

## **Acetaminophen Toxicity in Pets**

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While acetaminophen (APAP) enjoys a reputation of safety and efficacy for humans, it is probably one of the worst medications that can be administered to a dog or a cat. Acetaminophen represents the most common drug toxicity in cats and has also been responsible for many deaths in dogs. Between 1992 and 1997, the ASPCA Poison Control Center received 1,464 calls about dogs and cats having ingested APAP. While acetaminophen can be used safely at a dose of 15mg/kg orally every 8 hours in most dogs, there is no safe dose recommended for cats. APAP toxicity in cats is almost exclusively due to intentional administration by humans, and doses as small as 163mg (1/2 of a regular strength acetaminophen tablet) have resulted in death.

Veterinarians are frequently called upon to treat acetaminophen toxicity and must have available medications and antidotes ready for administration as soon as the animal presents to the clinic. A variety of therapies may be employed to preempt or treat acetaminophen toxicity. Many of these agents are commercially available, but unfortunately, equally as many are no longer commercially available or never were. It is in these two latter cases that the community pharmacist can be instrumental in assisting the veterinarian with providing life saving therapies. What follows is a current listing of medications and therapies used to treat acetaminophen toxicity from the point of ingestion until late in the course of the illness. This is not a complete description of acetaminophen overdose therapy, but is intended to provide the veterinarian with a reference for all products that have been used to treat acetaminophen toxicity in dogs and cats.

### ***Apomorphine***

Apomorphine is a potent emetic that can cause complete emptying of the stomach within a few minutes of ingestion. Apomorphine was once commercially available for humans but was taken off the market almost a decade ago. Various veterinary companies attempted to provide commercially available product, but at the time of this printing, apomorphine is only available through the services of a compounding pharmacist. Apomorphine is not recommended for cats due to excessive CNS stimulation and respiratory depression. Apomorphine stimulates dopaminergic receptors in the chemoreceptor trigger zone and the onset of reaction to the drug is a mere 5 minutes.

### ***Ipecac***

As apomorphine may cause excessive CNS stimulation in cats prior to the induction of emesis, many clinicians prefer to use ipecac to induce emesis in cats. This emetic is also quite effective in dogs. Since many pet owners have this medication in their home medicine cabinets, veterinarians will often advise clients to induce emesis prior to coming to the veterinary hospital in order to save valuable time in preventing gastric absorption of acetaminophen. Ipecac, which not only stimulates the chemoreceptor trigger zone but also is a direct gastric irritant, elicits reaction within 20 minutes and the dose may be repeated one time.

### ***Acetylcysteine***

Acetylcysteine acts in two ways to combat acetaminophen poisoning: (1) to enhance the glutathione supply, and (2) to reduce the reactive NAPQI metabolite to a non-toxic conjugate with cysteine. Acetylcysteine rapidly hydrolyzes to cysteine and interacts with the reactive metabolite NAPQI to form a non-toxic conjugate that is excreted in the urine. Reducing NAPQI frees up glutathione stores for conjugation with APAP to non-toxic metabolites. Acetylcysteine is most effectively administered within 24 hours of acetaminophen ingestion, but may be administered with beneficial effect even after 24 hours. Acetylcysteine is not commercially available as a solution for injection, but the solution for inhalation has been given intravenously to dogs and cats for acetaminophen overdose.

### ***Sodium Sulfate***

Sodium sulfate may be administered as a sulfate donor to promote sulfation of acetaminophen. Sulfation is the primary elimination pathway for cats but is quickly saturated leading to toxic NAPQI formation. Dogs have a very limited ability to conjugate with sulfate and providing a sulfate substrate may enhance this path of elimination. While sodium sulfate injection is not commercially available, it may be compounded by pharmacists into a 1.6 percent sterile solution for injection.

### ***Methylene Blue***

The toxic NAPQI metabolite binds covalently to sulfhydryl groups on hemoglobin molecules rendering them incapable of transporting oxygen. Animals with methemoglobinemia quickly progress to cyanosis and quickly die from hypoxia. Cats are more susceptible to methemoglobinemia due to having 8 sulfhydryl groups on their hemoglobin as opposed to 4 groups in most other mammals. One study has been conducted indicating that administration of methylene blue will not be as successful in treating methemoglobinemia in male cats as in female cats. Studies also indicate that only single doses of methylene blue can be administered intravenously to cats without inducing Heinz body formation. Administration of subsequent doses risks further oxidative damage to red cells. Methylene blue as a 1 percent injection in 1ml and 10ml ampules is sporadically available commercially. If veterinarians require compounded solutions, the chemical is readily available to pharmacists.

### ***Ascorbic Acid***

Ascorbic acid may also be useful in treating methemoglobinemia. Ascorbic acid acts as an antioxidant and may prevent NAPQI binding to hemoglobin to form methemoglobin.

### ***Cimetidine***

Cimetidine has been given to acetaminophen-poisoned patients to inhibit cytochrome P-450 enzyme oxidation and the formation of NAPQI. Human studies have indicated that cimetidine must be administered no later than 8 hours after exposure to provide hepatoprotection.