

Pemphigus Foliaceus in 91 Dogs

A retrospective study of 91 dogs with pemphigus foliaceus was performed. Clinical signs of the disease included crusts (n=79), pustules (n=36), and alopecia (n=33). Lesions were most common on the trunk (n=53), inner pinnae (n=46), face (n=37), and foot pads (n=32). Cytological evaluation revealed acantholytic keratinocytes in 37 of 48 dogs. Results of combination treatment with prednisolone and azathioprine were comparable to results with prednisolone therapy alone. More than half of the dogs achieved remission with appropriate therapy, and another 25% significantly improved. **J Am Anim Hosp Assoc 2006;42:189-196.**

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Introduction

Pemphigus foliaceus is the most common form of the pemphigus complex in small animals and possibly the most common of all immune-mediated dermatoses in the dog.¹⁻³ Although canine pemphigus foliaceus has been recognized since 1977, information regarding the disease has been mostly limited to case reports.⁴⁻⁷ Few studies have been performed to further characterize the disease and to evaluate the outcome of treatment.^{8,9} Pemphigus may occur spontaneously, may be related to drug administration, or be associated with neoplastic skin disease.¹⁰⁻¹² All forms of pemphigus share the presence of autoantibodies directed against keratinocyte desmosomal proteins, resulting in a loss of adhesions between keratinocytes.¹³ In pemphigus foliaceus, this loss of adhesion leads to intraspinal or subcorneal pustule or vesicle formation. These primary lesions are transient in nature and ultimately result in the formation of crusts.¹⁴

Definitive diagnosis of pemphigus foliaceus is based on histological features—the most important of which are pustules or vesicles with marked acantholysis of keratinocytes.¹⁵⁻¹⁷ Neutrophils or eosinophils are typically present in large numbers within pustules.¹⁷ The mainstay of pemphigus foliaceus treatment is immunosuppressive therapy.^{1,14} In a recent study, a poor prognosis in dogs was reported, with only 53% of treated cases surviving >1 year after initiation of treatment.⁹ The purposes of this study were to evaluate the clinical features, diagnostic modalities, and treatment options for pemphigus foliaceus and to determine whether they have any predictive value on the outcome of the disease in a large number of dogs.

Materials and Methods

Medical records of dogs evaluated for pemphigus foliaceus between September 1994 and November 2002 at three referral institutions, two specialty clinics (i.e., Animal Skin and Allergy Clinic in Melbourne,

Australia [n=25] and Dermatology for Animals in Campbell, California [n=31]), and a university veterinary teaching hospital (i.e., Colorado State University [n=35]) were reviewed. Dogs were included in the study if a definitive diagnosis of pemphigus foliaceus was made by histopathological findings diagnostic for or highly suggestive of pemphigus foliaceus in association with classical clinical signs, supportive cytology, and response to therapy. Breed, gender, and age of dogs, previous medications, and the presence of pruritus at the time of disease onset were recorded. Rate of onset of clinical signs was categorized as rapid (i.e., clinical signs developed within a period of <1 month) or slow (i.e., clinical signs developed within a period >1 month). Lesions were categorized as pustules (superficial lesions filled with pus), crusts (adherens of dried exudates, serum, or pus to the surface of the skin), scales (accumulation of loose fragments on the surface of the skin), and/or alopecia (loss of hair), and the specific locations of the lesions were noted where possible. If results of surface cytology were available, they were also recorded.

Medications used were recorded, as well as the duration of therapy until initial improvement and complete remission. Final treatment outcomes were recorded as remission, euthanasia, or improvement. Improvement was defined as one or more small areas of scaling, crusting, or erythema without the need for changes in therapy. If a dog was euthanized, the reason for the euthanasia was determined whenever possible. The follow-up period was determined for each animal.

A Fisher's exact test was used to determine if there was a significant difference in outcomes between therapy with prednisolone alone or in combination with azathioprine, and any adverse effects. The times to remission with prednisolone only versus prednisolone and azathioprine were compared with a two-tailed, unpaired *t*-test.^a A *P* value of <0.05 was considered significant.

Results

Signalment and History

Ninety-one dogs were included in the study. The average age at onset of clinical signs was 6 years (median age 6.5 years; range 0.5 to 16 years). No gender predisposition was identified. There were 46 males (34 castrated) and 45 females (41 spayed). Affected breeds with more than one dog are listed in Table 1. Because cases came from three different areas and institutions, breed predispositions were not identified. In 29 dogs, the course of the disease was determined to be rapid. The course was considered slow in 22 dogs and could not be determined from medical records for 40 dogs. The average time from onset of disease to presentation to a specialist was 17.2 weeks (range 3 days to 2 years).

Forty-four animals received medications before referral. In 18 of these dogs, antibiotics and/or glucocorticoids at various dosages were given with partial or no response. Prior to onset of clinical signs, 26 dogs had also received drugs for other reasons. Thirteen animals received antibiotics, and four were given L-thyroxine supplementation. Heartworm preventions with ivermectin or milbemycin

Table 1

Most Common Dog Breeds Diagnosed With Pemphigus Foliaceus

Breed	No. of Dogs
Mixed-breed dog	40
Akita	10
Labrador retriever	9
Cocker spaniel	5
German shepherd dog	3
Chinese shar pei	3
Chow chow	2
Boston terrier	2
Shih tzu	2
Australian cattle dog	2

oxime were administered in six dogs, and one animal each received fipronil, lufenuron, and mexiletine. In three animals, the disease onset was acute and occurred shortly after administration of fipronil, cephalixin, and amoxicillin, indicating a possible drug reaction. However, rechallenge of the animal to verify a drug reaction was not performed.

Clinical Findings

In 62 dogs, it was possible to verify from the records the degree of pruritus at disease onset. Forty-eight dogs showed no pruritus; in four (6%) dogs, there was severe pruritus; in seven (11%) animals, the pruritus was moderate; and in three (5%) it was mild. Crusts were the most common lesions noted (n=79). Pustules were described in 36 dogs; alopecia occurred in 33 dogs; and scaling affected 27 dogs. The locations of lesions are listed in Table 2. Lesions limited to the face were noted in 15 dogs, and exclusive foot pad involvement occurred in three animals. Focal disease affecting only the face and/or feet occurred in 31 dogs. In 60 dogs, pemphigus foliaceus was generalized. Of the dogs with nonoral mucous membrane lesions (n=2), one dog had erosions of the prepuce, and one had erosions of the vulva.

Of the 48 dogs in which results of skin surface or aspiration cytology were recorded, individual acantholytic cells were present in 37 dogs, high numbers of neutrophils were seen in 35 dogs, and numerous eosinophils were noted in eight cases. In the cytological preparations from two dogs, clusters of acantholytic cells were present. Intracellular bacteria were seen cytologically in nine animals. Extracellular cocci were noted in an additional 23 dogs. Histopathology was either strongly suggestive of or diagnostic for pemphigus foliaceus in all dogs, with acantholytic cells present in intraepithelial pustules and/or serocellular crusting.

Table 2**Locations of Dermatological Lesions in Dogs With Pemphigus Foliaceus**

Site	No. of Dogs (%)
Trunk	53 (58%)
Inner pinnae	46 (51%)
Dorsal muzzle	37 (41%)
Foot pads	32 (35%)
Periocular area	26 (29%)
Outer pinnae	23 (25%)
Planum nasale	23 (25%)
Interdigital area	10 (11%)
Lips	9 (10%)
Perianal area	5 (5%)
Mucous membranes	2 (2%)

Treatments and Outcomes

Of the 88 dogs treated for the disease, 46 went into remission with treatment, 31 improved greatly with treatment but still had mild focal lesions, and 11 were euthanized. Four dogs were euthanized because they had severe disease that did not respond to treatment. Two dogs were euthanized because of adverse effects from medications, and four were euthanized for other diseases or unrelated causes. In one dog, the reason for euthanasia was unknown.

The initial treatment for most dogs was glucocorticoids alone or a combination of glucocorticoids and azathioprine [Table 3]. Owners of three dogs refused treatment and were lost to follow-up. For the dogs achieving complete resolution with exclusively glucocorticoids, the average time to remission was 7 months (range 1.5 to 12 months). Sixteen of the 39 dogs initially treated with glucocorticoids received prednisolone long term (15 went into complete remission with this treatment). In 13 dogs, other drugs were added or replaced prednisolone. Adverse effects from prednisolone therapy included signs of iatrogenic hyperadrenocorticism, such as lethargy and polyuria/polydipsia, in 10 of 39 animals. One dog developed anorexia in addition to the polyuria and polydipsia, one dog lost weight, and one dog developed anorexia and pain. Of the 39 dogs treated with glucocorticoids only [Figure 1], five were euthanized 1 month to 4.25 years after therapy was initiated. Euthanasia for three dogs was related to other medical problems (i.e., an undiagnosed kidney mass, hematochezia, and collapse). One dog was euthanized because of its advanced age, and the reason for euthanasia in one dog was unknown.

The average time to remission for dogs that received a combination of prednisolone and azathioprine (n=33) was

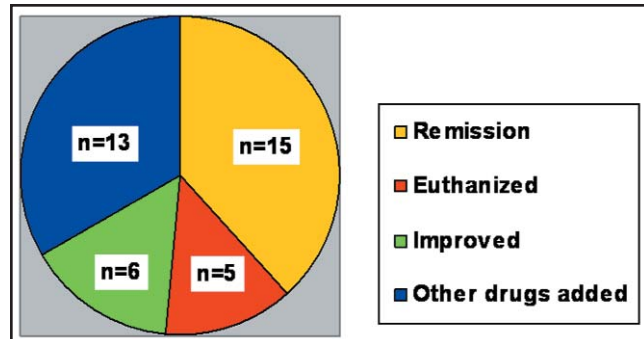


Figure 1—Treatment outcomes for 39 dogs with pemphigus foliaceus that were treated exclusively with glucocorticoid therapy.

11.7 months (range 2 to 29 months). There was no statistically significant difference between time to remission for dogs treated with glucocorticoids alone and those treated with azathioprine and prednisolone ($P=0.089$). Five dogs treated with azathioprine and prednisolone had received prednisolone from the referring veterinarian with unsatisfactory results, and two of these dogs went into remission with combination therapy. Over the long term, 17 of the 33 dogs continued to receive a combination of glucocorticoids and azathioprine, two received only azathioprine, two received only prednisolone, and two received a combination of prednisolone and aurothioglucose. For four dogs, other drugs replaced or were added to prednisolone and azathioprine. Adverse effects seen with the combination therapy of prednisolone and azathioprine included iatrogenic hyperadrenocorticism (n=13), hepatotoxicity (n=3), anemia (n=1), demodicosis (n=1), and gastrointestinal bleeding (n=1). Thus, adverse effects occurred more often with this combination than with prednisolone alone ($P=0.05$). Of the 33 dogs treated initially with a combination of prednisolone and azathioprine [Figure 2], three were euthanized 3 months to 2 years after diagnosis because of the pemphigus foliaceus. One dog suddenly died of unknown cause.

Eight dogs were initially treated with tetracycline and niacinamide. Pemphigus foliaceus was controlled in three of these dogs. In two dogs, prednisolone was added to the

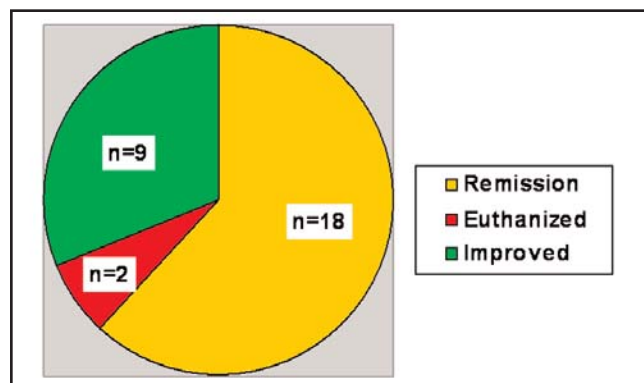


Figure 2—Treatment outcomes for 33 dogs with pemphigus foliaceus that were treated with a combination of azathioprine and prednisolone.

Table 3**Drugs Used Initially for the Treatment of Pemphigus Foliaceus in 88 Dogs**

Drugs	No. of Dogs
Prednisone/prednisolone (1.5 to 5 mg/kg/d PO*)	38
Methylprednisolone (1.3 mg/kg/d PO)	1
Prednisone/prednisolone (1 to 4.5 mg/kg/d PO) and azathioprine (1.5 to 2.6 mg/kg/d PO)	28
Triamcinolone (0.1 mg/kg/d PO) and azathioprine (1 to 1.8 mg/kg/d PO)	2
Dexamethasone (0.2 mg/kg/d PO) and azathioprine (1.8 mg/kg/d PO)	1
Methylprednisolone (0.7 to 1.6 mg/kg/d PO) and azathioprine (0.7 to 2.6 mg/kg/d PO)	2
Tetracycline and niacinamide†	6
Prednisolone (0.5 to 1 mg/kg/d PO), tetracycline, and niacinamide†	2
Azathioprine (2 mg/kg/d PO)	1
Prednisolone (0.7 mg/kg/d PO), doxycycline (5 mg/kg/d PO), and niacinamide†	1
Essential fatty acids‡	1
Prednisolone (3 mg/kg/d PO), azathioprine (1.5 mg/kg/d PO), and doxycycline (5 mg/kg/d PO)	1
Prednisolone, azathioprine, and fatty acids	1
Pimecrolimus topically	1
Prednisolone (0.7 mg/kg/d PO), doxycycline (5.2 mg/kg/d PO)	1
Triamcinolone (0.1 mg/kg/d PO), tetracycline†	1

* PO=per os

† Tetracycline and niacinamide were each given at 250 mg PO q 8 h in dogs <15 kg and at 500 mg PO q 8 h in dogs >15 kg.

‡ Essential fatty acid supplementation was administered according to the manufacturers' recommendations.

therapy, and in one dog this regimen resulted in complete remission. One dog was euthanized for lymphoma. Two dogs did not achieve remission. Adverse effects were not observed with this therapy.

Twenty-nine dogs had a rapid onset of disease and were referred within 1 month. Treatment outcomes for these dogs are illustrated in Figure 3. Two of the dogs were euthanized for lack of response to treatment. Onset of disease was gradual in 22 dogs, and the outcomes are depicted in Figure 4. Four of these dogs were euthanized—one from a lack of response, two from collapse, and one from an unrelated cause. Two dogs died suddenly of unknown causes. Control of the pemphigus foliaceus did not differ between the two groups ($P=0.16$).

Treatment outcomes for 31 dogs with localized disease are shown in Figure 5. In this group, three dogs were euthanized—one from severe pemphigus, one because of the adverse effects of therapy, and one from collapse. One dog died from unknown cause. The outcomes of 59 dogs with generalized disease are presented in Figure 6. In this group, three dogs were euthanized because of the severity of the pemphigus foliaceus. Four other dogs were euthanized for reasons other than pemphigus (i.e., lymphoma, old age, hematochezia, unknown cause). There were no significant differences in remission rates or death rates between dogs with localized disease and dogs with generalized disease ($P=0.66$ and $P=1.0$, respectively).

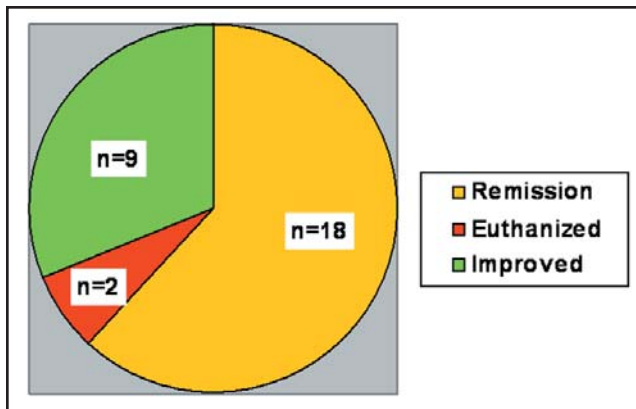


Figure 3—Treatment outcomes for 29 dogs with pemphigus foliaceus that had a rapid onset (i.e., <1 month) of clinical signs.

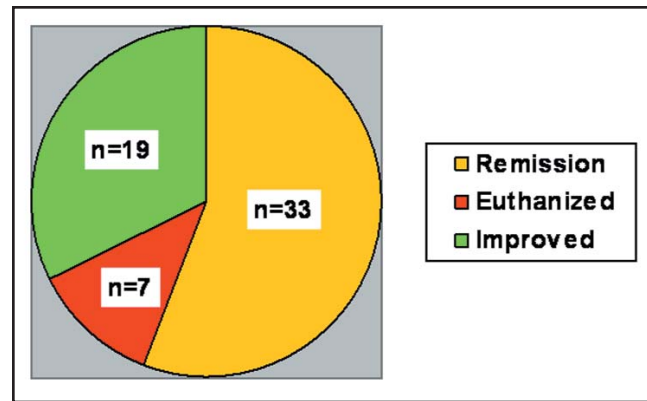


Figure 6—Treatment outcomes for 59 dogs with generalized pemphigus foliaceus.

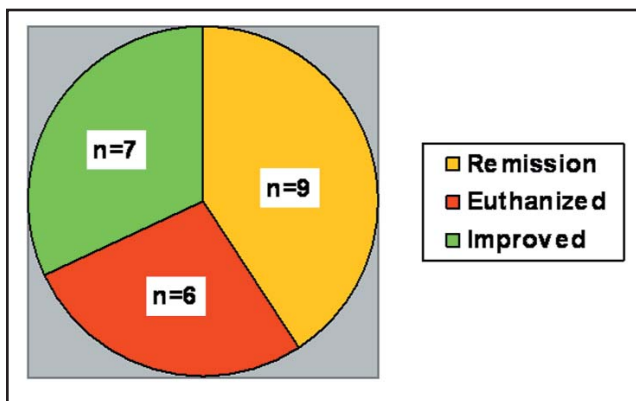


Figure 4—Treatment outcomes for 22 dogs with pemphigus foliaceus that had a gradual onset (i.e., >1 month) of clinical signs.

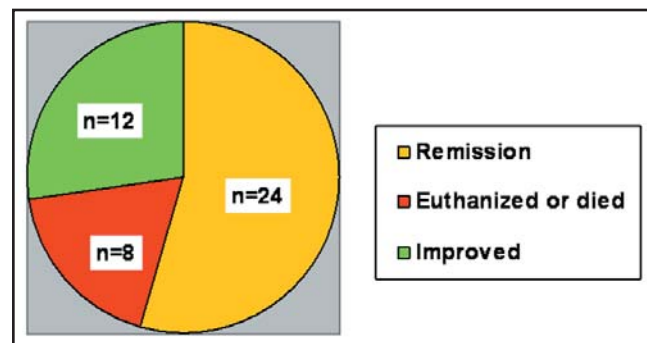


Figure 7—Treatment outcomes for 44 dogs with pemphigus foliaceus that received antibiotics either before or with immunosuppressive therapy.

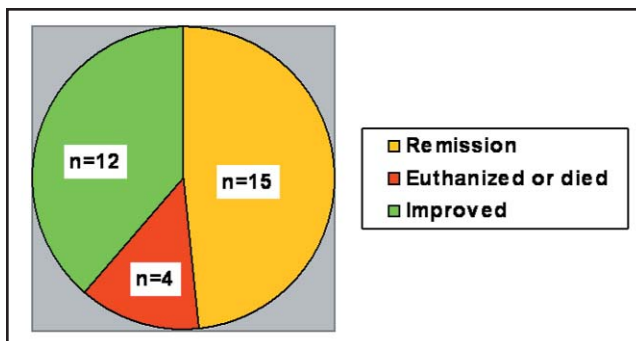


Figure 5—Treatment outcomes for 31 dogs with pemphigus foliaceus localized to the face.

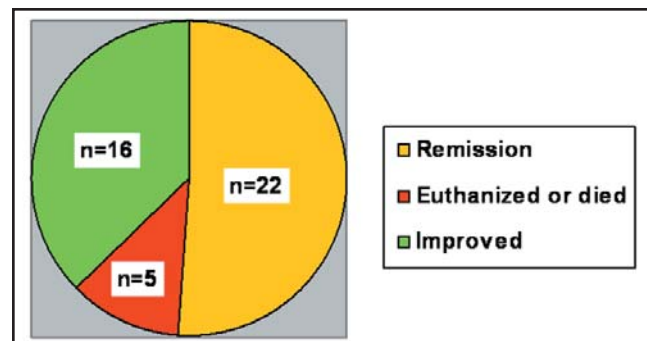


Figure 8—Treatment outcomes for 43 dogs with pemphigus foliaceus that did not receive antibacterial drugs.

A variety of drugs were used for long-term control of the pemphigus foliaceus [Table 4]. Two of the dogs were completely tapered off medications and had no recurrence of clinical signs. Interestingly, one of these dogs had received amoxicillin immediately prior to onset of the disease. Six dogs were lost to follow-up.

For the 91 dogs evaluated in this study, the average follow-up time was 1.5 years (median 1.1 years; range 1 month to 7.9 years). Average time to improvement was 6 weeks.

When achieved, average time to remission was 9.3 months (median 6.5 months, range 1 to 36 months). Forty-three dogs were followed for <12 months, and 12 of these dogs were euthanized (eight for other diseases and four for lack of response or for adverse effects of treatment for the pemphigus foliaceus). In 54 dogs, the follow-up time was >12 months. Four of these dogs were euthanized—one for unrelated cause, one for neoplastic disease, and two because of the pemphigus foliaceus. Twenty-two dogs never achieved

Table 4
Drugs That Achieved Final Control of Pemphigus Foliaceus in 80 Dogs

Drugs	No. of Dogs
Prednisolone (0.1 to 4 mg/kg/d PO*) and azathioprine (0.4 to 3 mg/kg/d PO)	24
Dexamethasone (0.09 to 0.1 mg/kg/d PO) and azathioprine (0.8 to 2 mg/kg/d PO)	2
Methylprednisolone (0.1 to 0.4 mg/kg/d PO) and azathioprine (1 to 2.2 mg/kg/d PO)	4
Triamcinolone (0.08 mg/kg/d PO) and azathioprine (1 mg/kg/d PO)	1
Prednisolone (0.1 to 4 mg/kg/d PO)	22
Methylprednisolone (0.1 mg/kg/d PO)	1
Triamcinolone (0.07 mg/kg/d PO)	1
Azathioprine (0.4 to 3 mg/kg/d PO)	9
Tetracycline† or doxycycline (3 to 18 mg/kg/d PO) and niacinamide†	8
Prednisolone (0.3 to 1.25 mg/kg/d PO) and aurothioglucose (0.07 to 0.15 mg/kg)‡	2
Essential fatty acids§ PO	2
Prednisolone (1 mg/kg/d) and cyclosporine (3 mg/kg/d PO)	1
Aurothioglucose‡ (0.15 mg/kg)	1
Methylprednisolone (0.2 mg/kg/d PO), tetracycline, and niacinamide† PO	1
Tacrolimus (0.1% topically)	1

* PO=per os

† Tetracycline and niacinamide were each given at 250 mg PO q 8 h in dogs <15 kg and at 500 mg PO q 8 h in dogs >15 kg.

‡ Aurothioglucose was given weekly or every other week as an intramuscular injection.

§ Essential fatty acid supplementation was administered according to the manufacturers' recommendations.

complete remission, and 12 of these cases were followed for <12 months.

Treatment method (i.e., prednisolone only versus prednisolone and azathioprine) had no influence on the number of dogs euthanized (12% and 13%, respectively; $P=1.0$). Similarly, the number of dogs that achieved clinical remission with only prednisolone initially (38%) was not significantly different from the number of dogs treated with azathioprine and prednisolone together (42%; $P=0.81$).

Forty-four dogs [Figure 7] were initially treated with antibiotics, and 43 dogs [Figure 8] received immunosuppressive therapy without antibiotics. There were no significant differences between dogs treated with or without

antibiotics with regard to remission (55% and 49%, respectively; $P=0.83$) or euthanasia rates (18% and 12%, respectively; $P=0.55$).

Discussion

This retrospective study of 91 dogs with pemphigus foliaceus was similar to previous reports, especially with respect to clinical signs, diagnosis, and treatments.⁴⁻⁹ Based on data from dogs in this study, prednisolone compared to prednisolone and azathioprine treatment had approximately the same impact on the rates of response and euthanasia. Additionally, the form of disease (i.e., localized versus generalized) and concurrent treatment with antibiotics had no predictive value in outcome.

Alopecia, scaling, crusting, and epidermal collarettes are the commonly reported lesions of canine pemphigus foliaceus.¹ In the study reported here, crusts were the most common clinical feature and were seen in 87% of the animals. Pustules were noted in more than one-third of the dogs. Pemphigus foliaceus can be localized or generalized, and lesions have usually been noted first on the head, particularly the dorsal aspect of the nose.⁸ In the current study, however, most dogs had a generalized distribution of lesions at presentation. Foot pad involvement has been common in pemphigus foliaceus and has been associated with lameness.¹⁹ Occasionally, the feet may be the only affected site.^{18,19} In the current study, more than one-third of the dogs had foot pad lesions, although exclusive pad involvement was rare. Involvement of mucous membranes and mucocutaneous junctions has been rare in pemphigus foliaceus.¹ In this study, nine dogs had lesions on the lips, and two showed changes of the nonoral mucous membranes. Pruritus has been reported as variable in pemphigus foliaceus, and some dogs in this study were pruritic.¹ However, many dogs had received glucocorticoids before presentation to the specialist, and in 29 dogs it was not possible to determine pruritus from the records.

Differential diagnoses for pemphigus foliaceus based on clinical findings include superficial folliculitis, dermatophytosis, demodicosis, discoid lupus erythematosus, and pemphigus erythematosus.^{1,20,21} Direct cytology can be strongly suggestive of pemphigus foliaceus, especially the cytological feature of acantholytic cells, either singly or in rafts. In the study reported here, 37 (77%) of 48 cytological specimens had acantholytic keratinocytes; thus, the presence of these cells in cytological preparations from crusted lesions should raise the index of suspicion for pemphigus. Microscopic evaluation of Tzanck preparations or impression smears is part of a routine diagnostic workup for pustular and crusty skin diseases; thus, the number of cytological samples recorded seemed very low. However, because of the retrospective nature of this study, it was unknown how many cytological samples were obtained but not recorded. Prospective studies are warranted to confirm the above findings. It must be remembered that superficial folliculitis (e.g., bacterial or caused by *Trichophyton* spp.) can occasionally result in acantholysis—most likely secondary to enzyme release from neutrophils or the organisms themselves. Therefore, acantholytic cells are not pathognomonic for pemphigus foliaceus.

Histopathologically, increased density of acantholytic cells, the presence of acantholytic rafts, and increased pustule size (with pustules spanning multiple hair follicles) are specific for pemphigus foliaceus.¹⁶ Direct immunofluorescence or immunohistochemical evaluation may support the diagnosis, but these tests are less sensitive than direct histopathological evaluation and are often prohibitive because of technical or cost factors.^{1,2} Indirect immunofluorescence staining of either circulating antibodies or circulating immune complexes is of little value in diagnosing canine pemphigus foliaceus, but it might be a valuable tool

in the future as sensitivity of these tests increases.^{2,22-24} None of the dogs in the current study underwent immune testing.

Secondary pyoderma is common in pemphigus foliaceus and may complicate the diagnosis.¹ Initial treatment with antibiotics prior to or concurrent with the onset of immunosuppressive treatment may be associated with better outcomes.⁹ However, antibiotic treatment did not influence treatment outcomes in the current study, and future prospective studies are needed to address this apparent discrepancy.

In recent studies, the initial recommended treatment for pemphigus foliaceus was oral glucocorticoids at immunosuppressive doses, which were tapered based on clinical improvement.^{1,8,14} The success rate with exclusively glucocorticoid therapy has been reported to be <50%, with a favorable response within the first 10 days of treatment being a good prognostic sign.^{1,8} The results of the study reported here concurred with these reports. Fourteen dogs responded to prednisolone therapy within the first 2 weeks, and 10 of these dogs ultimately remained on prednisolone alone to control their clinical signs. Thus, rapid response during early treatment may be a good prognostic sign.

Concurrent use of other immunosuppressive drugs, particularly azathioprine, has been advocated as the treatment of choice for pemphigus foliaceus.¹⁴ In the present study, 21 (64%) of 33 dogs initially treated with prednisolone and azathioprine showed satisfactory results. The number of dogs responding to combination therapy was not significantly higher than the number of dogs responding to glucocorticoids only. However, five of these dogs received glucocorticoid therapy prior to referral with unsatisfactory results. It is possible that owners chose combination therapy more often when pemphigus foliaceus was severe or previous drug therapy had failed, masking a better success rate with the drug combination. Prospective, blinded studies with random allocation of dogs to different treatment protocols are needed to clarify this further. The average time to remission was longer for dogs treated with combination therapy than for dogs exclusively treated with prednisolone (11 versus 7 months). This longer time to remission may have arisen because combination therapy was used in the more severely affected dogs.

Adverse effects of combination therapy were largely attributed to iatrogenic hyperadrenocorticism and were seen more often when prednisolone was used alone. A reason for this finding was not identified. In addition, hepatotoxicity was seen in three dogs. All liver enzymes were dramatically elevated shortly after initiation of therapy and were thought to be secondary to azathioprine administration. Anemia was observed in one dog and was also attributed to bone marrow suppression from azathioprine. These adverse effects emphasize the need for appropriate regular monitoring with complete blood counts and biochemical panels in all dogs receiving azathioprine.¹⁴

Cyclophosphamide, aurothioglucose, and cyclosporine, niacinamide, and tetracycline as adjunctive or single therapies have all been reported as treatments for canine pemphi-

gus foliaceus.¹⁴ Cyclosporine used as a single therapeutic agent had limited efficacy in one study; however, the number of dogs was small, and different formulations of cyclosporine exist today.²⁵ More studies are needed to evaluate this drug for the treatment of canine pemphigus foliaceus. Chrysotherapy with aurothioglucose alone or in conjunction with corticosteroid therapy may be effective in controlling some cases of canine pemphigus foliaceus.⁸ In one study, the following treatments were used to maintain remission of pemphigus foliaceus: chlorambucil; aurothioglucose; glucocorticoids with aurothioglucose; tetracycline or doxycycline with niacinamide; prednisolone; fatty acid supplementation; and tacrolimus.⁸ Animal numbers in these treatment groups were too small to perform statistical analysis.⁸ None of the dogs treated with these therapies showed any adverse effects.⁸ Further studies are needed to evaluate particular treatments (i.e., tetracycline in combination with niacinamide) with promising results and rare adverse effects.

Treatment-induced remission of canine pemphigus foliaceus after cessation of therapy has been recently reported.²⁶ In the current study, two dogs remained in remission after all drugs had been discontinued for approximately 1 year. One of these dogs had suddenly developed clinical signs of pemphigus while receiving amoxicillin for another problem, and drug-induced pemphigus may have been possible. Although a greater percentage of dogs with a rapid onset of disease responded better to therapy than those with gradual onset, this difference was not statistically significant. Similarly, control of clinical signs was achieved in dogs with generalized disease more than in dogs with localized disease, but the difference was not statistically significant.

Conclusion

Based on this study, canine pemphigus foliaceus was characterized by crusts and pustules and had either a generalized pattern or was limited to the face and feet. Cytological evaluation, a rapid and highly informative test, showed acantholytic cells in many specimens. Prednisolone or a combination of prednisolone and azathioprine was the treatment most commonly used. Side effects were more frequently seen with the combination therapy. More than half of the affected dogs achieved remission with appropriate therapy, and another 25% were improved.

^a GraphPad InStat; GraphPad Software, San Diego, CA 92121

References

1. Scott DW, Miller W, Griffin CE. Muller's and Kirk's Small Animal Dermatology. 6th ed. Philadelphia: WB Saunders, 2001.
2. Werner LL, Brown KA, Halliwell RE. Diagnosis of autoimmune skin disease in the dog: correlation between histopathologic, direct immunofluorescent and clinical findings. *Vet Immunol Immunopathol* 1983;5:47-64.
3. Carlotti DN. Autoimmune mediated skin diseases. *J Small Anim Pract* 1989;30:223-227.
4. Halliwell REW, Goldschmidt MH. Pemphigus foliaceus in the canine: a case report and discussion. *J Am Anim Hosp Assoc* 1977;13:431-436.
5. Noxon JO, Myers RK. Pemphigus foliaceus in two Shetland sheep-dog littermates. *J Am Vet Med Assoc* 1989;194:545-546.
6. McEwan NA, McNeil PE, Kirkham D. Pemphigus foliaceus: a report of two cases in the dog. *J Small Anim Pract* 1986;27:567-575.
7. Garman RH, Tompsett JW. A pemphigus foliaceus-like disease in the dog: a case report. *J Am Anim Hosp Assoc* 1978;14:585-588.
8. Ihrke PJ, Stannard AA, Ardans AA, *et al.* Pemphigus foliaceus in dogs: a review of 37 cases. *J Am Vet Med Assoc* 1985;186:59-66.
9. Gomez SM, Morris DO, Goldschmidt MH. Outcome and complications associated with treatment of pemphigus foliaceus in dogs: 43 cases (1994-2000). *J Am Vet Med Assoc* 2004;224:1312-1316.
10. Noli C, Koeman JP, Willemse T. A retrospective evaluation of adverse reactions to trimethoprim-sulphonamide combinations in dogs and cats. *Vet Q* 1995;17:123-128.
11. White SD, Carlotti DN, Pin D, *et al.* Putative drug-related pemphigus foliaceus in four dogs. *Vet Dermatol* 2002;13:195-202.
12. Turek MM. Cutaneous paraneoplastic syndromes in dogs and cats: a review of the literature. *Vet Dermatol* 2003;14:279-296.
13. Olivry T, Joubert S, Dunston SM, *et al.* Desmoglein-3 is a target autoantigen in spontaneous canine pemphigus vulgaris. *Exp Dermatol* 2003;12:198-203.
14. Rosenkrantz WS. Pemphigus: current therapy. *Vet Dermatol* 2004;15:90-98.
15. Yager JA, Wilcock BP. Colour Atlas and Text of Surgical Pathology of the Cat and Dog. London: Wolfe Publishing, 1994.
16. Kuhl KA, Shofer FS, Goldschmidt MH. Comparative histopathology of pemphigus foliaceus and superficial folliculitis in the dog. *Vet Pathol* 1994;31:19-27.
17. Gross TL, Ihrke PJ, Walder EJ. Veterinary Dermatopathology: A Macroscopic and Microscopic Evaluation of Canine and Feline Skin Disease. St. Louis: Mosby, 1992.
18. High M. An interesting case of pemphigus foliaceus in a dog. *Can Vet J* 1999;40:127-128.
19. Ihrke PJ, Stannard AA, Ardans AA, *et al.* Pemphigus foliaceus of the footpads in three dogs. *J Am Vet Med Assoc* 1985;186:67-69.
20. Rosenkrantz W. Pemphigus foliaceus. In: Griffin CA, Kwochka KW, MacDonald JM, eds. Current Veterinary Dermatology. St. Louis: Mosby, 1993.
21. Mueller RS. Dermatology for the Small Animal Practitioner. Jackson: Teon NewMedia, 2000.
22. Medleau L, Dawe DL, Scott DW. Complement immunofluorescence in sera of dogs with pemphigus foliaceus. *Am J Vet Res* 1987;48:486-487.
23. DeBoer DJ, Ihrke PJ, Stannard AA. Circulating immune complex concentrations in selected cases of skin disease in dogs. *Am J Vet Res* 1988;49:143-146.
24. Iwasaki T, Shimizu M, Obata H, *et al.* Effect of substrate on indirect immunofluorescence test for canine pemphigus foliaceus. *Vet Pathol* 1996;33:332-336.
25. Rosenkrantz WS, Griffin CE, Barr RJ. Clinical evaluation of cyclosporine in animal models with cutaneous immune-mediated disease and epitheliotropic lymphoma. *J Am Anim Hosp Assoc* 1989;25:377-384.
26. Olivry T, Bergvall KE, Atlee BA. Prolonged remission after immunosuppressive therapy in six dogs with pemphigus foliaceus. *Vet Dermatol* 2004;15:245-252.