Poisonous Plants that Affect the Liver  (9-Aug-1999)

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Chapter Sections

Xanthium spp. - Cocklebur
Senecio - Ragwort - Groundsel
Crotalaria - Rattlebox
Amsinckia - Fiddleneck
Echium spp.
Heliotropium (Heliotrope)
Microcystis Aeruginosa, M. Viridis, Anabaena Flos-Aquae, Nostoc spp., Oscillatoria Aghardii, and Nodularia Spumigena
Lantana and Lippia spp.
Helenium spp. - Sneezeweeds
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Kochia Scoparia
Lotus Corniculatus - Birdsfoot Trefoil
Cycad Poisoning

Xanthium spp. - Cocklebur

Xanthium strumarium - Common cocklebur
X. orientale - Cocklebur, Sheepbur
X. spinosum - Spiny clotbur

<table>
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<tr>
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<th>Usual Duration (if survives)</th>
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<td>Herbivores, swine</td>
<td>Hours to days</td>
<td>Days to permanent damage, often lethal</td>
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Family - Compositae (Composite Family)

Images

- Cocklebur, Xanthium strumarium. 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 .
- Common cocklebur, Xanthium strumarium - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org .
- Cocklebur, Sheepbur, X. orientale - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org .
- Spiny clotbur, X. spinosum - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org .

Description - Xanthium spp.

- Plant - rough, coarse, annual, herb 3 feet tall.
- Stem - Erect, stout, widely branched, often red-blotched.
Leaves - alternate, simple triangular or heart-shaped, rough-toothed or lobed; blades, 6 inches long, broad.
Flowers - inconspicuous, imperfect.
Fruit - bur-like, 2-beaked, covered with many spines; 2 compartments, each containing a seed.

Habitat

- Southern Canada, throughout USA, to Mexico.
- In fields, wastelands, flood plains, overgrazed pastures, roadsides.

Toxic Principle

- Carboxyatractyloside, a sulfated glycoside, which is present in high concentrations in the seed and cotyledon, is now thought to be the primary toxic principle.
- Susceptible species:
  - Pigs, cattle, sheep, fowl, horses.
  - Hogs between 20 - 50 pounds appear most susceptible.

Toxicity

- Cockleburs sprout in spring and a dry fall.
- Cotyledonary stages of plant are extremely hazardous to herbivores and omnivores (toxic plus apparently reasonably palatable).
- 0.75% of animal's weight of young seedlings may produce clinical signs of toxicosis in a few hours and death in 24 - 48 hours.
- 500 seedlings are lethal to a 40 pound pig.
- Toxicity is not lost on drying.
- Seeds are poisonous, but are contained in a bur and are seldom eaten. Toxic at 0.3% of animal weight. Toxicosis can result when seeds are milled and mixed in feed.

Mechanisms of Action

- Inhibits carrier mediated ADP and ATP transport across mitochondrial membranes.
- Death may occur even when kidney and liver damage are pharmacologically prevented.
- Severe hypoglycemia may occur.
- Burs may cause mechanical damage.

Signs

- General:
  - Appear a few hours to 2 days after ingestion.
  - If death occurs, it is usually within 3 days of the onset of signs.
  - Anorexia, reduced responsiveness.
  - Vomiting, evidence of abdominal pain.
  - Rapid weak pulse, dyspnea.
  - Muscular weakness, prostration.
  - Spasmodic contraction of leg and neck muscles.
- Pig:
  - Evidence of abdominal pain.
  - Opisthotonos, spasmodic running motions, convulsions occur if severely poisoned.
  - Death occurs about 48 hours after onset of signs.
- Cattle:
  - Blindness, extreme hypersensitivity, convulsions are prominent.
  - Calves die acutely within 12 hours.
- Fowl:
  - Pronounced depression, death.

Lesions

- Gastroenteritis, with thickening of the mucosa.
- Hepatic, cardiac and other hemorrhage may be seen.
- Toxic hepatitis with slight icterus is characteristic.
- Ascites may be seen.
- High probability of chronic liver damage.
- Hepatic cirrhosis in recovered animals.
- Renal tubular degeneration (similar to acorn poisoning).

**Diagnosis**

Identification of *Xanthium*, evidence of consumption and appropriate clinical signs.

**Treatment**

- Preferred treatment - Oral activated charcoal (may use dose syringe and administer slurry via nose in swine) - saline cathartic; avoid dehydration.
- Fluids, dextrose, B-vitamins, supportive care.

**Prevention**

- Remove from source of exposure.
- Control weeds with 2,4-D.

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**Composite Family, Compositae**

**Common Cocklebur**, *Xanthium strumarium* L. - 1, upper part of plant; 2, seed; 3, bur; 4, seedling plant. **Annual**, reproducing by seed. **Taproot** rather woody, stout. **Stem**, erect, normally bushy, 2 to 4 feet (0.6 to 1.2 m) tall, ridged, rough-hairy, often spotted. **Leaves** alternate, simple, triangular in outline, toothed or lobed, rough, with long petioles. **Flowers** small, male and female flowers separate but borne together in clusters in axils of the upper leaves. Two female flowers are enclosed in each oval bur. At maturity the bur is hard, woody, and covered with hooked prickles, and ends in 2 curved spines. Male flowers numerous, in clusters on short stalks, dropping soon after pollen is shed. **Seeds** about 1/2 inch (1.3 cm) long, dark brown, rather slender with pointed tips. **Found** in cultivated fields, abandoned land, poor pastures, and roadsides.
**Senecio - Ragwort-Groundsel**

*S. jacobaea* - Ragwort, stinking Willie, tansy ragwort  
*S. ridelli* - Riddell's groundsel  
*S. longilobus* - Threadleaf groundsel, wooly  
*S. spartioides* - Broom groundsel  
*S. integerrimus* - Lamb's tongue groundsel  
*S. burchellii*  
*S. douglasii*  
*S. erraticus*  
*S. glabellus*  
*S. ilicifolius*  
*S. lobatus*  
*S. plattensis*  
*S. vulgaris* - Common groundsel  
*S. confusus*  
*S. pauperculus* - Prairie groundsel

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**Family - Compositae**

**Images**

- Common groundsel showing coarsely toothed leaves, flowers with no ray florets, and the seed heads with white pappus that aids in wind dispersal (*S. vulgaris*). Knight A.P. and Walter R.G. (Eds.). A Guide to Plant Poisoning of Animals in North America. Ithaca: International Veterinary Information Service (www.ivis.org), 2003. - To view this image in full size go to the IVIS website at www.ivis.org . -
- Senecio, Groundsels, and Ragworts, *Senecio* spp.. Source: Cornell University, Poisonous Plants Informational Database (www.anisc.cornell.edu/plants/index.html). - To view this image in full size go to the IVIS website at www.ivis.org . -

**Description**

*Senecio* spp. Mostly perennial herbs, approximately 3 feet tall. Leaves are palmately dissected, narrow segmentations are present; leaves are whorled, but bracts are not overlapping and form a cup under the head. Flowers are yellow, in heads clustered at the top of the plant and are numerous. The seeds are in both the disc and in the ray florets.

**Habitat**

- *S. ridelli* - Nebraska to Colorado and New Mexico, West Texas.  
- *S. longilobus* - Colorado, Utah to Texas, Arizona and New Mexico.  
- *S. spartioides* - Nebraska to Wyoming, south to Texas and Arizona.  
- *S. integerrimus* - Minnesota to British Columbia, south to Nebraska and California.
The western Senecios tend to grow in rangelands. *S. jacobaea* grows in roadsides, pastures and waste places. The plants increase in number when pastures are overgrazed.

*S. vulgaris* is a common weed in hayfields in California and possibly other states. New plantings of alfalfa and alfalfa weakened by heavy weevil infestations are more susceptible to competition by the weeds.

Oat hay may also be contaminated. These plants are readily identified in baled hay; but it is almost impossible to identify them in hay that is cubed or pelleted.

*S. pauperculus* - Much of North America except for the southeastern states. In Illinois especially the northern and the western counties; some in east central Illinois.

### Toxic Principles

- *S. jacobaea* - Jacobine, jacobine, senecione.
- *S. ridelli* - Ridelliine.
- *S. longilobus* - Longilobine.
- *S. spartioides* - Seneciphylline.
- *S. integerrimus* - Integerrimine.
- *S. vulgaris* - Senecionine, seneciphylline, retrorsine.
- Of over 100 known pyrrolizidine alkaloids, only a few have proven to be toxic.

### Toxicity

- *S. plattensis* is not poisonous. *S. longilobus* (threadleaf groundsel) is eaten throughout the year, especially when the range forage is dry and during ice and snow storms, but stock losses are heaviest in the late spring and summer months. 
- Dry leaves retain their toxicity. One to 5% of an animal's weight fed at one time or over a few days may bring on acute toxicosis. 'In the field, acute poisoning is rare, but chronic poisoning is common. In this instance, 12 - 56% of the animal's weight must be eaten before symptoms appear.
- Poisoning tends to occur as a result of ingestion of contaminated hay, at least in the case of common groundsel (*S. vulgaris*) in California. Poisoning may also occur during the growing season when good forage is scarce and the animals are forced to eat these plants.
- In Texas, *S. longilobus* is evergreen and may be eaten in winter. Young leaves are believed to be of greater toxicity than more mature leaves and stems.
- Ensiling hay containing pyrrolizidine alkaloids does not ensure detoxification and multiple deaths have occurred in cattle consuming contaminated silage. However, the addition of molasses to the green chopped plants during the ensiling process may lessen the risk.

### Absorption, Distribution, Metabolism and Excretion (ADME) (Applies to All Pyrrolizidine Alkaloid Plants)

Pyrrolizidine alkaloids are rapidly absorbed from the intestine and thereby expose the liver first via the portal circulation. They are also rapidly excreted in body fluids such as milk and urine. Since pyrrolizidine alkaloids are considered to be carcinogens, there is a potential public health problem. In addition, the alkaloids pass across the placenta and can thereby affect the fetus.

### Mechanism of Action (Applies to All Pyrrolizidine Alkaloid Plants)

- The toxicity of pyrrolizidine alkaloids is believed to be due to pyrrole derivatives which arise as a result of dehydrogenation of pyrrolizidine alkaloids by hepatic microsomal enzymes. Phenobarbital induction of hepatic enzymes intensifies the hepatotoxicity of
pyrrolizidine alkaloids. The activated pyrrole form presumably alkylates macromolecules in the hepatocyte, principally DNA, which impairs cell division.

- In high doses, necrosis of the hepatocytes occurs. More often the metabolic lesion prevents the hepatocyte from undergoing binary fission to regenerate hepatocytes. The cell continues to grow although unable to divide. Both nucleus and cytoplasm expand, sometimes up to 10-fold (hepatocytomegaly and karyomegaly). Ultimately, the cell reaches a critical mass and dies. With mild necrosis, the histopathologic description will be one of parenchymal atrophy with hepatocytomegaly.
- With the death of larger numbers of hepatocytes, the necrosis triggers a regenerative response accompanied by bile duct proliferation. Thus, the 3 primary lesions of pyrrolizidine alkaloid poisoning are hepatocytomegaly (which is always present), fibrosis and bile duct proliferation. The latter 2 lesions are dose and time dependent.
- After chronic ingestion of pyrrolizidine alkaloids, the picture may be one of slow hepatic degeneration, until the hepatic reserve is depleted, at which time liver function collapses and the animal suffers from a generalized hepatic insufficiency syndrome.

**Susceptible Species**

- Cattle and horses are most often poisoned; sheep and pigs require a longer time to show signs. Although sheep were, at one time, used in reducing the *Senecio* contamination of pastures, they may be poisoned on some strains at doses only slightly higher than those affecting cattle.
- Young, growing animals are more susceptible to the hepatotoxic effects of those compounds than are adults.
- Chronic pyrrolizidine alkaloid poisoning occurs worldwide causing extensive livestock losses.

**Signs**

- Acute poisoning.
  - Dullness, weakness, abdominal pain and death in a few days to weeks. Horses may exhibit extreme nervous excitement. The acute form is infrequent.
- Chronic poisoning.
  - Clinical signs often may not appear for 2 - 8 months after the first ingestion of pyrrolizidine alkaloids containing plants.
  - Animals lose condition over months and develop icterus. In the later stages, cattle may exhibit nervous derangement and mania. Horses more frequently exhibit nervous signs, especially yawning, drowsiness and staggering. The condition in horses is called "sleepy staggers" and "walking disease". The signs in horses may appear abruptly. Animals may stand apart and lose appetite. An unpleasant, sweetish odor may emanate from the skin. Horses may chew fences and walk aimlessly (off ravines or into buildings, etc.). Head pressing may occur, perhaps due to hepatoencephalopathy. The course often results in death within about a week of onset.
  - Cattle may also exhibit secondary photosensitivity: subcutaneous edema, dry, scaly muzzle. There may also be a rough hair coat, and tenesmus associated with diarrhea or constipation; the straining may result in prolapse. Liver function tests may be worthwhile in subclinical *Senecio* poisoning. In spite of the absence of apparent illness in adult cows consuming pyrrolizidine alkaloids, calf losses may occur.
- Chronic poisoning of swine is associated with pyrexia and severe respiratory signs.

**Gross Lesions**

- Acute form.
  - Enlargement and congestion of the liver, necrosis and hemorrhage in lobules.
  - Gastroenteritis.
- Chronic toxicosis.
  - The liver may be enlarged and cirrhotic.
  - Patchy gastroenteritis.
  - Ascites.
- In the horse.
  - Chronic, toxic active hepatitis.
  - Intestinal edema.
  - Enlarged hepatic lymph nodes.
  - Toxic tubular nephrosis.
  - Cerebral edema.
- In swine.
  - Swine experimentally fed *S. jacobaea* for 2 months developed pulmonary edema, congestion and alveolar epithelialization.

**Histologic Lesions**

- Hepatocytomegaly and karyomegaly.
- Hepatic necrosis.
- Bile duct proliferation.
- Fibrosis and cirrhosis may develop.
Diagnosis

- Sufficient dietary exposure to plant materials.
- Compatible clinical signs and gross as well as histologic lesions.
- Detection of pyrrolizidine alkaloids in plant materials and liver of exposed animals. Contact the USDA Poisonous Plant Research Laboratory in Logan, UT, USA.

Treatment

Treatment is usually unsuccessful. Animals should be removed from access to the plant. It has been suggested that laxatives and a high protein, low carbohydrate diet (rationale?) and ensuring adequate fluid intake are beneficial.

Note

As previously mentioned, contaminated hay can serve as the source of pyrrolizidine alkaloids. Due to the prolonged delay in onset of clinical signs and since the affected hay is often no longer available, the likelihood of successful adjudication in the courts is at times quite small.

Threadleaf Groundsel - White wooly stems, showy yellow flowers (enlarged disc and ray flowers, center and lower right), pinnately lobed leaves, and achene fruit (upper right) characterize this unusual shrub.
Crotalaria - Rattlebox

*Crotalaria sagittalis* - Arrow Crotalaria, rattle box, wild pea
*C. spectabilis* - Showy Crotalaria
*C. retusa*
*C. mucronata var.giant-striate*
*C. incana*
*C. rotundifolia*
*C. burkeana*
*C. juncea*
*C. dura*
*C. equorum*
*C. globifera*

**Family** - *Leguminosae* (Pulse or Bean Family)

**Images**


**Description**

- *C. sagittalis*.
  - Plant - Annual to perennial branched herb up to 1.5 feet all.
  - Stem - Conspicuous whitish hairs.
  - Leaves - Simple, oval to linear, 1 - 2 inches long; conspicuous whitish hairs.
  - Flowers - Yellow, inconspicuous, 1/4 inch long.
  - Fruit - Legume pod, 3/4 - 1 inch long, turns black with maturity.
- *C. spectabilis*.
  - Plant - Dense, erect annual to perennial herb up to 6 feet tall.
  - Stem - Never hairy.
  - Leaves - Simple, ovate, dorsally hairless, ventrally covered with fine hairs.
  - Flowers - Yellow, tinged with purple, about 1 inch long.
- *C. retusa*.
  - Plant - Erect, annual herb, not dense, up to 2.5 feet tall.
  - Stems - Very fine hair.
  - Leaves - Simple, narrowly ovate, 2 1/2 - 4 1/2 inches long.
  - Flowers - Yellowish with purple tinge.
  - Fruit - Pod is narrow and up to 1 1/2 inches long.

**Habitat**

- *C. sagittalis* - Native from Connecticut, south to central Florida, through deep southern states, and into the western part of Illinois, eastern Great Plains, Oklahoma, Eastern Texas. Areas where perennial plants are weak, sandy soil, open areas of blackjack oak woods, extensive stands by Missouri River (cause of Missouri bottom disease of horses).
- *C. spectabilis* - Southern states and as far north as Virginia and Missouri. Roadsides, refuse heaps, farm stands, originally introduced...
as a soil building, green manure crop, but now naturalized. Seeds are a grain contaminant causing problems in swine and poultry.

- **C. retusa** - Florida Peninsula. Waste areas and along roadsides in sandy soil. Introduced as a soil builder.
- **C. mucronata** var. *Giant-striata*. Coastal plains of North Carolina. Introduced as soil builder in Southeast

**Toxic Principle**

- The pyrrolizidine alkaloid, monocrotaline has been identified in *C. spectabilis* and is thought to be in *C. sagittalis*.
- Monocrotaline is a diester of monocrotalic acid and the nitrogen-containing rectroecine.

**Mechanism of Action**

- Monocrotaline is a pyrrolizidine alkaloid (see Senecio handout), acting on the DNA, especially of hepatocytes, but also has a fundamental action causing constriction of the lumen in the medium and small veins of the hepatic venous tree via subendothelial swelling.
- The plant is pneumotoxic in some areas of the world and mast cells in the lungs of animals fed monocrotaline release 5-hydroxytryptamine which may have some role in the pulmonary vascular lesions.
- The toxic principle of *C. retusa* may be different since characteristic hemorrhage does not occur.

**Susceptible Species**

- **C. sagittalis** - Horses are more susceptible than cattle.
- **C. spectabilis** - Fowl, cattle, horses and swine are more sensitive than sheep goats and mules.
- **C. retusa** - Fowl are known to be susceptible to several species of *Crotalaria*.

**Toxicity**

- **General.**
  - Alkaloid is most concentrated in the seed, but it is also present in the leaves and stem.
  - Also toxic when dry (as in hay).
  - *Crotalaria* turns green early and remains green when other forage turns brown; consequently, most cases of poisoning occurs as a result of ingestion early in spring or late in fall.
- **Cattle.**
  - Steers fed *Crotalaria* developed clinical signs in 10 days. A total of 55% of the body weight was consumed over 67 days.
  - Nine lb of dried plant killed a 300-lb steer in 4 days.
- **Swine.**
  - *Crotalaria* fed at 0.05% of body weight produced clinical signs.
  - Two grams of ground seed fed daily produced acute toxicosis in a 50-lb pig in 7 days.
- **Fowl.**
  - Eighty to 160 seeds produces death in many fowl (30 - 60 days).
  - 0.05% seeds in a ration retards growth.
  - 0.2 lb/ton of seeds in poultry mash interferes with growth.
  - 0.3% seeds in a ration causes 100% mortality within 18 days.
- **Horses.**
  - *C. sagittalis.*
  - "Bottoms" disease in horses (occurs in horses on low lying areas).
  - One percent of animals body weight of seeds for 2 days produced death on the second day.
  - One quart of pods fed daily produces clinical signs in horses.
- **Lab animals.**
  - **C. spectabilis.**
  - Most toxic species.
- **Poultry.**
  - **C. retusa.**
  - One hundred seeds force fed to a white leghorn hen produced death in 1 1/2 - 2 weeks.
  - Ten seeds force fed every day produced death in chickens in 18 - 40 days.
- **Lab animals and poultry.**
  - **C. mucronata** var. *Giant-striata.*
  - One percent dietary level seriously affects weight gains in Wistar rats.
  - Three to 6% levels in poultry ration causes mortality.
  - Less toxic than *C. spectabilis.*
Signs

  - Slow emaciation, weakness, stupor.
  - Fatal in several weeks to months after signs appear.

- *C. spectabilis* (horses).
  - Incoordination, aimless walking and pushing against objects (head pressing) for hours.
  - Delirium, excitement, apparent blindness.
  - Death preceded by icterus, weakness and stupor.

- *C. spectabilis* (cattle).
  - Three syndromes: acute, intermediate, chronic.
  - Acute - Signs appear in 1 day, death in 4 days.
  - Intermediate - Signs appear in 2 months and last 2 - 3 months before death; clinical signs consist of weakness, emaciation, incoordination, constipation or diarrhea.
  - Chronic - Signs develop in a few days or months and consist of loss of appetite, poor condition, tenesmus, nervousness, excitability, blood in feces, prostration, bloody nasal discharge and death.

- *C. spectabilis* (swine).
  - Signs appear in several weeks.
  - Loss of hair, unthriftiness.

- *C. spectabilis* (fowl).
  - Characteristic comb discoloration in 29 hours.
  - Severe greenish-yellow diarrhea.
  - Birds are depressed, ruffled feathers.

- *C. retusa*.
  - Clinical signs are similar to *C. spectabilis* but are less acute and with much less hemorrhage.

- *C. mucronata* var. *Giant-Striata*.
  - Causes retardation of weight gain in chickens and rats, and probably other animals.

Gross Lesions

- *C. sagittalis*
  - Congestion and hemorrhage.
  - Degeneration of liver and spleen.
  - Stomach is abnormally full of undigested food.

- *C. spectabilis* (cattle).
  - Acute - Profuse hemorrhage on the serous membranes of the abdominal and thoracic cavities.
  - Intermediate - Hepatic cirrhosis, ascites, petechiae on the intestinal serosa.
  - Chronic - Widespread hemorrhage, petechiae or ecchymoses in nearly all tissues; ascites, edema in the mesenteries, occasional icterus; degeneration of parenchymatous organs, liver indurated and bluish-gray.

- *C. spectabilis* (swine).
  - Anemia, ascites.
  - Firm indurated liver.
  - Hemorrhages of heart.
  - Gastritis.

- *C. spectabilis* (fowl).
  - Odor of crushed leaves in carcass.
  - Dehydration, full crop.
  - Thickened air sacs and pericardial sacs.
  - Atrophic spleen.
  - Petechial hemorrhages of serous membranes of abdominal and thoracic cavities.
  - Petechial and suffusive hemorrhage of the visceral fat, heart and musculature.
  - Swollen kidneys.
  - Dark, small, marbled liver.
  - Liver may be ruptured.
  - Enlarged gallbladder.
  - Distended abdomen due to ascites.

- *C. mucronata* var. *Giant-Striata* (fowl).
  - Almost entirely limited to liver.
  - Fibrous thickening of liver capsules with or without edema.
Histologic Lesions

See Histologic Lesions section for *Senecio*.

Diagnosis

See Diagnosis section for *Senecio*.

Treatment

- Treatment has little value after signs appear.
- Protectants, blood transfusions and fluid therapy may be attempted.
- Symptomatic therapy may prolong life.

Prevention

Avoid grain contaminated by all *Crotalaria* species.

Comments

- *C. intermedia* has been shown to be non-toxic.
- *Crotalaria* spp. causes many problems in Australia.
- *Crotalaria* is an excellent green-manure plant.
- Modern harvesting of corn and other crops may result in the contamination of stains with *Crotalaria* seed.
- Spraying of pasture and crop land with broad-leaf killing herbicides has largely eliminated *Crotalaria* poisoning in the continental United States for the present.

*Rattlebox* (*Crotalaria sagittalis*) - *a*, whole plant; *b*, cross section of seed pod - both one-third natural size.
**Amsinckia - Fiddleneck**  
*Amsinckia intermedia* - Tarweed, fingerweed, fiddlenecks, fireweed

### Family
Boraginaceae (Borage Family)

### Images

### Description
- *A. intermedia*
  - Plant - Erect, annual, covered with numerous white bristly hairs, 13 feet tall.
  - Stem - Sparsely branched.
  - Leaves - Alternate, hairy, lanceolate-linear, thick, covered with bristly hairs.
  - Flowers - Inflorescence dense, 1-sided, coiled.
  - Fruit - 2-4 gray-black nutlets, about 2.5 mm long, small, long, ovoid, angular, rough.
- Native to Pacific Coastal states; spreading eastward locally.
- California, Oregon, Washington, Idaho.
- Grain fields, gardens, orchards, waste places, of semiarid regions, dry open cultivated ground; wheat screenings used to fatten animals.
- Frequently encountered as a weed in hayfields.

### Toxic Principle
- Pyrrolizidine alkaloid (see *Senecio*).
- Nitrates may accumulate to potentially lethal concentrations.

### Toxicity
- General.
  - Screenings from wheat contaminated with tarweed is toxic.
  - Lambs tolerated 25% nutlets mixed with wheat grain for 125 days.
  - Toxic effects appear to be cumulative.
  - Five percent *Amsinckia* seeds in diet, produced death of a pig in 2 months.
  - Leaves are also toxic.
  - Large amounts of seeds may cause death in a short time.
  - Sheep, lambs, mules and fowl are more resistant to poisoning.
- Chronic.
  - After ingesting small amounts over a long period, animals will fail to gain weight and lose condition.

### Signs
- Hemorrhage of the gastrointestinal tract and subcutaneous tissues.
- Unthriftiness, icterus, sluggishness, sleepiness.
- Delirium, aimless wandering.
- Anemia, failure to gain weight.
- Small ulcers on lip and gum mucosa with offensive odor.
- Horses.
  - "Walking Disease"
  - Sluggishness, sleepiness, furious delirium or aimless walking.
  - Small ulcers on mucosae of lips and gums accompanied by offensive odor.
  - Anemia may develop in later stages.
- Swine.
  - "Hard Liver Disease"
  - Failure to gain weight between 30 - 100 lb. Animals become long and narrow, head may appear to elongate due to muscle atrophy.
  - Appearance may be similar to severe parasitism.
  - Unthriftiness, icterus.
- Cattle.
  - "Hard Liver Disease".
  - Unthriftiness, icterus.
  - Poor condition.

Lesions

- Hepatic cirrhosis.
- Hemorrhage in the subcutaneous tissue or in the gastrointestinal tract.
- Primarily a hepatotoxic problem. Pigs and rarely, sheep and cattle may also develop renal megalocytosis.
- See Histologic Lesions section for Senecio.

Diagnosis

See Diagnosis section for Senecio.
**Echium spp.**  
*Echium vulgare* - Blue thistle, blue devil, viper's bugloss  
*E. plantagineum* - Paterson's curse, salvation Jane

### Images
- Blue thistle, Blue devil, Viper's bugloss, *Echium vulgare* - Google Image Search. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org). -  
- Paterson's curse, Salvation Jane, *E. plantagineum* - Google Image Search. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org). -

### Description
- *Echium* spp.
  - Plant - Rough, hairy, herb.  
  - Leaves - Alternate, entire.  
  - Flowers - Symmetrical, 4-lobed, single style; 5-parted calyx.  
  - Fruit - 4 - 1 seeded nutlets or 2 - 2 seeded nutlets.

### Habitat
- *E. vulgare* - Northeastern USA (East of Mississippi).  
- *E. plantagineum* - Southern states. Dry meadows and pastures; limestone regions.

### Poisonous Principle
Pyrrolizidine alkaloids (see *Senecio*).

### Susceptible Species
Sheep, cattle, horses, pigs.

### Toxicity
- General.
  - Contact with bristly hairs on the leaves or stem may produce dermatitis.  
  - All parts toxic.

### Clinical Signs
- General.
  - Dermatitis, itching.  
  - Hepatosis.

### Lesions
- See Histologic Lesions section for *Senecio*.  
- Hepatotoxic.
• Pigs and rarely sheep and cattle develop renal megalocytosis.
• Laboratory animals develop pulmonary disease.

**Diagnosis**

See Diagnosis section for *Senecio*.

**Prevention**

• Carefully control by grazing with closely observed, less valuable sheep (they are somewhat resistant).
• Supplemental feed.
Heliotropium (Heliotrope)  
*Heliotropium europaeum* - Heliotrope

**Family** - Boraginaceae

**Images**

**Description**
An annual weed (do not confuse with *Valeriana officinalis*, the garden heliotrope).

**Habitat**
The plant occurs rather sparingly in the southeastern states from Florida up to New Jersey and occasionally into New England; most problems have been reported in Australia.

**Toxic Principle**
- Two alkaloids of pyrrolizidine type; heliotrine and lassiocarpine, and their respective N-oxides.
- Allylic esters of pyrrolizidine alkaloids which are also hepatotoxic.
- Plant may contain up to 3% alkaloids, mostly as N-oxides.

**Toxicity**
- General.
  - No known losses in USA.
  - Toxicosis results from ingestion of a large quantity over an extended period.

**Absorption, Distribution, Metabolism and Excretion (ADME)**
- The N-oxides of the alkaloids are more soluble and therefore absorbed rapidly, intact; whereas the parent alkaloids are significantly degraded in the rumen.
- Metabolism to the much more toxic pyrrole compounds occurs in the tissues after absorption.

**Mechanisms of Action**
- Pyrrolizidine alkaloid (see *Senecio* handout).
- Slow acting liver toxin, sometimes with a high death rate.
- In most cases, animals can consume large amounts over an entire season without developing signs. However, the hepatocyte changes persist and predispose the affected animal to serious poisoning the second season.

**Signs**
- General.
  - Progressive loss of condition characteristic of liver atrophy.
  - Perhaps photosensitization.
  - Hemolytic jaundice (sudden) - high copper content of some plants is associated with this type of jaundice.
  - Death.
Lesions

Liver damage (atrophic hepatosis).

Diagnosis

Identification of *Heliotropium*, evidence of consumption, and appropriate clinical signs and lesions.

Treatment

- Remove animal from source of plant.
- Evidence suggests that cobalt may facilitate the detoxification of pyrrolizidine alkaloids via vitamin B12 before liver damage occurs.

Prevention

- Sheep have been used in Australia to graze infested areas during seedling stages.
- Supply ample cobalt to form vitamin B12 which may help to limit pyrrolizidine alkaloid effects.

Microcystis Aeruginosa, *M. Viridis, Anabaena Flos-Aquae, Nostoc spp., Oscillatoria Agardhii, and Nodularia Spumigena*

Hepatotoxic Blue-Green Algae

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Poisonous Plants that Affect the Liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>All species</td>
<td>Hours (usually) to chronic</td>
<td>Days to permanent damage; highly lethal</td>
<td></td>
</tr>
</tbody>
</table>

Images

- *M. Viridis* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.
- *Anabaena Flos-Aquae* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.
- *Nostoc spp.* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.
- *Oscillatoria Agardhii* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.
- *Nodularia Spumigena* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.

Habitat

- Potentially toxic blooms of *Microcystis aeruginosa, Anabaena flos-aquae, Nostoc spp.*, and *Oscillatoria agardhii* occur during sunny weather in stagnant bodies of freshwater with high nutrient (especially phosphate) concentrations, such as occur in eutrophic ponds, lakes, and reservoirs. Commonly animals are exposed to potentially toxic amounts when pastures or holding pens uphill have fertilized the pond with animal wastes and wind has concentrated the bloom near the side of the pond where the animals drink.
- *Nodularia* blooms occur in brackish water. Problems have been documented especially in Australia and the Baltic Sea.
- Microcystins have also been shown to cause liver failure in fish raised in net pens in marine coastal areas. The source of these microcystins is unknown, but nutrient enrichment associated with fish food and excreta may encourage algal growth.
- Microcystins from a reservoir in Brazil were present in water used in dialyze a number of kidney patients. Liver failure occurred as well as several deaths.
- Shrimp are relatively tolerant of microcystins and may bioaccumulate potentially toxic amounts.

Description

- Blue-green algae cells in water are green, blue-green or blue depending on their degree of deterioration. Fresh blooms are green, and the colonies of cells are approximately the size of grains of sand and often float at or near the surface of the water. Microscopically, colonies of *Microcystis* (Fig. 1) cells contain hundreds or thousands of marble-like cells grouped in a common mucilaginous matrix. Colony shape may be round or irregular. The individual cells are approximately the size of erythrocytes.
- Microscopically, *Nodularia* are more linear (Fig. 2) as are *Oscillatoria* (not shown) and *Anabaena*.
Toxic Principle

- Microcystins and nodularin are a group of similar cyclic peptides containing some very unusual residues (not all are amino acids of a structure common to animals), that are responsible for the hepatotoxic properties of Microcystis and Nodularia. In the older literature the microcystins were termed "fast-death factor".
- Blue-green algae also have lipopolysaccharide endotoxins in their cell walls.
- Most toxic strains of Anabaena and some toxic strains of Oscillatoria and Microcystis contain neurotoxins.

Mechanism of Action

- Hepatocytes are the primary target cell in liver.
- Specificity for hepatocytes is related to cell uptake of the toxins via bile acid carriers.
- The biochemical mechanism(s) of action of microcystins and nodularin is inhibition of protein phosphatases 1 and 2A; which results in excessive phosphorylation of specific intracellular proteins including cytokeratins 8 and 18 which are the major proteins in cytoskeletal intermediate filaments of hepatocytes.
- The hepatocytes round-up apparently due to a loss of the normal arrangement of intermediate filaments, microtubules, and actin microfilaments, the three major components of the hepatocyte cytoskeleton. The hepatic sinusoids are severely disrupted. The resultant intrahepatic hemorrhage and necrosis, as well as acute hepatic insufficiency, possibly accompanied by hypoglycemia, may result in severe circulatory shock and death.
- Toxicoses may be aggravated by endotoxins, but this has not been well documented at this time.

Signs

- Animals ingesting toxic amounts of Microcystis blooms often develop an acutely lethal syndrome characterized by gastrointestinal disturbances (vomiting depending on species, abdominal pain and often diarrhea which may be bloody), followed by weakness, pallor of the mucous membranes, severe reduction in both activity and responsiveness, and death.
- The syndrome often lasts less than 24 hours from the onset until death.
- It is also possible to have sublethal toxicoses with substantial liver damage but most animals not lethally exposed often seem to make a successful recovery. The area of sublethal toxicosis does, however, need further characterization.
- Secondary (hepatogenous) photosensitization sometimes develops in surviving herbivores.

Lesions

- The liver tends to be swollen and to contain abnormal amounts of blood.
- Often the lobular pattern may be exaggerated (depending on species) due to hemorrhage into the liver lobules. There may be significant edema in and around the wall of the gallbladder.
- Microscopically, the picture is one of acute separation of hepatocytes from one another, toxic centrolobular apoptosis followed in some cells by necrosis which may extend nearly to the entire liver lobule with replacement by hemorrhage.
- In time-course studies, intact hepatocytes and especially hepatocyte debris are evident in the central veins of the damaged liver. These can be observed even in pulmonary capillaries. At death, however, only granular debris may remain.
- Marked edema of the gall bladder may be evident.
- Secondary (hepatogenous) photosensitization due to blue-green algae has been documented in cases from the field.

Diagnosis

- Diagnoses are based on history, and appropriate clinical signs, gross and microscopic lesions, and identification of the algae in the water.
• Blue-green algae should be collected from a suspected source soon after the incident, so that human efforts to kill out the bloom or changes in wind direction or weather are not able to remove it before identification.
• One portion of the sample should be immediately examined microscopically to find the colonies of algal cells.
• A 1 ml specimen of cells should be shipped chilled (not frozen) to a laboratory capable of culturing the cells as rapidly as possible. Contact Dr. Val Beasley of the College of Veterinary Medicine, University of Illinois, 2001 S. Lincoln Avenue, Urbana, IL 61801, USA or Dr. Wayne Carmichael, Department of Biological Science, Wright State University, Dayton, OH 45435, USA.
• A smaller specimen (5 ml) should be combined with an equal amount of buffered, neutral 10% formalin in order to fix the algae and prevent its physical deterioration.
• The gastrointestinal tract contents of lethally poisoned animals may also contain the readily identifiable colonies of Microcystis cells.

Diagnostic Flow Chart for Suspected Blue-Green Algae Cases

- Careful collection of a dense portion of an algae bloom is mandatory; collection of filamentous algae or other plants, or water containing little algae is not likely to be toxicologically meaningful.

Thoroughly mix algae and divide into at least 5 portions

- Examine immediately under light microscopy for algal identification.
- Fix cells in an equal amount of 10% neutral buffered formalin for identification at a later time.
- Submit 2 L of frozen, concentrated algal bloom material to be freeze-dried for toxin analysis (see below*)
- Refrigerate and submit for culture if highly toxic (do not freeze).
- Cells at bottom of centrifuge tube. Decant water.
- Freeze and thaw or sonicate to rupture (faster but not as thorough as freeze and thaw).
- Centrifuge and collect supernatant.
- Bioassay 1.0 ml i.p. into mouse.

Hepatotoxin present: death usually within 3 hours; liver weight (as %b.w.) increased by 60% or more.

- Anabaena only.
- *Request analysis of freeze-dried algae for peptide hepatotoxins

Neurotoxin present: death usually within 30 minutes, often faster; no increase in liver weight, nervous signs.

- Aphanizomenon spp.
- *Request analysis of freeze-dried algae for saxitoxin or neosaxitoxin by HPLC.

Anabaena only.

- Profuse salivation and lacrimation.
- Submit brain and blood for cholinesterase activity; if a cyanobacterial cholinesterase inhibitor such as anatoxin-a(s) is present, brain activity will be normal and blood activity will be depressed—no acceptable methods for toxin analysis yet available.

Treatment

• No specific treatment for microcystin or nodularin toxicosis has been explored.
• Animals recently exposed should have measures taken to thoroughly evacuate their gastrointestinal tracts at the earliest possible time, and should be given activated charcoal and a saline cathartic. In small animals, cholestyramine, if immediately available, would be
preferred over activated charcoal.

- Steps to combat hemorrhagic shock are indicated, such as intravenous fluids and possibly blood transfusions, corticosteroids, and, if marked metabolic acidosis is present, sodium bicarbonate should be given slowly IV (in fluids).

**Note**

- Some species and strains of *Anabaena* produce microcystin-LR and/or other microcystins. Generally the same clinical effects would be expected and diagnostic and therapeutic approaches followed. However, *Anabaena*-associated hepatotoxicosis has not been documented often in cases from the field.
- Recently, a structurally-unrelated (cyclic guanine derivative) algal hepatotoxin, termed cylindrospermopsin from *Cylindrospermopsis raciborskii* has been identified. It seems to have caused liver failure in human beings. Its action is to interfere with synthesis of glutathion.

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**Lantana and Lippia spp.**

*Lantana camara* - Largeleaf Lantana

*L. involucrata*

*L. aculeata*

*L. ovatifolia*

*L. sellowiana*

*Lippia ligustrina* - White brush

### Major Species | Usual Time of Onset | Usual Duration (if survives) | Full Table for Poisonous Plants that Affect the Liver
---|---|---|---
Herbivores | Days to chronic | Weeks to permanent damage; often lethal

**Family** - Verbenaceae (Verbena Family)

**Images**

- *Lantana involucrata* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.
- *Lantana aculeata* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.
- *Lantana ovatifolia* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.
- *Lantana sellowiana* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.

**Description**

- **Lantana spp.**
  
  - Plant - Erect or spreading shrub.
  - Stem - Ridged, angular, prickly.
  - Leaves - Opposite, ovate, crenated or serrated margin, veined from base, spreading hairs, 1.5 - 5 inches long.
  - Flowers - Small, tubular, spreading lobes, long axillary peduncles, yellow or pink changing to orange or bright red.
  - Fruit - Fleshy, drupe-like, 2-celled or 2 one-seeded.

- **L. camara**
  
  - Plant - Low, perennial shrub, 3 - 6 ft tall.
  - Stem - Square, sparse weak spines, occasionally vine-like, hairy.
  - Leaves - Opposite or in whorls of 3, ovate, petaled, crenatedentate, 2 - 4 inches long, 1.2 - 2.4 inches wide, toothed, aromatic, rough
above, hairy beneath; leaf stalks, 0.4 - 0.8 inches long.

- Flowers - Small, tubular, yellow or pink changing to bright red, 0.4 - 0.5 inches long, 0.24 - 0.31 inches across; in flat-topped clusters, axillary umbels, 1.6 - 2.4 inches across.
- Fruit - Greenish-blue or black, fleshy, berry-like, 0.24 - 0.31 inches diameter, glossy; seeds, oval, 0.16 - 0.2 inches long, 0.12 - 0.14 inches thick, grooved on 2 sides, brown, rough, irregular.

**Lippia liquisina**

- Plant - Shrub, often spiny, 0.4-1.2 ft high.
- Leaves - Opposite, lanceolate to oblong, veinless, 0.2-1 inch long.
- Flowers - In slender, naked spikes.
- Fruit - 2-celled nutlets; 1 seed per cell nutlets, greenish-blue or black 1/4 inch in diameter.

**Habitat**

- General - Southern Africa; Australia; India.
  - *L. camara* - Central and Southern Florida; Northern USA and Canada as an ornamental; Australia; Mexico.
  - Fence rows, ditch banks, fields, waste areas, pastures, sandy soils, potted; cultivated as outdoor annual, dry woods.
  - *Lippia* spp. - Southwest Texas to Mexico
  - Also grown as a potted plant in Central and other parts of USA.

**Toxic Principle**

- Pentacyclic triterpene acids, including lantadene A and B, reduced lantadene A, dihydrolantadene A, and icterogenin.
- Hepatogenous photosensitizer.
- Gastrointestinal irritants.

**Susceptible Species**

- *Lantana camara* - Sheep, cattle, children.
- *Lippia* spp. - Cattle, sheep, goats, horses.

**Toxicity**

- **Lantana camara**.
  - Foliage and ripe berries contain toxic substance.
  - Green berries have a higher concentration of the toxin.
  - Berries may be lethal to children. However, some dark skinned people eat ripe berries without noticing ill effects.
  - Lantana is one of the main causes of poisoning in Florida.
  - Three-fourths to 1 lb of dry leaves may cause toxicosis of a 400 lb bovine (1% of animals weight) (green weight basis).
  - Two percent of sheep's weight produced fatal results in 5 days.
  - Toxicity of individual plants is genetically determined.
  - Fifty to 90% of animals newly exposed are affected.
  - High mortality of affected animals (90%).
  - All species of Lantana should be considered poisonous.
  - Poisoning commonly occurs among grazing animals.

- **Lantadene A**.
  - One dose of lantadene A, 1 - 3 mg/kg, produces mild liver injury, increased SGOT and SDH; but serum bilirubin does not increase.
  - One dose at 3 mg/kg or 7 doses at 1 mg/kg over 3 days causes cholestasis, elevated SGOT, SDH, and bilirubin; green discoloration of the liver; enlarged gallbladder; dry impacted feces may be found in rectum; renal tubular necrosis.
  - One dose of 4 - 8 mg/kg causes centrilobular, midzonal, and massive hepatic necrosis; hemorrhage into the intestinal tract is common.
  - One dose at 60 mg/kg given orally is toxic to sheep.

**Mechanism of Action**

- Hepatogenic photosensitizer; hepatotoxic; cholestasis.
- The toxins have effects on both hepatocytes and bile canaliculi.
Decrease in canaliculi ATPase activity.
Collapse of canaliculi.
Secretory function of hepatocytes is lost; metabolizing function is retained.
Literature is in disagreement as to whether or not normal bilirubin conjugation is retained.

Signs

**Lantana.**
- Acute toxicosis:
  - The major clinical effect of *Lantana* toxicosis is photosensitization, the onset of which often takes place in 1 to 2 days after consumption of a toxic dose (1% or more of animal's body weight).
  - Jaundice is usually prominent, and animals usually become inappetent, and they often exhibit decreased digestive tract motility and constipation.
  - Other signs may include: sluggishness, weakness, and transient, sometimes bloody diarrhea. In acute cases, death occurs in 2 to 4 days.
- Subacute and chronic toxicosis:
  - Subacute poisoning is more common.
  - Raw photosensitized surface areas are susceptible to invasions by blow fly maggots and bacteria.
  - In severely affected cattle, lesions may appear at the muzzle, mouth, and nostrils.
  - Ulceration may be present in the cheeks, tongue, and gums, while swelling, hardening, peeling of mucous membranes, and deeper tissues occur in the nostrils.
  - Death may occur after 1 to 3 weeks of illness and weight loss.

**Lippia** spp.
- Emaciation.
- Leg weakness.
- Incoordination.

Lesions

**General.**
- Highly pigmented liver.
- Icterus, general edema.
- Gallbladder paralysis and distention.
- Necrosis of renal tubules.
- Hemorrhages in some organs.
- Myocardial damage and intestinal paralysis has been suggested, but conclusive supportive evidence is lacking.

**Cattle (severe cases).**
- Lesions from muzzle to mouth and nostrils, ulceration of cheeks, tongue, and gums.
- Swelling, hardening, peeling of mucous membranes and deeper tissues in the nostrils.

**Human.**
- Acute pulmonary edema and "neurocirculatory collapse" has been reported in a 2 1/2 year old girl.

Diagnosis

Identification of *Lantana* or *Lippia*, evidence of consumption and appropriate clinical signs and lesions (browsing might be overlooked because of the small amount necessary to cause toxicosis).

Treatment

- Treat for 12 -24 hours to overcome reduction in gut motility.
- Physostigmine may initiate dramatic reversal of some of the signs within minutes.
- Contraindications for the use of physostigmine include: asthma, gangrene, cardiovascular disease, mechanical obstruction of the gastrointestinal or urogenital tracts.

Prevention

- Grubbing and destruction of plants is most practical.
- Herbicides.
**Lantana** - The oval, toothed, and veiny leaves; the square prickly stems; the terminal flower clusters; and the black berries are characteristic of this attractive ornamental shrub.
**Helenium spp. - Sneezeweeds**

- **H. autumnale** - Common or autumn sneezeweed, staggerwort, swamp sunflower
- **H. hoopesei** - Orange or western sneezeweed, yellowweed
- **H. microcephalum** - Small head sneezeweed
- **H. nudiflorum** - Purplehead sneezeweed
- **H. tenuifolium** - Bitter sneezeweed, bitterweed, fennel

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<tbody>
<tr>
<td>Esp. sheep and goats, cattle, horses, swine, rabbits</td>
<td>Hours to chronic</td>
<td>Days to weeks; often lethal</td>
<td></td>
</tr>
</tbody>
</table>

**Family** - Compositae (Composite or Sunflower Family)

**Images**

- Common or autumn sneezeweed, *Helenium autumnale* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.
- Orange or western sneezeweed, *Helenium hoopesei* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.
- Purplehead sneezeweed, *Helenium nudiflorum* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.

**Description**

- **H. autumnale** - Perennial, lanceolate leaves of equal size, flowers yellow, rays reflexed.
- **H. hoopesei** - Perennial; oblong/lanceolate leaves, smaller on the upper stem; flowers are orange-yellow, with large horizontal rays. Twenty to 40 inches tall.
- **H. microcephalum** - Annual, lanceolate leaves; numerous flower heads with yellow rays.
- **H. nudiflorum** - Perennial; linear to lanceolate leaves which are golden-yellow; rays may have a purplish base, not reflexed.
- **H. tenuifolium** - Annual; 6 - 30 inches high; linear leave, yellow flowers.

**Habitat**

- **H. autumnale** - Eastern North America, wet pastures, meadows, ditches, near streams.
- **H. hoopesei** - Western Montana to eastern oregon southward to California and New Mexico (5,000 - 12,000 feet elevation). Moist slopes and well- drained mountain meadows in high ranges.
- **H. microcephalum** - Southern Texas and Mexico. Moist ground, most toxic at flowering.
- **H. nudiflorum** - Eastern USA to Michigan and Texas. Wet pastures, meadows, ditches, along streams.
- **H. tenuifolium** - Southeastern USA to Texas. Sandy fields, woods, waste areas.

**Toxic Principle**

- Helenalin; helenanolide, tenulin sesquiterpene lactones. Helanin is believed to be the primary toxic constituent.
- The glycoside dugaldin.

**Mechanism of Action**

The effect of helanin is believed to be similar to that of hymenoxon (see handout on *Hymenoxys*).
Susceptible Species

Sheep and goats are more susceptible than horses, cattle and rabbits.

Toxicity

- All parts are toxic, especially the leaves and flowers.
- Poisoning is common in the late summer or fall when other forage is scarce.
- Among the most dangerous range plants to livestock.
- Also unsafe for human consumption.
- Stable toxic principle, resists drying.
- Toxicity of plants varies greatly.
- Somewhat cumulative effects.
- One percent of an animal's weight for 8 days may produce severe illness and death.
- Many species remain green even when covered with snow.
- *H. hoopesei* - Causes trouble in spring since it is green before other forage.
- *H. microcephalum* - 0.25% of sheep's body weight was rapidly fatal.
- 2.5 gm/kg of body weight may cause acute poisoning and death in cattle.
- *H. tenuifolium* - Bitter, sharp taste, but occasionally grazed in quantity, when more palatable foliage is scarce.
- Sneezeweed poisoning (spewing sickness) is more of a problem in sheep than in other species.

Signs

- Acute Syndrome.
  - Depression, decreased appetite, ruminal atony, mild tympany.
  - Arched back, grinding of teeth.
  - Serous nasal discharge, slight evidence of regurgitation.
  - Excessive salivation, bloating.
  - Severe abdominal pain.
  - Vomition and diarrhea.
  - Head pushing occurs terminally.
  - Apparently agonal seizures.
  - Recumbency with clonic and tonic convulsions.
  - Death within 4 - 24 hours after consumption.
- Chronic syndrome.
  - Several weeks of ingestion are required before signs appear (in the chronic syndrome).
  - Weakness and salivation as well as diarrhea and a febrile response may appear.
  - Vomiting is characteristic in sheep, and therefore a green nasal discharge is present and these signs give rise to the name spewing sickness.
  - Loss of muscular control has been suggested.
  - Death occurs with or without agonal spasms.
  - Milk may have a bitter taste.
  - Photosensitization may occur.

Lesions

- *H. microcephalum*.
  - Serosanguinous fluids accumulate in all body cavities.
  - Tubular nephrosis may be seen.
- *H. hoopesei*.
  - Liver degeneration.
- General.
  - A gastrointestinal irritation.
  - Hepatic and renal congestion.
  - Gastric edema.
  - Adhesion of necrotic areas of the lungs; probably a result of aspiration pneumonia.
  - Endocardial hemorrhage, pulmonary edema, fluid in pleural cavity, ascites.
  - Elevated serum transaminase activities, result of hepatic necrosis.
  - Renal damage.
Diagnosis

- Identification of sneezeweed.
- Evidence of consumption in sufficient quantities.
- Appropriate clinical signs and lesions.

Treatment

- Remove animals from access to the plant.
- The oral administration of lard and other oils, before the onset of spasms has been recommended.
- Administration of L-cysteine before clinical signs appear has been suggested.
- Activated charcoal and a saline cathartic are likely to be of benefit if animals have very recent exposure (hours) to a large amount of the plant.

Prevention

- Loose herding, avoiding dense areas of sneezeweed, results in less poisoning.
- Fence off or mow sneezeweed.
- Small patches may be eliminated by herbicides such as 2,4-D.

Comments: In the 1940s, it was estimated that 8,000 sheep were lethally poisoned by sneezeweeds annually.

Bitter Sneezeweed - *Helenium amarum* (Rafin), H. Rock. - 1, plant; 2, flower head; 3, seed. Annual, with short branching taproot. Stems smooth, erect, 6 to 30 inches (15 to 75 cm) tall, branching in upper portion. Leaves numerous, smooth, threadlike, without petioles, alternate, and crowded along main stem and branches. Flower heads about 3/4 inch (1.9 cm) in diameter, ray flowers yellow with toothed tip, surrounding dome-shaped mass of yellow disk flowers. Seed reddish-brown, hairy along edges, wedge-shaped, bearing bristle-tipped scales at top. Found in old feedlots, pastures, idle land, and wasteland. Does not persist under cultivation.
Common Sneezeweed, *Helenium Autumnale* L. • **1.** upper part of plant; **2.** lower stem and roots. **Perennial,** reproducing by seeds and a spreading crown. **Roots** much branched, somewhat fleshy, **Stems** slender, erect, smooth to rough, narrowly branched, with wide appendages along the stem, especially on upper part. **Leaves** alternate, slender, oblong to lanceolate, 2 to 4 inches (5 to 10 cm) long, gray and hairy when young, becoming greenish and smooth later. **Flower heads** sunflower-like, about 1 inch (2.5 cm) across. Ray flowers yellow, drooping, surrounding the greenish-yellow disk flowers. **Seed** about 1/16 inch (1.5 mm) long, hairy. **Found** around water holes and ditches where water is readily available. Whether dry or fresh, poisonous to livestock, especially sheep. Most serious in the Western areas.
Bitterweed plant in flower
Hymenoxys spp. - Rubberweed - Bitterweed

H. odorata - (Actinea odorata) bitter rubberweed, Colorado rubberweed, bitterweed
H. richardsoni (H. floribunda) - (Actinea richardsoni) pinque
H. lemmoni - Cockerell

Family - Compositae (Composite or Sunflower Family)

Images

- Bitter rubberweed, Hymenoxys odorata - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.
- Pinque, Hymenoxys richardsonii - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org.

Description

- H. odorata.
  - Plant - Annual, erect, bitter, small, bushy, up to 2 feet tall.
  - Stem - Usually purplish, thick, woody stalk, much branched from the base, base covered with a wooly growth, each ascending stem branches and terminates in a yellow-flowered head.
  - Leaves - Alternate to 3 times alternately divided into very narrow glandular, wooly divisions, not distinct from petiole.
  - Flowers - Composite flower heads at tips of stem branches, bright yellow, 1/5 - 1/2 inch in diameter. Sixty or more disc florets; 6 - 10 ray florets, rays tipped with 3 lobes; aster-like flowers, golden yellow or orange.
  - Fruit - 50 - 75 seeds from each head.
  - Note - Flowers in May or June. H. richardsonii is perennial.

Habitat

- H. odorata - Kansas to Mexico, and westward to California. Overgrazed ranges, along streams and low places.
- H. richardsonii - Saskatchewan to Texas, west to California and Oregon. Grassland, open forests, dry, sandy or gravelly soils.

Toxic Principle

The water soluble toxic principle is believed to be the sesquiterpene lactone hymenoxon, although other compounds including hymenolide, parcin and psilostrophin also present. Hymenorin is an epimeric mixture of hymenoxon.

Susceptible Species

Sheep are more susceptible than cattle and goats. Natural cases largely limited to sheep, and no notable reports of toxicosis in cattle, horses and goats. Sheep may develop a liking for it.

Toxicity

- General.
  - Toxicity is retained upon drying.
  - Wide variation in minimum lethal dose.
  - Bitterweed toxicity slowly increases with maturity.
  - Toxicity is greatly increased during drought.
  - Ingestion of 1.3% of body weight may be lethal to some animals during periods of normal rainfall and 0.5% may be lethal
during drought.
- Bitter taste, therefore, often avoided by range livestock.
- An animal may die from eating one large feeding, or repeated smaller feedings over extended periods of time.
- Winter and spring seems to be the most dangerous time.

- Sheep.
  - One percent of animal's weight as green plant is lethal, whether ingested at one time or in fractional amounts over several months.
  - A 100-lb animal may die if it eats 0.25 - 0.5 lb daily for 2 - 4 weeks.
  - Hymenovin is lethal to sheep when given orally at doses as low as 100 mg/kg.

**Mechanisms of Action**

- Binds to sulfhydryl groups (like arsenic and certain other metals) and other nucleophilic components.
- Mixed function oxidase inducers and inhibitors had no effect on toxicity of hymenoxon.
- Cysteine or methionine, a source of SH groups, or BHA (butylated hydroxyanisole), which increases glutathione and GSH transferase, reduced the toxicity of hymenoxon.

**Signs**

- Loss of appetite, anorexia, apparent abdominal pain.
- Cessation of rumination, bloating.
- Vomition, salivation.
- Green salivary discharge and stains about the muzzle, commonly seen in range cases.
- Affected sheep commonly lag behind the rest of the flock.
- Death may occur in 1 - 3 days.

**Lesions**

- Kidney, liver, lungs and abomasum may be congested.
- Liver may be friable.
- Abomasum and duodenum contain hemorrhages.
- Submaxillary and retropharyngeal lymph nodes are frequently congested or hemorrhagic.
- Spleen may be enlarged.
- Epicardium, endocardium and costal pleura may be hemorrhagic.
- Few if any lesions may be found in some chronic cases.

**Diagnosis**

- Identification of the plant.
- Evidence of consumption.
- Appropriate clinical signs and lesions.

**Treatment**

- If removed from access to the plant at the onset of signs, sheep may make an uneventful but slow recovery.
- See *Helenium*.

**Prevention**

- Reduce stocking rates.
- Since animals will seldom eat toxic amounts, heavy losses may be prevented, especially when sheep are being driven, by avoiding heavily infested areas or by supplemental feeding.
- When sheep losses become especially high, cattle should be grazed on the affected pasture in their place.
- Eradication of the plant is usually not practical. Efforts may include pulling by hand or the use of 2,4-D.

**Comments**

- Edward's plateau reports the most losses (in Texas).
- The name rubberweed is used because the plant contains a small amount of rubber.
Kochia Scoparia
*Kochia scoparia* - Kochia, Mexican fireweed, fireweed, summer cypress, burning bush

**Images**

- Kochia, Mexican fireweed, *Kochia scoparia* - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -

**Description**

- An annual plant reproducing by means of seeds.
- Stems - Smooth, green, much branched, from a few inches to over 6 feet in height.
- Leaves - Alternate, simple, hairy, 1 - 2 inches (2.5 - 5 cm) long, pointed, without petioles.
- Flowers - Small, greenish, without petals, in axils of upper leaves and in terminal panicles.
- Seeds - About 1/16 inch (1.5 mm) long, oval, flattened with groove on each side, finely granular, surface dull brown with yellow markings. Fragile star-shaped hull may enclose seed.
- Root - Taproot.

**Habitat**

- *Kochia scoparia* is extensively used as a forage plant for cattle in arid, infertile regions of the western and southwestern United States. Problems are sometimes encountered in areas of Colorado, New Mexico, and Texas.
- *Kochia* tolerates extremely high soil sodium concentrations and in areas of such soil may exist as virtually the only species present.

**Toxic Principles**

- Some *Kochia scoparia* plants contain a substance (which may or may not actually be a thiaminase) which destroys thiamine. This agent does not apparently account for the principle effects of *Kochia* toxicosis.
- May contain oxalates (at up to 6 - 7% of the dry weight), but usually no oxalate crystals are observed in the kidneys of *Kochia* poisoned animals.
- May contain nitrates (see section on nitrate toxicosis).
- May also contain "saponins and/or alkaloids".
- May also contain other, but as yet, unidentified hepatotoxic and nephrotoxic and possible neurotoxic substances.
- Often contains high sulfate concentrations.

**Toxicity**

- In the southwest USA, *Kochia* grows wild and is sometimes touted as a good forage plant. It is high in crude protein and may be fed to cattle and horses.
- Problems principally arise from mid-summer onward. Most poisoned animals are first clinically affected from mid-August to the first of September after grazing for 35 - 40 days.
- Drought seems to increase the likelihood of *Kochia*-related problems. Whether this is due to a reduction in the availability of other plants or increased concentration of the toxic chemicals in *Kochia* is not known.
- Seed maturation also seems to increase toxicity of the plant.
Mechanisms of Action

- Laxative effect is believed to be due to the high sulfate content of *Kochia*.
- Most common major toxic effect is due to hepatotoxicity.
- Photosensitization, which is not rare, is likely to be due to hepatotoxicity.
- Central nervous system derangement may be due to polioencephalomalacia secondary to thiamine deficiency as a result of *Kochia*-induced thiamine destruction.
- Nitrate toxicosis induces its effect as a result of gastrointestinal microbial conversion of nitrate to nitrite which oxidizes hemoglobin to methemoglobin which no longer carries oxygen.
- Soluble oxalates may be nephrotoxic and precipitate as calcium oxalate in the kidney or may cause acute hypocalcemia, also due to combination with available calcium.

Signs and Clinical Pathology

- Signs will vary depending upon which *Kochia*-induced toxic effect, if any, predominates.
- *Kochia scoparia* produces loose feces whenever it is grazed.
- Liver failure may be evidenced by an increase in liver-associated enzymes in the serum prior to the onset of clinical signs in addition to subsequent profound icterus. Bilirubin may also be quite high and elevations in pyruvate, lactic acid, and creatine kinase have also been observed. Signs referable to liver failure may also include lagging behind the rest of the herd, anorexia, evidence of abdominal pain, bilirubinuria, and death.
- Photosensitization may occur and be accompanied by icterus. Photosensitized animals display lesions similar to severe sunburn on the white (unpigmented) areas of the body.
- Blood urea nitrogen values may also increase.
- Animals with polioencephalomalacia (cerebrocortical necrosis) from any cause may display bizarre behavior, a severe drop in responsiveness to external stimuli, blindness, muscle tremors especially of the head, cerebral edema, and terminally, opisthotonus, nystagmus, and clonic-tonic convulsions.

Lesions

- Also vary depending upon the clinical syndrome present.
- Severe liver necrosis is the most common lesion, and hepatic cirrhosis may be seen.
- Lesions compatible with photosensitization or polioencephalomalacia (both of which are thoroughly described in other references) may be seen in some animals experiencing *Kochia* poisoning.
- Gastrointestinal tract inflammation may be seen.

Diagnosis

- Appropriate clinical signs and lesions and sufficient consumption of *Kochia* in addition to evidence of ruling out other causes.
- Criteria for the diagnosis of polioencephalomalacia are readily available in other references.
- See also Bracken Fern (*Pteridium*) under Diagnosis.

Treatment

- Terminate exposure to *Kochia*.
- There is no specific treatment for *Kochia*-induced hepatotoxicosis. Minimization of stress is appropriate. Manage as for other causes of liver failure.
- If possible, animals with photosensitization should be kept out of the sunlight by confinement indoors.
- Treat polioencephalomalacia cases with thiamine.
- Nitrate poisoning and oxalate toxicosis are discussed in separate handouts in this series.
Kochia, *Kochia scoparia* (L.) Schrad - 1, entire plant; 2, individual flower; 3, seeds. **Annual**, reproducing from seeds. **Stems** smooth, green, much branched, from a few inches to over 6 feet (1.8 m) high, growing from a taproot. **Leaves** alternate, simple, hairy, 1 to 2 inches (2.5 to 5 cm) long, pointed, without petioles. **Flowers** small, greenish, without petals, in axils of upper leaves and in terminal panicles. Seeds about 1/16 inch (1.5 mm) long, oval, flattened with groove on each side, finely granular, surface dull, brown with yellow markings. Fragile star-shaped hull may enclose seed. **Found** in cropland, dry pastures, and rangeland, where it is a serious weed. Also commonly known as Mexican fireweed.
Lotus Corniculatus - Birdsfoot Trefoil

<table>
<thead>
<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Poisonous Plants that Affect the Liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruminants; other herbivores</td>
<td>Chronic</td>
<td>Weeks to months; poisoning is rare</td>
<td></td>
</tr>
</tbody>
</table>

Family - Leguminosae (Pulse or Bean Family)

Images


Habitat

- Europe, Britain, Australia, Africa, and the USA.
- A forage crop (used in the midwestern USA and elsewhere).

Clinical Signs and Lesions

- Losses reported primarily in Australia.
- A cyanogenic substance is reportedly present in some strains, and cyanide toxicosis in various horses and mules was reported in Russia.
- Liver failure occasionally has been associated with trefoil pastures, apparently due to a different toxic principle.
- Dermatitis has been associated with exposure of several species of animals to this plant.
- This may be related to primary (or perhaps secondary) photosensitization.

- Potentially associated with bloat in cattle due to saponins.
- Grazing trefoil may slow the growth rate of young chickens.

Diagnosis

Toxicosis may be difficult to confirm and other possible causes must be ruled out.

Birdsfoot Trefoil, *Lotus corniculatus* L.

Family - Pea (Leguminosae).

Growth Form - Perennial herb from elongated roots.

Stems - Spreading to ascending, smooth or slightly hairy, up to 18 inches long.

Leaves - Alternate, divided into 5 leaflets, the leaflets oblong to obovate, rounded or pointed at the tip, up to 1/2 inch long, smooth or nearly so, up to 2/3 inch long.

Flower Arrangement - Flowers several, borne in umbels, the umbel borne on stalks.

Flowers - Bright yellow, up to 3/4 inch long, borne on short stalks.

Sepals - 5, green, united below.

Petals - 5, bright yellow, arranged to form a typical pea-shaped flower.

Stamens - 10.

Pistils - Ovary superior.

Fruits - Pods narrow, up to 1 inch long, pointed at the tip, with several seeds.

Habitat - Open, disturbed areas.

Range - Throughout the state.

Time of Flowering - June to September.
Cycad Poisoning

<table>
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<tr>
<th>Major Species</th>
<th>Usual Time of Onset</th>
<th>Usual Duration (if survives)</th>
<th>Full Table for Poisonous Plants that Affect the Liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>Herbivores, dogs, swine</td>
<td>Hours to a few days</td>
<td>Weeks to permanent damage; often lethal</td>
<td></td>
</tr>
</tbody>
</table>

Images

- Cycas spp. - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -
- Zamia spp. - Google Image Search. - To view this image in full size go to the IVIS website at www.ivis.org . -

Description

- Cycad palms occur in tropical and subtropical climates.
- Representative genera and their geographical locations include Encephalartos spp. (Africa), Dion spp., and Zamia spp. (Central America), Cycas spp. (Oceania, Australia), Lepidozamia spp., Bowenia spp., and Macrozamin spp. (all 3 in Australia).
- Cycads (Zamia spp.) are native to Florida, and many non-native species have been cultivated as ornamentals. Cycads (Cycas revoluta, common name: false sago palm) has also been a cause of toxicosis in dogs in Texas where it is grown as an ornamental.
- Zamia floridana - common name Coontie - fernlike plant with a thick starchy stem. Leaves (0.3 - 1 cm long) are feather-shaped. Slender cylindrical (7.6 - 18 cm) cones on male plants with thicker (13 - 18 cm) cones present on female plants.

Poisonous Principles

- Glucoside derivatives of methyl azoxymethanol (azoglycosides) including cycasin, macrozamin, and alpha-amino-beta-methylaminopropionic acid.
- Cycasin has been demonstrated to be responsible for acute hepatotoxic and carcinogenic effects following ingestion of cycads. However, cycasin is not responsible for neurotoxicity in livestock.
- Cycasin is not carcinogenic when administered parenterally. Cycasin must be hydrolyzed to its aglycone, methylazomethanol to induce tumors.
- Some evidence of additional neurotoxic compounds having a molecular weight of 1,000.
- Pois-Index® has listed cycads as containing cyanogenic glycosides. However, the authors are aware of no evidence for the presence of cyanogenic glycosides, and the clinical syndromes are not consistent with a cyanogenic compound ingestion.

Toxicity

- As few as 2 seeds of a cycad plant have caused poisonings in small dogs.
- Cycad-based meals are occasionally incorporated as a staple of the diet of some people.

Susceptible Species

- Cattle, sheep, dogs, swine, horses, goats.
- Humans.

Clinical Syndromes

- Acute intoxication characterized by hepatic (ascites, icterus) and gastrointestinal signs (vomiting, anorexia). Clinical signs develop within 12 hours of ingestion.
  - Polydipsia.
  - Hepatic cirrhosis. Icterus develops within 2 - 3 days postingestion.
  - Hemorrhagic gastroenteritis with gastric or abomasal ulceration.
  - Coagulopathy, subcutaneous bruising, and hemorrhage. Melena and hemoptyis occur terminally.
    - Thrombocytopenia. Prolonged PT, ACT, PTT.
    - May be due to hemorrhage, decreased synthesis of clotting factors, and/or DIC.
- Cattle, sheep.
  - Neurotoxic syndrome.
  - Cattle - "goose-stepping" gait, ataxia more severe when animals are exercised. Condition in cattle known as "derriergue" in
Dominican Republic.

- Goat, sheep - progressive hindlimb paralysis.
- Cardiotoxic effects reported.
- Cycasin potentially carcinogenic in laboratory animals.
- Associated with high incidence of amyotrophic lateral sclerosis and Parkinsonism - dementia in humans (Guam).

Clinical Pathology

- Hyperbilirubinemia, hypoproteinemia, hypocalcemia, hyponatremia, hypokalemia, azotemia, and a metabolic alkalosis may occur.
- Increased serum liver enzymes (may not be pronounced).
- Glycosuria, bilirubinuria, hematuria, and casts on urinalysis.

Lesions

- Centrilobular and midzonal hepatic necrosis. Distended bile ducts. Generalized icterus, petechial, and ecchymotic hemorrhage, and ascites may be present.
- Desquamation of renal tubular epithelial cells. Proteinaceous, red blood cell, and bilirubin casts may be present.
- Degeneration of fascilus gracilis and lateral spinocerebellar pathways. Axonal degeneration.

Treatment

- Symptomatic and supportive.
- Prognosis for cycad poisoned dogs is generally poor.

References

Xanthium spp. - Cocklebur


Microcystis Aeruginosa, M. Viridis, Anabaena Flos-Aquae, Nostoc spp., Oscillatoria Aghardii, and Nodularia Spumigena - Hepatotoxic Blue-Green Algae


**Lantana and Lippia spp.**


**Cycad Poisoning**


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