

Tremorgenic mycotoxin intoxication

by
Mary M. Schell, DVM

Dogs allowed to roam or get into the trash may ingest tremorgenic mycotoxins, which are neurotoxins that produce varying degrees of muscle tremors or seizures that can last for hours or days. Since 1998, the ASPCA Animal Poison Control Center (APCC) has consulted on 25 cases of suspected tremorgenic mycotoxin intoxication in dogs and one in a squirrel. Sources of tremorgenic mycotoxins for household pets have included moldy dairy foods, moldy walnuts or peanuts, stored grains, and moldy spaghetti.¹⁻⁷

These toxic secondary metabolites of many fungi vary in quantity and in their ability to produce clinical effects. Toxin production depends on seasonal growing conditions as well as the genus and species of the mold. At least 20 mycotoxins have been identified as tremorgens (compounds capable of inducing serious muscle tremor in one or more vertebrates), although only a few have been shown to have clinical relevance.^{3,8} *Penicillium* species are most often incriminated in producing tremorgenic mycotoxins; the most common are penitrem-A and roquefortine C.^{1,3,6,8} Intoxication with these mycotoxins has been documented in many animals, including dogs, cattle, sheep, rabbits, poultry, and rodents.

Several mechanisms of action have been proposed, and the mechanism may vary both between toxins and the individual susceptible species. Penitrem-A inhibits the inhibitory neurotransmitter glycine in mice. Studies in mice have shown that drugs such as mephensin or nalorphine, which increase glycine concentrations, halt tremors due to penitrem-A.³ A study in rats indicated that midazolam maleate, a gamma-aminobutyric acid agonist, reduced the tremors in rats that had been given penitrem-A without altering cerebellar tissue changes seen later.⁹ Another tremorgen - verruculogen - reduces concentrations of gamma-aminobutyric acid, an inhibitory neurotransmitter, in the brain.^{1,6,8}

Affected dogs may have a history of running unsupervised or of ingesting compost, garbage, or moldy foods (especially moldy dairy products) within two hours before the onset of signs. Toxins ingested in low quantities can cause fine muscle tremors that may last for several hours or days. With larger exposures, the tremors can become severe, progress to seizures, and may result in death. Tremors in cases of non-lethal intoxication may last several days. Vomiting often precedes the earliest tremors, which may help limit the severity of illness. Vomiting was reported in 13 of 26 APCC consultations mentioned above.

Diagnosis

Other substances can cause signs of central nervous system stimulation in dogs (*e.g.* hyperesthesia, tremors, and seizures) and must be considered in a list of differential diagnoses. These substances include strychnine, metaldehyde, ethylene glycol, cholinesterase inhibitors, methylxanthines, medications such as pseudoephedrine hydrochloride, and illicit drugs such as amphetamines and cocaine.^{3,10} If you suspect ethylene glycol exposure, an ethylene glycol test is useful. Stimulants such as amphetamines, methylxanthines, and pseudoephedrine frequently cause marked tachycardia and hyperactivity before the onset of tremors or seizures.

You can submit a sample of the suspect food or stomach contents to a diagnostic laboratory for analysis. The traditional means of evaluating for the presence of a tremorgenic mycotoxin involved administering an extract of the suspect food to mice and observing for any clinical signs. Currently, mass spectrometry techniques can identify common tremorgenic mycotoxins.⁴ A tremorgen screen that specifically identifies and quantifies tremorgens, including penitrem-A and roquefortine C as well as strychnine and metaldehyde, is now available at the Animal Health Diagnostic Laboratory at Michigan State University.^{4,11}

Treatment and Prognosis

The treatment goals for any animal presenting with tremors or seizures are to control the tremors or seizures, decontaminate the gastrointestinal tract, and stabilize the animal. Diazepam alone may not effectively control severe

mycotoxin-induced tremors. To control severe tremors, you may need to administer methocarbamol at a dose of 55 to 220 mg/kg given intravenously to effect at a rate of no more than 2 ml/min.¹² If the tremors have progressed to generalized seizures, you may need to administer diazepam initially (0.5 to 1 mg/kg intravenously¹³), followed by methocarbamol, or administer a barbiturate such as pentobarbital sodium (3 to 15 mg/kg slowly intravenously to effect¹³). Once tremors are controlled, decontaminate the gastrointestinal tract. Perform gastric lavage if the animal did not vomit. Activated charcoal (1 to 2 g/kg orally) and a cathartic such as 70% sorbitol (3 ml/kg orally) or magnesium sulfate (250 mg/kg or 1/4 level tsp/10 lb orally) may limit further absorption of toxins. Provide supportive therapy such as intravenous fluids, corticosteroids for managing the shock, and thermoregulation as necessary (affected animals are often hyperthermic on presentation and may become hypothermic as signs are controlled).

Tremorgenic mycotoxins are not uncommon, so don't overlook them as causes of acute central nervous system stimulation. With early and aggressive treatment, the prognosis is good, and no long-term sequelae are expected.

References

1. Abramson, D.: Toxicants of the genus *Penicillium*. *Handbook of Plant and Fungal Toxicants* (J.P. Felix, ed.). CRC Press, Boca Raton, Fla., 1997; pp 303-317.
2. Arp, L.H.; Richard, J.L.: Intoxication of dogs with the mycotoxin penitrem A. *JAVMA* 175 (6):565-566; 1979.
3. Beasley, V.R. *et al.*: Tremorgenic mycotoxins and various staggers syndromes. *A Systems Affected Approach to Veterinary Toxicology*. Department of Veterinary Biosciences, College of Veterinary Medicine, University of Illinois, Urbana, Ill., 1997; pp 137-142.
4. Braselton, W.E.; Rumler, P.C.: MS/MS screen for the tremorgenic mycotoxins roquefortine and penitrem A. *J. Vet. Diagn. Invest.* 8:515-518; 1996.
5. Hocking, A.D. *et al.*: Intoxication by tremorgenic mycotoxin (Penitrem A) in a dog. *Aust. Vet. J.* 65 (3):82-85; 1988.
6. Pitt, J.I.: *Penicillium*. *Foodborne Disease Handbook, Vol 2 Diseases Caused by Viruses, Parasites, and Fungi* (Y.H. Hui, *et al.*, eds.). Marcel Dekker, New York, N.Y., 1994; pp 617-630.
7. Puls, R.; Ladyman, E.: Roquefortine toxicity in a dog. *Can. Vet. J.* 29:569; 1988.
8. Cole, R.J.: Tremorgenic mycotoxins. *Mycotoxins in Human and Animal Health, Conference Proceedings* (J.V. Rodricks *et al.*, eds.) Pathotox Publishers, Park Forest South, Ill., 1977; pp 583-595.
9. Cavanagh, J.B. *et al.*: The effects of the tremorgenic mycotoxin penitrem A on the rat cerebellum. *Vet. Pathol.* 35 (1):53-63; 1998.
10. Lowes, N.R. *et al.*: Roquefortine in the stomach contents of dogs suspected of strychnine poisoning in Alberta. *Can Vet. J.* 33:535-538; 1992.
11. Personal communication, staff at the Animal Health Diagnostic Laboratory, Lansing, Mich., August 1999.
12. Fort Dodge Animal Health, Inc.: Robaxin-V product insert. Overland Park, Kan., 1999.
13. Plumb, D.C.: *Veterinary Drug Handbook*, 3rd Ed. Iowa State University Press, Ames, 1999.

"Toxicology Brief" was contributed by Mary M. Schell, DVM, ASPCA Animal Poison Control Center, 1717 S. Philo Road, Suite 36, Urbana, IL, 61802; (888) 4ANI-HELP.

Copyright © 2000, Veterinary Medicine Publishing Group. Reprinted with permission from the April 2000 issue of *Veterinary Medicine*. All rights reserved. For more on *Veterinary Medicine*, visit www.vetmedpub.com.