Assessment of exposure to *Leptospira* serovars in veterinary staff and dog owners in contact with infected dogs

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Objective—To assess patterns of seroreactivity to *Leptospira* serovars in veterinary professional staff and dog owners exposed to dogs with acute leptospirosis and to contrast these patterns in people with those observed in dogs.

Design—Cross-sectional study.

Sample Population—Human subjects consisted of 91 people (50 veterinarians, 19 technical staff, 9 administrative personnel, and 13 dog owners) exposed to dogs with leptospirosis. Canine subjects consisted of 52 dogs with naturally occurring leptospirosis admitted to the University of Bern Vetsuisse Faculty Small Animal Clinic in 2007 and 2008.

Procedures—People were tested for seroreactivity to regionally prevalent *Leptospira* serovars by use of a complement fixation test. A questionnaire designed to identify risk factors associated with seropositivity was used to collect demographic information from each study participant. Dogs were tested for seroreactivity to *Leptospira* serovars by use of a microscopic agglutination test.

Results—On the basis of microscopic agglutination test results, infected dogs were seropositive for antibodies against *Leptospira* serovars as follows (in descending order): Bratislava (43/52 [83%]), Australis (43/52 [83%]), Grippotyphosa (18/52 [35%]), Pomona (12/52 [23%]), Autumnalis (6/52 [12%]), Icterohemorrhagiae (4/52 [8%]), Tarassovi (2/52 [4%]), and Canicola (1/52 [2%]). All 91 people were seronegative for antibodies against *Leptospira* serovars. Therefore, statistical evaluation of risk factors and comparison of patterns of seroreactivity to *Leptospira* serovars between human and canine subjects were limited to theoretical risks.

Conclusions and Clinical Relevance—Seroreactivity to *Leptospira* serovars among veterinary staff adhering to standard hygiene protocols and pet owners exposed to dogs with acute leptospirosis was uncommon (*J Am Vet Med Assoc* 2011;238:183–188).

Infection caused by *Leptospira interrogans* is an important zoonotic disease worldwide, with millions of human cases of leptospirosis occurring annually and case fatality rates as high as 20% to 25% in some regions.¹ Human infection results from exposure of mucous membranes or broken skin to infected urine from carrier mammals, either directly or through contamination of soil or water.² Typical reservoir hosts of common *Leptospira* serovars are dogs (Canicola); rats (Icterohemorrhagiae and Australis); raccoons, squirrels, and skunks (Grippotyphosa); pigs (Pomona); and horses (Bratislava).²³ Human infection occurs in both industrialized and developing countries, but the incidence is higher in the tropics than in temperate regions because of longer survival of leptospires in the environment in warm and humid conditions.⁴ The reported incidence of leptospirosis in people reflects as much the availability of laboratory diagnostic methods and the index of clinical suspicion as the true incidence of disease.⁴ Leptospirosis has recently been classified as a reemerging infectious disease, particularly in tropical and subtropical regions.³ However, this may also reflect a greater awareness of the disease and more rigorous attempts to diagnose it.⁶

Important risk factors in zoonotic transmission of *Leptospira* organisms are the climate and biotic interactions between wildlife, companion animals, and humans. Human infections may be acquired through occupational, recreational, or vocational exposure. Indeed, occupation is a substantial risk factor as most infections in farm workers, veterinarians, abattoir workers, and meat inspectors

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**Abbreviations**

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<td>CFT</td>
<td>Complement fixation test</td>
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<td>IQR</td>
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<td>MAT</td>
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occur by direct contact with infected animals. The risk of occupational transmission to veterinarians has been well documented in farm animal practitioners but less so in companion animal veterinarians. Transmission to pet owners has also been reported.

Leptospirosis in dogs is fairly common in western Switzerland, in part because of its climate and wildlife populations. In 1 study on healthy dogs in the surroundings of Bern, 16 of 30 (53%) dogs were seropositive for antibodies against Leptospira serovars with titers ≥ 1:800 in 7 (23%) dogs. This high prevalence is similar to that observed in southern Europe; in a study of 240 dogs in Italy, 29% were seropositive for antibodies against Leptospira serovars. In addition, the University of Bern Vetsuisse Faculty Small Animal Clinic attracts a large number of dogs with leptospirosis because it is one of the few European centers offering intermittent hemodialysis for the treatment of acute kidney injury in companion animals. The hospital staff at this institution therefore has a high risk of exposure to infected urine or blood. Owners of dogs with leptospirosis have a similar high risk of infection (of which they are often unaware) because infection may occur either by direct inoculation from their pet or by exposure to leptospires in the same environment from which their dog acquired the infection. Despite these risks, serologic surveys designed to evaluate the rate of seropositivity in these human populations have not been described.

The purposes of the study reported here were to assess patterns of seroreactivity to Leptospira serovars in veterinary professional staff and dog owners exposed to dogs with acute leptospirosis and to contrast these seroreactivity patterns in people with those observed in dogs.

Materials and Methods

A cross-sectional study, designed as a mix of prospective and retrospective exposure, was performed to assess the pattern of seroreactivity to Leptospira serovars among dogs with acute leptospirosis and humans exposed to these dogs, including the veterinary professional staff of the teaching hospital (retrospective exposure) and the owners of the affected dogs (prospective evaluation). The study was approved by the institutional departmental board for clinical studies and fulfilled privacy regulations as well as ethical requirements.

Canine subjects—Dogs consisted of client-owned dogs with acute leptospirosis admitted to the University of Bern Vetsuisse Faculty Small Animal Clinic during the leptospirosis seasons of 2007 and 2008. Dogs with a diagnosis of leptospirosis in 2007 formed the canine contact population for the veterinary professional staff, and dogs with a diagnosis of leptospirosis in 2008 were the canine contact population for the dog owners. Inclusion criteria for dogs were clinical and clinicopathologic evidence of acute kidney injury, associated with either a single serologic MAT antibody titer ≥ 1:800, or a 4-fold increase in paired MAT antibody titers within an interval of 1 to 5 weeks. Data collection for analysis included initial serum urea and creatinine concentrations, outcome (survivor vs nonsurvivor), treatment (patient receiving dialysis vs patient not receiving dialysis), serodiagnosis (single high antibody titer vs paired antibody titers with a 4-fold increase), and pattern of seroreactivity to Leptospira serovars.

Human subjects—People consisted of veterinary staff at the University of Bern Vetsuisse Faculty Small Animal Clinic (including veterinarians, technical staff, and administrative personnel) and owners of dogs with acute leptospirosis. Informed consent was obtained from all human subjects.

All owners of dogs that had a diagnosis of acute kidney injury from leptospirosis in 2008 were considered for inclusion in the study. At the time of initial admission of dogs to the University of Bern Vetsuisse Faculty Small Animal Clinic, owners were provided with a general client information sheet regarding leptospirosis and its potential as a zoonotic disease. Two to 5 weeks later, regardless of the dog's outcome, owners were contacted and asked for study participation.

Blood sample collection from the veterinary staff was performed between April and June of 2008. Blood sample collection from the dog owners was performed between April and November of 2008. The 26 dogs of the 2007 leptospirosis season were determined to have leptospirosis between May and October. In 2008, 1 dog was determined to have leptospirosis in early April and the remaining 25 dogs were not admitted until after blood sample collection from the veterinary staff had been completed in June.

At the time of blood sample collection, each human subject was asked to complete a questionnaire designed to collect demographic data related to the identification of potential risk factors associated with seropositivity. The questionnaire was reviewed and approved by the institutional departmental board for clinical studies to fulfill privacy regulations and ethical requirements. The questionnaire was completed by the veterinary staff.

Data were collected with regard to routine interaction with healthy and infected dogs, other privately owned animals that were potential carriers, recent use of antimicrobials, general immune and health status, travel history, and whether hygienic measures had been adhered to during daily routine with potentially infected dogs. To assess the latter, the veterinary staff were asked to place a mark on a visual analogue scale between 0 and 10, with 10 being equivalent to thoroughly applying hospital hygiene policies, such as wearing protective gloves while handling animals and washing hands after animal contact on a routine basis. It is a general hospital procedure to maintain a high index of suspicion for leptospirosis for each dog with acute kidney injury throughout the entire hospital stay. This approach ensures the proper handling of dogs with leptospirosis that receive a diagnosis some time after hospitalization by seroconversion and guarantees the highest protection for the veterinary staff.

To assess the hygiene standard performed at home by dog owners with their diseased dogs before hospital admission, dog owners were asked to place a mark on a visual analogue scale between 0 and 10, with 10 being equivalent to thoroughly applying hospital hygiene policies such as wearing gloves or washing hands. Additionally, dog owners were asked to rate the frequency of contact with their dogs at home prior to hospital admission as
equal to, more frequent than, or less frequent than normal. The questionnaire was completed anonymously.

Serologic testing—Serologic testing of blood samples from humans was performed as previously described by use of a CFT to measure antibodies against the serovars Australis, Canicola, Grippotyphosa, Icterohemorrhagiae, Pomona, and Sejroe. Samples that had positive CFT results at a dilution of ≥1:10 were further evaluated by use of a MAT for seroreactivity to serovars Grippotyphosa, Australis, Pomona, Tarassovi, Canicola, Icterohemorrhagiae, Hardjo, Bratislava, Autumnalis, and Sejroe. Serologic testing of all blood samples from humans was performed by use of CFT and MAT.

Serologic testing of blood samples from dogs was performed by the National Reference Laboratory for leptospirosis by use of an MAT according to World Organisation for Animal Health guidelines. Briefly, the MAT was performed with a panel of live antigens representing both ubiquitous Leptospira serovars and locally prevalent Leptospira serovars, including Grippotyphosa, Australis, Pomona, Tarassovi, Canicola, Icterohemorrhagiae, Hardjo, Bataviae, Bratislava, Autumnalis, and Sejroe. Sera were initially screened at a dilution of 1:100. Those with a positive reaction for detection of serum antibodies against Leptospira serovars were titrated in a serial 2-fold dilution, and the endpoint antibody titer was recorded.

Statistical analysis—A statistical comparison was performed between the 2007 and 2008 dog populations with regard to patterns of seroreactivity, selected clinico-pathological variables, outcome, and treatment. Because most data were not normally distributed, statistical analyses were performed with a Wilcoxon rank-sum test for continuous data and with a Fisher exact test for categorical data; a statistical software package was used. Values of P < 0.05 were considered significant. Data are presented as median and IQR.

Results—Fifty-two dogs met the inclusion criteria (26 dogs each year). Each dog had marked azotemia at the time of initial admission. Median serum creatinine concentration was 6.6 mg/dL (IQR, 4.3 to 11.2 mg/dL; reference range, 0.6 to 1.3 mg/dL) and median serum urea concentration was 309 mg/dL (IQR, 246 to 420 mg/dL; reference range, 20.4 to 66.6 mg/dL). The most common clinical signs were lethargy, anorexia, weight loss, depression, and vomiting. Thirty of the 52 (58%) dogs required hemodialysis. Nineteen of the 52 (37%) dogs died (nonsurvivors), of which 16 were euthanatized during hospitalization or shortly after discharge. Ten of the 52 (19%) dogs were determined to have leptospirosis on the basis of seroconversion, whereas 42 (81%) dogs were determined to have leptospirosis on the basis of a single MAT antibody titer ≥1:800. Dogs were seropositive for antibodies against Leptospira serovars in the following descending order: Bratislava (43/52 [83%]), Australis (43/52 [83%]), Grippotyphosa (18/52 [35%]), Pomona (12/52 [23%]), Autumnalis (6/52 [12%]), Icterohemorrhagiae (4/52 [8%]), Tarassovi (2/52 [4%]), and Canicola (1/52 [2%]). No significant difference was found between the dog populations from 2007 and 2008 in relation to all variables examined.

Blood samples were obtained from 13 clients associated with 10 dogs (10/26 [38%]). Eight of these 10 dogs were considered survivors with a median serum creatinine concentration of 6.6 mg/dL (IQR, 4.8 to 11.2 mg/dL), which was not significantly different from that of the entire dog study population. Median time between initial recognition of clinical signs, recorded in the medical records of 9 of these 10 dogs, and blood sample collection from owners was 31 days (IQR, 27 to 37 days). From the veterinary staff, 78 subjects participated in the study, which included 50 veterinarians, 19 technical staff, and 9 administrative personnel. Questionnaires were evaluated to identify behaviors that are theoretical risks for exposure by contrasting responses from the veterinary staff and the dog owners. In the veterinary staff group, 82% (64/78) were female subjects with 79% (62/78) of these being <40 years of age with an approximately equal distribution between rural and urban residence, whereas in the dog owners group, 77% (10/13) were female subjects with 92% (12/13) of these being ≥40 years of age with a high percentage (85% [11/13]) of rural residence. Eighty-seven percent (79/91) of all human subjects (veterinary staff 72/78 and dog ≥5 years 7/13) had ≥5 years of contact with healthy dogs on a regular basis. Of the 50 veterinarians, 19 technical staff, 9 administrative personnel, and 13 dog owners, 56% (28/50), 68% (13/19), 44% (4/9), and 46% (6/13), respectively, had frequent contact with other potential carrier species of leptospirosis such as horses, rabbits, and cattle. The number of human subjects with regular contact to rats, sheep, and swine was negligibly small. The percentage of veterinarians, technical staff, and administrative personnel that were involved in the primary care of dogs with leptospirosis within the intensive care unit during the 12 months prior to blood sample collection were 68% (34/50), 84% (16/19), and 0%, respectively. Of the veterinarians and technical staff, 56% (28/50) and 68% (13/19), respectively, in their recent professional career had close contact with >10 dogs suspected of having acute leptospirosis. Within 3 weeks prior to blood sample collection, 1 human subject received antimicrobial treatment. Another subject self-reported having an impaired immune status. Veterinarians and technical staff rated their median adherence to hygienic measures when exposed to diseased dogs during the past 3 years as 8 (IQR, 6 to 9) and 8 (IQR, 5 to 7), respectively, on a visual analogue scale of 0 to 10. Dog owners rated the median hygienic standards performed at home between themselves and their diseased dogs before hospital admission as 0 (IQR, 0 to 1) on a visual analogue scale from 0 to 10. Three of the 13 dog owners associated with 2 diseased dogs rated the intensity of contact with their own dogs at home during disease state prior to hospital admission as more frequent than typical. One of these 2 dogs died. The remaining 10 of the 13 dog owners, who were associated with 8 diseased dogs, considered the frequency of contact as equal to a typical daily routine. One of these 8 dogs died.

All 91 human subjects were seronegative for antibodies against Leptospira serovars. The result from 1 veterinarian was considered suspicious after a screening CFT (antibody titer of 1:13). However, further evaluation with an MAT revealed that this veterinarian was also seronegative for antibodies against Leptospira serovars.
Discussion

Results of this study suggest that zoonotic transmission of *L. interrogans* with subsequent seroconversion is uncommon in people exposed to infected dogs, both in the modern hospital setting and at home. Hospital policies often regulate the handling of animals with suspected leptospirosis. Examples of routine preventative measures include wearing gloves while handling infected animals, washing hands after animal contact, and the use of a closed urinary collection system (indwelling catheter) for animals without anuric kidney failure. These precautions are usually sustained throughout the entire hospital stay. The results of this study suggest that either the standard hygiene precautions are sufficient to avoid disease transmission or that the zoonotic transmission potential of leptospirosis from infected dogs to people is low. To the authors’ knowledge, there are no data available that favor either of these potential explanations.

Leptospirosis is a seasonal disease, and the number of affected dogs presented in western Switzerland usually peaks in the summer and early fall. During the winter months, freezing temperatures and low humidity are not compatible with the survival of these bacteria in the outside environment. The likelihood of bacterial transmission from the environment is therefore greatly diminished during the winter season, and their continuing survival is dependent on reservoir hosts and carrier animals. Therefore, detection of antibodies among the veterinary staff before the start of the 2008 leptospirosis season would have required the persistence of a measurable antibody titer for at least 5 months after exposure from the previous fall (the last dog with leptospirosis of the 2007 leptospirosis season was seen at the end of October).

To the authors’ knowledge, the duration of immunity in naturally infected human or canine hosts has not been well evaluated, but a high patient-to-patient variability in relation to antibody response and duration of seropositivity appears to exist. In 1 study, MAT antibody titers in people after vaccination were significantly lower than those that developed after natural infection, and seroconversion occurred with low frequency (20% to 60%). Results of a study on vaccinated dogs indicate that a duration of immunity with clinical protection of approximately 1 year can be attained. Nevertheless, some routinely vaccinated dogs have low or no detectable antibody titers and are still considered reasonably protected. Unfortunately, most of the chronic infections are asymptomatic and antibody titers may fall below detectable concentrations. Although immunity against leptospirosis was thought to be primarily humoral, a recent study points to a role for cell-mediated immunity in protection from leptospirosis. On the other hand, a serologic follow-up for antibodies against serovars Australis and Bratislava over a 3-year period of 18 human patients involved in a localized outbreak of leptospirosis in Italy revealed that, although the highest antibody concentrations were reached soon after the acute phase of infection in most patients, others had highest concentrations only after several months. Serum antibody titers then tended to recede with varying rapidity, and antibodies against serovar Australis were still detectable in some patients after 5 years. In general, despite certain variability in absolute values, high-titer antibodies ≥ 1:100 were detected in all patients 9 months after infection. Results of another study evaluating the persistence of antileptospiral IgM, IgG, and agglutininating antibodies in human patients presenting with acute febrile illness in Barbados revealed that patients with severe leptospirosis commonly remained seropositive for antibodies against *Leptospira* serovars several years after infection. Thirty-nine percent of affected people were seropositive for antibodies against the antigen of serovars Australis and Bratislava (titers ≥ 1:100) after 1 year, declining to approximately 20% between the second and fifth years and to 16% in the sixth year after infection. In summary, the persistence of measurable antibody titers in humans varies greatly from study to study and has not been evaluated in subclinically infected humans. Therefore, it is possible that the veterinary staff exposed during the 2007 leptospirosis season had either never been infected or had cleared infection without leaving detectable antibody titers. The likelihood of these possibilities cannot be differentiated on the basis of our data.

On the other hand, all dog owners were tested at an optimal time after exposure to their diseased dogs but none of the 13 dog owners developed a detectable seroreactivity to the tested *Leptospira* serovars despite frequent contact with their dogs, with reportedly few hygiene precautions taken prior to admission. Even though the number of tested owners is small, these results may indicate that zoonotic transmission of *L. interrogans* with subsequent seroconversion is uncommon in people exposed to infected dogs.

Leptospirosis in humans results most commonly from exposure to infected urine of carrier mammals, either directly or through contaminated soil or water. Therefore, collection of urine in infected dogs with indwelling catheters to prevent human exposure is often recommended. Leptospirosis in dogs presents clinically in a biphasic manner with an acute, septicemic phase lasting about a week, followed by an immune phase, characterized by antibody production and excretion of leptospires in the urine. Assuming that most animals are admitted to the hospital toward the end of the acute phase, the collection of urine seems important. Moreover, data from 6 human patients suggest that urinary shedding of leptospires may continue despite appropriate treatment with antimicrobials. The same study also detected leptospires in urine samples that were taken during the first 7 days of illness. Therefore, the use of a closed urinary collecting system with an indwelling catheter is justified and recommended from the beginning of hospitalization.

The veterinary staff and dog owners are specific groups with significantly higher exposure risks to leptospirosis than the general human population in Switzerland. Leptospirosis is not a reportable disease in Switzerland. Therefore, data regarding incidence of infection or serologic prevalence within the healthy Swiss population are not available. However, they are assumed to be low. Still, sporadic instances of severe leptospirosis in people of Switzerland are reported. Serologic data from surrounding European countries examining the healthy
population are scarce. A study conducted in Italy found a highly variable seroprevalence among healthy populations. Most other studies on the incidence of leptospirosis in humans reflect either surveillance data from the past decades or point-source outbreaks and do not represent data from healthy populations. Annual incidence reports of leptospirosis vary from 0.53/100,000 population in tropical areas to 0.04/100,000 population in developed countries. Some of these studies conclude that leptospirosis is a reemerging disease and warrants more awareness.

Leptospirosis is no longer a nationally notifiable disease in the United States. An estimated 100 to 200 human cases of leptospirosis are identified annually with about 50% occurring in Hawaii. A recent seroepidemiologic survey among 511 US veterinarians attending the 2006 AVMA Annual Convention detected a seropositivity rate of 2.5%.

Given that no seropositive humans were found in the study reported here, analysis of risk factors from the questionnaire could not be performed. A theoretical risk factor is undoubtedly the hygienic measures adhered to. This was subjectively rated far higher by the hospital staff than by owners. Interestingly, both groups considered their personal risk of leptospirosis infection to be equally low.

A major limitation of this study is the small number of human subjects, especially dog owners, available for serologic testing. The negative results for the detection of serum antibodies against Leptospira serovars in all of the human subjects studied precluded statistical evaluation and leave room for speculation about potential risk factors and their importance. If similar prevalence ranges were expected as was observed in 311 US veterinarians in the study by Whitney et al., approximately 2 human subjects should have been seropositive for antibodies against Leptospira serovars in our study. However, the fact that all of the human subjects were seronegative and yet were exposed to a high number of affected dogs with clear diagnosis of leptospirosis adds weight to the results of this study despite the small number of human subjects. On the other hand, the University of Bern Vetsuisse Faculty Small Animal Clinic is essentially a referral hospital with a high index of suspicion for leptospirosis, and thus, protective measures used by staff might be more rigorous than those used in general practice clinics.

The cross-sectional design of this study was another major weakness. Optimally, all humans would have been tested prospectively both prior to exposure risk and afterward. Although dog owners were tested prospectively after exposure, the veterinary staff was largely tested in 2008 for retrospective exposure to the season of 2007. Given a minimum of 5 months elapsed between potential contact to Leptospira organisms and testing of the veterinary staff, this group had ample time to mount a measurable antibody response, and given previous studies showing persistence of antibodies over several months to years, they may still have been expected to have detectable antibodies against Leptospira serovars if exposure or infection had occurred.

For technical reasons, it was impractical to use the same screening tests for dogs and for people in this study. The CFT used for the human samples did not include testing for antibodies against the serovar Autumnalis, so seroreactivity to this Leptospira serovar may have been missed.

The gold standard to determine the serovar responsible for infection is bacterial culture. Although the MAT is a good serologic test to assess seroreactivity to Leptospira serovars among individuals, it is unable to differentiate between serovars within a serogroup and cross-reactions among serovars that occur, which hinders determination of the exact serovar in the early phase of detected seroreactivity. For example, test results for antibodies against serovars Australis and Bratislava, which belong to the same serogroup, were positive for more than 80% of all affected dogs. Results of the MAT are unable to determine which of these 2 serovars is truly present and disease causing. Additionally, cross-reactions among different serovars resulted in positive MAT results for antibody against up to 4 serovars in multiple dogs. Again, results of the MAT were unable to determine which or how many serovars were truly affecting these dogs. Because of this inherent limitation of the MAT, differences in the severity or duration of illness attributable to specific serovar infection could not be evaluated.

In conclusion, this study shows for the first time that seroreactivity to Leptospira serovars among dog owners and veterinary staff exposed to dogs with acute leptospirosis infection is uncommon. There is, nonetheless, a remaining risk, which may carry severe consequences to human health. Although this study was not designed to address the effect of hygienic measures on zoonotic disease transmission, continued use of such measures seems prudent.

References

Evaluation of orally administered famciclovir in cats experimentally infected with feline herpesvirus type-1

Sara M. Thomasy et al

**Objective**—To evaluate orally administered famciclovir for treatment of cats with experimentally induced disease attributable to feline herpesvirus type-1 (FHV-1).

**Animals**—16 nonvaccinated specific-pathogen-free cats.

**Procedures**—Cats were treated orally with famciclovir (90 mg/kg; n = 10) or a similar volume of lactose (400 mg; 8) 3 times/d for 21 days. Cats were inoculated with FHV-1 and administered the first treatment dose on day 0. Disease score; weight; results of urinalysis, serum biochemical analysis, and CBC; histologic conjunctivitis score; herpetic DNA shedding; goblet cell density; anti–FHV-1 antibody concentration; and plasma penciclovir concentration were measured.

**Results**—On days 4 to 18 following inoculation, disease scores were lower in famciclovir-treated cats than in lactose-treated cats. Lactose-treated cats decreased in weight during the first 7 days after inoculation, but famciclovir-treated cats increased in weight throughout the study. Percentage change in weight was greater in famciclovir-treated cats on days 7 and 14 than in lactose-treated cats. Serum globulin concentration was lower on days 3 through 9, conjunctivitis histologic score was lower on day 14, herpetic DNA was shed less frequently throughout the study, goblet cell density was lower on day 14, and circulating anti–FHV-1 antibody concentration at study end was lower in famciclovir-treated cats, compared with these measurements in lactose-treated cats. Approximate peak plasma penciclovir concentration was 20 µg/mL.

**Conclusions and Clinical Relevance**—Famciclovir administration improved outcomes for systemic, ophthalmic, clinicopathologic, virologic, and histologic variables in cats experimentally infected with FHV-1. Adjunctive topical mucinomimetic and antimicrobial treatments may also be necessary. (Am J Vet Res 2011;72:85–95)