

American author William Lyon Phelps once wrote that “a cat pours his body on the floor like water.” But during post-surgery or critical care, that tranquil creature can often turn into one agitated, keyed-up kitty — especially after a dose of conventional pain medication.

Yet pain must be dealt with. Besides causing great discomfort or even torment for a cat, pain delays healing and suppresses immunity. In some situations, it can even sensitize a cat’s nervous system in such a way that chronic pain results.

In the hope of finding better pain control options for cats, a research group at the Western College of Veterinary Medicine (WCVM) has begun testing the effectiveness of buprenorphine and medetomidine. Both are classed as *analgesics*, a diverse group of drugs that are used to treat pain in humans and animals.

During the study, the research team plans to evaluate the efficacy of each analgesic as well as the effectiveness of combining the two drugs. The study is still underway, but members of the WCVM research team already have a hunch that buprenorphine may very well be the ace up their collective sleeve. Although the drug isn’t licensed yet in Canada, it has proven more effective in some ways than other *opioid* drugs such as hydromorphone and morphine.

While buprenorphine’s use in treating cats has been studied widely, this project is the first to investigate the drug’s effects after *epidural* administration — a widely-accepted and effective technique for delivering analgesics. Rather than delivering a drug by mouth or by vein, epidural administration directly delivers the pain-killing drugs to the body’s pain receptors around the spinal cord.

“So far, any other drug that’s administered through the epidural route has been longer-acting since the actual pathways and receptors are right there in the spinal cord. You’re putting the drugs right there at the site of action,” explains Dr. Tanya Duke, a veterinary anesthesiologist and the research team’s leader.

Duke’s collaborators are Drs. Paulo Steagall and Stelio Luna of Brazil’s Sao Paulo State University, Dr. Polly Taylor of Ely, U.K., and Dr. Peter Gilbert of WCVM. Taylor and Luna are co-supervisors for Steagall, a PhD student who will use this study as part of his graduate program.

One analgesia or two?

As Duke explains, previous studies have shown that buprenorphine is quite effective in smothering pain. For example, common opioids like hydromorphone and morphine given via the muscle offer three to four hours of pain control while buprenorphine’s effects can last from six to eight hours. Buprenorphine’s effects don’t happen as quickly as other opioid drugs, but Duke points out that it doesn’t cause agitation, vomiting, or any of the other negative side effects linked with some opioids.

The study’s second drug, an alpha-2 agonist called medetomidine, is also relatively free of adverse side effects. As well, its close-chemical cousin — epidural dexmedetomidine — has been shown to kill pain in dogs without altering respiration, behaviour or motor function.

Although medetomidine is found on many veterinarians’ shelves and is considered a classic analgesic, the potential use of epidural medetomidine has only been studied in horses and dogs. In fact, Duke is the only researcher who looked at its potential use as a painkilling drug in cats



Stories by Matt Barron



during the 1990s, and based on her findings, medetomidine only keeps cats in its analgesic cradle for about four to six hours.

Although there are no published reports of administering epidural buprenorphine and medetomidine together, Duke says the analgesic combo shows great promise for treating pain in cats. Her reasoning is simple: previous research has shown that mixing an opioid with an alpha-2 agonist creates an effective synergy. And since buprenorphine and medetomidine are members of those two drug families, it’s a valid option for researchers to explore.

“Instead of getting the effect of one plus one equals two, you tend to get an effect that is more like one plus one is greater than two,” says Duke.

ABOVE: Dr. Paulo Steagall (top) and Dr. Tanya Duke with two of the project’s cats.

Proof is in the pain measurements

But studying the drug's pain-killing action and how it affects a cat's central nervous system isn't easy. As a first step, small animal surgeon Dr. Peter Gilbert had to surgically implant catheters in the study's eight cats so scientists could epidurally administer the drugs directly to the animals' spinal cord receptors.

Next, the research team had to come up with an effective way of objectively measuring any pain experienced by the cats — a crucial step in gauging when the painkilling effects of each analgesic (or drug combination) began to subside.

But before the research team could test each drug's ability to kill pain in a cat, they had to inflict slight pain. The answer to this challenge is an elastic, bracelet-like device that fits around each cat's chest. Tucked under the elastic band is a small probe that delivers heat to the cat's skin. As soon as the drug's effects wear off and each cat responds to the heat, the scientists quickly retract the probe.

The study's intensive, hands-on work with the cats began this summer and will wrap up during the fall of 2007. Studying the effectiveness of epidurally administering these painkilling drugs may be a painstaking process, but once their efficacy has been proven, a veterinarian can administer them "fairly easily," says Duke.

What is more difficult to pin down is the potential costs of using a drug like buprenorphine: so far, it's still classified as an experimental drug in Canada and isn't licensed for general practice in the country. Duke, who used the drug as a veterinary analgesic in Britain during the 1980s, says the price of buprenorphine exceeded that of morphine, but the cost wasn't prohibitive.

"The drug is a tad more expensive," says Duke, "but the benefits are very powerful."

Besides its remarkable pain-killing clout and its relative lack of side effects, buprenorphine has an interesting perk. Unlike morphine and other opioids that cause agitation in cats, buprenorphine makes feline patients experience a state approaching euphoria.

"The cats usually become happy, friendly, euphoric," describes Steagall. "They even start rolling around and rubbing on things."

In other words, the cats reclaim their fluid composure and once again, they can pour themselves on the floor like water. **V**

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Valerie Millette

Scientists' curiosity kills pain for cats

Curiosity may have killed the cat, but that inquisitive quality comes in handy when you're a scientist who is hunting for a better way to kill pain.

While Drs. Tanya Duke and Paulo Steagall share a boundless curiosity for finding better pain control for cats, the challenges involved in studying the topic this summer have demanded a range of expertise and a workload beyond what even they could offer.

That's partly why Duke's work in the field of feline analgesia became dormant in the first place. Back in the 1990s, the veterinary anesthesiologist developed methods for studying the epidural administration of analgesics to cats, "but I never had time to devote to research," says Duke, who had teaching and clinical duties. "And it would have been too much to take on myself."

Duke met Steagall in 2006 at an anesthesiology conference in Liverpool, England. At the time, Steagall was pursuing his Master of Science degree at Sao Paulo State University in Botucatu, Brazil. For his PhD work, the long-time cat enthusiast wanted to study buprenorphine — the same promising analgesic drug that had been studied by Duke. In clinical research, the drug had garnered slightly longer-lasting analgesic effects for cats and fewer side effects than morphine.

With financial support from WCVI's Companion Animal Health Fund and Pfizer Animal Health in place, Steagall could afford to rent some crucial equipment: a mechanical and thermal threshold device that detects an animal's pain threshold. The device indicates when a drug's effectiveness is wearing off — allowing scientists like Steagall and Duke to accurately measure how long the drug's analgesic would hold. The instrument's co-inventor is Dr. Polly Taylor, a British anesthesiologist

specialist who advises Steagall on his PhD alongside Brazilian Dr. Stelio Luna.

But before the study could begin, the cats had to be implanted with catheters, a tricky operation in which small animal surgeon Dr. Peter Gilbert slipped the drug-delivery tube under the skin. "He's done a wonderful job. Not one cat has had post-operative complications," says Duke. She adds that the research group plans to find good homes for all of the cats once the study ends.

Additional research support also had to be found at the last minute, and second-year veterinary student Valerie Millette was, as Duke puts it, "emailed at the eleventh hour." One of her roles was to test three different stimuli for pain detection using Taylor's device, or in other words, "to find the best way to annoy the cat," says Duke. Millette's testing showed that the sensation of heat gave researchers an accurate measure of how well the drugs stifle pain.

Given cats' propensity for agitation, Millette worked hard to familiarize the cats with the researchers and equipment. "It may not sound like an important job," says Duke, "but you need the cats to be as calm as possible because it's good for the cats and yields more accurate results."

Millette proved quite successful in making the cats comfortable despite never having owned a cat herself. As for Steagall, Duke is enthusiastic about his easy way with the cats. "You should see him," she says. "He's like the cat whisperer."