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L-Lysine Administration for Feline Herpesvirus Infection

L-lysine is an amino acid with antiviral activity against feline herpesvirus type 1 (FHV-1) and the analogous human herpesvirus, HSV-1.

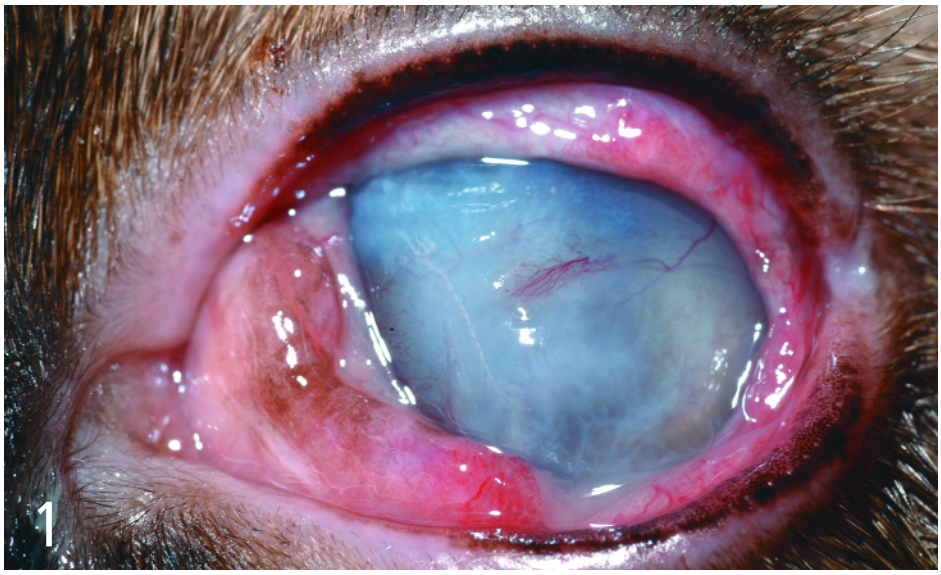
Despite the availability of vaccines and antiviral drugs effective against FHV-1, this virus remains a common cause of acute, chronic, and recurrent conjunctivitis and ulcerative and stromal keratitis (**Figure 1**). It has also been associated with corneal sequestrum (**Figure 2**), eosinophilic keratoconjunctivitis (**Figure 3**), anterior uveitis, dermatitis (**Figure 4**), and rhinosinusitis.

Kittens are usually infected early in life, experience acute upper respiratory tract and ocular disease, and typically become latently infected for life. These carrier cats then shed virus intermittently throughout life, with or without clinical evidence of disease. Some studies show that up to 50% of normal cats can shed FHV-1 at the ocular surface. Chronic, recurrent disease is especially prevalent in multicat environments.

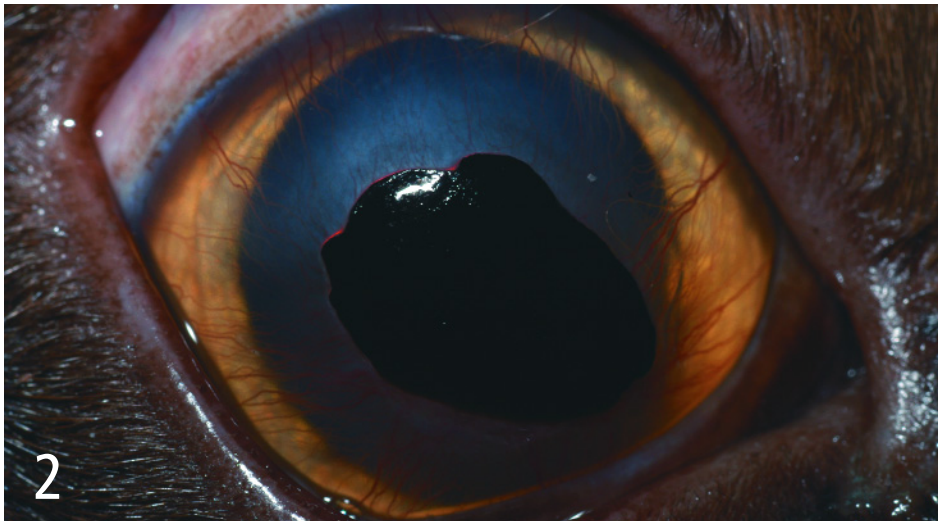
Although some antiviral medications developed for humans infected with HSV-1 can be used safely in cats and are effective against FHV-1, no

continues

FHV-1 = feline herpesvirus type 1, HSV-1 = herpes simplex virus type 1



Left eye of an 11-year-old spayed female Siamese cat with stromal keratitis believed to be herpetic in origin. The corneal surface is not ulcerated; however, conjunctival hyperemia, extensive corneal stromal edema, neovascularization, and white blood cell infiltration are present.



Right eye of a 9-year-old castrated male Burmese cat with an extensive corneal sequestrum and associated corneal neovascularization. FHV-1 DNA can be detected in 50% to 80% of corneal scrapings from cats with this syndrome.[8]

Courtesy Christine C. Lim, DVM

medications or vaccines reduce establishment of latency or frequency of viral reactivation.[1] In addition, other human antiviral drugs are ineffective against FHV-1, toxic to cats, expensive, or cannot be administered for protracted periods. This has led to investigation of adjunctive antiviral therapies, such as L-lysine therapy, that are safe, effective, and inexpensive and can be given long term.

Evidence of Efficacy

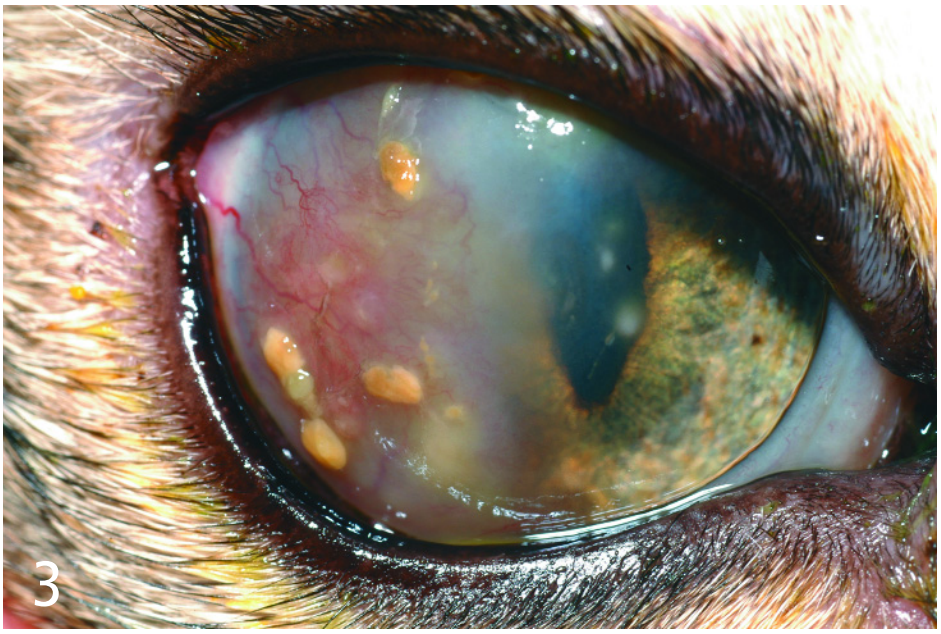
Originally, lysine was administered to FHV-1–infected cats on the basis of data in humans that supported its efficacy against HSV-1. It was assumed that the agent would be safe in cats. However, excessive lysine administration has been shown to competitively inhibit arginine absorption in some species. This could have devastating effects in cats because arginine is an essential amino acid in this species. In one study,[2] a single meal of a complete amino acid diet without arginine produced fatal encephalopathy in some near-adult cats. Therefore, careful investigation of lysine's antiviral efficacy against FHV-1 and its safety in cats is warranted.

In Vitro Research

Lysine limits the in vitro replication of many viruses, including FHV-1. The antiviral mechanism is unknown; however, many investigators have demonstrated that concurrent depletion of arginine is essential for lysine supplementation to be effective. This finding suggests that lysine exerts its antiviral effect by antagonism of arginine. This is certainly true for FHV-1: Arginine is an essential amino acid for replication of the virus, but, in the presence of small amounts of arginine, lysine supplementation reduces viral replication by about 50%.[3] However, this effect was not seen in media containing higher arginine concentrations, suggesting that a high lysine:arginine ratio is critical for efficacy.

In Vivo Research

Results of 2 independent in vivo studies have supported the clinical use of L-lysine in cats. In the first of these studies,[4] 8 FHV-1–naive cats were administered 500 mg of lysine Q 12 H PO beginning 6 hours before, and continuing for 3 weeks after experimental inoculation with FHV-1. Lysine-treated cats had significantly less severe conjunctivitis than cats that received placebo.



Courtesy J. Seth Eaton, VMD

Right eye of a 13-year-old spayed female domestic shorthair cat with feline eosinophilic keratoconjunctivitis. Note the white plaques in the lateral part of the cornea, the corneal edema, the cellular infiltration, and the vascularization. FHV-1 DNA can be detected in approximately 75% of corneal scrapings from cats with this syndrome.[8]

In the second study,[5] 14 latently infected cats received 400 mg of lysine Q 24 H PO. Viral shedding was monitored for 30 days. Lysine administration in these cats was associated with a statistically significant reduction in basal viral shedding compared with levels in cats that received placebo. Since these cats were normal, latently infected carrier cats, little or no clinical disease was seen during the month-long study in the placebo or lysine group. In both studies, plasma arginine concentrations remained in the normal range, and no signs of toxicity were observed, despite notably elevated plasma lysine concentrations in treated cats.

Of note, both studies reported results of lysine administration to experimentally infected cats; therefore, the applicability of these data in naturally infected cats remains to be tested.

Indications & Course of Treatment

On the basis of the in vitro and in vivo data described, L-lysine is now commercially available in veterinary formulations and is recommended by many veterinarians for cats infected with FHV-1. Unlike the protocol for HSV-1–infected humans, owners of cats receiving L-lysine for FHV-1 are not advised to restrict the cat's arginine intake. There are no published data on dose, frequency of administration, course of therapy, or timing of lysine administration relative to herpetic disease episodes in clinical patients; thus, information on these issues is anecdotal.

I administer 500 mg Q 12 H PO to adult cats that show evidence of recurrent herpetic dis-

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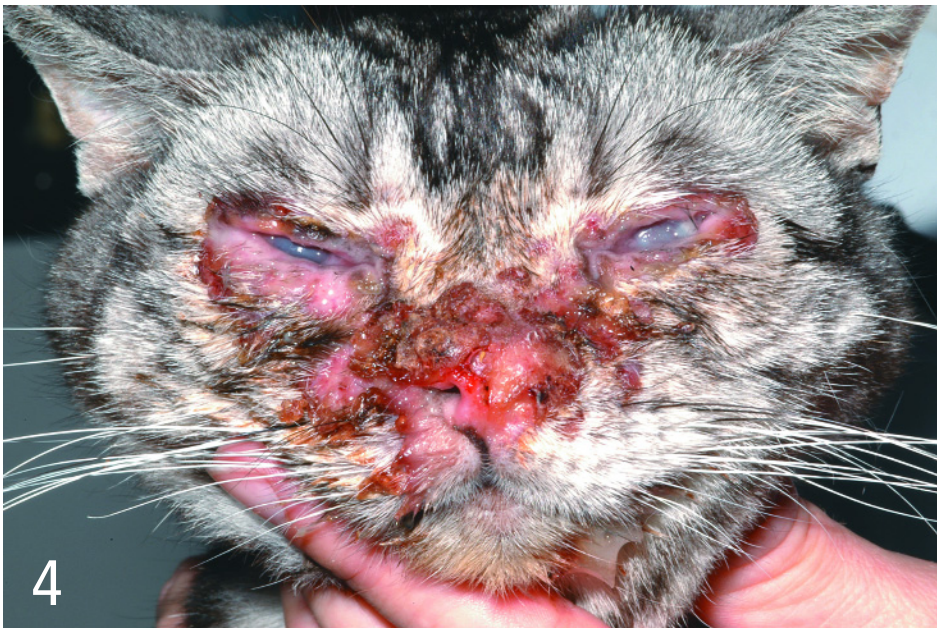

Courtesy J. Seth Eaton, VMD

Periocular and nasal skin of a 14-year-old spayed female domestic shorthair cat with herpetic dermatitis. Note the extensive hyperemia and the crusting and excoriations of the skin. Sensitivity and specificity of the FHV-1 polymerase chain reaction assay performed on skin biopsy specimens were 100% and 95%, respectively, for this disease.[9]

ease. I administer it therapeutically at the time of recrudescent disease and encourage owners of cats that have frequent recurrences to administer this same dose over the long term as a prophylactic measure. This approach is based on data from clinical trials in humans in which lysine administration reduced severity, frequency, and duration of recurrent disease episodes.

Means of Administration

Lysine is available in many formulations—tablets and capsules intended for human use and, more recently, veterinary gels, pastes, chews, and powders. All of these are intended for bolus administration. Bolus administration is sometimes impractical, however, for several reasons. Cats receiving lysine frequently require very protracted courses and often live in multicat environments in which all cats should be treated. In addition, twice-daily oral administration techniques may stimulate further viral reactivation through stress or facilitate transfer of infectious organisms among cats by operators.

Thus, the safety and efficacy of L-lysine incorporated into cat food have been studied. Results of an initial safety trial were encouraging.[6] Cats fed a diet supplemented with up to 8.6% (dry matter) L-lysine showed no signs of toxicity, had normal plasma arginine concentrations, and had normal food intake. Mean plasma lysine concentration of these cats was increased to levels similar to that achieved with bolus administration. In a subsequent study,[7] 25 cats with enzootic upper respiratory tract disease were fed a diet supplemented to 5.1% lysine for 52 days while subjected to rehousing stress (which is known to cause viral reactivation).

Ironically, food (and therefore lysine) intake decreased coincident with peak disease and viral presence. As a result, cats did not receive lysine at the very time they needed it most. Perhaps because of this, disease in cats fed the supplemented ration was more severe than that in cats fed the basal diet. In addition, viral shedding was more frequent in cats receiving the supplemented diet. On the basis of these data, dietary lysine supplementation cannot be recommended at this stage.

Veterinary chews containing lysine have recently become available. The amount of lysine in these chews is not always described on a milligram basis and they may contain other supplements not necessarily required in individual patients. Veterinarians are advised to carefully assess the amount of lysine and other agents in these products.

Summary & Future Considerations

To date, data indicate that lysine supplementation decreases in vitro replication of FHV-1, bolus administration of lysine safely reduces basal viral shedding in latently infected cats and disease severity in acutely infected cats, and dietary lysine supplementation of cats appears ineffective. However, much remains to be investigated in this field.

So far, both bolus studies have assessed small populations of specific pathogen-free or random-source cats experimentally infected with only 2 strains of only 1 of the organisms known to cause upper respiratory tract disease in cats. Therefore, these studies may not truly reflect circumstances in larger, clinically important populations—especially multicat environments, where control of enzootic upper respiratory tract disease is extremely challenging because of variable vaccination history, intercurrent disease, physiologic stresses, and high turnover of cats of diverse genetic composition and with varied exposure to infectious diseases.

In addition, to my knowledge, the effect of lysine on other organisms important in the pathogenesis of infectious upper respiratory tract disease has not been investigated; however, this also may be clinically important, especially in multicat environments where infectious upper respiratory tract disease is prevalent. Despite this, bolus administration of lysine (probably 500 mg Q 12 H) in cats with chronic or recurrent herpetic disease appears justified. ■

See Aids & Resources, back page, for references, contacts, and appendices.

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