Comparison of pulse administration versus once daily administration of itraconazole for the treatment of *Malassezia pachydermatis* dermatitis and otitis in dogs

Lauren R. Pinchbeck, BA; Andrew Hillier, BVSc, DACVD; Joseph J. Kowalski, DVM, DACVM; Kenneth W. Kwochka, DVM, DACVD

Objective—To compare clinical efficacy of pulse administration with itraconazole versus once daily administration for the treatment of cutaneous and otic *M pachydermatis* infection in dogs.

Design—Randomized controlled trial.

Animals—20 dogs.

Procedure—Dogs were treated with itraconazole orally (n = 10/group), using a pulse administration regimen (5 mg/kg [2.3 mg/lb], PO, q 24 h for 2 consecutive days per week for 3 weeks) or once daily administration (5 mg/kg, PO, q 24 h for 21 days). No other treatment was permitted. On days 0 and 21, clinical severity of cutaneous and otic disease was assessed, and samples were collected for cytologic examination and yeast culture. Cytology (sum of the mean number of yeast organisms per oil immersion field for affected sites) and culture (mean of the score for extent of yeast growth for samples from affected sites) scores were calculated.

Results—For dogs in both treatment groups, clinical severity of cutaneous and otic disease was significantly decreased by day 21, but decrease in severity was not significantly different between groups. Similarly, skin cytology, skin culture, and ear culture scores were significantly decreased on day 21, compared with day 0, for both groups, but decreases were not significantly different between groups except that dogs in the pulse administration group had a significantly greater decrease in ear culture scores than did dogs in the daily administration group. However, when cytology scores only for ear samples were analyzed, day 21 score was not significantly decreased, compared with day 0 score, for either group.

Conclusions and Clinical Relevance—Results suggested that both pulse administration and once daily administration of itraconazole were efficacious in the treatment of *M pachydermatis* cutaneous infection in dogs. However, adjunctive treatment may be needed in dogs with *M pachydermatis* otitis. (*J Am Vet Med Assoc* 2002;220:1807–1812)

From the Department of Veterinary Clinical Sciences, College of Veterinary Medicine, The Ohio State University, Columbus, OH 43210.

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Address correspondence to Dr. Hillier.

Malassezia pachydermatis is a lipophilic, non–lipid-dependent, nonmycelial, saprophytic yeast that inhabits normal and abnormal skin, the ear canals, the oral and anal mucosal surfaces, the anal sacs, and the vagina of dogs.[1-3] Infection with *M pachydermatis* is recognized as a secondary complication of hypersensitivity disorders, keratinization defects, endocrinopathies, and staphylococcal pyoderma.[4] Affected dogs are pruritic and typically have seborrheic dermatitis, erythema, alopecia, and evidence of self-trauma.[4,5] Dogs with chronic *M pachydermatis* infection develop severe greasy scale, hyperpigmentation, and lichenification and often have an offensive, rancid, or yeast-like odor.[4,5] The most commonly affected areas include the ventral aspect of the neck, axillae, ears, muzzle, interdigital spaces, and perianal skin.[4,6]

Current recommendations for treatment of *M pachydermatis* infection include topical and systemic treatments.[4,6] Shampoos, conditioners, sprays, lotions, and leave-on products with degreasing or antimycotic properties, or both, have been recommended for topical treatment.[4-7] However, topical treatment may fail to completely resolve the infection, in part because of failure of the owner to comply with the labor-intensive regimen that is required. Systemically administered antimycotic agents that have been recommended in textbooks for the treatment of cutaneous *M pachydermatis* infection include ketoconazole, itraconazole, and fluconazole.[4,6] However, the clinical efficacy of these drugs has not been documented in controlled studies.

Itraconazole is a lipophilic triazole antifungal agent approved for treatment of cutaneous and systemic fungal diseases in humans.[8-12] It has activity against *Candida* spp and *Malassezia* spp in humans and, thus, has the potential to be useful for the treatment of cutaneous and otic *M pachydermatis* infection in dogs. To our knowledge, the efficacy of oral itraconazole treatment in dogs with *M pachydermatis* infection has not been determined.

In humans, itraconazole is characterized by keratinophilic and lipophilic properties that result in retention of the drug in the skin.[13] The drug is administered orally, and the principal routes of delivery of itraconazole to the stratum corneum include excretion, passive diffusion, and transfer via the sebum.[13] The drug accumulates in the sebaceous glands, so that peak sebum concentration is 5 to 10 times the peak plasma concentration, and the sebum concentration remains high for up to 7 days after administration is discontinued.[14] It has also been reported that incorporation of

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itraconazole in the sebum and stratum corneum enables itraconazole to be detected in the skin surface for 3 to 4 weeks after administration is discontinued.[13] Itraconazole has better tissue penetration, has a longer elimination half-life, and is less toxic,[12,15,16] compared with ketoconazole.

The pharmacokinetic profile of itraconazole, along with the sustained high concentrations of the drug that develop in the skin following oral administration, suggests that pulse administration (ie, intermittent administration of a drug at the recommended dose with a longer interval between doses than is commonly accepted) could be as efficacious as once daily administration for the treatment of cutaneous *M pachydermatis* infection in dogs. Compared with daily administration, the benefits of pulse administration include decreased potential for side effects and adverse reactions, increased owner compliance, and reduced treatment cost.

The purpose of the study reported here, therefore, was to compare the clinical efficacy of pulse administration with itraconazole versus once daily administration for the treatment of cutaneous or otic *M pachydermatis* infection in dogs.

Materials and Methods

Dogs—Twenty client-owned adult dogs examined at The Ohio State University Veterinary Teaching Hospital because of *M pachydermatis* dermatitis or otitis were considered for inclusion in the study. A diagnosis of *M pachydermatis* infection was made on the basis of history, clinical signs, and cytologic evidence for at least 1 body site having a mean of ≥ 1 yeast organism**/oil immersion field (OIF)** during microscopic examination of 10 consecutive OIF with corneocytes.[3] All body sites with lesions suggestive of *M pachydermatis* infection were sampled for cytologic examination. When multiple locations existed for a particular body site (eg, nail beds, interdigital spaces, axilla, lip folds), the single most severely affected location was chosen to represent that body site.

Dogs with physical examination findings suggestive of staphylococcal pyoderma (eg, pustules, crusts, or epidermal collarettes) or microscopic evidence of bacterial infection (ie, abundant bacteria evident during microscopic examination of skin preparations) for which systemic antibiotic treatment was indicated were excluded. Diagnosis and treatment of primary dermatologic disease (eg, hypersensitivity, keratinization defects, endocrinopathies) were not pursued at the time of entry into or during the course of the present study. No new treatments (including bathing, topical application of any product, and systemic administration of antibiotics or corticosteroids) were permitted during the course of the study, with the exception of itraconazole. However, in dogs that were receiving hypoallergenic diets, allergen immunotherapy, flea control treatments, or antihistamines because of previously diagnosed allergic disease, treatment was continued without any change throughout the present study. Owners gave written consent for inclusion of their pets in the study after they reviewed written information explaining drug administration, potential adverse reactions, and details regarding study participation.

Experimental protocol—This study was conducted as a randomized controlled trial. Dogs included in the study were randomly assigned to 1 of 2 groups. Dogs assigned to the **pulse administration group** (**PAG**; n = 10) were treated with itraconazole oral solution (10 mg/ml)[a] at a dosage of 5 mg/kg, PO, every 24 hours for 2 consecutive days and did not receive any treatment for the following 5 days. This 7-day cycle was repeated for 21 days, so that dogs in the PAG received a total of 6 doses of itraconazole. Dogs assigned to the **daily administration group** (**DAG**; n = 10) were treated with itraconazole oral solution at a dosage of 5 mg/kg, PO, every 24 hours for 21 days. Itraconazole was administered without food.[17] Dogs with *M pachydermatis* otitis and moderate or severe otic exudate underwent ear flushing with warm sterile saline (0.9% NaCl) solution prior to initiation of systemic treatment, but no further ear cleaning or topical otic treatments were permitted thereafter.

For all dogs included in the study, a history was obtained, a physical examination was performed, samples for cytologic examination and yeast culture were collected, and a ***Malassezia* index (MI)** score was generated on day 0. Owners were then instructed to begin drug administration and return for reevaluation in 21 days. On day 21, samples were collected for cytologic examination and yeast culture from the same anatomic locations where day 0 samples had been collected, and an MI score was generated. Owners were asked whether all treatments had been successfully administered and whether any adverse effects related to itraconazole administration had been observed. A single investigator who did not know to which group dogs had been assigned performed all physical examinations, collected all samples for cytologic examination and yeast culture, and performed all cytologic examinations. The group assignment was only revealed to this investigator once the clinical data and cytology and culture results for all the dogs were recorded.

MI score—Before and after treatment with itraconazole, an MI score was assigned to each dog. The MI score represented a semiquantitative measurement of the severity of skin disease and was calculated with the following equation:

$$\text{MI score} = \text{CLS} + (\text{VASP} \times 1.8)$$

where CLS is the clinical lesion score and VASP is the visual analog score for pruritus. The equation was adapted from clinical scoring systems used in human[18-21] and veterinary dermatology.[22,23] The CLS was calculated by examining each of the 6 body sites typically involved in dogs with *M pachydermatis* infection (ventral aspect of the neck, axillae, perineum, feet, left ear, and right ear) and assigning a score from 0 to 3 (0 = absent, 1 = mild, 2 = moderate, 3 = severe) for each of 4 features (erythema, greasy scale or exudate, hyperpigmentation and lichenification of the skin [or hyperplasia of the ear canal], and odor) for each site. The CLS was determined by summing scores for all 4 features for each of the 6 sites; maximum CLS, therefore, was 72.

The VASP was calculated by asking owners to assess the severity of pruritus during the 3 days preceding examination (ie, prior to day 0 and day 21) on a scale from 0 to 10, with 0 indicating no pruritus and 10 indicating constant pruritus. The VASP was multiplied by 1.8; maximum VASP, therefore, was 18, and maximum MI score was 90.

Cytologic examination—Samples for cytologic examination were collected from the skin by scraping the skin surface with a No. 10 scalpel blade and from the ears by swabbing the ear canal with a sterile swab. Material collected was smeared onto a glass slide, stained with Gram stain,[b] and examined microscopically. The number of yeast organisms at each body site was quantitated as the mean number of yeast organisms per OIF during examination of 10 consecutive OIF with corneocytes.

Yeast culture—Samples for yeast culture were collected from all sites for which mean number of yeast organisms per

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OIF was ≥ 1. Samples were collected by scraping the skin surface or swabbing the ear canal and were plated on Sabouraud agar with dextrose and chloramphenicol. Plates were incubated in 5% CO_2 at 37 C for 48 to 72 hours. A veterinary microbiologist identified colonies as *M pachydermatis* on the basis of gross morphologic and microscopic characteristics.[24] A yeast culture score from 1 to 5 was assigned on the basis of extent of growth obtained, with 1 = no growth, 2 = few colonies, 3 = light growth, 4 = moderate growth, and 5 = heavy growth.

Statistical analyses—A cytology score was calculated for each dog by adding mean number of yeast organisms per OIF for all sites examined on that dog that had a mean number of yeast organisms per OIF ≥ 1. Additional cytology scores were calculated by adding mean number of yeast organisms per OIF for all skin sites only and for the left and right ears only. Yeast culture scores were calculated by averaging the scores for extent of yeast growth for all sites examined. Additional yeast culture scores were calculated by averaging the scores for extent of yeast growth for all skin sites only and for the left and right ears only.

Day 0 median values for MI score, CLS, VASP, cytology scores, and yeast culture scores were compared between groups with the Kruskal-Wallis test to determine whether groups were significantly different prior to initiation of itraconazole treatment. For each group, the sign-rank test was used to determine whether median values obtained on day 21 were significantly different from values obtained on day 0. Day 21 median values were compared between groups by means of regression analysis, using day 0 median values as a covariate, followed by the Kruskal-Wallis test. The same procedure was used to compare the percentage change between day 0 and 21 values between groups. All analyses were performed with standard software.[c] For all analyses, values of $P \leq 0.05$ were considered significant.

Results

Owners did not report any adverse effects related to itraconazole administration.

Dogs in the PAG ranged from 1 to 7 years old (mean, 2.7 years). Seven were male, and 3 were female. There were 2 Beagles, 2 Labrador Retrievers, 2 Cocker Spaniels, 2 mixed-breed dogs, 1 German Shepherd Dog, and 1 American Staffordshire Terrier. At the time of entry into the study, 2 dogs were confirmed to have atopic dermatitis, 7 were suspected to have atopic dermatitis, and 1 had pruritic dermatitis of undetermined origin.

Dogs in the DAG ranged from 2 to 10 years old (mean, 5.8 years). Four were male, and 6 were female. There were 3 Beagles, 2 mixed-breed dogs, 1 Cocker Spaniel, 1 Yorkshire Terrier, 1 Miniature Schnauzer, 1 Boxer, and 1 Lhasa Apso. At the time of entry into the study, 5 were confirmed to have atopic dermatitis, 3 were suspected to have atopic dermatitis, and 2 had pruritic dermatitis of undetermined origin (1 of these dogs was later confirmed to have a cutaneous adverse food reaction).

Day 0 values for MI scores, CLS, VASP, cytology scores, and culture scores were not significantly different between groups.

MI score—For both groups, median MI score on day 21 was significantly less than median MI score on day 0 (Table 1). However, neither the median absolute decrease in MI score ($P = 0.364$) nor the median percentage decrease in MI score ($P = 0.112$) was significantly different between groups.

Similarly, median CLS on day 21 was significantly less than median CLS on day 0 for both groups (**Table 1**). However, although the median absolute decrease in CLS was not significantly different between groups ($P = 0.096$), the median percentage decrease in CLS for the PAG was significantly greater than the median percentage decrease for the DAG. Finally, for both groups, median VASP on day 21 was significantly less than median VASP on day 0. However, neither the median absolute decrease in VASP ($P = 0.427$) nor the median percentage decrease in VASP ($P = 0.678$) was significantly different between groups.

Cytology scores—Cytologic examination of samples collected on day 0 revealed that a total of 50 sites (25 sites on dogs in the PAG and 25 sites on dogs in the DAG) had a mean number of yeast organisms per OIF ≥ 1. Fifteen of these samples were from the interdigital space (PAG, 9; DAG, 6), 13 were from the ear canal (PAG, 7; DAG, 6), 11 were from the lip fold (PAG, 6; DAG, 5), 4 were from the nail bed (PAG, 2; DAG, 2), 2 were from the distal aspect of the extremities (PAG, 1; DAG, 1), 2 were from the ventral aspect of the neck (DAG), 1 was from the axilla (DAG), 1 was from the perineum (DAG), and 1 was from the caudal aspect of the abdomen (DAG). Follow-up samples were collected on day 21 only from these 50 sites. Only 15 of these 50 samples were found to contain a mean number of

Table 1—Changes in clinical severity of skin and ear disease in 20 dogs with *Malassezia pachydermatis* dermatitis or otitis treated with itraconazole orally (n = 10/group), using a pulse administration regimen (5 mg/kg [2.3 mg/lb], PO, q 24 h for 2 consecutive days per week for 3 weeks) or once daily administration (5 mg/kg, PO, q 24 h for 21 days)

	Pulse administration				Daily administration			
			Decrease				Decrease	
Variable	Day 0	Day 21	Absolute	Percentage	Day 0	Day 21	Absolute	Percentage
MI score	25.2 (14.0, 45.0)	10.6* (2.0, 26.4)	12.9 (9.6, 29.4)	54 (41, 86)	33.0 (16.0, 61.0)	18.1* (6.0, 47.0)	14.1 (5.0, 24.8)	41 (19, 67)
CLS	15.0 (4.0, 22.0)	5.0* (2.0, 12.0)	7.5 (1.0, 14.0)	60† (25, 82)	19.5 (3.0, 43.0)	9.5* (5.0, 38.0)	6.0 (–2.0, 19.0)	31 (–67, 66)
VASP	5.0 (2.0, 10.0)	2.0* (0.0, 8.0)	2.5 (–2.0, 6.5)	56 (–50, 100)	7.5 (4.0, 10.0)	2.0* (0.0, 10.0)	5.0 (–4.0, 7.0)	75 (–67, 100)

Data are given as median (range).
*Significantly ($P \leq 0.05$) different from day 0 value. †Significantly ($P \leq 0.05$) different from value for the other group.
MI = *Malassezia* index. CLS = Clinical lesion score. VASP = Visual analogue score for pruritus.

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yeast organisms per OIF ≥ 1 (1/33 samples from skin sites other than the nail beds [DAG], 2/4 samples from the nail beds [DAG], and 12/13 samples from the ears [PAG, 6; DAG, 6]).

For each dog, cytology scores were calculated using values only for these 50 sites. When values for all 50 sites were analyzed, median cytology score was significantly lower on day 21 than on day 0 for dogs in both groups (**Table 2**). However, neither the median absolute decrease in cytology score ($P = 0.174$) nor the median percentage decrease in cytology score ($P = 0.174$) was significantly different between groups.

When values only for the 37 skin sites were analyzed, median cytology score was significantly lower on day 21 than on day 0 for dogs in both groups (Table 2). However, neither the median absolute decrease in cytology score ($P = 0.068$) nor the median percentage decrease in cytology score ($P = 0.102$) was significantly different between groups.

When values only for the 13 ear samples were analyzed, median cytology score on day 21 was not significantly lower than on day 0 for either the PAG ($P = 0.063$) or the DAG ($P = 0.075$; Table 2). In addition, neither the median absolute decrease in cytology score ($P = 0.391$) nor the median percentage decrease in cytology score ($P = 0.391$) was significantly different between groups.

Yeast culture—Samples for yeast culture were collected on days 0 and 21 only from the 50 sites that had a mean number of yeast organisms per OIF ≥ 1 on day 0. For 46 of the 50 (92%) samples collected on day 0, results of yeast culture were positive for *M pachydermatis*. Results of yeast culture were positive for 33 of the 37 (89%) samples collected from skin sites and for all 13 of the samples collected from ears.

Results of yeast culture were positive for only 11 of the 50 (22%) samples collected on day 21. Results were positive for 3 of the 37 (8%) samples collected from skin sites and 8 of the 13 samples collected from ears. Results of cytologic examination were positive for samples collected on day 21 from 9 of the 11 sites from which *M pachydermatis* was isolated on culture. Results of cytologic examination were also positive for samples collected on day 21 from 6 of 39 (15%) sites from which *M pachydermatis* was not isolated on culture.

When values for all 50 sites were analyzed, median culture score was significantly lower on day 21 than on day 0 for dogs in both groups (**Table 3**). However, the median absolute decrease in culture score and the median percentage decrease in culture score for all 50 sites were significantly greater in dogs in the PAG than dogs in the DAG.

When values only for the 37 skin sites were analyzed, median culture score was significantly lower on day 21 than on day 0 for both groups. However, neither the median absolute decrease in culture score ($P = 0.917$) nor the median percentage decrease in culture score ($P = 0.446$) was significantly different between groups.

Finally, when values only for the 13 ear sites were analyzed, culture score was significantly lower on day 21 than on day 0 for both groups. However, although the median absolute decrease in culture score was not significantly ($P = 0.087$) different between groups, the median percentage decrease in culture score for dogs in the PAG was significantly greater than the median percentage decrease in culture score for dogs in the DAG.

Table 2—Changes in cytology scores (sum of the mean number of yeast organisms per oil immersion field for all affected sites in each dog) for 20 dogs with *M pachydermatis* dermatitis or otitis treated with itraconazole orally (n = 10/group), using a pulse administration regimen or once daily administration

	Pulse administration				Daily administration			
			Decrease				Decrease	
Sample site (n)	Day 0	Day 21	Absolute	Percentage	Day 0	Day 21	Absolute	Percentage
All sites (50)	40.4 (13.8, 184.0)	2.7* (0, 33.7)	33.2 (13.6, 174.0)	96 (33, 100)	55.1 (14.7, 137.0)	17.6* (0.2, 86.4)	32.2 (–1.6, 110.0)	71 (–2, 99)
Skin sites only (37)	24.5 (3.5, 92.8)	0.1* (0.0, 0.2)	24.5 (3.4, 92.6)	100 (97, 100)	29.1 (1.9, 59.8)	0.2* (0, 22.3)	14.5 (1.9, 48.8)	98 (31, 100)
Ears only (13)	32.8 (15.3, 91.5)	10.5 (0.7, 33.6)	28.3 (–11.6, 81.0)	80 (–71, 98)	55.8 (14.9, 137.0)	23.2 (8.3, 86.4)	15.9 (–5.7, 110.0)	54 (–7, 81)

See Table 1 for key.

Table 3—Changes in culture scores (mean of the score for extent of yeast growth for samples from all affected sites in each dog) for 20 dogs with *M pachydermatis* dermatitis or otitis treated with itraconazole orally (n = 10/group), using a pulse administration regimen or once daily administration

	Pulse administration				Daily administration			
			Decrease				Decrease	
Sample site (n)	Day 0	Day 21	Absolute	Percentage	Day 0	Day 21	Absolute	Percentage
All sites (50)	3.2 (2.7, 4.0)	1.0* (1.0, 3.0)	2.0† (0.3, 3.0)	67† (9, 75)	3.2 (2.0, 5.0)	1.6* (1.0, 4.0)	1.5 (0.0, 2.7)	46 (0, 73)
Skin sites only (37)	3.0 (2.0, 3.5)	1.0* (1.0, 2.0)	2.0 (0.5, 2.5)	67 (20, 71)	2.8 (1.3, 3.7)	1.0* (1.0, 2.0)	1.5 (0.0, 2.7)	60 (0, 73)
Ears only (13)	4.0 (2.0, 5.0)	1.0* (1.0, 5.0)	2.0 (0.0, 4.0)	67† (0, 80)	5.0 (4.0, 5.0)	4.0* (2.0, 4.0)	1.0 (0.0, 3.0)	20 (0, 60)

See Table 1 for key.

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Discussion

Results of the present study suggested that both pulse administration (5 mg/kg, PO, q 24 h for 2 consecutive days per week for 3 weeks) and once daily administration (5 mg/kg, PO, q 24 h for 21 days) of itraconazole were efficacious in the treatment of *M pachydermatis* dermatitis and otitis in dogs. This was demonstrated by significant improvement in semiquantitative assessments of the severity of cutaneous and otic disease (MI score, CLS, VASP) and quantitative indicators of infection (cytology and culture scores).

In the present study, we did not detect any significant differences between groups in regard to the median absolute or percentage decrease in MI score, CLS, or VASP, except for a significantly greater median percentage decrease in CLS among dogs in the PAG, compared with dogs in the DAG. Further evaluation of the data revealed that dogs in the DAG had higher median CLS on day 0, compared with dogs in the PAG, although the difference was not significant. Similarly, on day 21, dogs in the DAG had higher median CLS than did dogs in the PAG. Thus, although the median absolute decrease in CLS from day 0 to day 21 was similar for the 2 groups, the median percentage decrease was not as great for the dogs in the DAG because of the higher CLS. We did not make any attempts in the present study to determine or treat the primary dermatologic disease causing *M pachydermatis* infection in these dogs, and we suspect that clinical lesions associated with the primary dermatologic diseases may have been more severe in dogs in the DAG. Nevertheless, results of this study do indicate that even without addressing the primary disease, systemic treatment of secondary *M pachydermatis* infection results in overall clinical improvement, in that dogs in the PAG had a median 60% decrease in CLS and a median 56% decrease in VASP, and dogs in the DAG had a median 31% decrease in CLS and a median 75% decrease in VASP. Thus, the contribution of secondary *M pachydermatis* infection to overall clinical signs in animals with dermatologic disease is appreciable, and our findings underscore the importance of evaluating and treating secondary *M pachydermatis* infection in dogs with primary dermatologic diseases such as atopic dermatitis.

The significant decrease in the skin site cytology scores from day 0 to day 21 in both treatment groups indicates that both treatment protocols were efficacious in treatment of *M pachydermatis* dermatitis. Evaluation of data for individual dogs revealed that 2 dogs in the PAG with *M pachydermatis* nail bed infections had cytologic resolution of these infections, whereas the 2 dogs in the DAG with nail bed infections did not have cytologic resolution of the infections at this site on day 21. This disparity is unlikely the result of greater efficacy of the pulse administration protocol of itraconazole. Rather, the 2 dogs in the PAG with nail bed infections had low cytology scores (3.1 and 1) at this site on day 0 and no organisms on day 21, whereas the 2 dogs in the DAG with nail bed infections had higher cytology scores on days 0 (26.6 and 41.7) and 21 (21.1 and 10.6). Thus we conclude that severe infection of the nail bed may require additional treatment, such as adjunctive topical antimycotic treatment, use of a higher dosage of itraconazole, or use of itraconazole for a longer period.

Analysis of cytology scores for the 13 ear samples revealed that the cytology score on day 21 was not significantly lower than the cytology score on day 0 for either group. In addition, neither the median absolute decrease nor the median percentage decrease in scores was significantly different between groups. However, the sample size was small, indicating that the power of these analyses was low, and it is possible that inclusion of more dogs with *M pachydermatis* otitis may have resulted in significant decreases in ear cytology scores. On the other hand, yeast organisms were seen in 12 of 13 ear samples collected on day 21, suggesting that resolution of infection was uncommon and that adjunctive ear cleaning, topical antimycotic treatment, use of higher dosages of itraconazole, administration of itraconazole for a longer period, or control of the primary dermatologic disease may be necessary for resolution of *M pachydermatis* otitis.

Analysis of culture scores for samples from all sites, skin sites only, and ears only indicated that culture scores were significantly lower on day 21 than on day 0 for both groups in the present study. However, the median absolute decrease and the median percentage decrease in culture score for all 50 sites were significantly greater for samples from dogs in the PAG, compared with dogs in the DAG, as was the median percentage decrease in culture scores from the ear sites only. Although these findings could suggest that pulse administration of itraconazole is more efficacious than daily administration, there is no pharmacologic basis for this possibility, and we do not believe it to be the case. We have established in this study that culture was less sensitive than cytology in detecting *M pachydermatis* infection (only 46/50 sites that were cytology positive on day 0 were culture positive, and only 11/15 sites that were cytology positive on day 21 were culture positive), particularly for infection of the ears (12/13 ears were cytology positive on day 21, compared with 8/13 ears that were culture positive on day 21). Further, discrepancies between cytology and culture scores were most noticeable in the ears of dogs in the PAG on day 21, when 6 infected ears had positive cytology results, but only 2 yielded growth of *M pachydermatis*. In contrast, in the DAG, 6 ears had positive cytology results on day 21, with all 6 also yielding growth on culture. The reasons for this disparity are not clear but may include differences in itraconazole pharmacokinetics between individual patients, differences in the susceptibility of *M pachydermatis* to itraconazole, and the cytology and culture techniques employed in this study. The first 2 possibilities were not evaluated in the present study. A previous study[25] reported that sensitivity of fungal culture with contact plates was lower than sensitivity of cytologic examination of tape-strip samples when low numbers of the organism were present, whereas another study[1] found that *Malassezia* organisms were identified more frequently by use of adhesive tape and fungal culture than by 3 different methods of cytologic examination. These findings suggest that the cytology and culture method-

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ologies used may affect detection of infection with *M pachydermatis*, and these differences are the most likely cause of the differences between groups in the present study in regard to mean decrease in culture scores.

Results of yeast culture of samples collected on day 21 were positive for only 11 samples, including 8 ear samples, 2 samples from the lip folds, and 1 sample from an interdigital site. Surprisingly, results of cytologic evaluation were negative for the 2 samples from the lip folds. The reason for this disparity is not known; however, it is possible that the technique used to collect cytologic samples from the lip folds did not allow collected material to adhere to the glass slide.

[a]Sporanox, Janssen Pharmaceutica, Titusville, NJ.
[b]Sigma Diagnostics Inc, St Louis, Mo.
[c]Intercooled Stata 7.0 for Windows 98, version 7, Stata Corp, College Station, Tex.

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