Amitraz toxicity is a rare clinical presentation. The mortality rate is less than 5% in dogs if appropriate treatment is instituted but is higher in young, old and debilitated animals and, reportedly, toy-breed dogs (e.g., Chihuahuas, Pomeranians). Amitraz toxicity may be seen with doses of 10 mg/kg. Signs of toxicity may appear within 1 hour of ingestion and are mostly related to α2-adrenergic activity. Common clinical signs include cardiovascular, gastrointestinal (GI), and neurologic signs.

**DIAGNOSTIC CRITERIA**

**Historical Information**

**Gender Predisposition**
- None reported.

**Age Predisposition**
- Animals younger than 3 months and geriatric animals.

**Breed Predisposition**
- Toy breeds (e.g., Pomeranian, Chihuahua).
- Cats are more sensitive than dogs and more likely to develop toxic effects.
- Rabbits and small rodents are very sensitive to the toxic effects of amitraz.

**Owner Observations**
- Lethargy.
- Ataxia.
- Vomiting.
- Loss of consciousness.
- Collapse.
- Sedation.
- Anorexia.
- Diarrhea.
- Dyspnea.
- Hypersalivation.
- Polyuria/polydipsia.
- Death.
- Mild to severe depression (lasting 24–72 hours).

**Other Historical Considerations/Predispositions**
- Witnessed ingestion of acaricide-impregnated collars or pieces of collar.
- Inappropriate direct application of amitraz-containing products.
- Use of undiluted amitraz-containing products. After application of properly diluted and applied solution, toxic effects are less common and transient.
- Toxic effects are more severe and recovery is slower in debilitated animals.

**Physical Examination Findings**
- Lethargy.
- Ataxia.
- Hypothermia.
- Bradycardia.
- Tachypnea/dyspnea.
- Mydriasis.
- Vomiting.
- Dehydration.
- Seizures.
- GI stasis.
- Hypertension or hypotension

**Laboratory Findings**
- Hyperglycemia—common.
  - Secondary to effects on pancreatic β cells and consequent inhibition of insulin release.
  - Secondary to effects on α cells of the islet of Langerhans and increased glucagon secretion.
  - May worsen clinical signs in diabetic animals.
- Elevated liver enzyme activity—rare.
  - Secondary to metabolism in the liver.
- Glycosuria.
- Isosthenuria.
- Secondary to glycosuria and decreased secretion of antidiuretic hormone and renin.
Other Diagnostic Findings

- Abdominal radiography.
  - May help visualize a collar buckle in the stomach or small intestine.
- Liquid chromatography.
  - Used to evaluate for the presence of amitraz in body fluids (i.e., gastric contents), plasma, and hair. This method has only been used to prove exposure and absorption as toxic levels have not been determined for tissue. (Only performed in specialized laboratories.)
- Pathologic findings—mainly secondary to high-dose or prolonged exposure.
  - Increased liver weight.
  - Slight enlargement of hepatocytes.
  - Thinning of the zonae fasciculata and reticularis of the adrenal glands.
  - Slight hyperplasia of the zona glomerulosa of the adrenal glands.

Summary of Diagnostic Criteria

- Previous or suspected history of exposure to amitraz-containing products:
  - Application of acaricide collars.
  - Application of spot-on acaricide solution.
  - Bathing or dipping in amitraz-containing solution.
- Compatible clinical signs.

Diagnostic Differentials (Box 1)

- \( \alpha_2 \)-Adrenergic toxicity (e.g., medetomidine, xylazine).
  - \( \alpha_2 \)-Adrenergic agonists are widely used in veterinary medicine for their sedative and analgesic effects. Toxicity may occur if these drugs are used inappropriately or if an overdose is erroneously administered. Clinical signs of toxicity include bradycardia, occasional atrioventricular block, decreased respiration, hypothermia, urination, and vomiting.
- Organophosphate and carbamate compound toxicities.
  - These compounds interfere with the metabolism or breakdown of acetylcholine at cholinergic sites. Clinical signs can be grouped into three categories. Muscarinic signs are summarized using the acronym SLUD: salivation, lacrimation, urination, defecation. Nicotinic signs include generalized muscle tremors of head and body and generalized muscle fasciculation. Central nervous system (CNS) signs include anxiety and restlessness, seizure, and coma. Patients display classic miosis versus the more common mydriasis seen with amitraz toxicity.
- Recreational drugs: opioids, marijuana.
  - Clinical signs associated with opioid intoxication in dogs include miosis, salivation, diarrhea, depression, bradycardia, and ataxia.
- \( \alpha_2 \)-Adrenergic agonists are used as an inhibitory neurotransmitter. Clinical signs are mainly tremors, ataxia, and CNS depression with no effects on the cardiovascular system.
- Barbiturates activate inhibitory GABA-ergic receptors and inhibit excitatory glutamate receptors. They do not cause mydriasis. Clinical signs associated with intoxication include depression, ataxia, recumbency, coma, tachycardia, or bradycardia.
- Tricyclic antidepressant drugs inhibit the fast sodium channels in the ventricular myocardium, causing a prolongation of the QRS intervals. The CNS toxicity is not fully elucidated. Clinical signs initially include hyperthermia, vomiting, hyperexcitability, tremors, and seizure and then progress to bradycardia, coma, hypotension, and cardiac arrhythmias.
- Ethanol.
  - Ethanol affects the lipids and proteins of cell membranes, resulting in reduced sodium and potassium conduction in nerve membranes. Ethanol mainly causes signs of CNS depression. Other clinical signs include ataxia, lethargy, sedation, hypothermia, and metabolic acidosis.
- Ethylene glycol.
  - Acute toxicity results in neurologic signs, including sedation and depression.
- Pyrethrin and pyrethroid.
  - These compounds prolong the sodium conductance in nerve axons, resulting in repetitive nerve firing. Mild clinical signs are hypersalivation, twitching, paw flicking, mild depression, and vomiting. Moderate to severe toxicosis can cause protracted vomiting, diarrhea, marked depression, ataxia, muscle tremors, seizure, coma, and death.
- Primary CNS disease.
  - History consistent with CNS trauma.
- Diabetes mellitus.
  - Diabetes mellitus can occur secondary to a decrease or absence of insulin secretion by the pancreatic \( \beta \) cells or loss and/or inactivity of
insulin receptors at a cellular level. This causes a failure of glucose uptake into the cells, leading to hyperglycemia, glycosuria, and cellular starvation. Clinical signs associated with diabetes mellitus are polyuria/polydipsia, polyphagia, and weight loss. Clinical findings are hyperglycemia and glycosuria.

TREATMENT RECOMMENDATIONS

**Initial Treatment**

- Mild, transient sedation after correct application of product.
  - This often does not require any specific treatment.
- Mild signs after application of topical product.
  - Decontaminate skin by washing with mild detergent and copious warm water. Wear personal protective garments (gloves, apron).
- Recent ingestion of a collar or pieces of a collar with minimal clinical signs.
  - Induction of emesis. As amitraz can delay gastric emptying, emesis can be induced for up to 12–24 hours.
    - 3% hydrogen peroxide at a maximum dose of 2 mL/kg PO can be used. Administer a maximum of 45 mL after feeding a moist meal.
    - Apomorphine 0.02–0.04 mg/kg IV, SC, IM. This may cause CNS and respiratory depression, so use only if there are no clinical signs.
  - Endoscopic retrieval of pieces in the stomach and small intestine if emesis is unsuccessful or there are small pieces in the small intestine.
- Incomplete retrieval of collar in asymptomatic or mildly symptomatic patients.
  - Activated charcoal 2 g/kg PO. Oral activated charcoal-based toxin absorbers may help to bind any released amitraz. Charcoal may be readministered multiple times until the collar is retrieved or eliminated in the stools. This may prevent further absorption of amitraz from the collar.
- Laxative. Administer a nonoily laxative (oil-based laxatives may increase the extraction of amitraz from the collar and facilitate greater absorption). An enema to evacuate the colon may be administered about 12–18 hours after ingestion, if diarrhea has not occurred or the laxative does not produce the desired results.
  - Bulky diet to decrease intestinal transit time. This can be used with charcoal and laxative therapies.
- In patients with moderate to marked clinical signs after ingestion of collar or topical application.
  - Atipamezole: Specific α₂-adrenergic antagonist. Starting at the lower end of the range, administer 0.05–0.2 mg/kg IM slowly. The IV administration of atipamezole is off label but could be considered in an emergency situation.
    - This will reverse bradycardia, sedation, hypertension, hypotension, and GI effects within 10–15 minutes.
    - Because atipamezole has a short half-life (1.5–2 hours), dosing may need to be repeated every 2–4 hours, particularly if the animal has ingested an amitraz-containing collar that has not been retrieved from the GI tract and there are persistent clinical signs.
  - Yohimbine: α₂-adrenergic antagonist. Administer 0.1 mg/kg IV slowly or IM.
    - This will reverse bradycardia, sedation, hypertension, hypotension, and GI effects in minutes.

---

**BOX 1. CLINICAL SIGNS OF TOXICITIES THAT COULD BE CONFUSED WITH AMITRAZ INTOXICATION**

<table>
<thead>
<tr>
<th>Clinical signs</th>
<th>Amitraz</th>
<th>Opioids</th>
<th>Barbiturates</th>
<th>Tricyclic Antidepressants</th>
<th>Ethanol/ethylene Glycol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lethargy</td>
<td>Salivation</td>
<td>Miosis</td>
<td>Depression</td>
<td>Hyperthermia</td>
<td>Depression</td>
</tr>
<tr>
<td>Sedation</td>
<td>Lacrimation</td>
<td>Salivation</td>
<td>Ataxia</td>
<td>Vomiting</td>
<td>Ataxia</td>
</tr>
<tr>
<td>Ataxia</td>
<td>Urination</td>
<td>Diarrhea</td>
<td>Recumbency</td>
<td>Tremors</td>
<td>Lethargy</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>Defecation</td>
<td>Depression</td>
<td>Coma</td>
<td>Seizure</td>
<td>Sedation</td>
</tr>
<tr>
<td>Hypothermia</td>
<td>Muscle tremors/fasciculation</td>
<td>Bradycardia</td>
<td>Bradycardia</td>
<td>Bradycardia</td>
<td>Hypothermia</td>
</tr>
<tr>
<td>Tachypnea</td>
<td>Anxiety</td>
<td>Ataxia</td>
<td>Coma</td>
<td>Hyperthermia</td>
<td>Metabolic acidosis</td>
</tr>
<tr>
<td>Mydriasis</td>
<td>Seizure</td>
<td>Tachycardia</td>
<td>Bradycardia</td>
<td>Vomiting</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Coma</td>
<td>Bradycardia</td>
<td>Coma</td>
<td>Tremors</td>
<td></td>
</tr>
<tr>
<td>Hypoperfusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Collapse</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Because yohimbine has a short half-life (1.5–2 hours), dosing may need to be repeated every 4 hours, particularly if the animal has ingested an amitraz-containing collar that has not been retrieved from the GI tract and there are persistent clinical signs.

Yohimbine has been associated with tachycardia and tachypnea because of residual α1-adrenergic antagonism. It may also cause vomiting and shivering.

Supportive Treatment
- Fluid therapy based on maintenance fluid therapy and correction of any dehydration.
- Maintenance of normal body temperature.

Patient Monitoring
Close observation for possible recurrence of clinical signs is advocated for at least 24–72 hours in moderately to severely affected patients. Important parameters to monitor are:
- Heart rate.
- Blood pressure.
- Body temperature.
- Urine production.
- Serum glucose.

Home Management
If clinical signs are mild, the owner can be advised to bathe the animal with a mild hand soap or dishwashing detergent (owners should be advised to wear gloves to protect themselves from toxicity).

Milestones/Recovery Time Frames
- Mild and transient sedation after correctly applied treatment.
  — Recovery is expected after 24–36 hours.
- Moderate to severe clinical signs after institution of treatment:
  — Reversal of bradycardia, hypothermia, depression, and sedation within minutes from antidote’s administration, but it may take up to 24–72 hours for complete recovery.

Treatment Contraindications
- Use of atropine to reverse bradycardia.
  — Atropine does not reverse the α2-agonist effect of amitraz. It increases the heart rate and may potentiate hypertension.
  — The resultant increase in myocardial oxygen consumption may predispose patients to cardiac arrhythmias.
  — Atropine aggravates GI hypomotility.
- Use of xylazine as an emetic.
  — This may increase the toxic effects of amitraz and worsen CNS depression.
- Administration of insulin to correct hyperglycemia.
  — Inefficient in decreasing hyperglycemia. The administration of an α2-antagonist causes a rapid restoration of euglycemia.
- Induction of emesis after ingestion of amitraz solution.
  — This may be ineffective because the peak of absorption through the GI tract is 1 hour, and patients rarely present this quickly. It may be contraindicated if the patient is sedated.
- Gastrostomy to remove ingested collar.
  — Increases the risk of gastric dilatation secondary to gastrointestinal hypomotility.

PROGNOSIS
The prognosis is usually good with rapid institution of treatment. Mortality from amitraz toxicosis is rare (<5%) in dogs. The prognosis is less favorable in cats.

Favorable Criteria
- Mild and transient sedation (24–72 hours).
- Reverse of clinical signs (CNS depression, bradycardia, respiratory depression, and GI hypomotility) following rapid decontamination and institution of therapy.

Unfavorable Criteria
- Tachycardia.
- Dyspnea.
- Signs consistent with hypoperfusion.

RECOMMENDED READING
ARTICLE #2 CE TEST

1. The clinical signs of amitraz toxicity are due to
   a. the metabolism or breakdown of acetylcholine at cholinergic sites.
   b. α₂-adrenergic activity.
   c. the release of catecholamine from synaptic sites.
   d. interference with coagulation factors.

2. Amitraz causes
   a. bradycardia.
   b. constipation.
   c. hypoglycemia.
   d. miosis.

3. Animals considered to be more sensitive to the toxic effects of amitraz include
   a. young, old, and toy-breed animals.
   b. German shepherds.
   c. adult animals.
   d. giant-breed animals.

4. Which statement is correct concerning the use of atropine in patients with amitraz toxicosis?
   a. It is the antidote of choice.
   b. It reverses the cardiovascular effects of amitraz.
   c. It has no side effects when administered to patients with amitraz toxicosis.
   d. It may cause hypertension.

5. The treatment of patients with clinical signs of amitraz toxicosis includes
   a. administration of atropine.
   b. gastric lavage.
   c. administration of antibiotics.
   d. administration of α₂-adrenoreceptor antagonists such as atipamezole and yohimbine.

The Auburn University College of Veterinary Medicine approves these articles for 1 contact hour each of continuing education credit. Those who wish to apply this credit to fulfill state relicensure requirements should consult their respective state authorities regarding applicability. Subscribers may take individual CE tests online and get real-time scores free of charge at SOCNewsletter.com.