

## Ivermectin Toxicity

Brandy R. Sobczak, DVM, ASPCA Animal Poison Control Center, Urbana, Illinois

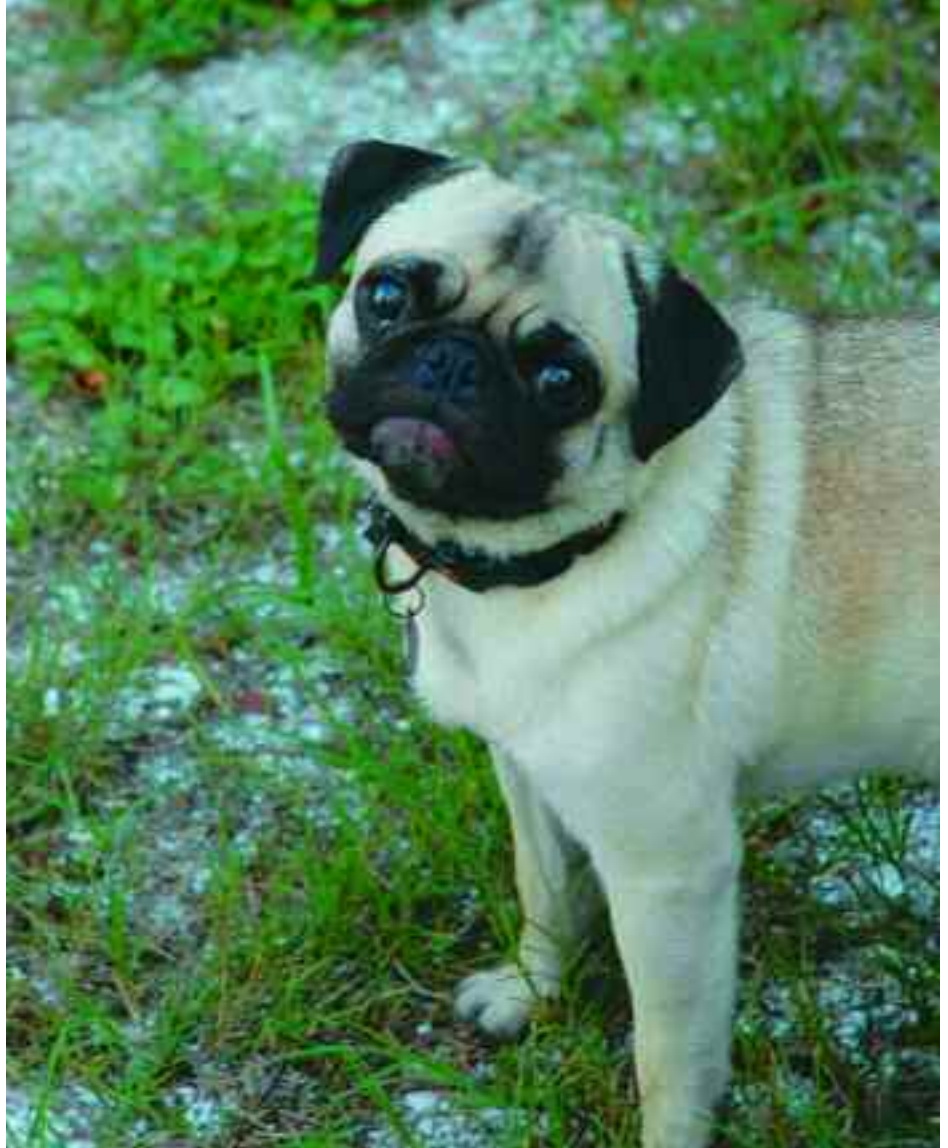
A 7.95-kg, 2-year-old male pug presented with ataxia and acute onset of blindness.

**History.** The dog had been prescribed a 1% concentration of ivermectin for treatment of demodicosis. The owner was instructed to give the medication with a syringe. Instead, she poured some of the liquid onto the dog's food. An estimated 3 ml had been used, making a possible dose of 3.77 mg/kg. Signs were noted within 5 hours of exposure to the medication.

**Physical Examination.** The dog was ambulatory on examination but moderately ataxic and depressed. Both pupils were mydriatic; the menace reflex and the pupillary light response were absent. The dog seemed to be clinically blind. Vital signs were within normal limits.

**Laboratory Results.** CBC, serum chemistry profile, and blood glucose were within normal limits.

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### ASK YOURSELF ...

Which of the following is the best treatment approach?

- A. Induce emesis, give charcoal, and explain to the owner that the blindness is permanent.
- B. Conduct gastric lavage, give charcoal, and perform an ophthalmic examination.
- C. Perform an ophthalmic examination, do not induce emesis but give charcoal, and treat supportively.
- D. Give atropine as an antidote and send the dog home.

CBC = complete blood count

## INSIGHTS FROM CLINICAL CASES . DISCUSSION

### Correct Answer: C

**Perform an ophthalmic examination, do not induce emesis but give charcoal, and treat supportively.**

Because the dog was already symptomatic, emesis was not indicated. Also, because the exposure occurred at least 5 hours previously and the product was a liquid, emesis or lavage would not be beneficial. Ivermectin has no antidote; treatment is symptomatic and supportive.



**Pathophysiologic Mechanism.** Ivermectin works against nematodes and arthropods by releasing GABA at presynaptic neurons in the peripheral nervous system. As an inhibitory neurotransmitter, GABA leads to paralysis and death of parasites by blocking postsynaptic stimulation of muscle fibers and neurons. In mammals, GABA receptors are found in the CNS and retina instead of at neuromuscular junctions. Ivermectin does not readily cross into the CNS, making it fairly safe for use in mammals. However, for young animals and sensitive breeds (those lacking P-glycoprotein) as well as in cases of overdose, ivermectin can more easily penetrate the blood–brain barrier, resulting in toxicosis.

**Clinical Signs.** Dogs often exhibit ataxia, mydriasis, CNS depression, and blindness. Depending on the animal and the dose, other signs may include recumbency, tremors, hypersalivation, hypothermia, seizures, respiratory depression, coma, and possibly death. Signs may take hours to days to develop. Laboratory results are often unremarkable.

**Treatment.** Emesis may be induced if the animal is asymptomatic and ingestion has occurred recently (within the past 1 to 2 hours). Ivermectin has a long half-life in dogs (about 2 days), and most of the drug is excreted

in the feces. It is speculated that ivermectin may undergo enterohepatic recirculation; thus, repeated charcoal doses may hasten recovery. There is no antidote for ivermectin; treatment is supportive, and recovery may take days to weeks. Depending on the patient's condition, IV fluid therapy in addition to thermoregulation can be helpful in severely depressed animals. Turning animals frequently to prevent decubital ulcers, urine scald, and pneumonia are critical in recumbent or comatose patients. Atropine is indicated only if bradycardia is present. Ventilatory support may also be necessary. Physostigmine has been used in comatose animals to encourage them to move around, eat, and possibly interact with owners. However, the effects of the drug are short-lived and should be reserved for severe cases. Nutritional support may also be required for recumbent animals. Picrotoxin is a GABA antagonist, but its use can be associated with seizures and is therefore not recommended.

Blindness caused by ivermectin is often transient, but recovery of sight may take up to 14 days. Fundic examinations may reveal a slightly swollen optic disk, retinal edema, and retinal folds.

**Differential Diagnoses.** Other substances that can cause similar CNS or cardiovascular signs

include loperamide or other opioids, benzodiazepines, ethylene glycol, alcohol, or marijuana. For acute onset of blindness, rule out sudden acquired retinal degeneration, trauma, glaucoma, or retinal detachment.

**Outcome.** This patient was treated with IV fluids and repeated doses of activated charcoal; his ataxia resolved within 36 hours. The blindness persisted but gradually improved. Fourteen days after exposure, the dog's eyesight had returned completely. ■

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

### Tx at a glance

- Induce emesis if the patient is asymptomatic and ingestion has occurred within the past 1–2 hours.
- Give a low-end dose of activated charcoal with a cathartic. Repeat every 6–8 hours at one quarter to one half of the original dose; this may need to be continued for 24 or more hours.
- Monitor cardiovascular function, respiratory function, and particularly body temperature for at least 24 hours. Monitor electrolytes (especially sodium) if repeated charcoal doses are given.
- Perform an ophthalmic examination in animals presenting with blindness.
- Provide supportive care to recumbent or comatose animals: IV fluids, ventilatory support, and nutritional support; turn frequently to prevent decubital ulcers, pneumonia, and urine scald.
- Atropine (0.01–0.02 mg/kg IV) is indicated only if bradycardia is present.
- Physostigmine (1–2 mg IV; effects may last 30–90 min) may be used in severely affected animals to allow short-term motor function and an opportunity to eat or interact with owners.

#### TAKE-HOME MESSAGES

- There is no antidote for ivermectin; treatment is symptomatic and supportive.
- Blindness associated with ivermectin generally is transient.
- Ivermectin should be used with caution in juvenile animals and sensitive breeds.

CNS = central nervous system; GABA = gamma aminobutyric acid