Bufotoxin

Bufotoxins are bufogenins conjugated with suberyl arginine, and they have a similar mechanism of action as bufogenins.

From: Veterinary Toxicology (Third Edition), 2018

Related terms:

Bufotenin, Toxic Injury, Toxin, Animal, Serotonin, Vomiting, Heart Arrhythmia, Amphibia, Anura, Bufo

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Toxic Exposures

Peter M. Rabinowitz, ... Lora E. Fleming, in Human-Animal Medicine, 2010

AMPHIBIAN INTOXICATIONS

Toads (genus *Bufo*) produce a potent toxin (bufotoxin) in their parotid gland that is similar to cardiac glycosides such as digoxin. Human cases of intoxication are rare, but in Asia ingestion of toad egg soup has led to significant toxicity. Treatment involves gastric decontamination and management of arrhythmias. In serious human poisonings a digoxin antidote (digoxin-specific Fab fragment) has been used.

Poisoning by toads is a significant problem in dogs that try to ingest them. Large toads such as the marine toad (*Bufo marinus;* also known as *cane toads* or *giant neotropical toads*) carry a higher load of venom (Figure 8-35).

Mouthing of the toad by the dog releases toxin into the dog's mouth and contact with mucous membranes, leading to systemic absorption. Poisoned dogs develop excess salivation, anxiety, and vomiting almost immediately, and death can occur within 15 minutes after exposure. Treatment involves decontamination of the oral cavity through irrigation with water and forced emesis if a toad has been swallowed. Endoscopic or surgical removal of the toad may be necessary. If cardiac complications develop in a dog, the use of digoxin-specific Fab fragment should be weighed against its high cost.[10] Bradycardia can be treated with atropine (0.04 mg/kg IM, SC).

Toads

Michael E. Peterson DVM, MS, Brian K. Roberts DVM, DACVECC, in Small Animal Toxicology (Third Edition), 2013

Mechanism of Toxicity

The biologically active substances produced by Bufo toads include dopamine, epinephrine, norepinephrine, serotonin, bufotenine, bufagenins, bufotoxins, and indolealkylamines.[1,3] All *Bufo* species produce these substances, but there is variation in the quantity of each substance produced by different toads. For instance, Bufo marinus and *Bufo viridis* contain the highest known plasma level of endogenous digitalis-like substances, which are collectively known as *bufadienolides.*[7] Indolealkylamines have been characterized as similar to the hallucinogen lysergic acid diethylamide.[2]

Bufotenine, or 5-hydroxydimethyltryptamine, has been definitively identified as a pressor, but there is also evidence that this compound may be a hallucinogen or have a "psychedelic" effect.[1,8] The hallucinogenic effects of bufotenine may be

this compound may be a hallucinogen or have a "psychedelic" effect.[7] The hallucinogenic effects of bufotenine may be secondary to the known systemic pressor activity and oxygen starvation of the optic nerve.[1] Only the Colorado River toad (*Bufo alvarius*) releases 5-methoxydimethyltryptamine from the methylation of serotonin; it acts as a true hallucinogen.[9]

Bufagenins and bufotoxins are cardioactive steroids also known as digitalis-like substances.[7] The bufagenins act like digitalis to inhibit potassium-dependent adenosine triphosphatase, which is the enzyme that allows active transport of sodium out of and potassium into cells.[7] Digitalis-like substances can cause alterations in heart rate and rhythm. Any type of arrhythmia can result from digitalis overdose, especially bradycardia and supraventricular and ventricular tachycardias. Bufotoxins are vasoconstrictors and add to the pressor effect of bufotenine to increase systemic vascular resistance.[1]

Although many of the substances released from *Bufo* toads are known to cause vasoconstriction and an increase in blood pressure, there has been no documentation to support this pressor activity.[3]

Role of pathology in diagnosis

Manu M. Sebastian, in Veterinary Toxicology, 2007

Toads

The most common toad seen in United States is the giant tropical toad, *Bufo marinus* which produce toxins which include bufagins, bufotoxins, bufotenins and other compounds. Dogs and rarely cats are exposed to the toxin. Bufagin's and bufotoxin's action is described as digitalis-like, often resulting in ventricular fibrillation. The common clinical signs are related to cardiac and CNS. Profuse salivation, head shaking, pawing at mouth and wretching are the common initial signs. Other clinical signs include seizures, cardiac arrhythmia, dyspnea, vomiting and recumbency or collapse. No specific histopathological lesions are observed in exposure to these toxins. Toad poisoning is mostly reported from Florida and Texas (Roberts *et al*., 2000; Kahn, 2005).

Invasive and Introduced Reptiles and Amphibians

Robert N. Reed, Kenneth L. Krysko, in Current Therapy in Reptile Medicine and Surgery, 2014

Frogs

Relatively few introduced frogs are established in the United States, but two species are of considerable veterinary interest. When stressed or molested, the Cane Toad (Figure 28-8) excretes bufotoxin from its large parotid glands, which can cause extreme pain or even death in domestic pets such as cats and dogs by causing a digitalis effect, hallucinations, uncontrollable salivating, coughing, vomiting, and convulsions. Domestic pets frequently attack or consume Cane Toads, especially in southern Florida. While collecting Cane Toads in a remote area near Lake Okeechobee in March 2002, K.L. Krysko observed an adult (approximately 35-kg) Rottweiler swallow a Cane Toad followed by the aforementioned effects for 45 minutes and death of the dog.

With females sometimes exceeding 130 mm snout-vent length, the Cuban Tree Frog (*Osteopilus septentrionalis*, Figure 28-9) far exceeds the length of most native tree frogs in the United States and is known to prey on these and a variety of native vertebrates. This species also excretes toxins from its skin, which can cause extreme irritation to mucous membranes of humans and other animals. Individuals have gone to the hospital for prolonged extreme pain after touching a Cuban Tree Frog then rubbing their eyes, and similar incidents may occur with companion animals.

Neurotoxic Animal Poisons and Venoms

Terri L. Postma, in Clinical Neurotoxicology, 2009

Toxin

Bufo toads contain bufotenine (5-OH-DMT) and an alkaloid tryptamine (5-MeO-DMT), a potent hallucinogenic. Experts have concluded that psychotropic effects are most likely from contact with *B. alvarius*.[222] Bufotoxin is a toxic cardiac glycoside, which is dried and used as a preparation in Chinese medicine.[223] Trace amounts of morphine have also been detected from *B. marinus*.[224]

Dendrobates and *Phyllobates* species contain several alkaloids. Batrachotoxins are the principle toxins found in *Phyllobates* species, potent inhibitors of sodium channel deactivation causing persistent ACh release, and are used in Columbian Indian blowguns to poison darts for hunting.[225,226] Other alkaloids include pumiliotoxins and histrionicotoxins.[226]

Cardiovascular Effects of Systemic Diseases

Francis W.K. SmithJr., ... Carl D. Sammarco, in Manual of Canine and Feline Cardiology (Fourth Edition), 2008

TOAD POISONING

- The Colorado river toad (*Bufo alvaritus*) and the marine toad (*Bufo marinas*) secrete toxins from the parotid glands that can cause profound cardiotoxicity. The parotid gland secretions contain epinephrine, norepinephrine, dopamine, serotonin, bufotenine, bufagenins, and bufotoxins. The animal does not have to ingest the toad to become poisoned. Toxic parotid secretions can be absorbed through the oral mucous membranes just holding the toad in its mouth.

Cardiac Pathophysiology

- Bufagenins and bufotoxins can have digitalis-like effects on the heart.

Diagnosis

History and Physical Examination

- The pet is often observed playing with the toad.
- Clinical signs occur within minutes and may include hypersalivation, vomiting, diarrhea, weakness, pulmonary edema, and seizures. Coma and death can occur within 30 minutes.

Electrocardiography

- In experimental studies, the digitalis-like effect of the toxin may result in any type of arrhythmia. In natural exposure, arrhythmias are rare. The most common rhythms noted are sinus arrhythmia and sinus tachycardia.
- Severely intoxicated dogs with bradycardia, tachycardia, neurologic disability or signs of shock should get an initial ECG. Monitoring the ECG is recommended if significant arrhythmias are noted.

Therapy

- The patient's mouth should be rinsed immediately. Atropine may help decrease salivation, but is reserved for patients with heart rates less then 50 bpm. Using atropine to treat excess salivation in dogs with normal heart rates or tachycardia can lead to more severe arrhythmias.
- Vomiting should be induced if ingestion was recent. The venom may enter enterohepatic circulation. Therefore, multiple doses of activated charcoal should be administered. Sorbitol cathartic is advised.
- Provide supportive care, including anticonvulsive and antiarrhythmic medication as needed.
- Pentobarbital anesthesia will control seizures.
- Propranolol is quite effective for tachyarrhythmias. In patients without asthma or pre-existing heart disease, doses of 0.5 to 2 mg/kg can be given slowly IV, to effect.

Poisonings in the Captive Reptile

Kevin T. Fitzgerald PhD, DVM, DABVP, Kristin L. Newquist BS, AAS, CVT, in Small Animal Toxicology (Third Edition),

2013

Amphibian Toxins

Certain amphibians are poisonous and can cause intoxications. In the United States two toad species (genus *Bufo*) are the source of the majority of toad poisonings. The cane or marine toad (*Bufo marinus*) and the Colorado River toad (*Bufo alvarius*) are the two species most implicated.[75,76]

All *Bufo* species of toads have parotid glands that release toxic substances when the animals are threatened. These toxic substances are biologically active compounds, such as dopamine, norepinephrine, epinephrine, serotonin, bufotenine, bufogenin, bufotoxins, and indolealkylamines. Severe toxicosis has been seen in small animals that bite, masticate, or hold these toads in their mouths. The active compounds secreted from the toad's parotid gland are rapidly absorbed by the mucous membranes of the predator and enter the systemic circulation.

Once these compounds have entered the circulation, the greatest effects are seen on the peripheral vascular system, the CNS, and the heart. Bufotenine has pressor effects on blood vessels, but may act as a hallucinogen as well. Bufogenin has digitalis-like effects.[77] It causes alterations in heart rate and rhythm. Bufotoxins are vasoconstrictors and add to the pressor effects. Indolealkylamines have activity similar to the hallucinogen LSD.

Dogs are the animals most commonly affected by amphibian parotid toxins. However, cats and ferrets have been reported to be affected. Exposure in reptiles has not been documented; however, it is logical to assume predatory reptiles that include amphibians in their diet might encounter and ingest poisonous toads. No specific antidote is available, and treatment is basically supportive. Therapy includes thoroughly flushing the oral cavity with running water. Severely affected animals may require seizure intervention and medications to stabilize heart rhythms. Supportive care involving fluids may be necessary in badly debilitated animals. Many other toxicoses and conditions can lead to neuropathies, and cardiac arrhythmias can present with signs very similar to those of toad poisonings.

Emergency Care

Elisa M. Mazzaferro, Richard B. Ford, in Kirk & Bistner's Handbook of Veterinary Procedures and Emergency Treatment (Ninth Edition), 2012

Other Poisonous Creatures

Bufo Species Toxicosis

Bufo toad species (*Bufo marinus*, also known as the *cane toad, marine toad,* and *giant toad;* and the Colorado River toad or Sonoran desert toad, *Bufo alvarius*) can be associated with severe cardiac and neurotoxicity if an animal licks the toad's skin. The severity of toxicity depends largely on the size of the dog. Toxins in the cane toad, *B. marinus,* include catecholamines and vasoactive substances (epinephrine, norepinephrine, serotonin, dopamine) and bufotoxins (bufagins, bufotoxin, and bufotenine), the mechanism of which is similar to that of cardiac glycosides. Clinical signs can range from ptyalism, weakness, ataxia, extensor rigidity, opisthotonus, and collapse to seizures. Clinical signs associated with *B. alvarius* toxicity are limited largely to cardiac dysrhythmias, ataxia, and salivation.

Immediate Action and Treatment

The animal should have its mouth rinsed out thoroughly with tap water even before presentation to the veterinarian. If the animal is unconscious or actively seizing and cannot protect its airway, flushing the mouth is contraindicated. Once an animal is presented to the veterinarian, the veterinarian should place an intravenous catheter and monitor the patient's ECG and BP. Attempt seizure control with diazepam (0.5 mg/kg IV) or pentobarbital (5 to 15 mg/kg IV to effect). Ventricular dysrhythmias can be controlled first with esmolol (0.1 mg/kg). If esmolol is ineffective, administer a longer-acting parenteral β-antagonist such as propranolol (0.05 mg/kg IV). Ventricular tachycardia also can be treated with lidocaine (1 to 2 mg/kg IV, followed by 50 to 100 mcg/kg/min IV CRI).

Management

Case management largely depends on supportive care and treating clinical signs as they occur. Monitor baseline acid

Case management largely depends on supportive care and treating clinical signs as they occur. Monitor baseline acid-base and electrolyte balance because severe metabolic acidosis may occur that should be treated with intravenous fluids and sodium bicarbonate (0.25 to 1 mEq/kg IV). Monitor ECG, BP, and mentation changes closely. Control seizures and cardiac dysrhythmias.

Regurgitation/Vomiting

In Clinical Veterinary Advisor, 2013

Basic Information

Definition

- Regurgitation is the passive discharge of undigested food within a few hours of consumption.
- Vomiting is the ejection of food from the stomach or the anterior intestine.
- Vomiting is controlled by the autonomic and somatic nervous systems.

Synonym

Emesis

Epidemiology

Species, Age, Sex

- All species of any age susceptible
- Commonly reported in recently fed snakes in stressful situations (e.g., handled) or kept at a low temperature

Risk Factors

- Elevated stress levels due to overstimulation and overcrowding
- Consumption of too large a meal
- Temperature below digestive requirement
- Infection altering physiologic or digestive processes
- Anatomic intestinal obstructions
- Neonatal congenital gastrointestinal defects
- Medication (e.g., tortoises with parenteral enrofloxacin)
- Bufotoxins

Contagion and Zoonosis

- Infectious causes are common.
- Cryptosporidiosis in snakes
- Inclusion body disease (IBD) virus in boid snakes (see Inclusion Body Disease in Snakes)
- *Chlamydophyla* in a gaboon viper (*Bitis gabonica*) (see Chlamydophilosis)
- Parasites associated include cryptosporidiosis, amoebiasis, cestodiasis, and ascariasis.

Associated Conditions and Disorders

Diarrhea (see Diarrhea)

Clinical Presentation

History, Chief Complaint

- A complete history and thorough physical exam are needed to narrow down potential causes of regurgitation and

- A complete history and thorough physical exam are needed to narrow down potential causes of regurgitation and vomiting.
- Expelled food found on the cage floor
- It is often difficult for owners to differentiate between regurgitation and vomiting.
- Some clients may provide feeding records that may help clinicians to associate a pattern for the regurgitation/vomiting and to determine the severity of the condition.
- Inactivity and increased basking frequency
- Snakes housed at a temperature that is too cool will expel food that is relatively fresh and undigested.
- Regurgitation and vomiting are uncommon in chelonians and when seen are considered serious symptoms of illness. One exception to this is iatrogenic regurgitation/vomiting associated with parenteral injections of enrofloxacin.
- Animals demonstrating symptoms of regurgitation and vomiting may display prolonged disinterest in feeding.

Physical Exam Findings

- Animals suffering from frequent vomiting may present dehydrated with acid-base and electrolyte imbalances.
- Emaciation/cachexia may be evident in an animal that is unable to keep food items down over an extended period of time.
- Animals with advanced symptoms may be dull, inactive, and unresponsive.

Etiology and Pathophysiology

- Improper husbandry is the most common cause of regurgitation and vomiting in reptiles.
- The most common mistakes include keeping the reptile at a lower temperature than required for adequate digestion and postprandial handling, especially in snakes.
- Infectious causes for gastritis and subsequent regurgitation/vomiting are common, including:
    - Gram-negative bacteria
    - *Chlamydophyla*
    - Viral disease such as IBD virus in boid snakes
    - Gastrointestinal parasites, including coccidia (cryptosporidiosis and others), amoebae, cestodes, and nematodes (ascariasis)
    - Toxins such as pesticides, including organophosphates and bufotoxins, may cause vomiting. Iatrogenic vomiting can be caused by drugs such as enrofloxacin, miticides, levamisole, xylazine, and apomorphine.
    - Intestinal obstructions or lesions associated with food consumption, surgery, or disease may induce regurgitation and vomiting.
    - Metabolic disease such as renal or hepatic insufficiency
- These causes disrupt normal esophageal or gastric function and/or motility, resulting in impaired digestion, stasis, putrification, and passive (regurgitation) or active (vomiting) discharge of ingesta.
- Regurgitation typically is associated with an esophageal or pharyngeal problem.
- Gastroesophageal sphincter incompetence is a common gastric issue that causes regurgitation.
    - These events disrupt normal esophageal or gastric functions or motility.
- Both vomiting and regurgitation are symptoms of an underlying problem, not diseases themselves.