy. However, there is one anecdotal report of a dog with lupoid onychodystrophy whose initial treatment with tetracycline and niacinamide led to a good response, but clinical signs recurred with subsequent substitution of doxycycline administered once daily for the tetracycline three times daily. Once the patient was administered tetracycline and niacinamide again, clinical signs subsided.^P Almost all dogs were treated with a combination of tetracycline/doxycycline and niacinamide, and the authors were unable to ascertain the contribution of the individual drugs to the benefits observed.

Pentoxifylline

Pentoxifylline is a methylxanthine derivative with hemorrheological properties.²⁰ It is also an immune-modulator which decreases endothelial leukocyte adhesion and neutrophil degranulation, inhibits T- and B-lymphocyte activation, decreases natural killer cell activity in humans,²¹ and prevents contact dermatitis in humans²² and dogs.²³ Pentoxifylline was administered to five dogs that failed treatment with tetracycline and niacinamide, with or without fatty acids. The response was excellent in two dogs

(case nos. 8, 13), good in one dog (case no. 19), and poor in two dogs (case nos. 10, 18). A sixth dog was treated with azathioprine and pentoxifylline for 1 month (case no. 29) and was subsequently maintained on exclusive pentoxifylline therapy with a good response. Thus, pentoxifylline is a useful therapeutic agent in some patients with lupoid onychodystrophy. One of the dogs with an excellent response (case no. 13) had shown spontaneous remission 6 months prior to treatment after fatty acids, doxycycline, and niacinamide were discontinued because of a partial response only. In light of the previous spontaneous remission, however, it is unclear how much of the improvement could be attributed to pentoxifylline therapy.

Prednisolone

Prednisolone has significant antiinflammatory and immunosuppressive activity and is used for the therapy of many immune-mediated skin diseases in veterinary medicine.²⁴ Prednisolone was used in five dogs. Four of these responded well to this treatment (case nos. 11, 18, 28, 30). One dog (case no. 11) responded excellently to prednisolone in combination with allergen-specific immunotherapy,⁹ but died 6 months later from acute pancreatitis. One dog (case no. 14) did not improve further after prednisolone was added to doxycycline and niacinamide therapy. Adverse effects led to cessation of these drugs in two of the dogs (case nos. 14, 28). In one of these dogs (case no. 14), prednisolone was part of a multidrug protocol, and it is unclear which drug specifically was responsible for the adverse effects observed. Although prednisolone is an effective drug for the treatment of canine lupoid onychodystrophy, based on these findings as well as other reports,^{5,6} the common and potentially severe adverse effects suggest that other drugs may be better initial options.

Other Drugs

Clofazimine is a rhimophenazine dye with both antiinflammatory and antimicrobial activity. It scavenges hypochlorous acid, reduces the chlorination of proteins by neutrophils, inhibits mitogen-induced stimulation of mononuclear cells, and stabilizes lysosomal membranes in macrophages.²⁵ Clofazimine has been reported effective in the treatment of discoid lupus erythematosus in humans.²⁶ It was used in one dog (case no. 10) that did not improve on doxycycline, niacinamide, pentoxifylline, and an elimination diet. Clinical signs resolved, and the dog was kept in remission for 6 months before recurrence of claw disease was noted in the spring in conjunction with cutaneous signs of atopic dermatitis. It was not clear whether initial improvement was due to the clofazimine administration or was a result of spontaneous remission, or whether the claw disease was related to the atopic dermatitis.

Azathioprine is a purine antagonist used for the treatment of immune-mediated skin disease. It was administered to one dog (case no. 29) in combination with pentoxifylline; this dog responded well and was subsequently maintained solely on pentoxifylline.

Onychectomy is a more radical treatment of onychodystrophies that reportedly resolves clinical signs reliably,¹² but due to successful medical management or reluctance of owners to pursue this option, none of the dogs in this study underwent this procedure.

Concurrent Diseases

A major problem in evaluating the efficacy of drug therapy for lupoid onychodystrophy relates to the unpredictable course of clinical signs. In an earlier study, it was postulated that lupoid onychodystrophy is a syndrome caused by a variety of diseases.⁷ Although most cases are thought to be immune-mediated, food adverse reactions and bacterial infections were also incriminated.⁷ In the authors' study, 12 of 30 dogs had concurrent documented diseases, but their relationship to lupoid onychodystrophy remains unclear. It seems unlikely that orthopedic problems such as hip dysplasia and osteoarthritis of one single joint would have any correlation with claw disease affecting all feet. Similarly, the dog with generalized demodicosis was successfully treated and in remission for years before onset of claw disease. Thyroid evaluation has been recommended in the diagnostic evaluation of dogs with claw disease.² To the authors' knowledge, no clear cause-effect relationship between hypothyroidism and claw disease has been reported to date in a scientific report. The hypothyroid dogs in this report were diagnosed long before the onset of claw disease and were on maintenance hormone replacement therapy with adequate post-pill T₄ values and no other clinical signs. However, 17% of the patients in this study had hypothyroidism confirmed by thyroid assays, adequate response to T₄ supplementation, and post-pill T₄ concentrations in the upper reference range. This is much higher than would be expected in the general population. The most common cause for primary thyroiditis in dogs is immune-mediated lymphocytic thyroiditis, and there may be a genetic predilection for the development of concurrent diseases. Another possibility may be the binding of antithyroid antibodies to claw matrix proteins.

Food adverse reaction has been reported as a cause of lupoid onychodystrophy.⁷ One dog (case no. 4) in this study responded to fatty acid supplementation and an elimination diet. Clinical signs recurred upon rechallenge, and the dog was subsequently maintained in remission for 6 months without fatty acids on a different preservative-free dog food. Traumatizing one claw then apparently triggered a relapse of clinical signs. The second recurrence may have been due to the development of a new dietary hypersensitivity or may have been totally unrelated to the dog's diet. The second dog (case no. 5), which apparently responded to an elimination diet, only partially responded to therapy with doxycycline and niacinamide and subsequently went into complete remission on the diet and niacinamide alone. After 6 months of therapy, niacinamide and the diet were discontinued, and clinical signs did not recur until 8 weeks later. Based on dietary challenge studies of dogs with cutaneous signs from adverse food reactions,²⁷ recurrence of

claw disease may have been expected sooner. In addition, niacinamide was discontinued at the same time. Thus, it is unclear if this dog relapsed due to a food adverse reaction, the cessation of niacinamide therapy, or another unrelated cause. The dog was subsequently lost to follow-up.

Atopic dermatitis was diagnosed in four dogs. One of these dogs (case no. 9) had an initial excellent response to a combination of doxycycline and niacinamide, was maintained on fatty acid supplementation, and developed clinical signs of atopic dermatitis without claw involvement 18 months later. Another dog (case no. 10) initially showed only signs of claw disease and failed to respond to an elimination diet, doxycycline, niacinamide, and pentoxifylline; but she went into complete remission with clofazimine only to relapse 6 months later in the spring with concurrent cutaneous signs of atopic dermatitis. One dog (case no. 11) developed cutaneous signs of atopic dermatitis while on doxycycline, niacinamide, and an elimination diet for the claw disease. Diagnosis was confirmed by exclusion of other differential diagnoses. An intradermal test showed positive reactions to a number of allergens. This dog's claw disease and cutaneous signs resolved completely on a combination of prednisolone and allergen-specific immunotherapy. While the prednisolone was being tapered, the dog died of acute pancreatitis. One dog (case no. 25) developed claw disease and atopic dermatitis simultaneously. Treatment of the latter involved antihistamines; there was improvement but not complete resolution of atopic signs and no apparent improvement of the claw disease. It is possible that allergen-specific T lymphocytes also recognize a cross-reactive epitope expressed in the claw matrix. Exacerbation of atopy could, therefore, result in the development of clinical signs. However, no direct evidence to support this hypothesis is available from this study.

In one dog (case no. 3), the clinical signs completely subsided with antibiotic therapy. Six months after cessation of treatment, flea allergy dermatitis developed simultaneously with recurrence of claw disease. All clinical signs resolved with flea control and fatty acid supplementation, and the dog was kept in remission with both treatments. Again, a relationship between flea allergy dermatitis and claw disease cannot be established based on this evidence. The initial improvement on antibiotics may have been due to the successful treatment of secondary infection. Spontaneous remission unrelated to drug administration cannot be ruled out. The above findings suggest that lupoid onychodystrophy may be a reaction pattern to a variety of insults.

Clinical Course of Lupoid Onychodystrophy

Spontaneous remission of lupoid onychodystrophy has not been addressed in previous publications. Scott *et al.* noted that when left untreated, lupoid onychodystrophy is a chronic, recurrent problem.⁵ In five dogs of the authors' study, the following initial treatments resulted in excellent or good responses: doxycycline, niacinamide, and elimination diet (case no. 7); tetracycline, niacinamide, and fatty acids (case no. 20); cephalexin (case no. 24); clavulanic

acid/amoxicillin (case no. 1); and prednisolone and fatty acids (case no. 30). In all dogs, treatment was discontinued completely with no relapse observed during a 2-year follow-up period. Thus, improvement may have been due to the administered medications or spontaneous remission of the underlying disease. Another possibility would be that a temporary insult caused the classic clinical and histopathological changes of lupoid onychodystrophy. In one dog (case no. 13), treatment first with fatty acid supplementation and later with doxycycline and niacinamide only resulted in partial improvement; but clinical signs completely resolved once all medications were discontinued, only to recur 6 months later in the next summer. The potential for multiple underlying etiologies and an uncertain natural course for lupoid onychodystrophy make the assessment of various therapies difficult. It is interesting that almost half of the dogs with excellent responses stayed in complete remission after therapy was discontinued. It may be prudent to recommend that in dogs having an excellent response to therapy, the medications be tapered and possibly discontinued to identify patients that do not require maintenance therapy.

Conclusion

Lupoid onychodystrophy is a syndrome that may be caused by a number of factors, and further studies evaluating pathogenesis and therapy are clearly needed. Based on the authors' experience, the diagnostic approach for dogs with suspected lupoid onychodystrophy should include a biopsy to rule out diseases such as pemphigus foliaceus, cytopathology of the claw fold, and, if indicated clinically or cytopathologically, an antibacterial trial therapy (to evaluate how much of the clinical signs are from bacterial infection) as well as a food elimination diet. If neither antibiotic therapy nor diet lead to remission, the authors recommend initial trial therapy with tetracycline and niacinamide *q* 8 hours for a period of 8 weeks. With good or excellent response, treatment may be tapered to *q* 12 hours or switched to doxycycline and niacinamide *q* 24 hours. If there is insufficient response, pentoxifylline or fatty acid supplementation may be used for 8 weeks. In dogs with nonresponsive disease or owners requesting immediate results, treatment with immunosuppressive drugs, such as glucocorticoids, will be the treatment of choice; however, owners need to be made aware of the possible adverse effects with this therapy. In any dog with an excellent response, tapering medications to determine the need for maintenance therapy is recommended. Veterinarians must be aware that spontaneous remissions and waxing and waning clinical signs for as-of-yet unknown reasons may make evaluation of drug efficacy difficult.

^a Emily Walder, 626 Venice Boulevard, Venice, CA

^b Tetracycline hydrochloride; Barr Laboratories, Pomona, NY

^c Niacinamide; Major Pharmaceuticals, Livonia, MI

^d Doxycycline hydrochloride, Vibravet; Pfizer, West Ryde, New South Wales, Australia

^e Omega 3 fatty acids; Biochemical Veterinary Research, Mittagong, New South Wales, Australia

^f Derm Caps; DVM Pharmaceuticals, Miami, FL

^g 3VCaps; DVM Pharmaceuticals, Miami, FL

^h Pentoxifylline, Trental; Aventis, Lane Cove, New South Wales, Australia

ⁱ Clofazimine, Lamprene; Novartis, Ryde, New South Wales, Australia

^j Prednisolone; Vet-A-Mix, Shenandoah, IA

^k Azathioprine; Roxane Laboratories, Columbus, OH

^l Clavulanic acid/amoxicillin, Clavulox; Pfizer, West Ryde, New South Wales, Australia

^m Cephalexin; Teva Pharmaceuticals, Sellersville, PA

ⁿ Efa-Vet 1; Efamol, Guildford, United Kingdom

^o Efa-Vet Regular; Efamol, Guildford, United Kingdom

^p Personal communication, Linda Messinger, 2000; Veterinary Referral Center of Colorado, Englewood, CO

^q Allergen extract formulated from individual allergens; Greer Laboratories, NC

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References

- McEwan NA. Nail disease in small animals. *Vet Derm News* 1987;11:18-20.
- Rosychuk RAW. Diseases of the claw and claw fold. In: Bonagura DJ, ed. *Kirk's current veterinary therapy XII*. Philadelphia: WB Saunders, 1995:641-647.
- Foil CS, Conroy J. Dermatoses of claws, nails and hoof. In: Von Tscharner C, Halliwell REW, eds. *Advances in veterinary dermatology*. Philadelphia: Baillière Tindall, 1990:420-422.
- Scott DW, Miller WH. Disorders of the claw and claw bed in dogs. *Comp Cont Ed* 1992;14:1448-1457.
- Scott DW, Rouselle S, Miller WH. Symmetrical lupoid onychodystrophy in dogs: a retrospective analysis of 18 cases (1989-1993). *J Am Anim Hosp Assoc* 1995;31:194-200.
- Auxilia ST, Hill PB, Thoday KL. Canine symmetrical lupoid onychodystrophy: a retrospective study with particular reference to management. *J Sm Anim Pract* 2001;42:82-87.
- Mueller RS, Friend S, Shipstone MA, Burton G. Diagnosis of canine claw disease: a prospective study of 24 dogs. *Vet Derm* 2000;11:133-141.
- Harvey RG, Markwell PJ. The mineral composition of nails in normal dogs and comparison with shed nails in canine idiopathic onychomadesis. *Vet Derm* 1996;7:29-34.
- Bergvall K. Treatment of symmetrical onychomadesis and onychodystrophy in five dogs with omega-3 and omega-6 fatty acids. *Vet Derm* 1998;9:263-268.
- Verde MT, Basurco A. Symmetrical lupoid onychodystrophy in a crossbred pointer dog: long-term observations. *Vet Rec* 2000;146:376-378.
- Mueller RS, Olivry T. Onychobiopsy without onychectomy: description of a new biopsy technique for canine claws. *Vet Derm* 1999;10:55-59.
- Boord MJ, Griffin CE, Rosenkrantz WS. Onychectomy as a therapy for symmetric claw and claw fold disease in the dog. *J Am Anim Hosp Assoc* 1997;33:131-138.
- Mueller RS, Sterner-Kock A, Stannard AA. Microanatomy of the canine claw. *Vet Derm* 1993;4:5-11.

References (cont'd)

14. Brakman M, Westerhof W. Treatment of generalized bullous pemphigoid with oral tetracycline. *J Am Acad Dermatol* 1994;30:145-146.
 15. Fivenson DP, Breneman DL, Rosen GB, Hersh CS, Cardone S, Mutasim D. Nicotinamide and tetracycline therapy of bullous pemphigoid. *Arch Dermatol* 1994;130:753-758.
 16. White SD, Rosychuk RAW, Reinke SI, Paradis M. Use of tetracycline and niacinamide for treatment of autoimmune skin disease in 31 dogs. *J Am Vet Med Assoc* 1992;200:1497-1500.
 17. Rothstein E, Scott DW, Riis RC. Tetracycline and niacinamide for the treatment of sterile pyogranuloma/granuloma syndrome in a dog. *J Am Anim Hosp Assoc* 1997;33:540-543.
 18. Plumb DC. *Veterinary drug handbook*. White Bear Lake: PharmaVet Publishing, 1991:492-496.
 19. Bellahsene A, Forsgren A. Effect of doxycycline on immune response in mice. *Infect Immun* 1985;48:556-559.
 20. Marks SL, Merchant S, Foil C. Pentoxifylline: wonderdrug? *J Am Anim Hosp Assoc* 2001;37:218-219.
 21. Bruynzeel I, Stoof TJ, Willemze R. Pentoxifylline and skin inflammation. *Clin Exp Derm* 1998;23:168-172.
 22. Schwarz T, Schwarz A, Crone C. Pentoxifylline suppresses allergic patch test reactions in humans. *Arch Derm* 1993;129:513-514.
 23. Marsella R, Kunkle GA, Lewis DT. Use of pentoxifylline in the treatment of allergic contact reactions to plants of the *Commelinaceae* family in dogs. *Vet Derm* 1997;8:121-126.
 24. Calvert CA, Cornelius LM. The most common indications for using steroid hormones in veterinary practice. *Vet Med* 1990;8:826-845.
 25. Arbiser JL, Moschella SL. Clofazimine: a review of its medical uses and mechanisms of action. *J Am Acad Derm* 1995;32:241-246.
 26. Mackey JP, Barnes J. Clofazimine in the treatment of discoid lupus erythematosus. *Brit J Derm* 1974;91:93-96.
 27. Harvey RG. Food allergy and dietary intolerance in dogs: a report of 25 cases. *J Sm Anim Pract* 1993;34:175-179.
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