Black Widow Spider (*Latrodectus* spp.)

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Toxicants that Cause Paresis or Paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>All species</td>
<td>Within 6 hours</td>
<td>Hours, infrequently lethal</td>
<td></td>
</tr>
</tbody>
</table>

Black widow spider (*Latrodectus mactans*) and other *Latrodectus* spp., e.g. brown widow spider, red widow spider, and red-legged spider.

**Images**


**Description**

- Medium-sized (10 - 18 mm) spider, black widow abdomen is shiny black with a red hourglass or red spots.
- Both male and female are poisonous, however, only females' mouth parts are of sufficient size to penetrate skin (human).

**Distribution**

Widely distributed in the warmer portions of the USA. Red widows reportedly occur in Florida.

**Toxic Principle**

- Several biologically active proteins identified including neurotoxins.

**Mechanism of Action**

- One lethal fraction, alpha-latrotoxin, causes release and depletion of acetylcholine.
- Binds to glycoproteins or gangliosides on neuromuscular synaptic membranes, allowing cationic ion-channels to remain open. Results in depolarization and calcium-independent release of neurotransmitter. Inhibits presynaptic neurotransmitter reuptake.
- In vitro, the sharp increases in nerve potentials are followed by a decline until no nerve impulses occur.

**Clinical Signs**

- Dull numbing pain at sight of injection of venom, muscle cramps, muscle fasciculations, tonic clonic convulsions, sweating, excess salivation, flaccid paralysis.
- Weakness with dyspnea followed by paralysis may occur within 6 hours in an acute case.

**Treatment**

- Corticosteroids, IV fluids, prophylactic antibiotics.
- Methocarbamol, calcium gluconate, meperidine, and atropine may be used to control muscle spasms, pain, and excessive secretions.
- Most envenomations are self-limiting and clinical signs resolve within 4 - 6 hours.
- Black widow spider antivenom (Wyeth Laboratories) is available.

**Neuromuscular Blocking Agents**

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Toxicants that Cause Paresis or Paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>All species</td>
<td>Minutes</td>
<td>2 - 4 hours; potentially lethal</td>
<td></td>
</tr>
</tbody>
</table>

**Introduction**

- Neuromuscular blocking agents are drugs that decrease the response to acetylcholine at the neuromuscular junction of skeletal muscle tissue.
- These drugs are classified into depolarizing (e.g., succinylcholine chloride) or nondepolarizing (e.g., curare) agents on the basis of their mechanism of action.

**Source**

- Nondepolarizing agents:
  - Curare is a generic term for various South American "arrow poisons". Derived from various *Strychnos* and *Chondrodendron* plant species.
  - The active alkaloids in curare are quaternary amines which induce a neuromuscular blocking effect.
  - Nondepolarizing ("curare-like") skeletal muscle blocking agents include tubocurarine, vecuronium, pancuronium, atracurium, and others. Predominately used for skeletal muscle relaxation after general anesthesia has been induced.
- Depolarizing agents:
  - Decamethonium.
  - Succinylcholine chloride-primarily used as a skeletal muscle relaxant.

![Curarine-1](image1.png) ![(+)-Tubocurarine Chloride](image2.png) ![Succinylcholine](image3.png)
Mechanism of Action

- Nondepolarizing agents:
  - Combine with the cholinergic receptor at the postjunctional membrane of skeletal muscle and thereby competitively blocks the transmitter action of acetylcholine.
  - Compete with Ach for cholinergic receptors at autonomic ganglia.
  - Decrease Ach release by presynaptic cholinergic nerve membrane.
  - May also cause the release of histamine with resultant effects.
- Depolarizing agents:
  - Stimulate sympathetic ganglia.
  - Have high affinity for postjunctional Ach receptor sites; stimulation followed by a depolarized blocked postsynaptic receptor. Resistant to acetylcholinesterase as compared to acetylcholine.
  - Less effective at stimulating release of histamine.

Signs

- Motor weakness followed by total flaccidity and inexcitability of the muscles.
- Small rapidly moving muscles or the jaws, ears, eyes are affected first and later the limb and trunk muscles become involved.
- Finally, intercostal muscles and the diaphragm are paralyzed resulting in terminal asphyxia.
- Terminal convulsions, if they occur are probably hypoxic in origin and very weak due to muscle effects. Generally have no direct CNS effects.
- Bronchospasms, hypotension, and excessive bronchial or salivary secretion may be a result of histamine release. Hypotension may occur due to direct actions.
- Malignant hyperthermia has been reported in man, swine, and horses and is more likely when muscle relaxants are used during surgery.

Absorption, Distribution, Metabolism and Excretion (ADME)

- Quaternary ammonium neuromuscular blocking agents are poorly absorbed from GI tract.
- Nondepolarizing agents undergo variable metabolic degradation by liver.
- Succinylcholine is hydrolyzed by butyrylcholinesterase of liver and plasma to less pharmacologically active agent succinylmonocholine.

Treatment

- Usually the effects last up to 4 hours and generally less. Therefore the use of artificial respiration as needed may be sufficient to allow survival in some animals.
- Reversal of nondepolarizing agents neuromuscular blockade by administration of cholinesterase inhibitor, e.g., neostigmine.

Note - Because cholinesterases normally degrade succinylcholine, neostigmine and other cholinesterase inhibitors should not be concurrently administered with this depolarizing agent.

Note - Considerable study and experience are recommended prior to the use of curariform drugs. Taylor, in Goodman and Gilman, editors, The Pharmacologic Basis of Therapeutics, recommends their use only by individuals with "extensive training in their use and in a setting where facilities for respiratory and cardiovascular resuscitation are immediately at hand". This text is recommended for those contemplating the use of these agents.
**Delphinium - Larkspur**

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mostly cattle</td>
<td>1 - 4 hours</td>
<td>Often rapidly lethal</td>
</tr>
</tbody>
</table>

**Introduction**

- Most Larkspur poisoning occurs in the western USA.
- Synonyms include poison weed and stagger weed.

**Habitat**

- Majority of Larkspur species are found west of the Mississippi River.
- Western USA, 2 major groups based upon growth characteristics.
  - Dwarf-low larkspurs occur in lowland slopes and grasslands. Less than 3 feet in height.
    - Include *D. nelsonii*, *D. geyeri*, *D. virescens*, and *D. bicolor*.
  - Tall larkspurs-upper slopes and among open stands of trees in draws. Are 4 - 6 feet in height. Generally occur in high altitude.
    - Include *D. barbeyi*, *D. occidentale*, *D. glaucum*, and *D. trolliifolium*.
- Eastern USA.
  - *Delphinium tricorne*.
    - Occurs in moist wooded areas-e.g. ravines and along streams.
    - Occasional poisoning-East Central USA.
- Also in cultivation as garden perennials.

**Description**

- Most are perennial, herbaceous, erect herbs. Simple or branching stems.
- Palmately lobed or palmately divided alternate leaves.
- Flowers are blue, purple or white, in a terminal raceme above the leaves; with a prominent spur formed from 1 sepal + 2 petals.
- Clustered (3 - 5 follicles) fruits contain irregular, ridged, brown seeds.

**Toxic Principle**

- The polycyclic diterpene alkaloid methyllycaconitine is the principle toxic alkaloid.
- In *D. occidentale* and *D. barbeyi*, the alkaloid content is high in early growth and then drops rapidly so poisoning is rare after flowering, unless the toxic seeds are ingested. Poisoning generally in spring and fall.
- Nevertheless-dried plants are poisonous-so drying alone is apparently not the cause of detoxification.
Mechanism

Methyllycaconitine functions as a potent neuromuscular blocking (curare-like) agent. Acts at postsynaptic, nicotinic, cholinergic receptor in the CNS and at neuromuscular junctions.

Toxicity

- LD₅₀ cattle 0.5% bw. *D. barbeyi* can cause fatalities in cattle at 17 g green plant/kg bw.
- May occur on any range but is more common when ranges are overgrazed.

Susceptible Species

- Causes more cattle losses than any other plant on western ranges.
- Horses and sheep rarely affected. Sheep are less susceptible than cattle.
- Grazing an area with sheep will not make it safe to subsequently graze cattle. Sheep eat different parts of the larkspur plant than cattle.

Signs

- Most common clinical sign in cattle may be sudden death.
- Clinical signs are primarily related to the nervous system.
- Hyperirritability, confusion, nausea.
- Mild muscle tremors, stiffness, weakness.
- May see constipation, bloat, oral irritation, vomiting (or regurgitation), salivation which may be followed by a dry mouth.
- Collapse, prostration. Inhalation pneumonia common in recumbent animals as a result of vomiting.
- Convulsions.
- Death is a result of respiratory paralysis or bloat as animals often fall into recumbency with the head downhill. Fatalities usually occur within 3 - 4 hours of ingestion of a fatal dose.

Note - Cardiovascular disturbances including hypotension and myocardial depression and associated arrhythmias may be difficult to manage pharmacologically. The arrhythmias may be comprised of supraventricular tachycardia and conduction disturbances.

Postmortem

Nonspecific lesions including ruminal bloat, venous congestion, inhalation pneumonia, and GI inflammation.

Prognosis

Guarded even in mildly affected.

Treatment

- Activated charcoal, magnesium sulfate as a saline cathartic.
- Excitable range cattle may be left untreated and moved to a new pasture.
- Physostigmine (0.04 to 0.08 mg/kg bw IV) is effective as a treatment for larkspur poisoning. Best if given early, and repeated injections are generally necessary.
- Turn so head is uphill.
- Relieve bloat, antibiotic therapy for inhalation pneumonia.

Prevention

- Spot spraying of larkspur patches with herbicides, followed by attempts to revegetate with other types of plants (i.e., grass).
- Some sources report $10,000 per year (in an average cow herd) in 500 losses and management costs due to poisoning.
**Cultivated Larkspur** - These plants have finely divided leaves, blue to white or pink spurred flowers, a dry splitting seed pod, and a rough seed (enlarged, right center).
Low Larkspur (*Delphinium Menziesii*). This is the most common of the low larkspurs, extending from Colorado to the Sierras, and causes heavy losses of cattle.

**Distribution of Larkspur**

- D. barbeyi and D. nelsonii
- D. tricorne
Tall larkspur (*Delphinium trolliifolium*) - This is the tall larkspur of the Northwest, and is conspicuous because of its large and beautiful flowers.
Introduction

- Botulism is the disease caused by any one of 7 serotypically different, but functionally similar toxins produced by strains of *Clostridium botulinum*. They are among the most potent toxins known. Of these 7 serotypes (A-G), types C and D have historically been the most commonly implicated in domestic mammals and poultry. These proteinaceous toxins are only slightly cross-reactive and can generally be regarded as immunologically specific.

Serotypes of *C. botulinum* toxins:
- A, B serotypes: primarily isolated from soil. B serotype has been a problem especially in horses, and also is implicated in toxicoses of cattle. Most often implicated with human infant botulism.
- C serotype: is the most commonly implicated serotype in dogs, waterfowl, and poultry. Reports now also implicate this toxin in horses.
- D serotype: birds are somewhat resistant to type D, but cattle are quite sensitive.
- E serotype: isolated from mud and water of estuaries and sea food. Dogs are reportedly extremely sensitive to type E toxin.

Sources

- The most common source of botulinus toxin causing poisoning in most if not all species of domestic animals is carrion. Carcasses of decaying animals form an anaerobic environment and the toxin may be present in maggots feeding on the contaminated tissues.
  - Waterfowl: Decaying vegetation and invertebrates in flooded areas or other stagnant water, such as ponds, may serve as the primary source of botulinus toxin causing death in the first affected birds. Subsequently, birds which are simultaneously poisoned and inoculated with *C. botulinum*, become the anaerobic carcasses for additional toxin production and the source for additional animals to become poisoned. This often results in a mass die off due to botulism. Maggots often serve as the vector of botulinus toxin.
    - Treatment: Drain areas, remove dead birds, frighten off incoming birds temporarily.
  - Carnivores: Carrion.
  - Cattle: Carrion incorporated into feed is one source (dead rodents or other animals in feed bins). "Osteophagia", the eating of the bones of dead animals associated with hypophosphatemia, is another source that occasionally results in botulism (sometimes referred to as "loin disease"). Adding pond water, from a stagnant pond, to corn silage resulted in a massive, highly lethal episode of botulism in dairy cattle.
  - Feeding poultry litter is a strongly suspected cause of botulism in ruminants in Australia.
  - Horses: Horses are extremely sensitive to the effects of botulinus toxin and suffer from toxicosis as a result of incorporation of carrion into their feed, as well as "toxicoinfectious botulism". The latter is a result of colonization of necrotic tissue in the animal by *C. botulinum* organisms and apparent production of toxin *in situ*. Sites may include the navel, wounds, gastric ulcers and possibly other necrotic areas, such as foci of necrosis in the liver and the gut in association with such problems as sand ingestions. Botulism has not been reproduced by the feeding of *C. botulinum* to healthy horses. "Toxicoinfectious botulism" (Shaker foal syndrome) of horses has been associated primarily with *C. botulinum* type B toxin. Signs suggestive of botulism have been reported in horses fed haylage. Proof of botulinus toxin involvement remains to be demonstrated in these cases.
  - Affected foals are typically less than 8 months of age and are commonly less than 2 months of age.
  - Humans: Three forms of the disease occur as a result of: 1) Ingestion of preformed botulinus toxin in improperly canned foods, especially in high protein foods such as meats and beans; 2) Wound botulism; and 3) Infantile (gastrointestinal) botulism. An association has been made with the latter and the feeding of honey.
    - General:
      - Affected animals may shed *C. botulinum* spores in their feces which may result in further environmental contamination.

Toxicity

- One of most toxic compounds known, particularly on a mole/kg basis. Because of its high molecular weight, botulinus toxin is 36 times as toxic as parathion on a mg/body weight basis, but over 100,000 as toxic on a molecule/body weight dosage basis.
  - LD<sub>50</sub> mouse 0.3 mg/kg bw; minimal LD mouse 0.12 mg/kg.
  - A single maggot from a dead pheasant was sufficient to kill a 3 week old chicken.
Mechanism of Action

- Botulinus toxin enters presynaptic membranes of cholinergic nerve endings via receptor mediated endocytosis. The toxin acts intracellularly via a metalloendoprotease action to cleave 3 proteins essential for neurotransmitter release (synaptobrevin, syntaxin, and SNAP-25). Thus, the toxin inhibits degranulation or exocytosis of acetylcholine granules. A small number of molecules of this toxin binds irreversibly to the sites of action, producing an essentially irreversible cessation of all cholinergic transmission. Death results from respiratory failure.

Schematic drawing of the blockage of acetylcholine release by botulinal toxin at the neuromuscular junction. The toxin prevents exocytosis of acetylcholine. From: Greene CE. Clinical Microbiology and Infectious Diseases of the Dog and Cat. WB Saunders, 1984.

- Lower motor neuron effects include paresis to paralysis, hypotonia and hyporeflexia.
- Some pharmacologic actions of various botulinus toxins and specific binding difference between toxins indicate the possibility of different mechanisms of action.

Signs

- Myasthenia.
- Inability to swallow.
- Progressive muscle paralysis with muscle weakness first in the hindquarters and then progressing to the forequarters, then the head and neck become involved. Humans are atypical in that in some aspects the effects are descending in sequence.
- Humans:
  - Latent period after ingestion of preformed toxin is from 2 hours to 8 days; usually 12 - 48 hours.
  - In 1949 over 60% of human victims died, but by 1980 only 13 - 15% succumbed.
  - Early vomiting indicates a greater degree of exposure and may be a cause of aspiration pneumonia.
  - Bilateral cranial nerve involvement and double vision. Pupils dilated and fixed or normal size and fixed.
  - Diarrhea, then obvious constipation.
  - Nasal voice. Dry painful mouth.
  - Weak neck muscles and limbs
  - Drowsy, but otherwise mental processes seem normal.
  - Death due to respiratory paralysis.
- Birds: All Anseriformes (waterfowl) are susceptible (other species vary).
  - Signs start with the progressive paralysis of the neck (limberneck), legs and wings.
  - Gasping for air and sometimes greenish diarrhea.
  - Usually die in coma within 24 - 48 hours due to respiratory and circulatory failure.
  - May drown from inability to hold head and body in normal position.
- Birds (Pheasants):
  - Pheasants exhibited paralysis of the legs, labored breathing and diarrhea.
  - Type C antisera was able to prevent the disease.
- Dogs:
  - General weakness is followed by an ascending paresis and paralysis with cranial nerve involvement (facial paralysis may be present). Remain alert and responsive, wag tail and move head even when paralyzed. (In this respect is the same as tick paralysis and "coonhound paralysis" [polyradiculoneuritis]; however in the latter conditions, there is less cranial nerve involvement than with botulism)
- Mydriasis with slow pupillary reflexes, decreased palpebral reflexes.
- Poor jaw tone, dysphagia. Vomiting, pain in cranial abdomen.
- May have secondary dehydration and/or urinary tract infections as well as secondary respiratory infections.
- Occasionally may have slow heart rate, rarely see megaesophagus and associated regurgitation. Decreased gag reflex.

**Cattle:**
- Inability or decreased ability to stand. Sternal and sometimes subsequent lateral recumbency. Often down with head down or turned to the side, like a cow with milk fever, may die in sternal recumbency.
- Rumen motility decreased or absent.
- Hypermotility. Paralysis of muscles of mastication and cannot resist forced opening of the mouth.
- Tongue may have normal tone, but often exhibits varying degrees of flaccid paralysis. This is most apparent after pulling the tongue out of the mouth repeatedly.
- Urinary bladder distended: with severe toxicosis become less likely to urinate when "feathered" or may not urinate at all until stimulated by attempts to introduce a urinary catheter.
- Proteinuria in some cows exhibiting paresis or paralysis.
- Concentrated urine and reduced rumen fill indicate decreased ability to drink water and resultant dehydration. Dry feces with large amount of mucus.
- Slow pupillary response to light.
- Animals sense pain stimuli but withdrawal reflexes from pin pricks or other pain are weak or absent.
- Rectal temperature, heart rate and respiratory rate remain normal until late in the syndrome.
- Death occurs without agonal respiratory gasps.
- Deaths in a herd may occur in one to several cows per day every day or every few days.
- Hyperglycemia may be noted.

**Foals and Horses:**
- Progressive symmetrical muscle paralysis, with stilted gait.
- Muscle tremors, inability to remain standing for longer than 4 - 5 minutes, drop to sternum. If helped to feet after a rest, signs reoccur and duration of standing decreases as time progresses.
- Dysphagia: In foals, milk runs out of their mouths as they attempt to suckle. Difficulty swallowing water, tongue and pharyngeal paralysis. Loss of tongue tone is often an early clinical sign in adult horses.
- Reduced intestinal peristalsis. Constipation. Frequent attempts to urinate with voiding of only a few ml of urine.
- Mydriasis.
- Later see dyspnea with extension of the head and neck. Tachycardia.
- Respiratory arrest, generally after a period of lateral recumbency, with the neck extended.
- Generally, the body temperature and hemograms remain normal throughout the syndrome.
- Creatine kinase may be elevated due to prolonged recumbency.
- Mortality is high in all ages, and is greater than 90% in foals. Foals less than 3 weeks old usually die within 24 hours and those 4 weeks or older live up to 72 hours.

**Lesions**

- In all species, lesions are generally nonspecific.
- **Cattle:**
  - Abomasal hyperemia.
  - Fluid-filled large intestine.
  - Aspiration pneumonia may be present.
- **Horses:**
  - Abscesses may occur in the navel, the lungs or in wounds of the skin or muscle. These may be sites of toxin production.
  - Foci of necrosis may occur in the liver.
  - Gastric ulcers may be present at the margo plicatus or less often at the pyloris.
  - Congestion and edema of the lungs.
  - Excessive pericardial fluid with free floating strands of fibrin.
  - Often there is generalized fatty change of the liver.
  - The urinary bladder is often distended with urine.
  - Aspiration pneumonia is sometimes present.
- The rectum is often filled with hard, mucus-coated feces.
- Occasionally the mare and foal are both affected and in such cases, the mare often has adrenocortical hyperplasia.
Diagnosis

- Most species:
  - Diagnosis is difficult to confirm. The mouse inoculation test is becoming obsolete but some labs may still use it. Tests for botulinus toxin can be used in cases where the animal is still alive or has just died. After a longer postmortem interval, the carcass may no longer represent the antemortem state.
  - Mouse inoculation test:
    - Positive test is manifested by a "wasp-wasted" appearance with respiratory distress and progressive paralysis and death within 24 hours in most cases.
    - Specimens to test include: food, carrion, maggots, spoiled bone meal, silage, bones, decaying vegetation; serum, gastrointestinal tract contents, feces, etc.
    - These specimens may be tested to determine if the toxin is present by the mouse inoculation test and may also serve as materials for the culture and identification of \( C. \) botulinum.
    - Mouse inoculation/protection test procedure: Mice are inoculated with a suspect specimen with and without a specific or polyvalent antiserum. The production of typical botulism, and concurrent protection of the appropriate antitoxin treated mice allow delineation of the specific toxin type.
- An immunodiffusion test using agar impregnated with antitoxins may sometimes be recommended as an alternative to the mouse protection test. One of the best labs is at the College of Veterinary Medicine of the University of Pennsylvania.
- Poultry labs are generally set up to run tests to identify the Type C toxin, commonly implicated in small animals.
- Type D toxin is difficult to isolate, and therefore it may be more practical to reproduce the syndrome in 1 group of animals with comparison to toxoid-vaccinated groups rather than through the usual practice of antitoxin administration.
- Culture:
  - Under the microscope, the bacteria appear as single or short chains of rod-shaped organisms. They are slightly motile via the action of 4 - 20 flagella.
  - One isolation medium that has been recommended is 25 x 200 mm tubes of chopped meat glucose starch (CMGS) medium made with freshly ground horse meat. A 2 - 3 gram sample of necrotic tissue or other specimen is cultured in duplicate tubes of such medium. The tubes are heated for 15 minutes at 70 °C in an attempt to kill bacterial contaminants. One tube is incubated at 30 °C and the other at 35 °C for 5 days. Routine culture methods may also be used for initial isolation from most specimens but check on laboratory capabilities.
- Horses:
  - Serum from horses generally will not have enough toxin present to be of value in the mouse inoculation test. This is the case because the horse is more sensitive to the toxin than are mice and the concentration of toxin in lethally affected horses will not affect the test mice. Because of the difficulties of the test procedures, tentative diagnoses may be the only possible diagnoses in some cases.

Differential Diagnosis

- Cattle:
  - Mineral imbalances (Ca or Mg deficiencies), including parturient paresis.
  - Other paralytic toxicoses (cholinesterase inhibitors and many others).
- Horse:
  - Dysphagia-esophageal or pharyngeal obstruction, leukoencephalomalacia, yellow star thistle, rabies.
  - Tick paralysis, hypocalcemia, white snakeroot poisoning.

Treatment

- In cases of recent ingestion of preformed botulinus toxin, measures to remove the contents of the gastrointestinal tract as well as activated charcoal and a cathartic are indicated.
- Antitoxins are the product (serum) of an animal (horse), which has received injections of a toxoid (inactivated toxin). Use of polyvalent antitoxin early in the course of the syndrome greatly enhances survival rates. The following dosage schedules have been recommended.
  - Horse:
    - 200 ml for foal and 500 ml for adult (> 400 lb bw).
    - Debride and treat any deep wounds.
    - Sodium/potassium penicillin 22,000 - 44,000 IU/kg QID IV to eliminate proliferating \( C. \) botulinum organisms. Oral penicillin therapy as well as aminoglycosides and tetracyclines are contraindicated in the horse.
  - Dog:
    - Trivalent antitoxin used in human medicine contains types A, B, and E antitoxins, if available type C antitoxin should be used but may be difficult to obtain.
    - 5 ml of a polyvalent antitoxin was administered IV and IM to a coonhound with type C botulism.
Antibiotic therapy with 20,000 IU/kg penicillin IM BID and ampicillin 16 mg/kg PO or 8 mg/kg IM QID has been recommended.

- Supportive care including padding, provision of a warm, dry environment and turning the animal with assistance in eating, drinking, urination and defecation are indicated. Supportive alimentation is required in a large number of cases. Prolonged ventilation for respiratory paralysis is probably not going to be practical for any animal patient.
- The possibility of respiratory or urinary tract infections should be reason for frequent monitoring and, if necessary, appropriate therapeutic measures.
- In cattle, carbamylcholine to stimulate gastrointestinal motility and enhance removal of the toxin seemed to enhance the probability of survival in a small number of animals.
- The use of guanidine HCl at 15 - 30 mg/kg/day orally in divided doses to increase the release of acetylcholine has been debated. Is not advocated for therapy.
- 4-aminopyridine at 2 - 3 mg/kg IP reversed the paralysis due to botulism in rats.
- Recently a therapeutic regimen of cholinesterase inhibitors, such as physostigmine and neostigmine, have been recommended along with atropine sulfate to block the muscarinic effects of the cholinesterase inhibition. Such measures should be used only in life-threatening toxicoses and with the utmost caution!

Recovery

Recovery in dogs may occur within 14 days or longer. Recovery of function occurs in the reverse order of the loss of function during the development of the syndrome.

Notes

- Mares on a high-protein, reasonably high caloric diet are believed to be predisposed toward having foals with toxicoinfectious botulism. Therefore, a less concentrated diet may be indicated on such farms.
- Secretion of corticosteroids by the mare has been postulated as contributing to the development of toxicoinfectious botulism in the suckling foal.

Tick Paralysis

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Toxicants that Cause Paresis or Paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle, sheep, dogs, cats deer, llamas</td>
<td>3 - 9 days</td>
<td>Days sometimes lethal</td>
<td></td>
</tr>
</tbody>
</table>

Images

- Dermacentor andersoni - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org. -
- Dermacentor variabilis - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org. -
- Ixodes holocyclus - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org. -

Introduction

- Ticks and mites are important arachnid ectoparasites of humans and animals and have a well-established role in the transmission of certain diseases.
- A number of tick species have been reported to cause paralysis.

Source

- Female ticks of certain species, especially Dermacentor andersoni or D. variabilis, in the USA secrete a neurotoxin from their salivary glands when feeding. Ixodes holocyclus and other Ixodes spp. as well as Amblyomma spp. have been implicated in tick paralysis in Australia. Autonomic involvement (cardiovascular) with Ixodes has been reported.
- Similar condition reported due to soft ticks of poultry and is primarily due to immature tick forms.
Dermacentor

Toxicity

- One feeding tick is enough to cause clinical signs.
- Cases of tick paralysis coincide with seasonal activity of ticks in a given geographical region.

Mechanism of Action

- Affects the lower motor neuron.
- Either inhibits depolarization of the terminal portion of motor nerves or blocks the release of acetylcholine at the neuromuscular junction. Electrophysiologic parameters favor the former site of action. EMGs show depressed evoked muscle potentials and slowed transmission across the neuromuscular junction. Nerve conduction velocity is consistently lowered.
- Result is paresis to paralysis and hypotonia as well as hyporeflexia.
- May have CNS effects as well.

Susceptible Species

Cattle and sheep have been commonly affected in the northwestern United States. Horses have been less commonly affected, but paralysis can result from 1 female tick. Reported more commonly in dog, rarely in cat. Wildlife rarely affected, however mule deer have been affected experimentally.

Signs

- Onset is generally 3 - 9 days after the attachment of the tick. Clinical signs may be transient or intermittent if the feeding ticks disengage and fall off. Female ticks found on the body, look carefully.
- Paresis begins in the pelvic limbs and ascends.
- Ataxia may be an early clinical sign. Animals may appear apprehensive and will assume a wide-based stance.
- Signs become generalized within 1 or 2 days.
- Cranial nerve dysfunction is not usually prominent and, if present, is usually limited to facial nerve diplegia (bilateral paresis or paralysis) and mild depression of gag reflexes. In some cases, mydriasis and anisocoria may occur as may dysfunction with other cranial or peripheral motor nerves.
- Dogs may develop anorexia and a change in phonation may be noted.
- Animals generally remain bright and alert unless secondary complications such as dehydration or infection occur.
- Respiratory paralysis can occur within 5 days of the onset of signs.
- There are usually no sensory deficits.

Diagnosis

- Finding feeding female ticks of the Dermacentor or other toxigenic genus.
- Nerve conduction velocity is consistently slower than normal.
- EMG changes appear approximately 5 days after onset of peripheral weakness.
- No notable effects on hematology, blood chemistry, or cerebrospinal fluid parameters occur in uncomplicated cases.
- Recovery upon removal of the ticks and the lack of reoccurrence in their absence confirms the diagnosis.

Lesions

None.
Treatment

- Removal of the tick or ticks results in marked improvement within 24 hours followed by complete recovery within days.
- It is essential to examine the ear canals closely, as well as the ear folds and interdigital areas in order to remove all ticks.
- Even when no ticks are found, but the signs are still suggestive of tick paralysis, a tick dip solution may be indicated.
- Assisting respiration could be necessary in severe cases, it may be essential to continue this assistance for up to several hours.
- Immunity to *D. andersonii* toxin has not been demonstrated.

Phenylarsonics

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Swine, poultry</td>
<td>Days</td>
<td>Weeks to permanent damage (common); potentially lethal</td>
<td></td>
</tr>
</tbody>
</table>

Source

- Four Compounds:
  - Arsanilic acid (p-aminophenylarsonic acid) and its salt, sodium arsanilate.
  - 3-nitro-4-hydroxyphenylarsonic acid (Roxarsone; or "3-Nitro").
  - 4-nitro-phenylarsonic acid (Nitarsone or Histostat-50).
  - p-ureidobenzenearsonic acid (Carbarsone or Carb-o-sep).
- Phenylarsonics are used as feed additives for disease control and to improve weight gain and feed efficiency. Had been used previously for blood parasites.
- Recommended concentrations:
  - Arsanilic acid (AA) and sodium arsanilate:
    - 50 - 100 ppm (0.005 - 0.01%) 45 - 90 gm/ton prolonged feeding for weight gain and feed efficiency in swine and poultry (chickens and turkeys only).
    - Late gestating sows require approximately 45 ppm because of their increased feed consumption.
    - 250 - 400 ppm (0.025 - 0.04%) for 5 - 6 days for treatment of swine dysentery.
  - 3-Nitro:
    - 25 - 37.5 ppm for swine diets to improve weight gain and feed efficiency.
    - 200 ppm for 5 - 6 days for swine dysentery.
    - 25 - 50 ppm for chickens and turkeys for improved weight gain and feed efficiency.
  - 4-Nitro:
    - 188 ppm for weight gain and feed efficiency in chickens and turkeys.
  - p-ureidobenzenearsonic acid:
    - 250 - 375 ppm for prevention and control of blackhead in turkeys.

Toxicity

- Arsanilic acid and sodium arsanilate:
  - Swine.
    - 250 ppm - Clinical signs appear within 3 - 6 weeks of first feeding.
    - 1000 ppm - Clinical signs appear in 3 - 10 days after begin feeding.
  - Turkeys.
• Maximum safe level is 300 - 400 ppm.
  • Rat.
    • Newborn LD50 oral - 216 mg/kg.
    • Adult LD50 oral - over 1,000 mg/kg.
  • 3-Nitro:
    • Swine.
      • 250 ppm - Clinical signs develop in 3 - 10 days.
      • 100 ppm - Clinical signs and lesions have been seen within 3 weeks. 75 ppm can cause problems.
      • 187 mg/kg for 30 days fed to swine resulted in paraparesis which progressed to paraplegia. Episodes of incoordination were observed from day 11 which could be illicit by exercise.
    • Dogs - oral LD50 is 50 mg/kg.
    • Rat - oral LD50 is 155 mg/kg.

Conditions of Poisonings

• Poisoning with either compound is most often a result of misformulation with excessive amounts.
• May result from feeding the high (therapeutic) levels too long.
• Can be due to treating excessively susceptible animals such as those with severe diarrhea or lactating sows.
• Water deprivation for any reason increases susceptibility.
• Use of "3-Nitro" at same levels as arsanilic acid.
• Arsanilic acid and sodium arsanilate are used most and most often are associated with toxicosis. Second in prevalence of use is "3-Nitro" and because of its greater toxicity, persons confusing its dosing level with that of arsanilic acid may misformulate feeds with resultant overdose.

Absorption, Distribution, Metabolism and Excretion (ADME)

• Absorbed orally or via the skin.
• Arsanilic acid is excreted in the urine, primarily as unchanged compound. Dehydration increases the likelihood and the severity of poisoning. Therefore diarrheas, limited water supply or lactation greatly increase the likelihood of clinical toxicoses. Generally poor absorption from the gut and rapid urinary excretion. Slower excretion from nervous tissue.

Mechanism of Action

• Not the same mechanism as inorganic, alphatic or trivalent organic arsenic poisoning. In these types of poisoning, sulfhydryl (-SH) groups are bound by arsenic, inactivating enzymes with -SH groups important to their structure and function.
• The phenylarsonics do not bind to sulfhydryl groups and, in pigs, are apparently excreted almost entirely unchanged, so that little if any reactive metabolites are formed to exert such an effect.
• Theory (not tested) is that the phenylarsonics may, in some way, interfere with the function of B-vitamins such as B1 or B6.
• By whatever mechanism, the phenylarsonics cause demyelination and gliosis (inflammation) in peripheral nerves.
• In functioning ruminants, however, it is theorized that the phenylarsonics may be broken down in the rumen and with sufficient exposure a syndrome similar to inorganic arsenic toxicosis develops (see below).

Signs

• Swine.
  • Acute (very high dose) phenylarsonic (arsanilic acid) toxicosis.
    • Earliest clinical signs roughened hair coats, diarrhea.
    • Incoordination, ataxia and hyperesthesia developed next.
    • After a few days, lose control of limb movements and animals become paralyzed (posterior paresis to quadriplegia) but, if have access to food and water, will eat and drink. Occasionally head tilt develops. Animals may develop loss of prehensive ability.
    • Arsanilic acid and sodium arsanilate may cause blindness, but this is rarely seen with "3-Nitro" (Roxarsone ®).
    • Reddening of the skin is seen in white animals and sensitivity to sunlight may occur (very characteristic).
    • Signs will completely abate if acute (high dose) toxicosis is caught and clean feed is provided within a few days of the onset. If delay in removal from arsanilic acid (e.g., paresis or paralysis present), then demyelination/paralysis can be progressive.
    • Die of thirst, cannot get to water (dehydration).
  • Chronic (excessive but not massive overexposure) toxicosis: gradual onset.
    • Goose stepping, knuckling of the hocks.
    • Poor growth, poor feed efficiency.
  • Experimental toxicosis of swine with "3-nitro" compounds (187.5 mg/kg, 30 days) produced a syndrome which was slightly different
from arsanilic acid toxicosis.

- Paralysis: mild peripheral and only minimal optic neuropathies.
- No EEG abnormalities were seen.
- Erythema of skin present, prolonged discoloration of skin where animal was handled.
- Arousing animals resulted in urination, defecation, then tremors and episodes of struggling and anxiety evidenced by squealing.
- Blindness was not detected.
- Animals continued to eat and drink.

**Poultry.**

- Arsanilic acid: anorexia, depression, coma and death.
- "3-Nitro": Incoordination and ataxia.

**Cattle.**

- Arsanilic acid: More resistant than swine but with sufficiently high overdose show signs like those of inorganic, aliphatic or trivalent organic toxicosis (diarrhea, shock, etc.).

**Dog.**

- Limited study LD50 (approximately 50 mg/kg)-renal hemorrhages.

---

**Lesions**

- Ruminants and rats
  - Severe gastrointestinal lesions as in inorganic arsenic toxicosis.
- Swine
  - Gross.
    - Usually no lesions are notable.
    - Erythema of the skin.
    - Muscle atrophy in chronic cases.
    - Abnormally full urinary bladder in some swine.
  - Histopathology.
    - Demyelination of peripheral nerves, optic tracts, optic nerves. Necrosis of myelin-supporting cells and degeneration of axons, with gliosis of affected tracts.
    - These lesions are usually not evident until 6 - 10 days of feeding excessive amounts of phenylarsonics. First the myelin fragments into granules and globules and then, after several days, the axons begin to break down. Lesions are progressive.
    - With "3-nitro" toxicosis, affected swine developed myelin and axonal degeneration of white matter of spinal cord. Degeneration began at 11 - 15 days, was progressive, and corresponded with the development of episodes of extreme incoordination. Peripheral and mild optic neuropathies were also observed. Brain lesions were not observed grossly or on histopathological examination.

**Diagnosis**

- High morbidity, low mortality.
- Affected swine and poultry often eat and drink but cannot move about due to extreme incoordination (mentally sane).
- Histopathologic findings:
  - Longitudinal sections of long nerves must be examined. In order to achieve this, the nerve must be fixed in a manner which will prevent curling up during fixation. This is readily accomplished by stapling the nerve to a tongue depressor before placing in the fixative. Optic nerve lesions will usually not be evident until 10 days of overexposure and sciatic or brachial nerves will show lesions only after 2 weeks of excessive phenylarsonic treatment.
  - If still getting treated feed or treated water prior to killing, 3 - 10 ppm in kidney and liver or 1 - 2 ppm in blood would be diagnostically significant. Likely to be found in urine, but diagnostic concentrations have not been established.
  - Usually, because of paralysis, affected animals have not been able to get to feed and since most is excreted within a few days, the kidney and liver arsenic concentrations are often normal.
  - Feed, the usual source, is the most worthwhile specimen for diagnostic confirmation. Arsanilic acid at 250 ppm or "3-Nitro" at 100 ppm with concurrent evidence of diarrhea or water restriction tends to confirm the diagnosis.
  - Labs can determine arsenic levels in feed and then calculate the amount of arsanilic acid or "3-nitro" present.
  - There is also a simple direct spectrophotometric method to detect "3-nitro" in feeds. Contact Iowa State University, Veterinary Diagnostic Laboratory by phone at 515-294-1213.
  - Consult with a veterinary toxicologist for interpretation on first few cases.
Differential Diagnosis

Includes nitrofuran or mercury poisoning, Ca/P deficiency, water deprivation, pseudorabies, B vitamin deficiency.

Treatment

- Withdrawal from the source, provision of clean feed and water in such a manner that paralyzed animals are able to eat and drink.
- B-vitamins can be tried, although not tested and shown to be worthwhile.
- Swine showing significant signs may fail to make a complete recovery due to irreversible nerve damage.

Organophosphorus-Induced Delayed Neuropathy (OPIDN)

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Toxicants that Cause Paresis or Paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle, swine, cats, chickens</td>
<td>2 - 4 weeks</td>
<td>Weeks to permanent (common)</td>
<td></td>
</tr>
</tbody>
</table>

Sources

- This syndrome can result from single or multiple exposures.
- The appearance of clinical signs are delayed for an average of 1 - 2 weeks in many animals and 2 - 4 weeks in man.
- Most, but not all, of the implicated phosphate esters causing OPIDN are insecticides.
- Related compounds (e.g., triarylphosphates) are used in industrial applications such as hydraulic systems, as additives to high-temperature fire-resistant lubricants, and as plasticizers. This class includes triorthocresyl phosphate (TOCP).

Toxicity

- The tendency to cause OPIDN does not parallel the tendency to inhibit acetylcholinesterase. Many OPs have not been associated with OPIDN in spite of their capacity to cause acute toxicosis due to acetylcholinesterase inhibition. Other compounds with comparatively low acute toxicity with respect to cholinesterase inhibition may be potent inducers of OPIDN in the absence of any previous toxicoses. In addition, some compounds such as O-ethyl-0-4-nitro-phenyl phenylphosphonothioate (EPN) are so toxic with regard to cholinesterase inhibition that the significance of their capacity to induce OPIDN is diminished by the small number of poisoned individuals that live long enough to develop the "delayed neurotoxicity" syndrome.
- If death occurs as a result of the induction of OPIDN, it is usually a result of respiratory paralysis or inability to get to water.

Specific Examples

   - Lubricant, plasticizer, sometimes an adulterant of human foods, beverages.
   - During prohibition was incorporated into Jamaica Ginger, which resulted in an epidemic of "Ginger Jake Paralysis" affecting thousands of humans.
   - At least 6 other TOCP incidents have also occurred, most a result of cooking oil contamination.
   - 7 - 14 day or longer delay before onset. Most other implicated OPs have been associated with an 18 - 21 day lag period before onset.

   Signs (general):
   - Affects motor and sensory neurons.
   - Abnormal sensation in the feet and legs such as tingling and burning.
   - High stepping.
   - Weakness, ataxia.
   - Ascending paralysis, may be flaccid. Gradual progression anteriorly.
   - Effects may be extremely persistent or permanent after exposure terminated.
   - Decreased reflex responses.
   - Muscle atrophy.
   - Severe dyspnea and absence of vocalization may be observed in cattle and pigs.
   - Recovery, if any, is generally slow and often incomplete.
   - Cattle: diarrhea, posterior weakness, ataxia, stiff, difficulty rising, weaving back legs, wide stance. Animals often recumbent.
2 - 6 days before death, although occasional sudden death noted. Animals dribble urine.

- Cattle and pigs: After a few days to several weeks, the peak of the process is reached and thereafter improvement in the functional disturbances begins.
- Cat: Cats may recover some function, probably dependent upon the extent of lesions.

Recovery:
- Mild cases: very slow recovery. Recovery generally more rapid in cat than in man.
- Severe cases: no recovery.
- Occasionally can ascend to result in quadriplegia and can cause death, from respiratory paralysis but this is rare. Prevalence:
  - 20,000 human victims of Ginger Jake (Jake Leg) Paralysis.
  - 10,000 human victims from poisoning of Morocco cooking oil which contained 3% mixed cresol phosphates.
- TOCP is biotransformed via the liver microsome P450 system to the more neurotoxic metabolite saligen cyclic-o-tolyl phosphate.

2. Leptofos (Phosvel ®), produced by Velsicol.
- Insecticide. Never marketed in the USA although registration applied for.
  - Sold in Egypt: caused an epidemic of OPIDN among water buffalo.
- Also causes mental and emotional dysfunction. Reports of "Leptophos zombies"; name used to describe workers in a leptophos plant in the USA. Workers were also exposed to n-hexane which may have contributed to the development of some clinical signs.
  - Confusion, headache, disorientation, and altered mental and emotional state.
- Some variation seen between species in ability to metabolize (oxidation, reduction, and dehalogenation reactions) leptofos associated with some variability in susceptibility among species.

3. Other OP insecticides and anthelmintics implicated in delayed neuropathy.
- DFP.
- Fenitrothion - Insecticide.
- EPN - Insecticide: extremely toxic as far as acute cholinesterase inhibition is concerned, OPIDN seen in survivors who are able to survive as a result of therapy.
- Cyanofenphos - Insecticide (Amaze, Oftanol).
- Trichlorinate - Insecticide.
- Mipafox - Insecticide.
- EPBP (S-7)-Insecticide.
- O-methyl-S-methyl, phosphoroamidate - Insecticide.
- Trichlorfon - Insecticide and anthelmintic.
- Carbofenothion (Trithion) - Insecticide.
- Haloxon - Anthelmintic causes OPIDN in some breeds/strains of sheep.

4. Other organophosphorus compounds implicated in OPIDN.
- DMPA (Zytron) - Herbicide.
- Butifos.
- Merphos - Defoliant.
- DEF - Defoliant.

5. Other compounds suggested as capable of causing delayed neurotoxicity, not OPs.
- Diallate (Avadex) - Carbamate herbicide.
- Sulfallate (Vegadex) - Carbamate herbicide discontinued product.

Mechanism of Action (Postulated)
- The development of OPIDN does not correlate with inhibition of acetylcholinesterase.
- The occurrence of delayed neuropathy has a high correlation with the inhibition of an enzyme called neuropathy target esterase (NTE). Maximal inhibition of > 70% at 1 - 2 days after exposure usually is associated with the onset of delayed neuropathy 8 - 14 days later. NTE does not have an identified function in the body. Whether or how NTE inhibition actually leads to OPIDN is therefore unknown. NTE is present in peripheral nerves, lymphocytes, brain, placenta, and several other sites.
- Three mechanisms of action of these OPs have been proposed:
  - A primary toxic effect on the metabolic machinery of the nerve cell perikaryon.
  - A direct action on the axon at certain vulnerable sites without affecting axonal transport.
  - Alteration or interruption of axonal transport.
- Many OP and carbamate insecticides can inhibit NTE but do not produce OPIDN. Besides inhibiting NTE, a compound must be able to undergo "aging" once it is bound to the enzyme before it will produce OPIDN.
- Inhibitors of NTE can be put into 2 groups:
  - Group A (phosphates, phosphoramidates, and phosphonates) are axonopathic, can "age" and are therefore potentially neurotoxic.
  - Group B (sulphonates, phosphinates, and carbamates) are not axonopathic, will bind to esterase, do not age and can therefore be protective.
- The essential difference between these 2 groups is the ability of Group A compounds to undergo aging. Prior administration of a compound from Group B can be protective against the delayed neurotoxic effects of subsequently administered Group A compounds.

Species Sensitivity (Varies at Least with Some Compounds)

Susceptible Species

Chicken, duck, turkey, horse, cow, sheep, pig, dog, cat, baboon, rat, and man.

![Graph](image)

Mean percent inhibition of lymphocyte neuropathy target esterase (LNTE) activity in cats exposed to a single, im dose of corn oil (vehicle control), DFP (positive control), or chlorpyrifos. Data points are expressed as a percentage of the group's mean predose LNTE activity. The mean (+ SD) predose LNTE activity for the corn oil, DFP, and chlorpyrifos groups were 8.97 ± 1.50, 10.16 ± 1.83, and 9.48 ± 2.61 nmol of phenyl valerate hydrolyzed/min/mg of protein, respectively. *indicates significantly different (p<0.05) from vehicle controls.
Cerebral cortex (frontoparietal lobe) from a cat treated with 300 mg of chlorpyrifos/kg of body weight. Vacuolar change confined to white matter. H & E, x 35.

Longitudinal section of lumbar (L4) spinal cord from a cat treated with chlorpyrifos at 300 mg/kg of body weight. Vacuolar change with associated myelin debris and macrophage infiltration. H & E, x 215.

Higher magnification. Multifocal axonal swelling (arrows). Bodian's stain, x 1060.
Nonsusceptible Species

- Mouse, rabbit, guinea pig, hamster, and gerbil.
- The adult hen (greater than 180 days of age) appears highly sensitive and is used in OPIDN screening of OPs. For an unknown reason, young chickens and probably the young of other species are more resistant to OPIDN.
- Suffolk sheep appear genetically predisposed (at least to Haloxon).
- Humans are extremely sensitive.

Lesions

- Characterized as a central-peripheral distal axonopathy (axons injured first, myelin damage is secondary).
- Histopathological analysis requires longitudinal section of spinal cord and peripheral nerves (staple nerves to tongue depressor during fixation).
- Clumping of myelin, foamy appearance of myelin, broken axons (axonal degeneration).
- The distal nerves of the peripheral nervous system are affected earlier and more severely than proximal fibers "dying-back polyneuropathy".
- Large diameter fibers appear more affected than small diameter fibers.
- Lesions are symmetrical and involve both sensory and motor pathways. Axon degeneration occurs largely in spinal cord tracts and peripheral nerves in hindlimbs.
- Demyelination occurs as a secondary event after the primary axonopathy.

Treatment

- No effective therapy is recognized.
- Treatment with atropine and oximes (2-PAM) minimize initial development of signs related to cholinesterase inhibition but do not prevent the development of OPIDN.

Lathyrus spp. - Vetchlings
(Equine Cystitis-ataxia and Teratogenesis Syndromes)

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Toxicants that Cause Paresis or Paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horses, cattle</td>
<td>10 days to 2 months</td>
<td>Weeks to permanent damage</td>
<td></td>
</tr>
</tbody>
</table>

Images

- *Lathyrus* spp. Source: Cornell University, Poisonous Plants Informational Database (www.anisci.cornell.edu/plants/index.html). - To view this image in full size go to the IVIS website at www.ivis.org . -
- Caley pea, *Lathyrus hirsutus* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -
- Wild pea, *Lathyrus incanus* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -
- Caley pea, *Lathyrus hirsutus* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -
- Singletary pea, *Lathyrus pusillus* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -
- Everlasting pea, *Lathyrus sylvestris* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -
- Sweet pea, *Lathyrus odoratus* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -

Source

- Most reports of serious lathyrism have come from Europe, Northern Africa, Russia and India. These outbreaks, which are now generally of historical interest, arose primarily from conditions of poverty and drought in which people were forced to subsist on a diet composed largely of *Lathyrus* sp. seeds. Large quantities of these seeds in the diet can produce a paralytic syndrome in man and livestock.
Toxic species of *Lathyrus* in the USA and Canada include:

- **L. hirsutus** (Caley pea, wild winter pea, singletary pea).
  - This plant has legume fruit pods, 1 - 1.75 inches long, 1/4 inch across, flat, hairy, many seeded, splitting in two halves which become tightly twisted when dry. Used as an annual winter forage or cover legume in the southern USA, California and Oregon.
- **L. incanus** (wild pea).
  - Native to the dry, sandy plans of Nebraska, Colorado, and Wyoming.
- **L. pusillus** (singletary pea).
  - Winter cover crop in the Gulf states, naturalized in area from Texas to Kansas to Florida to North Carolina.
- **L. sylvestris** (everlasting pea, flat pea).
  - Coarser, persistent perennial, with 2.5 inch (6 cm) long, 0.5 inch (1.25 cm) wide pods. Naturalized in the northern USA and southern Canada.
- **L. odoratus** (sweet pea).
  - This popular climbing vine is a favorite among gardeners for its sweet-smelling blossoms. The clusters of flowers may be white, pink, lavender, red or purple. The leaves are slightly elongated ovals with pointed tips, appearing in pairs on the winged green stems. Small, hard, green peas about 1/4 inch (0.6 cm) in diameter are borne in green seed pods.

**Susceptible Species**

- Different species of livestock vary considerably in susceptibility. The horse is particularly sensitive to the toxic principle and is most often poisoned.
- A diet of exclusively *L. sativus* seeds brings on signs in the horse in approximately 10 days. When fed 1 or 2 quarts of seeds per day, signs are delayed in onset for 2 - 3 months and may appear a month or more after withdrawal of the seeds from the diet.

**Toxic Principle (in Sweet pea)**

- The toxic principle of the sweet pea is beta-(gamma-L-glutamyl)-aminopropionitrile. It is localized primarily in the pea or seed of the plant. Once ingested this compound may be converted in vivo to beta-aminopropionitrile, which appears to be the substance responsible for the toxic effects.
- Neuotoxin is heat labile and can be destroyed by cooking.
- When the seed is ingested chronically, as in India where it makes up part of the native diet, it causes skeletal deformities due to inhibition of cross-linking during the formation of collagen. In the development of vascular walls, elastic fiber formation is inhibited, thus lowering the resistance to vascular wall stretching. The end result is a predisposition to vascular aneurysms. During pregnancy, the developing fetus is especially sensitive to the poison.
- Primary neurotoxin in *L. sativus*, ß-N-oxalyl-L-a-g-diaminoproprionic acid (ODAP), appears to cause direct neurotoxicity. Signs of neurolathyrism in man include muscular rigidity and paralysis of legs.

**Clinical Signs**

- Two forms of lathyrism are recognized: neurolathyrism and osteolathyrism.
- The acute toxicity of sweet pea ingestion is manifested as a paralytic syndrome; although the pea has to be consumed in rather large quantities before clinical signs develop. Other signs may include a slow, weak pulse, depressed and weakened respiration, and convulsions.

**Signs in Cattle (L. Hirsutis)**

- Osteolathyrism predominately affects livestock.
- Lameness in cattle may appear between the 3rd and 5th day of consumption when seeds are present at the time of poisoning. Lameness may rarely be severe. In experiments on pasture, and in feeding forage, no lameness occurred when the seeds were absent.

**Signs in Horses**

- Weight shifted to front legs.
- Hind legs held forward and a hopping gait.
- Seem normal when in a recumbent position.
- When get up, pain is associated with locomotion and may appear as if "tied up" due to stiffness in hindquarters.
- Sometimes the head is held low.
- Paralysis of recurrent laryngeal nerve leading to dyspnea and roaring.
Signs in Other Species

*L. hirsutus* - Experimentally, reproductive problems (chickens) and lameness and skeletal abnormalities (swine and chickens) have been reported.

Specific Syndromes

- *L. incanus.*
  - In Wyoming, *L. incanus* has been suspected of producing lameness in horses on range.
- *L. pusillus.*
  - Reported to cause livestock poisoning, experimental lameness and bone deformities in chickens.
- *L. sylvestris.*
  - Experimentally produces characteristic nervous signs of hyperexcitability, convulsions, and death without skeletal lesions.

Lesions

Neuronal degeneration in the spinal cord and nerves to the hind legs (neurolathyrism).

Prognosis

- Some animals make a full recovery.
- Others are chronically affected: for example, 2 years after *Lathyrus* toxicosis some affected horses exhibit stringhalt-like signs (incoordinated when forced to back up; legs stay flexed too long).

Treatment

If large quantities of the seed have been ingested, induce emesis and perform gastric lavage. Administer activated charcoal and a saline cathartic. Thereafter, symptomatic and supportive therapy is indicated.
Sweet Pea - The conspicuous and colorful butterfly-shaped flower, the pinnately divided leaves with tendrils, and the hairy seed pod and enlarged seed (upper right) characterize this colorful garden forb.

Sorghum spp. - Hybrid Sudan (Equine Cystitis-ataxia and Teratogenesis Syndromes)

*Sorghum vulgare,* var. *sudanesis* - Sudan grass

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Toxicants that Cause Paresis or Paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Horses</td>
<td>Average 8 weeks</td>
<td>Often permanent neurologic damage; secondary urinary tract infection may be lethal; also teratogen in horses</td>
<td></td>
</tr>
</tbody>
</table>

Images

- *Sorghum* spp.. 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 . -
- Sudan grass, *Sorghum vulgare* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -
- Sudan grass, *Sorghum sudanense* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -
Source

- Sudan grass is a member of the *Sorghum* spp. which are most often associated with cyanide or nitrate toxicoses.
- In horses, especially females, a syndrome of cystitis and ataxia has been associated with the consumption of Sudan grass in the southwest United States. Observed in Texas, Oklahoma, New Mexico, Arizona, California, Kansas, and Colorado.
  - Area incriminated most definitely is between Corpus Christi, Texas, and Fort Dodge, Kansas, and 300 miles either side of a line connecting these two cities.
  - All breeds of horses are involved.
- Similar ataxia-incontinence syndrome reported in horses and cattle of Australia grazing sorghum.

Toxic Principle

- Believed to be the lathyrogenic agent, beta-cyanoalanine.
- May also contain cyanogenic glycosides and nitrate in toxic amounts (which cause other syndromes).

Toxicity

- Associated with grazing of hybrid Sudan pastures. Grazing periods varies from 1 week to 6 months, average period 8 weeks in 1 report.
- Not associated with eating the cured hay from the pastures. Freshly cut hay has been implicated.
- Poisoning occurs from July to December or until frost kills the plant. Generally occurs during seasons of high rainfall. Young rapidly growing plants most commonly involved.
- Fertilization of the pasture seems to have no effect on toxicity of the Sudan grass.

Signs

- Posterior ataxia and incoordination in the rear legs is the most commonly observed clinical sign. May appear normal when standing but when forced to move may almost drop to the ground with one or both legs flexed. Horse may then recover and walk off more or less normally.
- When backed may sit or fall down into lateral recumbency. Flaccid paralysis of hind limbs may develop within 1 day of onset of ataxia.
- May weave as each foot is placed on the ground and may be confused with equine wobbler disease.
- Frequent opening and closing of the lips of the vulva (winking) and constant or frequent dribbling of urine (urinary incontinence).
- Urine scalding and contamination with associated irritation and exudation of the area ventral to the vulva and to a lesser degree the rear legs down to the hocks. Yellow putty-like sediment (urine odor) is deposited in skin.
- Mares may appear to be in constant estrus. Usually due to constant irritation of the urethra and vagina due to passage of urine and exudate from a constantly full urinary bladder.
- Cystitis results from sediment accumulation, urine stasis, and bacterial over growth. In general, cystitis is relatively uncommon in the horse.
- Males may squirt urine and the penis may be partially relaxed. With chronic toxicosis may constantly dribble urine. Partial alopecia on ventral abdomen.
- Dribbling urine in both sexes increased if animal is forced to move suddenly.
- Normal body temperature, pulse and respiration rates, appetite, and maintenance of body condition unless pyelonephritis occurs.

Teratogenesis

- Fetal malformations may occur when mares graze hybrid sudans during the 20th - 50th day of gestation. Foals may be born with extreme flexion of the joints or ankylosis. May result in dystocia.
- Abortions may also result.

Clinical Pathology

- Leukocytosis and lymphocytosis.
- Commonly see a normal urine pH of 8 and normal specific gravity of 1.030. Proteinuria may be present.
- Sediment: blood, epithelial cells, many bacteria, large numbers of calcium carbonate crystals. Hyaline and granular cysts present in some sediment exams.
- Urine culture: *E. coli* most commonly isolated in combination with *Corynebacterium* spp., *Staphylococcus* spp., *Proteus vulgaris*, and/or *Pseudomonas aeruginosa*.
Lesions

- Urinary bladder - Cystitis with markedly thickened bladder wall (2.5 - 3.5 cm) with large volumes of urine present. Mucosa and ureters may be hyperemic. Bladder contains amorphous, semisolid yellow deposit (calcium carbonate). Bladder mucosa occasionally ulcerated.
- Vagina - Reddening and sometimes coated with sediment.
- Kidneys - Pyelonephritis is sometimes present and may be the cause of death.
- Thoracic, lumbar and sacral spinal cord: neuronal degeneration and mild myelomalacic change in these areas of the cord.
- Arthrogryposis in foals (especially contracted joints).
- Histologic findings include acute, occasionally necrotizing cystitis. Degeneration of axons and demyelination in cervical, thoracic, lumbar, and sacral spinal cord segments.

Prevention

Keep horses off Sudan or Hybrid Sudan pastures.

Treatment

- Generally unsuccessful; antibiotics, nitrofurans, acidification of the urine and DMSO have all been tried. Changing of the diet from hay to grain and the use of antibiotics may provide temporary relief, but the syndrome generally recurs in 1 - 2 weeks after the therapy is stopped. Once the animal exhibits significant incoordination or dribbling or urine, complete recovery seldom if ever occurs.
- Note - A similar contracted foal syndrome in Europe has been described, but no connection with sudan grass or other causative agent has been made.

Sorghum - fruit cluster with leaf.
**Acacia spp.**  
*Acacia berlandieri* - Guajillo (pronounced Wah-hee-O)  
*A. georginae* - Gidyea  
*A. greggi*

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sheep, goats</td>
<td>6 - 9 months</td>
<td>Months; may be lethal; up to 50% may die</td>
</tr>
</tbody>
</table>

**Family** - *Leguminosae* (pulse or bean family)

**Images**

- Guajillo, *Acacia berlandieri* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.
- Catclaw acacia, *Acacia greggii* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.

**Introduction**

- Cause of "limberleg" or "Guajillo wobbles".
- Chronic ingestion of large amounts of the leaves and fruit (15 times the animal's weight) has been associated with toxicosis.
- This plant is considered a valuable forage species in some areas.
- Drought may result in this plant being the only forage available.
- Losses may be negligible during years of average rainfall.
- N-methyl-beta-phenyl-ethylamine hydrochloride administration (orally) to sheep at 375 mg/kg caused clinical toxicosis.
- Goats cannot be successfully maintained on ranges where Guajillo is present.

**Habitat**

- *A. berlandieri*: Texas, especially in the southern part of the Edward's plateau and Trans-Pecos (Chisos Mountains) areas. Rangelands.
- *A. greggi*: Limestone areas of Arizona; other areas?
- *A. georginae*: Queensland, Australia.
- *A. nilotica* subsp. *kraussiana*: South Africa.

**Toxic Principle**

- *A. berlandieri*  
  - Sympathomimetic amines.
  - Tyramine, N-methyl tyramine.
  - N-methyl-beta-phenylethylamine.
- *A. georginae*.  
  - Fluoroacetate.
- *A. greggi*.  
  - Cyanide.

**Toxicity**

- General (*A. berlandieri*).  
  - Oral lethal dose is approximately 450 mg/kg.
- *A. georginae.*
  - Six to 9 months on a diet containing this species is generally sufficient to produce toxicosis.
  - Mortality is generally low, but may reach 50% during drought years.
- *A. nilotica* subsp. *kraussiana.*
  - In goats the lethal dose is 30 g/kg, but 5 g/kg can be harmful if fed over long periods.
- *A. greggii.*
  - Potentially lethal in the limestone areas of Arizona.
  - Cases generally appear in the Fall or at the first frost.
- **Note** - Remainder of section pertains exclusively to Guajillo (*A. berlandieri*).

**Description**

- **A. berlandieri**
  - Plant - Perennial, pubescent shrub or small tree; 3 - 14 feet tall.
  - Stem - Leaf branches, 3 - 9 pairs.
  - Leaves - Alternate, twice pinnate; leaflets 3 - 6 mm long, numerous, 24 - 45 pairs, oblong-linear, oblique, acute, veiny with few or no prickles.
  - Flowers - White to yellow, sweet scented, axillary, leguminous, in dense groups, in globose heads.
  - Fruit - Legume, flattened, 4 - 6 times as long as wide; somewhat thickened margins, obvious at maturity, scattered among the foliage.

**Mechanism of Action**

Proposed mechanism of action is that the sympathomimetic amines of *A. berlandieri* compete for and then inactivate monoamine oxidase.

**Susceptible Species**

Sheep, goats.

**Signs (*A. berlandieri*)**

- General.
  - Clinical signs develop after 6 - 9 months ingestion as the sole diet.
  - Ataxia develops in the hind legs and occasionally the front legs.
  - Rubbery appearance of rear legs is first noticed when animals are forced to move.
  - Animals may get excited and become prostrate.
  - Generally animals remain alert and retain their appetite.
  - Nevertheless, many deaths on the range may be due to starvation and thirst.
- Sheep.
  - After grazing almost exclusively on Guajillo, sheep sometimes develop locomotor ataxia referred to as limber leg.
  - Stilted gait of the rear limbs, side to side swinging of the hips.
  - Forelimbs may then be affected.
  - Signs become exaggerated, animals are forced to move about.
  - Prostration.

**Diagnosis**

Identification of Guajillo, evidence of prolonged consumption, appropriate clinical signs.

**Treatment**

- Remove animals from access to the plant.
- Feed prostrate animals.
- Recovery usually occurs in a few months.
**Prevention**

- Do not allow animals to graze exclusively on Guajillo.
- When poisoning does occur, supplement feed and reduce stocking rates.
- Guajillo may be killed with herbicides.

---

**Karwinskia humboldtiana - Coyotillo**

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Toxicants that Cause Paresis or Paralysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cattle, sheep, goats, horses</td>
<td>Weeks to months</td>
<td>Weeks to permanent damage</td>
<td></td>
</tr>
</tbody>
</table>

**Synonyms** - Buckthorn, tullidora, capulin tullidor, capullincillo, cacatsi

**Images**

- Coyotillo, *Karwinskia humboldtiana* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -

**Habitat**

- Southwestern Texas into northwestern Mexico and Baja California.
- Rangelands, gravelly hills, canyons, river valleys, along arroyos.

**Description**

Spineless woody shrub or tree, 1 - 7 m tall. Leaves are veined opposite, petioled and elliptical to ovate (3 - 8 cm long) and have prominent veins. Small flowers are yellow-green, clustered in leaf axils with 5 sepals and 5 petals. Fruits (drupes) are ovoid, brownish-black or dark purple at maturity, 1 cm in length, is a several seeded berry, in the axils of the leaves. May flower at any time of year depending on weather. Fruits most often present from November to February.

**Toxic Principle**

Unknown. Contains anthracenones as well as a cumulative neurotoxic C-15 polyphenol.

**Toxicity**

Seeds (fruit) are the most toxic followed by the leaves. Toxic dose of whole fruit on a dry weight basis varies from .05 - 0.3% of body weight. For green foliage, this figure is 15 - 20% of the animals weight. Paralytic condition is caused by fruits not by the leaves. Winter season is most dangerous due to lack of good forage. Poisoning may result from a single feeding; however, most toxicoses occur after several days or even weeks of exposure.

**Mechanism of Action**

Unknown, but one component reportedly uncouples oxidative phosphorylation.

**Susceptible Species**

- Cattle - goats, sheep, and horses have experienced naturally occurring toxicosis.
- Sheep - 0.2% of the body weight of the ground fruit may be lethal. Similarly 20 - 25 lb of the leaves may be required to cause death. Sheep are the most commonly affected species.
- Frogs, snakes, chickens, rats, rabbits, chickens, and possibly dogs are susceptible experimentally.
- Children and soldiers-have been poisoned by eating the berries. In one outbreak, 10% of the affected soldiers died and others were still disabled 14 months after exposure. Recovery in man does occur but may take over 1 year.
- Snow monkeys (Macaca fuscata).
Signs

- Unthriftiness, depression, weakness, trembling, hindlimb incoordination, hypermetric respiratory distress, and dyspnea. As condition progresses, forelimbs may become affected.
- Paralytic condition affecting especially the hindquarters.
- "Limberleg", of cattle and sheep. Severely poisoned animals may jump and move backwards.
- Goats may walk on their knees.
- There is a lag period prior to appearance of signs from a few days to several weeks. Appetite remains normal. Most severely poisoned animals do not recover.
- "Bulbar weakness", respiratory, and possibly cardiac failure may lead to death.
- Reduced conduction velocities in affected nerves.
- The chronic wasting condition produced by the leaves is associated with signs of nausea, progressive weakness and death.

Lesions

- The motor paralysis is attributable to a segmental demyelinating neuropathy. Schwann cells swell and myelin laminae split at the intraperiod lines with formation of myelin vacuoles.
- Demyelination is more prominent than axonopathy. Chromatolysis, especially in the anterior horn cells of the spinal cord (probably secondary to peripheral damage), with time remyelination and axonal regeneration may occur. Swollen axons in white matter of cerebellum of goats.
- There may also be a lymphadenopathy, and small hemorrhages on the heart.
- Inflammatory lesions may be present on the mucosa of the stomach and intestines. In lethal cases, severe pulmonary edema tends to occur, and there may be microscopic degeneration of skeletal and cardiac muscle. Mild toxic nephritis and centrilobular hepatic necrosis and fatty change has been described. Demyelination of posterior spinal cord.
- Elevated CPK and SGOT due to indirect muscle damage.

Prevention

Avoiding exposure of unfamiliar animals to the plant and do not overstock ranges.

Differential Diagnosis

Acacia (also produces condition called limberleg). Syndrome is similar to triaryl phosphate (TOCP) toxicosis.

Treatment

Daily administration of thiamine has been reported to be of value in humans.
Coyotillo (*Karwinskia humboldtiana*) - Showing the leaves and fruit.

Citreoviridin and Patulin: Mycotoxins Causing Paralysis

<table>
<thead>
<tr>
<th>Specific Agents</th>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citreoviridin (Mycotoxin)</td>
<td>Cattle</td>
<td>(Importance of this mycotoxin in the field has not been well established)</td>
<td></td>
</tr>
<tr>
<td>Patulin (Mycotoxin)</td>
<td>Cattle</td>
<td>(Toxicosis is very rare)</td>
<td></td>
</tr>
</tbody>
</table>

### Citreoviridin

- A *Penicillium* spp. mycotoxin sometimes found in rice (and probably other substrates).
- Can cause ascending paralysis with convulsions and respiratory paralysis resulting in respiratory arrest.
- Cardiovascular and respiratory failure may occur 3 days after the initial onset of paralysis.

### Patulin

- Mycotoxin produced by *Penicillium* spp., *Aspergillus* spp., *Byssoschlamys fulva*, and *B. nivea*.
- Produced in apples, pears, grapes, barley, malt, rice, and wheat straw. Detectable to 1 mg/l apple juice.
- Unstable if mixed with wheat flour, ground sorghum or ground wet corn; and unstable if SO₂ (sulfur dioxide) is used as a preservative in apple products.
- Fermentation with *Saccharomyces* spp. (as is used in cider production) also inactivates patulin.
- Cattle have reportedly exhibited an ascending paralysis of motor nerves with convulsions, excitement and cerebral hemorrhage.
- Lesions may include pulmonary and cerebral edema, ascites, congestion of liver, spleen, and kidneys in addition to the effects described above.
- Inhibitor of RNA polymerase.
- LD₅₀ mice (SC) 8 - 15 mg/kg, oral LD₅₀ mice 35 - 48 mg/kg.
  - Mice displayed restlessness, heavy labored breathing, and convulsions.

**Note** - The importance of either of these mycotoxins (citreoviridin or patulin) in the field has **not** been established.
## Additional Toxicants

<table>
<thead>
<tr>
<th>Specific Agents</th>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Avidin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>in raw egg white (causes biotin deficiency), however, egg yolks are rich in biotin</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Locewod</strong> (Astragalus and Oxytopis) (Miserotoxin = 3-nitro compounds)</td>
<td>(See Toxicants with Mixed Effects on the Central Nervous System)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Solanum dimidiatum</strong></td>
<td>Cattle</td>
<td>Unknown</td>
<td>Chronic to permanent damage; potentially lethal</td>
</tr>
<tr>
<td><strong>Cycad palms</strong> (Cycas or Zamia)</td>
<td>Herbivores, dogs, swine</td>
<td>Hours to a few days</td>
<td>Weeks to permanent damage; often lethal</td>
</tr>
<tr>
<td><strong>Lolitrem B</strong> from Acremonium lolii in perennial ryegrass (Lolium perenne)</td>
<td>Sheep, cattle, sometimes horses</td>
<td>Chronic</td>
<td>Chronic; rarely lethal</td>
</tr>
<tr>
<td><strong>Tetrodotoxin</strong> (sodium channel blocker) in: - Puffer fish (Tetraodon and Fugu) - California newt (Taricha; a salamander) - European newt (Tarituras; a salamander) - Unk (Bombia; a salamander)</td>
<td>Pet animals (carnivores)</td>
<td>Minutes to hours</td>
<td>Days to several weeks</td>
</tr>
<tr>
<td><strong>Saxitoxin and neosaxitoxin</strong> (sodium channel blockers). Responsible for paralytic shellfish poisoning-from cocles, mussels, clams. Name derived from the Alaskan butter clam, Saxidomas giganticus). Poisoning is much more commonly a result of eating oysters. All acquire the toxin from the dinoflagellate, Gonyaulax spp., usually evident as &quot;red tides&quot;. The same toxins are produced by certain strains of at least 2 species of blue-green algae (Aphanizomenon flos-aquae and Anabaena flos-aquae)</td>
<td>Pet animals (from eating shellfish); All species (from drinking blue-green algae in surface waters)</td>
<td>Minutes to hours</td>
<td>Hours to months. Human cases often reported; potentially lethal</td>
</tr>
<tr>
<td><strong>Ciguatera</strong> (ichthyosarcotoxin, that causes sodium channels to stay open) in red snapper, barracuda, and other warm water, carnivorous, marine fish that bioaccumulate the toxin synthesized by marine benthic dinoflagellates, e.g., Gambierdiscus spp. Ciguatera causes neurologic, gastrointestinal, and cardiac dysfunction.</td>
<td>Pet animals</td>
<td>Hours to two days</td>
<td>Days to weeks; rarely lethal</td>
</tr>
<tr>
<td><strong>Sulfonamides</strong> (cause peripheral neuritis)</td>
<td>All species esp. chickens and cattle</td>
<td>Days to weeks</td>
<td>Weeks to permanent damage; potentially lethal</td>
</tr>
<tr>
<td><strong>Mephenesin</strong></td>
<td>Small animals</td>
<td>Hours to days</td>
<td>Hours to days; unlikely to be lethal</td>
</tr>
<tr>
<td><strong>Selenium</strong> (Lycopersicon) (may also contain toxic amounts of nitrate)</td>
<td>Swine; other species</td>
<td>Seven weeks to months</td>
<td>Damage may be permanent; potentially lethal</td>
</tr>
</tbody>
</table>

- Mephenesin
- Tetrodotoxin (sodium channel blocker)
  - Puffer Fish (Tetraodon and Fugu)
  - Poison Dart Frogs-Central and South America
  - California Newt (Taricha) (a salamander)
  - European Newt (Tarituras) (a salamander)
  - Unk (Bombia) (a salamander)

Full Table for Toxicants that Cause Paresis or Paralysis
- Saxitoxin and Neosaxitoxin (sodium channel blocker)
  - in Paralytic Shellfish Poisoning - From cockles, mussels, clams. (Especially the Alaskan butter clam, *Saxidomas giganticus*) and especially oysters - All from the Dinoflagellate (*Gonyaulax* spp.). Also contain the similar acting neosaxitoxin.
  - in Red Tide. Same Dinoflagellate in Fishes
  - in Blue-Green Algae (Aphanizomenon) - May contain both saxitoxin and the similar acting neosaxitoxin

- Ciguatera
  - Ciguatera is the neurologic, gastrointestinal, and cardiac syndrome produced by ciguatoxins, which are oxidative metabolites of gambiertoxins. The latter are produced by the benthic dinoflagellate *Gambierdiscus toxicus*.
  - The toxins bioaccumulate in food chains. People and pet animals may be exposed through consumption of warm-water, carnivorous, marine fish, such as red snapper and barracuda.
  - The mechanism of action of ciguatoxins is to cause sodium channels to stay open.
  - Avidin in raw egg white (causes biotin deficiency), however, egg yolks are rich in biotin.
  - Sulfonamides (peripheral neuritis) (See Toxicants that Affect the Kidneys)
  - Selenium (subchronic selenosis in swine (See Toxicants Causing Skin Effects Other Than Photosensitization)
  - Cycad Palms (See Poisonous Plants that Affect the Liver)

References

**Black Widow Spider (*Latrodectus spp.*)**


**Neuromuscular Blocking Agents**


**Delphinium - Larkspur**


**Botulism**


**Tick Paralysis**

Phenylarsonics

Organophosphorus-Induced Delayed Neuropathy (OPIDN)

Lathyrus spp. - Vetchlings

Sorghum spp. - Hybrid Sudan

Karwinskia humboldtiana - Coyotillo

Citroveridin and Patulin : Mycotoxins Causing Paralysis

All rights reserved. This document is available on-line at www.ivis.org. Document No. A2610.0899.