



## Q+A with Dr. David Maggs and Dr. Sara Thomasy

For nearly a decade, Dr. David Maggs, BVSc, DACVO, a UC Davis professor of veterinary ophthalmology, and Dr. Sara Thomasy, DVM, PhD, DACVO, a vision researcher in the university's Murphy-Russell Laboratory, have been revolutionizing veterinary medicine with their studies of the drug famciclovir. Almost 97 percent of cats carry herpesvirus type-1, a disease that stays latent in their body for life and is known to cause painful and chronic eye problems. Drs. Maggs and Thomasy, along with their fellow researchers, were the first to establish the efficacy and safety of famciclovir in treating these flare-ups—a discovery widely hailed as a true breakthrough in veterinary medicine. In this Q+A, Drs. Maggs and Thomasy talk about the discovery, why it was so significant, and where their continued research into the drug is leading them.

**Q:** What is feline herpesvirus type-1?

**Dr. Maggs:** It's a highly contagious virus that cats tend to get exposed to right around the time they start to lose the immunity transferred to them from their mother. Almost inevitably they get it from either the mother cat or another cat they come into contact with. Some cats become seriously ill when they're first infected and occasionally they can die, but usually they get over the initial exposure. However, once cats are exposed to the virus, they stay infected for life—even if they don't show signs. About 97 percent of cats carry herpesvirus.

**Q:** What are the long-term effects of having the virus in their system?

**Dr. Maggs:** The virus lives inside their brain tissue, and in a notable number of infected cats it reactivates throughout their life. It's an analogous virus to the human cold sore virus. Humans who suffer recurrent cold sores are not infected with an unusual virus; rather, they have an immune system that simply lets that virus come out more often. In cats, the recurrent effects are sometimes respiratory—they start sneezing and snuffling—but most of the time they are ocular. In these cats, we see a lot of chronic recurrent conjunctivitis, corneal ulcers, and ocular discharge. This is why veterinary ophthalmologists like us are so interested in this disease.

**Q:** Before your famciclovir studies, what sorts of treatments were available for these herpes-related eye problems?

**Dr. Thomasy:** For cats with mild disease, we would often try topical antivirals—but they need to be given very frequently and often cause irritation. For cats with severe disease, we were really

without a good treatment. We had only one oral drug—called acyclovir—but it was particularly unsafe. Acyclovir is one of the most commonly used drugs for herpes infections in people, but cats don't absorb or tolerate the drug very well.

**Dr. Maggs:** There are no antiviral drugs on the market to date that were developed for cats, and there are none that were developed for feline herpesvirus. Therefore we are forced to take drugs that were developed for a different species—that is, humans—and developed to target a different virus—that is, the human herpesviruses—and discover whether they are both safe for cats and effective against feline herpesvirus. So it's two giant leaps of faith that have taken some very stepwise work.

**Q:** How did you come to study famciclovir, even though it is in the same family as acyclovir, which is so dangerous in cats?

**Dr. Thomasy:** Veterinary ophthalmologists have a listserv, and it started to pop up that vets were giving famciclovir to cats and just estimating the dose. They were reporting that it was working really well and that it seemed safe. But they were experimenting with a potentially toxic drug. So we felt that it was critical to study it.

**Dr. Maggs:** Given how closely related famciclovir is to acyclovir, we had to move really slowly, beginning with some in vitro work. We wanted to make sure that this drug would inhibit the virus's growth in vitro so that we didn't endanger any cats' lives.

**Dr. Thomasy:** In our first study with cats, we looked at how the drug distributes within the body. We used a very similar dose to what everybody else was using, and we found that the concentrations that resulted from that dose were much lower than what we would expect for the drug to have efficacy. We didn't give the drug for very long—just long enough to see if there were any side effects. Based on this initial study, the safety of the drug looked good. But we thought that we probably had to increase both the dose and the dose frequency.

Then we did a second study—our major study—looking at the efficacy of the drug. We gave the drug three times a day. Ten cats received the drug, and the remaining six cats received a placebo. All 16 cats were infected with feline herpesvirus. The results were astounding. The cats on the placebo were so much sicker. We had six cats that were sneezing, just feeling awful, not eating, and looking terrible. And then we had 10 cats that were playing and looked amazing. And we saw that difference in just a few days.

**Dr. Maggs:** It was an amazingly exciting moment in research. These cats were virtually normal compared to the cats on the placebo. In my almost 30 years as a veterinarian, there have been two absolutely revolutionary moments in ophthalmology. The first was the introduction of cyclosporine for dry eye, which is the most common cause of conjunctivitis in dogs. That drug was introduced in the late '80s and revolutionized veterinary ophthalmology. This discovery of famciclovir was the second moment for me. It has completely revolutionized our ability to treat the most common form of conjunctivitis in cats. These two discoveries have changed the way we practice veterinary medicine.

**Q:** And your studies were funded in part by CCAH?

**Dr. Maggs:** Yes. And it was very farsighted of them—this was really “out there” research when CCAH began funding our work several years ago. I really commend them for taking the risk. So

far, eight studies have come from this work, each one of which has added another layer to our understanding.

**Q:** And that research continues. What are you looking at now?

**Dr. Thomasy:** We're pursuing several lines of research at the moment. For one, we're continuing to work on the drug's dosage. Famciclovir has very complex pharmacokinetics—that is, the way it distributes and metabolizes in the body. So we're trying to find a dose that we know will be efficacious in 99 percent of cats, which is a challenge.

**Dr. Maggs:** Figuring out what dose to give is normally a simple step—but with this drug it's been an incredibly complex step, taking us eight or nine years to date. And we're still not there. In terms of other related research, we've also started working with zoos—and also with a cheetah conservancy in Namibia—to look at the usefulness of this drug in nondomestic cats. This virus appears to have some similar effects in zoo animals, but we don't have anything like the data in wild cats that we do in domestic cats. So it looks like it too is going to be complicated. Additionally, famciclovir is used right now to treat outbreaks, but we've started looking at whether it can prevent outbreaks as well. For example, we're studying the prophylactic effect of using famciclovir in shelters, because feline herpes remains the most common reason for euthanasia among shelter cats. A lot of this work we are doing collaboratively with teams of researchers from around the world.