**Bufo** species toxicosis: Big toad, big problem

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It is common for companion animals to mouth toads. Oral exposure to larger toad species such as marine and Colorado River toads can be life-threatening. Fortunately, mouthing other toad species found throughout the United States usually results in nothing more than signs of oral irritation, including profuse ptyalism, gagging, and pawing at the mouth.

True toads, from the genus *Bufo*, are represented by 18 species in the continental United States. Only two species—*Bufo marinus* and *Bufo alvarius*—have been reported to cause serious signs after oral exposure.

*Bufo marinus*, also known as the cane, marine, or giant toad, is found in the southern tip of Florida and Texas and in Hawaii. *Bufo marinus* was introduced from Puerto Rico into Hawaii in 1932 in an effort to control an insect threat to the sugar cane industry. Adults range from 4 to 9.5 in long. The toad's size and its extremely large, raised parotid poison glands extending caudally over the shoulders aid in its identification (Figure 1).

The Colorado River toad, *B. alvarius*, is found in the southern half of Arizona, southeastern California, and southwestern New Mexico. Also known as the Sonoran Desert toad, this species ranges from 3 to 7 in long and has comparatively smooth skin. Besides its parotid poison glands, this species has an additional pair of poison glands on the forelimbs and several pairs on the hindlimbs.

All toads from the genus *Bufo* produce poisonous glandular secretions. The biochemical classes of the components in the secretions are similar, although individual components vary among species. *Bufo marinus*, followed by *B. alvarius*, has the largest parotid poison glands and the largest volume of secretions from the glands.

**Toxins and their mechanisms of action**

Parotid glands in toads are not salivary glands. They are aggregations of skin glands that have several small orifices that empty on the skin's surface. The secretions' primary toxins are bufogenins, such as marinobufagin, and bufotoxins, such as marinobufotoxin. Bufogenins are similar to cardiac glycosides. These compounds inhibit Na⁺, K⁺-ATPase activity in the myocardial cell membrane, similar to digitalis. This effect leads to an increase in intracellular sodium and, by stimulating sodium-calcium exchange, ultimately increases calcium concentrations in the myocardial cells, resulting in arrhythmias. Bufogenins also block sodium channels, similar to local anesthetics. Bufotoxins are conjugates of a bufogenin with suberyl arginine. Their mechanism is thought to be similar to that of the bufogenins.

Secondary toxins produced by parotid glands include the bufotenines serotonin and 5-hydroxytryptophan as well as catecholamines. Bufotenines can potentially cause signs such as seizures, depression, tremors, hyperesthesia, hyperthermia, vomiting, and diarrhea if absorbed in sufficient quantities. Catecholamines may cause signs such as tachycardia, hypertension, anxiety, and respiratory difficulty. However, dogs that were experimentally given *Bufo* species toxins orally did not experience an elevation in blood pressure. Generally, the oral mucosa prevents marked absorption of most compounds. The role of serotonin is questionable because of its rapid degradation in the gastrointestinal tract. Other bufotenines such as 5-hydroxytryptophan are better-absorbed through the gastrointestinal tract and may play a more important role. Catecholamines are also inactivated by the intestine and the liver, but endogenous cate-
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BRIEF SUMMARY
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CAUTIONS:
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- Do not administer Baytril Tablets to dogs or cats with known or suspected sensitivity to quinolones.
- Do not administer Baytril Tablets to dogs or cats with known or suspected sensitivity to other antibacterials.
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TOXICOLOGICAL BRIEF
Continued

Cholamine release may instead serve to potentiate the toxicosis. The clinical signs of poisoning may occur as a result of a combination of factors that may differ from one kind of compound to another.

Signs of Clinical and Diagnoses
Signs of Baytril toxicity manifest immediately and can progress to advanced signs in less than 15 minutes. The most common noncardiac signs of dogs results from B. marinus exposure include neurological abnormalities (seizures, stupor, ataxia, and dystagmus), pyalism (usually profuse), hyperemic mucous membranes, recumbency or collapse, tachypnea, and vomiting. Hyperthermia or hypothermia may also develop. The most common electrocardiographic findings in dogs following B. marinus exposure were sinus arrhythmia, sinus tachycardia, and normal sinus rhythm. However, 10 of 94 dogs evaluated required treatment for bradycardia, while only two dogs required measures to slow tachycardia. A variety of arrhythmias can be seen after oral exposure in dogs and people, but hypocalcemia has also been reported.

The severity of signs likely depends on the volume of the secretion released by the toad and the patient's size. Exposure to larger toads, such as B. marinus or B. altavus, is more likely to produce more severe signs, especially in smaller animals. For example, smaller dogs were hospitalized longer in one case series. However, exposure to any Bufo species can potentially produce advanced signs, especially if a patient is small, geriatric, or in poor health.

Consider other possible causes of these clinical signs if an exposure was not witnessed. Inquire about recent pesticide use, because organophosphorus, carbamate, pyrethroid, metaldehyde, or chlorinated hydrocarbon exposure can cause similar signs. Also ask about medications in the home. Toxicosis from ingestion of a sympathomimetic such as pseudoephedrine or amphetamine, a methylxanthine such as theophylline, a 3β-blocker, a 3β-agonist, or one of many antidepressants can have a similar presentation. Exposure to common outdoor plants such as Rhododendron species, Nerium oleander (oleander), and Digitalis purpurea (foxglove) can also manifest with similar signs. Oral signs such as pylralis can be induced by oral exposure to agents such as freshly applied topical flea products, caustic cleaning products, liquid potpourri, and plants such as Dieffenbachia and Philodendron species that contain insoluble calcium oxalate. Finally, other medical conditions such as seizure disorders, vehicular trauma, and heat stroke can have a similar presentation.

Treatment
Oral lavage is recommended for all exposures. The most effective way to
decrease oral absorption of secretions is to have the owner lavage the mouth with running water from a tap or a hose pointed in a rostral direction through the oral cavity. This is indicated only if exposure is likely and the patient is exhibiting either no signs or mild signs such as gagging or ptysialism. If the patient is exhibiting advanced signs such as depression or tachypnea, oral lavage should be performed at the veterinary facility. If possible, intubate the patient before oral lavage to decrease the risk of iatrogenic aspiration. If the patient is from an area where B. marinus or B. alterans is found, immediate evaluation is recommended after oral lavage, regardless of the patient's size. In other areas of the country, advise the owner of the small likelihood of serious exposure, and tell the owner to watch for the clinical signs. Evaluate the patient immediately if any serious signs emerge.

The ingestion of a whole toad is potentially more life-threatening than the mouthing of a toad. If a toad is ingested, emesis is indicated unless signs other than ptysialism are present. Other means of decontamination in this situation can include endoscopic retrieval, surgical removal, or multiple doses of activated charcoal with a cathartic.

Activated charcoal may help adsorb Bufo species toxins, but its efficacy for this use has not been evaluated. Nevertheless, activated charcoal is recommended if advanced signs are developing. If any abnormality in cardiac rate or rhythm is auscultated or if severe neurologic signs develop, monitor an electrocardiogram continuously. Evaluate serum electrolyte activity and monitor serial potassium concentrations if hyperkalemia or hypokalemia is detected. Correct any electrolyte imbalances as needed.

A dog exhibiting severe signs of toxicosis should receive an initial shock dose of fluids (45 to 90 ml/kg intravenously). The shock dose of fluids in cats is 25 to 60 ml/kg.15 Once the animal's condition stabilizes, the fluid rate may be lowered to a maintenance rate. Measure the serum potassium concentration, and administer potassium supplementation or take steps to lower the potassium concentration as needed. Frequently monitor the body temperature of severely affected animals. Control agitation, seizures, or tremors with diazepam (0.5 to 2 mg/kg...
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0.04 mg/kg intravenously or intramuscularly is appropriate in dogs and cats to treat severe bradycardia.13 Very high propranolol hydrochloride doses to treat arrhythmias have been recommended based on experimental trials,4 but empirical use of propranolol is not advisable because of the high incidence of bradydysrhythmias seen with toad intoxication.12 For ventricular and supraventricular arrhythmias that are not responsive to fluids, propranolol (0.02 to 0.06 mg/kg slowly intravenously in dogs and 0.04 mg/kg slowly intravenously in cats) is indicated. Lidocaine can be used for ventricular arrhythmias, but it is ineffective for supraventricular arrhythmias. Lidocaine can be given to dogs as a slow intravenous bolus (2 to 4 mg/kg) followed by a constant-rate infusion of 25 to 100 µg/kg/min. Cats can be given a slow intravenous bolus (0.25 to 0.75 mg/kg) followed by a constant-rate infusion of 10 to 40 µg/kg/min.16 Cats are more likely to experience side effects such as twitching and seizures from lidocaine, so be cautious with its use in this species.16 Esmolol hydrochloride has been recommended for treating prolonged sinus tachycardia as a result of *B. marinus* exposure.2 A recommended dose of esmolol for supraventricular arrhythmias in dogs consists of a loading dose of 0.5 mg/kg slowly intravenously followed by a constant-rate infusion of 50 to 200 µg/kg/min. Esmolol's advantages include a rapid onset of action and a rapid cessation of action once the infusion is discontinued. Hypotension is a common adverse effect. Esmolol can increase serum digoxin concentrations by up to 20% if the two drugs are concomitantly administered.14 It is unknown whether esmolol would have a similar effect on the digoxin-like bufogenins and bufotoxins absorbed after oral exposure.

Using diuretics such as furosemide (1 to 2 mg/kg intravenously) and hyperosmolar agents such as mannitol (0.25 to 1 g/kg slowly intravenously over 15 to 20 minutes) has been advocated in dogs experiencing severe signs such as collapse or coma.2 If you give furosemide to a hypokalemic patient, monitor the patient's potassium concentration. Dexamethasone sodium phosphate (0.5 to 1 mg/kg intravenously) and methylprednisolone sodium succinate (15 to 30 mg/kg intravenously) have also been administered in affected dogs.2 The finding of perivascular edema in the brains of dogs that were intravenously dosed with *B. marinus* secretions lends support to these recommendations.1 The above medications are acceptable for use in cats at similar doses.14

Digoxin-specific antigen-binding fragments (digoxin immune Fab) have been given in large empirical doses to people that developed signs after ingesting products containing glandular secretions from *Bufo* species toads. Digoxin immune Fab may especially be of value in treating patients that exhibit advanced arrhythmias, hyperkalemia,12 or neurologic signs, but the use of this product may be cost-prohibitive.18,19

**Prognosis**

Prompt treatment and supportive care initiated soon after exposure to *B. marinus* or *B. alvarius* usually result in a favorable outcome. However, fatalities can occur, especially if treatment initiation in the face of advanced signs has been delayed. Exposure to other *Bufo* species typically results in mild signs that should be self-limiting once the mouth is lavaged. Since all *Bufo* species contain similar toxins in their glandular secretions, the possibility for advanced signs always exists and should not be ignored.
REFERENCES