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Acetaminophen (Tylenol) Toxicity

My client, Ann, was dismayed when I told her that my physical examination and blood tests failed to reveal why Oscar, her 10 year-old talkative Siamese cat, had recently taken to loudly vocalizing in the middle of the night. Siamese cats have a reputation for being garrulous, and Ann had always found this charming. But not at three o'clock in the morning.

"This has been going on for almost a week now", said Ann, through bloodshot eyes. "I'm trying to recover from a cold, and I really need a good night's sleep. Last night I took Nyquil®, and slept through most of Oscar's howling. I'm tempted to give a little to Oscar, so maybe he'll sleep through the night as well", she told me. I was shocked. "Nyquil contains acetaminophen!" I told Ann. "If you give Nyquil® to Oscar", he may fall into a sleep that he never wakes up from!"

Ann prefers that I not use her last name in this article; she is embarrassed, as a cat owner, that she didn't know that acetaminophen is very toxic to cats. She shouldn't be. Despite the dangers of acetaminophen being published in numerous journals and magazines, many cat owners and enthusiasts still are unaware of how toxic this drug can be to cats, or that many common over-the-counter (OTC) drugs contain acetaminophen as one of their main ingredients.

Companion animals are at risk for developing toxicosis to prescription drugs as well as over-the-counter (OTC) medications, either by deliberate administration of the medication by owners, or by accidental consumption of improperly stored drugs. Dogs are more likely to chew on pill vials or tubes of ointment, eating the pills or ointment when the container finally breaks open. Cats, on the other hand, are generally more discrete about what they put in their mouths and are less likely to voluntarily ingest medications. With cats, toxicity tends to occur when well-intentioned owners unknowingly administer a seemingly harmless OTC medication, often with devastating results.

Veterinarians occasionally use OTC drugs to treat a variety of their patients' maladies. The most common of these are probably the non-steroidal anti-inflammatory drugs (NSAIDs). We prescribe these to treat musculoskeletal inflammation and pain, control fevers, and sometimes to inhibit blood clotting. Aspirin is clearly the best known of the NSAIDs. Aspirin is a non-steroidal anti-inflammatory drug (NSAID) that, for many years, had been used to control musculoskeletal pain and inflammation in dogs, and sometimes cats. In recent years, a multitude of safer and more effective oral pain relievers have been

developed, making aspirin an uncommon first choice for joint and skeletal disease in companion animals. In cats, we still use aspirin occasionally, mainly to inhibit blood clotting. Cats with certain heart diseases like hypertrophic cardiomyopathy are at increased risk for developing dangerous blood clots. Aspirin is frequently prescribed in an effort to inhibit blood clot formation, however, the dose must be strictly adhered to. Acetaminophen is often grouped with the NSAIDs, although technically it is somewhat different. "Veterinarians occasionally prescribe low doses of acetaminophen for pain control in dogs, but *never* for cats" says Dr. Jill Richardson, consulting editor of toxicology for the Veterinary Information Network and Director of Consumer Relations and Technical Services for Hartz. "In dogs, the dose is 5 – 10 mg per kg. Dogs show signs of toxicity when the dose exceeds 75 mg per kg." Cats, however, are very sensitive to acetaminophen toxicity. "There have been reports of toxicity developing in cats at doses as low as 10 mg/kg." Acetaminophen is one of the top two most common household medications, and it is no surprise that acetaminophen toxicity is commonly reported. In fact, between January 1998 and March 2000, veterinarians at the ASPCA Animal Poison Control Center consulted on over 1050 cases of accidental exposure to acetaminophen in dogs and cats.

Although most readily recognized by the trade name Tylenol, acetaminophen is the major ingredient of most aspirin-free pain relievers and cold remedies, including Excedrin®, Panadol®, Anacin®, Midol®, Pamprin®, BromoSeltzer®, and Percogesic®. Many decongestant products and "cold" or "flu" formulas also contain acetaminophen. For example, a single adult dose of Nyquil® syrup contains 1000 milligrams of acetaminophen, the equivalent of more than three Tylenol tablets. This is a frighteningly large dose, considering that ingestion of one 325-mg tablet by a cat results in severe toxicosis, and two tablets ingested within 24 hours is fatal. "Any dose is potentially life-threatening to a cat" says Dr. Richardson.

The enzymes responsible for the metabolism of most drugs are found in the liver. One particular enzyme, called glucuronyl transferase, is responsible for attaching a large molecule called glucuronide to a drug, rendering the drug inactive and water-soluble. The process of attaching a large molecule to a drug is called "conjugation". Cats, as a species, have low levels of glucuronyl transferase. Thus, many drugs that are quickly excreted as glucuronyl conjugates in other species are very slowly removed from the bloodstream in cats. Toxic metabolites accumulate in the bloodstream, causing severe organ damage.

At toxic doses, acetaminophen often causes hepatic necrosis – death of liver cells – especially in dogs. Cats, however, are more likely to develop a condition called methemoglobinemia, in which there is an excess amount of methemoglobin in the bloodstream. Methemoglobin is an abnormal form of hemoglobin that is incapable of transporting oxygen. As methemoglobin levels start to rise, clinical signs develop, such as chocolate-brown mucous membranes, fast heart rate, labored breathing, depression, vomiting, edema (swelling) of the face, neck and limbs, hypothermia, ataxia (incoordination) and coma. Cats may become jaundiced as liver failure develops.

Treatment for acetaminophen toxicity involves providing supplemental oxygen, administering intravenous fluids, and giving several drugs intravenously, including vitamin C, cimetidine (Tagamet), and N-acetylcysteine, a drug that provides the body with excessive amounts of the amino acid cysteine. This amino acid is necessary for the liver to repair itself and counteract acetaminophen's toxic effects.

Time is of the essence in treating acetaminophen toxicity. Treatment tends to be less efficacious when initiated more than 8 hours after ingestion.

Other over-the-counter NSAIDs such as ibuprofen (Advil®, Nuprin®, Motrin®) or naproxen (Aleve®) should never be given to cats. Ibuprofen has a narrow margin of safety in dogs, and cats, with their inability to metabolize these drugs, are thought to be twice as sensitive as dogs to ibuprofen's toxic effects.

Ultimately, any oral medication can potentially cause toxicosis in companion animals, especially cats, with their small body size and unique metabolic pathways. Cat owners should be certain to keep all medications safely stored, and have the phone number of their veterinarian and national poison control center readily accessible in case of a toxin-related emergency. No product, over-the-counter or otherwise, should be given to a cat without the advice of a veterinarian.

Sidebar 1: What to do if you suspect acetaminophen toxicity

"Acetaminophen toxicity is an emergency situation" says Dr. Jill Richardson, Director of Consumer Relations and Technical Services for Hartz, and consulting editor for toxicology for the Veterinary Information Network. "You should contact your veterinarian immediately, even if the cat ate only one pill, or even if the owner simply suspects that it was eaten. Early aggressive treatment by a veterinarian is extremely important. Even if you only suspect your cat may have eaten an acetaminophen tablet, still see a vet immediately. There is a test that can confirm exposure, but treatment for poisoning should be initiated while you wait for test results to see if the cat was actually exposed."

Sidebar 2: Clinical signs of acetaminophen toxicity

- Brownish-gray gums
- Labored breathing
- Swollen face, neck and limbs
- Hypothermia (low body temperature)
- Uncoordinated gait
- Coma
- Jaundice

My source for much of the info in the article came from Dr. Jill Richardson herself, and from an article she wrote, which can be found here:
http://www.aspca.org/site/DocServer/veccs_july00.pdf?docID=132