Cardioglycoside Toxicosis Including Red Squill and Scirriloside  (9-Aug-1999)

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Chapter Sections

Digitalis Purpurea and Other Species of Digitalis - Foxglove
Nerium - Oleander
Convallaria - Lily of the Valley
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Digitalis Purpurea and Other Species of Digitalis - Foxglove

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<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
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<tr>
<td>Most species</td>
<td>Hours</td>
<td>Days; often lethal</td>
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Images

- Foxglove, *Digitalis purpurea*. Source: Cornell University, Poisonous Plants Informational Database (www.ansci.cornell.edu/plants/index.html). - To view this image in full size go to the IVIS website at www.ivis.org.
- Foxglove, *Digitalis purpurea* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.

Description

- Plant - An erect biennial herb, which can attain a height of 4 feet.
- Leaves - The leaf shape varies widely, depending on the particular strain and species of *Digitalis*. Leaves may be large and broad, up to 12 - 15 inches long, or small, narrow leaves, 3 - 4 inches in length.
- Flowers - Are born during the second year in large numbers (in a pendant raceme) on the tall stalk of the plant: tubular-bell-shaped with spots frequently found on the inside bottom surface of the tube. The flowers vary in color depending on the variety (yellow, white, lavender, violet or purple); with most wild plants bearing purple flowers.
- Seeds - Many seeds are present in the small dry capsules (the fruit of the plant).

Habitat

- A common garden flowering plant originally introduced from Europe.
- Now naturalized and locally common in open rich lands, logged-off areas and roadsides from British Columbia to northern California as well as numerous other localities.
Toxic Principles

Contains about a dozen chemically and physiologically related cardiac or steroid glycosides. These include digitoxin, digoxin, gitoxin and others.

Toxicity

- Drying does not reduce the toxicity of the plant.
- Poisoning has resulted in children from drinking the water in a vase containing foxglove plants.
- Eating the flowers, seeds or leaves may also cause toxicosis.

**Signs, lesions, and treatment** are the same as for toxicoses induced from other sources of cardioglycosides.

*Foxglove (Digitalis purpurea)*
**Nerium - Oleander**

*Nerium oleander* - Common pink oleander

*N. odorum* - Rose laurel, adelfa

*N. indicum* - Rosenlorbeer

### Description

- **Plant** - Evergreen shrub about 5 - 25 feet tall, looks like a small tree if all but one stem is cut; gummy, sticky sap.
- **Stem** - Bark smooth, green until several years old.
- **Leaves** - Simple, evergreen, leathery, narrow, entire, smooth edges, oblong lanceolate, sharply pointed, 4 - 12 inches long, whorled or sometimes opposite.
- **Two primary parallel veins run perpendicular to the midrib.**
- **Flowers** - Spring or early summer, showy, white, pink, yellowish, rose, deep red, large cluster.
- **Fruit** - Pods, several inches long, narrow, contain many seeds; seeds have a tuft of brown hairs; pods often not produced in USA.

### Habitat

Native to Asia. Now an ornamental shrub in Southern and Southwestern USA. Common in Florida and widely planted in California. Sometimes used as a houseplant in the Northern USA.

### Toxic Principle

- Highly toxic cardiac glycoside similar to digitoxin. The cardiac glycosides: neroside, oleandroside, oleandrin, digitoxigenin, neriin and folinerin; oleandromycin (antibiotic), and rosagenin (strychnine-like).
- *N. indicum* contains odoroside (a steroidal glycoside).

### Mechanisms of Action

- Specific action is inhibition of Na/K ATP-ase enzyme system; causing increased intracellular sodium and decreased potassium concentrations.
- Bradycardia and/or tachycardia.
- Severe hyperkalemia may occur. Serum potassium concentrations may increase 2-fold.
- Marginal hypocalcemia and hypoglycemia may occur.
- Oleander has pharmacodynamic effects on the autonomic and central nervous systems, on the myocardium and on the gastrointestinal...
tract. The predominant effects are in response to different forms of conduction alterations in the heart.

**Susceptible Species**

All.

**Toxicity**

- Stems, flowers, leaves are all toxic.
- Toxicity is not lost on drying.
- Garden cuttings thrown into dry lots are a major cause of poisoning.
- Since 400 B.C. oleander has been known to poison man via eating meat cooked over oleander branches, eating porridge stirred with oleander stems and eating honey manufactured from the nectar of oleander blooms.
- One leaf can kill an adult human.
- The glycosides are distributed throughout the plant, but growing tops may be most toxic; dried leaves and bark are also poisonous.
- Males may be more sensitive to toxic effects.
- Contact may produce dermatitis in sensitive individuals.
- Oleandrin has digoxin-like action and is only slowly eliminated from the body (1 - 2 weeks).
- Extracts from the common oleander have been used as potent rat killers, insecticides and fish poisons, and are extremely toxic to all mammals.
- Oleandrin is water soluble, so leaves falling in a pond can poison the water, but the water is usually made unpalatable, so animals may avoid it.
- Plant is bitter and usually avoided.
- Using oleander twigs as skewers for roasting hot dogs may cause toxicosis.
- Monkey.
  - The cumulative toxic dose was 30 - 90 mg/kg orally in divided doses of 7.5 and 30 mg/kg at intervals of 48 hours.
  - Survival times ranged from 33 - 341 hours. The toxic effect was negligible when a dose of 3 mg/kg was given even though a total cumulative dose of 60 mg/kg was administered.
- Mice, Rats, Chickens.
  - Relatively insensitive to the cardiac effects of Oleander; neurotoxic at high doses.
- Dog.
  - The cumulative toxic dose orally was 150 - 225 mg/kg in 3 divided doses of 50 - 75 mg/kg at intervals of 24 hours. Survival time ranged from 76- 90 hours.
  - When 2 dogs were anesthetized and administered oleander tincture at 20 and 25 mg/kg, the animals developed A-V conduction defects, bradycardia, and ventricular ectopic beats. Four dogs injected with 30 mg/kg of oleander extract died within 6 hours of dosing.
- Cat.
  - The cumulative toxic dose of dried oleander leaves was 220 and 450 mg/kg BW orally in divided doses of 37.5 and 75 mg/kg at intervals of 24 hours. Survival times included 114, 240 and 36 hours.
- Goats.
  - The cumulative toxic dose was 200 mg/kg orally in divided doses of 100 mg/kg at intervals of 24 hours. The survival time was 33 - 35 hours.
- Sheep.
  - Ingestion of just 2 or 3 leaves is lethal.
  - One to 5 grams is toxic to sheep (green or dry).
- Cattle.
  - Lethal dose is 1 - 20 grams (green) or 15 - 25 grams (dry) leaves.

**Signs**

- General.
  - Onset is usually several hours after ingestion.
  - Signs may persist for 24 hours after plant material is evacuated from the gastrointestinal tract.
  - Signs are mainly referable to the heart and gastrointestinal tract.
  - Local irritation of the mucous membranes of the mouth and stomach.
  - Abdominal pain, nausea, vomiting, sweating in some species.
  - Anorexia.
  - Digitalis-like effects on the heart (pulse rapid and weak or slow and strong, depending on the stage of the disease).
  - Constriction of the blood vessels, cold extremities.
  - Pupillary dilation, blurred vision, fever.
- Dizziness, drowsiness, ataxia.
- Colic, bloody diarrhea (may be severe).
- Cardiac arrhythmias, unconsciousness, hypotension, hypothermia, bradycardia.
- Respiratory paralysis, dyspnea, shallow breathing.
- Tremors followed by progressive paralysis, coma and death (fibrillation in terminal stages).

- Goat.
  - Bleating and suppressed ruminations in addition to general signs.

- Man.
  - Excessive salivation, nausea, vomiting, mydriasis, incoordination, depression, prostration, convulsions, dyspnea, cyanosis; contact dermatitis.

Lesions

- General.
  - Severe catarrhal or hemorrhagic gastroenteritis.
  - Agonal hemorrhages are commonly encountered on the heart and serous and mucous membranes.
  - Clear or blood-stained fluid may be present in the serous cavities.

- Monkeys.
  - Pale mottling of the myocardium; subepicardial and subendocardial hemorrhage.
  - Hemorrhagic gastroenteritis and colitis.
  - Contraction of the myocardium, gall bladder and uterus.
  - Endometrial hemorrhage.
  - Multiple focal hemorrhages of the skeletal muscles.
  - Subcapsular ecchymoses of the ovaries and adrenals.
  - Congestion of the liver, lymph nodes, thyroid and adrenals.
  - Pancreatic weight reduced, adrenal weights increased.

- Goats.
  - Similar to monkeys, plus aspiration of rumen contents and foreign body pneumonia.

Diagnosis

Identification of oleander, evidence of consumption, and appropriate clinical signs and lesions.

Treatment

- Treat as for other cardioglycoside toxicoses.
- Dipotassium edetate has been used in the treatment of Oleander toxicosis and acts by antagonizing the cardiotoxicity via increasing membrane permeability through reduction of the calcium ion concentration and, consequently enhanced re-entry of potassium ions into the cardiac myofibers.
Oleander (*Nerium oleander*) - The narrow leathery leaves, the colorful flowers, and the hairy seed and slender seed pod (lower right) are characteristic of this deadly plant.
**Convallaria - Lily of the Valley**

**Convallaria majalis - Lily of the Valley**

**C. montana**

<table>
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<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Toxic Principle</th>
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<tr>
<td>Most species</td>
<td>Hours</td>
<td>Days; potentially lethal</td>
<td>Cardiac glycosides - Convallarin, convallamarin, and convallatoxin.</td>
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</tbody>
</table>

**Family** - Liliaceae (Lily family)

**Images**

- Lily of the valley (*Convallaria majalis*). Source: Cornell University, Poisonous Plants Informational Database (www.ansci.cornell.edu/plants/index.html). - To view this image in full size go to the IVIS website at www.ivis.org.
- Lily of the valley (*Convallaria majalis*) - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.

**Description**

- *C. majalis.*
  - Plant - Perennial herb, usually forming a dense mat that is persistent and excludes other plants.
  - Leaves - Basal, broad, 2 oblong, to oval, smooth.
  - Flower - Slender stalk bears a 1-sided row of waxy, bell-shaped, tiny white or pale pink, nodding, fragrant flowers.
  - Fruit - Fleshy, red, orange, 1/2 inch in diameter berry; seldom forms.
  - Rootstock - Horizontal.

**Habitat**

- *C. majalis.*
  - Escaped from cultivation in flower gardens throughout the USA and Canada.
- *C. montana.*
  - Virginia and Georgia, native to the high mountain areas of the southern states.

**Toxic Principle**

Cardiac glycosides - Convallarin, convallamarin, and convallatoxin.

**Susceptible Species**

Livestock (all), pets, humans.

**Toxicity**

- Leaves, flowers, roots are toxic; berries may also be toxic.
- Cardiac glycosides in all parts of the plant; both green and dried.
- A child died after drinking the water from a vase containing Lily of the Valley.
- Dermatitis can occur upon contact with the leaves.
- Has a purgative effect.
Signs

- Cardiac signs may be delayed for days and may persist for 3 weeks.
- The heart becomes hyperirritable and premature ventricular contractions and ventricular tachycardia may occur.
- Leaves may cause dermatitis.
- Vomition, diarrhea, nausea, anorexia, cramps.
- Large dose.
  - Mental confusion, extreme weakness, depression.
  - Collapse of circulation and death.

Lesions

Gastroenteritis.

Diagnosis

Identification of Lily of the Valley, evidence of consumption, and appropriate clinical signs and lesions.

Treatment

Treat as for digitalis overdose, recognizing the need for sufficiently sustained therapy.

Lily of the Valley. - The delicate white fragrant flowers (enlarged, right), the long lance-shaped leaves, and the horizontal rootstocks are characteristic of this hardy ornamental.
**Apocynum - Dogbanes**

- *Apocynum androsaemifolium* - Spreading dogbane
- *A. cannabinum* - Hemp dogbane, Indian hemp
- *A. sibiricum* - Prairie dogbane

**Family** - Lily of the Valley, Apocynaceae (dogbane family)

**Images**

- Spreading dogbane, *Apocynum androsaemifolium* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.

**Description**

- *A. androsaemifolium.*
  - Plant - Perennial, erect, 1 - 1 3/4 feet tall, contains milky juice.
  - Stem - Somewhat woody, smooth.
  - Leaves - Opposite, paired, smooth margined, ovate to oblone, mucronate tipped, slender petioled, dull dark green and smooth above; pale and somewhat pubescent below, loosely spreading or drooping.
  - Flowers - Fragrant, mostly nodding; cymes flowers simultaneously, terminal one is usually largest; corolla pink.
  - Fruit - Pods long, narrow, pencil-like, cottony mass within; seeds long, narrow, each with a tuft of long white hairs.
  - Rootstock - Spreading.
- *A. cannabinum.*
  - Plant - Erect perennial herb which grows to 5 feet tall. Contains milky juice.
  - Leaves - Opposite, simple untoothed.
  - Flowers - Small pinkish, appear in early summer.
  - Fruit - Slender, 2 inches long, hanging follicle or shoot which hangs in pairs and contain long, narrow seeds; seeds are covered with long silky hairs.

**Habitat**

Widely distributed in the USA and Canada. Open places, coarse soil, along streams, roadsides, pastures and infrequently tilled fields.

**Toxic Principle**

Cardiac glycosides.

**Susceptible Species**

Horses, cattle and sheep.

**Toxicity**

- Fifteen to 30 grams of green leaves has been reported as causing death of a horse or a cow.
- Reportedly very distasteful and animals usually avoid; poisoning is thus infrequent. Consumed primarily when other forage is in short supply.
- Green and dried dogbane is toxic.
The root of *Apocynum cannabinum* has been employed therapeutically to "retard the heart in systole" and was therefore used for "dropsy" and "heart trouble".

**Signs**
- Increased temperature and heart rate (or slow heart rate).
- Coldness of extremities.
- Dilation of pupils.
- Discoloration of mouth and nostrils, sore mouth.
- Sweating, gastric upset.
- Death.

**Lesions**
Nonspecific.

**Diagnosis**
Identification of *Apocynum*, evidence of consumption and appropriate clinical signs.

**Treatment**
Treat as for digitalis overdose, recognizing the need for sufficiently sustained therapy.

**Note** - Although still regarded as toxic, some of the literature is based upon confusion of *Apocynum* with *Nerium*, both members of the Apocynaceae family.

**Dogbane** - Note the paired, entire, variable-shaped leaves, the clusters of small flowers (enlarged, right), and the slender pods and tufted seeds (far right) of this milky-juiced herb.
Bufo Toxicosis - Toad Poisoning

Source

- The giant tropical toad, *Bufo marinus*, was introduced to the southern states and Hawaii approximately 40 years ago for insect control. The toads produce toxin in the parotid glands which are situated behind the tympanum and extend backward over the shoulders. There are numerous pin hole openings on the surface skin of these glands from which toxin can be manually expressed. The toads, therefore, are a threat to unsuspecting people who may be exposed to the toxin through an open wound, but more commonly, the threat is to animals mouthing the toads.
- *Bufo alvarius* also produces similar toxic secretions.

Toxic Principle

- The parotid gland secretions of *Bufo* toads contain bufagins, bufotoxins, bufotenins, and other compounds. Bufotoxins are conjugated bufagins. Bufagin's and bufotoxin's action is described as digitalis-like, often resulting in ventricular fibrillation. Bufotenins have oxytocic action and frequently a marked pressor action.
- Other compounds found in *Bufo* toxin are epinephrine, cholesterol, ergosterol, and 5-hydroxytryptamine (5-HT) (also called serotonin or "serum vasoconstrictor").

Species Affected

Canine, feline rarely.

Toxicity

The *Bufo marinus* in Florida seems to produce a more potent toxin than that produced by the Hawaiian or Texan *Bufo marinus*. Mortality in Hawaii of exposed and untreated dogs is approximately 5% as compared with nearly 100% in Florida.

Signs

- Signs vary according to the animal's age, concurrent disease, amount of toxin absorbed, and length of time since exposure.
- There are three primary aspects to *Bufo* toxicosis: a) the cardiac glycoside-like effects of the bufagins; b) the pressor effects of the catecholamines, and c) the hallucinogenic effects of the indolealkylamines.
- Salivation, head shaking.
- Ataxia, polyneum, emesis, diarrhea.
- Increased respiratory rate and depth.
- Apparent blindness.
- Convulsions.
- In early intoxication, monitoring reveals a gradual deterioration of the ECG with progressive negative ventricular deflection. This
eventually results in ventricular fibrillation and death if untreated.

**Clinical Pathology**

- Moderate increase in packed cell volume, hemoglobin content, and icterus index.
- Increase in blood glucose, blood urea nitrogen (BUN), potassium, and calcium.
- Sedimentation rate increases.
- Serum sodium and chloride concentrations decrease slightly, but serum inorganic phosphorus content is markedly reduced.
- Total protein usually decreases.
- Total white blood cell count decreases, principally because of neutropenia.
- Initial spike of SGOT which returns to normal.

**Treatment**

- First, when possible it is highly important to rinse mouth thoroughly. Often practitioners recommend using a garden hose to rapidly rinse *Bufo* secretions from the oral mucous membranes. Follow with activated charcoal and a saline or sorbitol cathartic. Activated charcoal may be repeated after 2 hours.
- In a patient **without** a history of asthma or cardiac disease:
  - Administer pentobarbital anesthesia.
  - Insert endotracheal tube.
  - Wash mouth out vigorously with running water.
  - Administer propranolol - 2 mg/kg body weight, IV; normal heart rate should return within 15 seconds.
  - Monitor ECG, repeat propranolol after 20 minutes if necessary.
  - **Note** - These doses of propranolol are for *Bufo* intoxication **only**.
  - Administer fluids if considered appropriate.
- If asthma or cardiac disease signs or history exist:
  - Monitor ECG and administer propranolol IV slowly at 0.5 mg/kg BW until cardiac rate returns to normal.
  - Administer fluids if appropriate.
  - Animals should be monitored for at least 24 hours after exposure.
- For life-threatening hyperkalemia, administration of glucose, insulin, and bicarbonate (slow IV in the fluids) is recommended. ECG monitoring during administration is warranted.
- Atropine may be of value for asystole and/or bradycardia.
- Phenytoin or lidocaine may be warranted for unresponsive clinically significant arrhythmias in small animals.
- A recent report described the use of Digibind ® (digoxin antibody fragments) for life threatening toxicoses in young men caused by chan su, which contains various bufo toxins.

**Note**

Anesthetics may further compromise an already diseased myocardium and should be used with discretion. Also, beta-adrenergic blocking drugs such as propranolol may block the endogenous catecholamines that asthmatics depend on for bronchodilation, and that animals with heart failure depend on to drive the heart. They should, therefore, be used with caution in older, asthmatics or cardiac diseased dogs.
### Additional Toxicants

<table>
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<tbody>
<tr>
<td><strong>Red squill (rodenticide)</strong></td>
<td>Dogs, cats</td>
<td>Minutes to days</td>
<td>Days; often lethal; not widely available</td>
</tr>
<tr>
<td><strong>Scilliroside (rodenticide)</strong></td>
<td>Dogs, cats</td>
<td>Minutes to hours</td>
<td>Days; often lethal; not widely available</td>
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<tr>
<td><strong>Some milkweeds (Asclepias)</strong></td>
<td>(See Toxicants Associated with CNS stimulation or Seizures)</td>
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### References

**Bufo Toxicosis**


**Pieris - Japanese Pieris**


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