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Plants Causing Sudden Death (20-Aug-2002)

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Plants Containing Cyanogenic Glycosides

Cyanogenic glycosides are substances present in many plants that can produce highly toxic hydrogen cyanide (HCN) or prussic acid. Specific plant enzymes released when plant cells are damaged when chewed, crushed, wilted, or frozen, hydrolyze the glycosides to cyanide. At least 2000 plant species are known to contain cyanogenic glycosides with the potential to produce HCN poisoning [1-6]. However, relatively few of these plants are frequent causes of cyanide poisoning in humans or animals because they are infrequent food sources for humans or animals [1,2]. Plants that have been most frequently associated with cyanide poisoning in animals are listed in Table 1 - 1. Some of these plants are grown as food sources for humans and animals, for example, sorghum (*Sorghum* spp.), corn (*Zea mays*), clovers (*Trifolium* spp.), and manihot or cassava (*Manihot esculenta*), and can be used safely provided attention is paid to the circumstances under which these plants accumulate cyanogenic glycosides.

Most plant-induced cyanide poisoning in humans occurs in tropical countries where cassava is commonly used as food. The chronic consumption of poorly prepared cassava diets produces a disease syndrome in humans known as tropical ataxic neuropathy [7]. Pigs and goats have been similarly poisoned when fed cassava tubers and leaves [8]. Plants such as blue flax (*Linum* spp.), grown for fiber (linen) and linseed oil, will also accumulate toxic levels of HCN under the right growing conditions [9].

Table 1 - 1. Plants Associated with Cyanide Poisoning	
Botanical Name	**Common Name**
Acacia spp.	Catclaw, acacia
Amelanchier alnifolia	Service, June, or Saskatoon berry
Bahia oppositifolia	Bahia
Mannihot esculentum	Cassava, manihot, tapioca
Cercocarpus montanum	Mountain mahogany
Chaenomales spp.	Flowering quince
Cynodon spp.	Star grass
Eucalyptus spp.	Eucalyptus, gum tree
Glyceria grandis	Tall manna grass
Hydrangea spp.	Hydrangea
Linum spp.	Flax
Lotus spp.	Bird's foot trefoil
Malus spp.	Crab apple
Nandina domestica	Heavenly or sacred bamboo
Phaseolus lunatus	Lima bean
Photinia spp.	Christmas berry
Prunus spp.	Choke-cherry, pin cherry
Pteridium aquilinum	Bracken fern
Sambuccus spp.	Elderberry
Sorghum spp.	Johnson, Sudan grass
Sorghastrum nutans	Indian grass
Stillingia texana	Texas queen's delight
Suckleya suckleyana	Poison suckleya
Trifolium repens	White clover
Triglochin maritima	Arrow grass
Vicia sativa	Common vetch
Zea mays	Corn, maize

Cyanide poisoning of livestock is most commonly associated with Johnson grass (*Sorghum halapense*), Sudan grass (*Sorghum vulgare*), and other forage sorghums [10,11]. Choke-cherries (*Prunus* spp.), [12] service berry (*Amelanchier alnifolia*), [13-15] and arrow grass (*Triglochin* spp.) [16-19] are less frequent but long recognized sources of cyanide poisoning. Crab apple leaves (*Malus* spp.), and sugar gums (*Eucalyptus cladocalyx*) have caused cyanide intoxication in goats, [20,21] and even wild deer have become victims of cyanide poisoning after eating service berry [22]. Occasionally cattle have consumed lethal doses of cyanogenic glycosides from eating acacia tree leaves and poison suckleya (*Suckleya suckleyana*) [23,24]. Under some undetermined growing conditions, certain grasses such as tall manna grass (*Glyceria grandis*) and Indian grass (*Sorgastrum nutans*) accumulate toxic levels of cyanogenic glycoside [25,26].
Cyanogenic glycosides in the leaves and stems of plants are not toxic unless acted on by the plant or rumen microorganism enzymes, b-glucosidase and hydroxynitrile lyase, to form HCN [1,27]. Enzymatic conversion of the glycosides is enhanced

when plant cells are damaged or stressed as occurs when the plant is chewed, crushed, droughted, wilted, or frozen [28]. In the process, the glycosides, which are normally isolated in cell vacuoles, come into contact with the cell enzymes and HCN is formed. Generally most parts of the plant contain cyanogenic glycosides; the young rapidly growing portion of the plant and the seeds contain the highest concentrations. The flesh of the ripe fruits is edible. Drying the plants decreases their cyanogenic potential especially over time. Ensiling plants will reduce cyanogenic glycoside content by as much as 50 percent, with free cyanide being liberated from silage pits or silos in the curing process [28,29].

The concentration of cyanogenic glycosides in plants varies with the stage of growth, time of year, soil mineral and moisture content, and time of day. Cool moist growing conditions enhance the conversion of nitrate to amino acids and cyanogenic glycosides instead of plant protein. As the glycosides accumulate they further inhibit nitrite reductase in the plant, favoring the conversion of nitrate to cyanogenic glycoside rather than to amino acids [28]. Nitrate fertilization of cyanogenic plants therefore has the potential to increase the cyanogenic glycoside content of plants. Frost and drought conditions may also increase cyanogenesis in some plant species. Young plants, new shoots, and regrowth of plants after cutting often contain the highest levels of cyanogenic glycosides. Application of herbicides (2,4-dichlorophenoxyacetic acid [2,4-D]) can also increase the cyanogenetic glycoside content of plants.

At least 55 cyanogenic glycosides are known to occur in plants, many being synthesized from amino acids as part of normal plant metabolism [1,8,30]. Some of the better known glycosides include amygdalin (laetrile) from bitter almonds, peach, apricot, cherry and apple seeds; [31] prunasin from choke-cherries and service berry leaves; linamarin and lotaustralin from flax and white clover [9]; dhurrin from sorghum; and triglochinin from arrow grass. In the 1970s, laetrile received considerable attention as a potential cure for cancer, but its efficacy has never been proven, and, in fact, it was shown to have the potential to be highly toxic to humans and animals [32,33].

Selective breeding of certain varieties of plant species with naturally low glycoside content has resulted in varieties that are low cyanogenic glycoside; and has increased their food value for humans and animals. The development of sweet almond varieties with low cyanogenic glycoside content has facilitated the human consumption of almond seeds. Similarly sorghum varieties low in cyanide have been developed that have greatly increased the safety of feeding sorghums, such as Sudan grass, to livestock.

Ruminants are more susceptible to cyanide poisoning than other animals because the normally mildly acidic to alkaline rumen contents (pH 6.5 - 7), high water content, and microfloral enzymes in the rumen hydrolyze the cyanogenic glycosides to HCN [34]. Water drunk after animals have eaten cyanogenic plants enhances the hydrolysis of the glycosides. Conversely, ruminants that are on high energy grain rations where the rumen is more acidic (pH 4 - 6) have a slower release of HCN than if they were fed a grass, hay, or alfalfa diet [34]. Humans, pigs, dogs, and horses that have a highly acidic stomach (pH 2 - 4) tend to have a reduced rate of glycoside hydrolysis and cyanide production in their digestive systems and therefore rarely suffer from cyanide poisoning of plant origin. Atypically, donkeys have been reported to develop acute cyanide poisoning from eating the new shoots from wild choke-cherries [35].

Mechanism of Acute Cyanide Poisoning

Hydrogen cyanide (HCN) is highly poisonous to all animals because it rapidly inactivates cellular respiration thereby causing death [36-38]. The cyanide ion is readily absorbed from the intestinal and respiratory tracts and has a strong affinity for binding with trivalent iron of the cytochrome oxidase molecule, inhibiting its enzymatic action and preventing cellular respiration [37,39-41]. The characteristic cherry red venous blood seen in acute cyanide poisoning results from the failure of the oxygen-saturated hemoglobin to release its oxygen at the tissues because the enzyme cytochrome oxidase is inhibited by the cyanide. Normally, small quantities of cyanide are detoxified by cellular enzymes and thiosulfates in many tissues to form relatively harmless thiocyanate, which is excreted in the urine. When large quantities of cyanide are rapidly absorbed and the body's detoxification mechanisms are overwhelmed, cyanide poisoning occurs. In most species, the lethal dose of HCN is in the range of 2 to 2.5 mg/kg body weight [36-38]. However, if plenty of other plant material and carbohydrates are present in the stomach, formation and absorption of cyanide may be slowed, allowing animals to tolerate higher doses.

Chronic Cyanide Poisoning - In addition to the acute toxic effects of cyanide poisoning, low levels of cyanide will over time cause a variety of chronic effects in humans and animals. Chronic cyanide poisoning is thought to be a form of lathyrism, a neurotoxicity recognized in people in some eastern Asian countries where the seeds of certain peas (*Lathyrus* spp.) are eaten when other foods are scarce. The neurotoxin in the uncooked peas results in damage to the spinal cord leading to paralysis. Similarly, a chronic neuropathy occurs in people who consume poorly cooked cassava (*Manihot esculenta*).

The perennial sweet pea (*Lathyrus latifolius*) and the annual sweet pea (*L. odoratus*) seeds contain neurotoxins (lathyrogens) capable of producing osteolathyrism in animals, especially horses [42]. The primary lathyrogen in the annual sweet pea is b-amino proprionitrile, which causes defective cross-linking of collagen and elastin molecules [42]. This disease in horses is characterized by skeletal deformities and aortic rupture caused by defective synthesis of cartilage and connective tissue [42]. A similar syndrome of musculoskeletal deformities in foals and calves has been associated with pregnant mares and cows chronically eating Sudan grass (*Sorghum sudanense*) or sorghum hybrids containing low levels of cyanogenic glycosides [43-

48]. In addition to limb deformities (arthrogryposis), calves also develop severe degeneration of the spinal cord and brain [44]. Affected animals develop posterior ataxia, urinary incontinence, and cystitis resulting from lower spinal cord degeneration [48]. The cystitis may become complicated by an ascending infection of the kidneys.
The underlying problem is the loss of the myelin sheath surrounding peripheral nerves with resulting loss of nerve function. The demyelinization of the nerves is thought to result from the conversion of the cyanide glycoside to T-glutamyl β-cyanoalanine, a known lathyrogen that interferes with neurotransmitter activity [46]. Neuronal degeneration in the brain associated with chronic cyanide poisoning may be associated with the depletion of hydroxycobalamin [45]. Animals may slowly recover if the source of the toxic aminonitrile is removed before neuronal degeneration becomes severe.
Low doses of cyanide are also goitrogenic in humans and animals. Enlargement of the thyroid gland is caused by the formation of thiocyanate, which inhibits the intrathyroidal transfer of iodine and elevates the concentration of thyroid-stimulating hormone [8]. Pregnant ewes grazing star grass (*Cynodon* spp.) have developed goiter because of the presence of cyanide in the grass [29].

Clinical Signs of Acute Cyanide Poisoning
Sudden death is often the presenting sign of acute cyanide poisoning. Affected animals rarely survive more than 1 to 2 hours after consuming lethal quantities of cyanogenic plants and usually die within a few minutes of developing clinical signs of poisoning [29]. If observed early, poisoned animals show rapid labored breathing, frothing at the mouth, dilated pupils, ataxia, muscle tremors, and convulsions. The heart rate is usually increased and cardiac arrhythmias may be present. Regurgitation of rumen contents occurs when ruminants become recumbent and bloating occurs. High blood ammonia levels coupled with increases in neutral and aromatic amino acids may be a significant cause for the loss of consciousness associated with terminal cyanide poisoning [49]. The mucous membranes are bright red in color because oxygen saturates the hemoglobin. Cyanosis of the mucous membranes occurs terminally when the animal's tissues become depleted of oxygen.

Postmortem Findings
Animals poisoned by cyanide may have characteristic cherry red venous blood if examined immediately after death. Generalized congestion and cyanosis of the internal organs is often seen at necropsy. The blood clots slowly and the musculature is dark and congested. Hemorrhages occur commonly in the heart, lungs, and various other organs. The smell of bitter almonds reputedly characteristic of cyanide may occasionally be detected in the rumen gas when performing a fresh postmortem examination.

Diagnosis
Cyanide is rapidly lost from animal tissues unless specimens are collected within a few hours of death and frozen for chemical analysis. Liver, muscle, and rumen contents should be collected and frozen in air-tight containers before shipment to a laboratory capable of doing cyanide analysis. Levels of cyanide in liver or blood exceeding 1 ppm, or in muscle exceeding 0.63 g/mL are considered diagnostic for cyanide poisoning [29,50]. Cyanide poisoning can be confirmed by demonstrating toxic levels of HCN in the rumen contents or the suspect plants (or both) using the sodium picrate paper test [39]. Filter paper strips soaked in yellow sodium picrate and suspended over the suspect plant material in an air-tight jar turn brick red in a few minutes if significant cyanide is present. Commercial test kits are available for testing plants and rumen contents for cyanide. More precise determination of cyanogenic glycoside and cyanide levels is possible through the use of liquid chromatography and colorimetry [41]. Plant material containing more than 20 mg HCN/100 g (200 ppm = 200 mg/kg) is potentially toxic to all animals [36,50]. Liver or blood levels greater than 1 ppm are highly suggestive of cyanide poisoning [50]. Because many factors can alter cyanide determinations in tissues, the most consistent and diagnostically valuable HCN levels can be obtained from the brain and ventricular myocardium. Levels of HCN in excess of 100 g/100 g wet tissue are diagnostic of cyanide poisoning [51].

Treatment
Many remedies for cyanide poisoning in man and animals have been evaluated over time. In all cases the successful treatment of acute cyanide poisoning depends on the rapid inactivation and removal of cyanide by metabolizing or complexing it with other compounds to allow its excretion via the kidneys [41,52]. In animals this has been traditionally accomplished by injecting sodium nitrite and sodium thiosulfate intravenously [53]. Sodium nitrite converts some hemoglobin to methemoglobin for which cyanide has a strong affinity, producing cyanmethemaglobin [41]. This complexing of cyanide reactivates the cytochrome oxidase system essential for cellular respiration. Sodium thiosulfate in the presence of the tissue enzyme rhodanese combines rapidly with the cyanide molecule cleaved from cyanmethemaglobin to form relatively nontoxic and excretable sodium thiocyanate [37,54].
A recommended treatment for cyanide poisoning is the intravenous administration of a mixture of 1 mL of 20 percent sodium nitrite and 3 mL of 20 percent sodium thiosulfate. This dose is given intravenously per 100 lb of body weight [53]. The dose

may be repeated in a few minutes if the animal does not respond. Additional sodium nitrite should be given cautiously because excess will compound the toxicity by producing, in effect, nitrite poisoning. Better results have been obtained in sheep experimentally poisoned with cyanide by administering 660 mg/kg sodium thiosulfate and 22 mg/kg sodium nitrite intravenously [54]. Thiosulfate is the safest and most effective agent tested for treating cyanide poisoning in dogs. The effectiveness of these compounds given in combination is enhanced if oxygen is given simultaneously [55]. The oral administration of a 5 percent solution of cobaltous chloride at a dose of 10.6 mg/kg body weight further improved the effectiveness of the combination [54]. Alpha-ketoglutaric acid is an effective treatment if administered in conjunction with thiosulfate [56,567]. It is also beneficial to administer orally via stomach tube a solution of sodium thiosulfate (30 g to an adult cow) to detoxify free cyanide still present in the rumen. Animals suspected of consuming cyanogenic plants but that show no clinical signs should also receive oral sodium thiosulfate prophylactically. Administered via stomach tube, 1 gallon of vinegar diluted in 3 to 5 gallons of water will help acidify the rumen and reduce the production of hydrogen cyanide.

Prevention of Cyanide Poisoning

Appropriate pasture management to avoid exposing livestock to potentially toxic plants will help prevent animal losses. Animals should be prevented from grazing sorghums during early regrowth after the plants have been cut, droughted, or frosted, when they are likely to be most toxic [58]. Allowing sorghum forages to grow at least 2 feet high before allowing animals to graze them significantly reduces the potential for poisoning. Where uncertainty exists about the cyanogenic content of plant crops for animal forage, a sample of the plants should be tested for cyanide content. Properly curing hay and silage destroys the cyanogenic glycosides. Selecting forage sorghums and white clover varieties that have been specifically developed for low cyanogenic glycoside content further reduces the chances for poisoning and allows their safe use as forage crops [59-61].

The selective use of herbicides in localized areas can be used to control dense stands of cyanide-containing plants such as choke-cherry. Whenever herbicides are used as a control measure, it is important to follow manufacturer recommendations for the herbicide and observe local herbicide application ordinances.

Acacia, Gregg's Catclaw Acacia, Guajillo

Acacia greggii - Fabaceae (Legume family)

Habitat

Acacia is found in the limestone cliffs and calcareous rocks of flats and valleys of the southwestern desert areas of North America.

Habitat of Acacia, Gregg's Catclaw Acacia, Guajillo. *Acacia greggii* Fabaceae (Legume family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description

This shrub or small tree grows up to 20 feet (6 meters) in height and forms thickets (Fig. 1-1A). Branches are armed with stout curved spines. Leaves are bipinnately compound with three pairs of branchlets, each divided into two to seven pairs of leaflets. Flowers are pale yellow and clustered in dense round spikes 2 to 3 inches (5 to 8 cm) long and 2 cm in diameter (Fig. 1-1B). Fruits are curled, contorted leguminous pods containing numerous seeds.

Figure 1-1A. Catclaw acacia (*Acacia greggii*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-1B. Catclaw acacia flowers (*Acacia greggii*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
Cyanogenic glycoside, prunasin [1,6].

Note - There are many species of acacia, some of which are commonly browsed by livestock especially when other forages are scarce. Being high in protein, acacias often form an important part of the diet of range animals. Some species of acacia (*A. berlanderieri*), when eaten for prolonged periods in times of drought, can also cause neuro- muscular weakness and ataxia, and can adversely affect fertility in animals. These effects are possibly induced by one or more of the various amines and alkaloids including nicotine, nornicotine, mescaline, mimosine, and amphetamines that have been identified in acacias [62].

Western Service Berry, Saskatoonberry, June Berry

Amelanchier alnifolia - Rosaceae (Rose family)

Habitat
Service berry is common on rocky slopes, canyons, and alongside streams at altitudes from 5000 to 9500 feet throughout North America.

Habitat of Western Service Berry, Saskatoonberry, June Berry. *Amelanchier alnifolia* - Rosaceae (Rose family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description
Service berry shrubs or small trees grow up to 13 feet (4 meters) tall with simple, alternate, petioled leaves, that are oval to suborbicular in shape (Fig. 1-2A). The margins are coarsely serrate or dentate to the middle or below, rarely entire. The flowers are perfect and regular. The calyx has five lobes, with five white petals each up to 0.5 inches (6 to 10 mm) long (Fig. 1-2B). The ovary has five styles and develops into a purple pome when ripe.

Figure 1-2A. Service berry shrub in bloom (*Amelanchier alnifolia*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-2B. Service berry flowers (*Amelanchier alnifolia*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
Cyanogenic glycoside, prunasin [13].

Note - Livestock will browse on the plants and usually do not have problems unless they consume excessive quantities of new growth or wilted leaves in times of drought. It is not advisable to plant service berry shrubs in livestock enclosures. The ripe dark red to black fruits are edible.

Mountain Mahogany

Cercocarpus montanus - Rosaceae (Rose family)

Habitat

This woody shrub is common in the drier foothills, chaparrals, and Ponderosa pine terrain of the Rocky Mountains.

Habitat of Mountain Mahogany. *Cercocarpus montanus* - Rosaceae (Rose family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description

The shrub or small tree is up to 6 feet (2 meters) tall (Fig. 1-3A). Leaves are simple, oval to linear, entire or toothed, often prominently veined beneath. The flowers are small and inconspicuous with yellowish sepals and no petals; they are either single or in clusters. The fruit consists of a small seed inside a hairy achene with a long, twisted style (Fig. 1-3B). The sharp pointed basal end of the fruit and the corkscrew style enable the seed to bore into the soil as the style coils and uncoils in response to changes in humidity.

Figure 1-3A. Mountain mahogany (*Cercocarpus montanus*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-3B. Mountain mahogany showing pointed fruits with twisted, hairy style (*Cercocarpus montanus*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin

Cyanogenic glycosides [1,2].

Note - Livestock poisoning is seldom a problem with mountain mahogany because animals rarely browse on it. Wild deer commonly use it as a food.

Wild Blue Flax

Linum lewisii - Linaceae (Flax family)

Habitat

Blue flax is widely distributed from the plains to higher mountain elevations, growing in meadows, open forest, and along roadsides.

Habitat of Wild Blue Flax. *Linum lewisii* - Linaceae (Flax family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description
This native herbaceous perennial has slender stems and alternate very slender eaves. The light powdery-blue flowers have 5 sepals and 5 petals that drop off by midday (Fig. 1-4). New flowers open each day. Fruits are capsules that have 5 to 10 compartments, each containing a flattened, shiny, black seed. *L. perenne* is a perennial species introduced from Europe and tends to be a more robust plant with deep blue petals, and sepals with entire margins. Flax that is used for linen and linseed oil production comes from the annual *L. usitatissimum*. It has deep blue flowers, and inner sepals with a fringed margin. Of the approximately 200 species of flax that occur globally, some including *L. flavum* (yellow flax), *L. grandiflorum* (red flax) are popular ornamental garden plants.

Figure 1-4. Blue flax (*Linum* spp.) - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
Cyanogenic glycoside, linamarin (lotaustralin) [3,9]. Highest concentrations of the glycosides are found in the seedling tops and seeds (910 mg/100 g) [6]. There however, appears to considerable variation in the quantity of cyanogenic glycoside present depending upon the species and growing conditions of flax. Yellow pine flax (*L. neomexicana*) has been reported as poisonous to sheep, but no cyanogenic glycosides were detected.

Note - Flax is rarely a problem for animals unless they have little else to eat. Linen flax (*L. usitatissimum*), commonly grown as a crop plant in Europe, is the principal source of linseed meal (cake), a by-product of linseed oil production. Cyanide poisoning results when uncooked linseed cake is fed to cattle. Commercially produced linseed cake should be boiled for 10 minutes before feeding it to ruminants in order to destroy the enzyme linamarase that liberates cyanide from the glycoside linamarin [63].

Western Choke-Cherry
Prunus virginiana var. melanocarpa - Rosaceae (Rose family)

Habitat
This shrub or small tree grows in thickets, along waterways, mountainsides below 8000 feet, and occasionally in the drier plains. It is common in the western states especially in the Rocky Mountain area.

Habitat of Western Choke-Cherry. *Prunus virginiana var. melanocarpa* - Rosaceae (Rose family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description
The shrub or small tree growing up to 16 feet (5 meters) in height, has gray bark with obvious lenticels. The leaves are generally ovate to obovate, occasionally lanceolate, with serrate margins. The leaves are simple, glossy, and alternate with a few glands on the petiole or base of the blade. The inflorescence is a cylindrical raceme of showy white fragrant flowers appearing in early spring after the leaves have appeared (Fig. 1-5A). The fruit is a dark purple drupe when ripe and is the only edible part of the plant (Fig. 1-5B).
Other members of the genus known to be toxic include pin cherry (*P. pennsylvanica*) and wild black cherry (*P. serotina*) (Fig. 1-5C). These species vary from choke-cherry (*P. virginiana*) in leaf shape or inflorescence, or both.

Figure 1-5A. Western choke-cherry showing cylindrical flower raceme (*Prunus virginiana*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-5B. Western choke-cherry ripe berries (*Prunus virginiana*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
Choke-cherries contain two cyanogenic glycosides-amygdalin, which is commonly found in the seed, and prunasin, which is found in the leaves, bark, and shoots [1,4,12].

Note - The larger succulent leaves are the most toxic with concentrations of cyanogenic glycosides reaching 368 mg/100 g of fresh leaves. Ruminants consuming 25 percent of their body weight in green leaves are likely to suffer fatal cyanide poisoning. Wilted leaves and branches and new growth are especially toxic. The ripe berries are edible, although the seeds are toxic. It is inadvisable to plant choke-cherry shrubs or trees in or adjacent to animal enclosures.

Figure 1-5C. Black cherry (*Prunus serotina*). - To view this image in full size go to the IVIS website at www.ivis.org . -

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Elderberry

Sambucus canadensis - Caprifoliaceae (Honeysuckle family)

Habitat
Elderberry plants generally prefer open areas in the rich moist soils surrounding ponds and along ditches and streams throughout North America.

Habitat of Elderberry. *Sambucus canadensis* - Caprifoliaceae (Honeysuckle family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description
The woody shrubs grow to 10 feet (3 meters) in height, forming colonies from underground runners. The stems are thick and are filled with white pith. The leaves are opposite, pinnately compound with lanceolate serrated leaflets. Conspicuous, terminal, round, or flat topped clusters of numerous white, five-petaled flowers 0.25 inches (4 to 6 mm) in diameter (Fig. 1-6A). Drooping clusters of dark purple (*S. canadensis*) (Fig. 1-6B) or red (*S. racemosa*) (Fig. 1-6C) berries with several seeds form July through September. Some species of elderberry have been hybridized for ornamental purposes.

Figure 1-6A. Elderberry (*Sambuccus racemosa*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-6B. Elderberry fruits (*Sambuccus canadensis*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
Elderberries contain a cyanogenic glycoside, sambunigrin, and an irritant alkaloid that acts as a cathartic [2].

Note - All parts of the elderberry plant are potentially toxic to animals although animal poisoning is rarely encountered. Cultivated varieties of elder- berry should be considered potentially toxic and probably should not be planted in or around animal enclosures. The purple to black ripe berries are edible if well cooked and are often used for making jams and wine.

Figure 1-6C. Elderberry (*Sambuccus canadensis*). - To view this image in full size go to the IVIS website at www.ivis.org . -

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Johnson Grass

Sorghum halepense - Poaceae (Gramineae) (Grass family)

Habitat
Johnson grass is a common weed grass found in alluvial bottom land and along roadsides and ditches throughout most areas east and south of the Rocky Mountains. Sudan grass (broom corn, kafir corn), *Sorghum sudanense*, and its hybrids are frequently grown as a forage crops.

Habitat of Johnson Grass. *Sorghum halepense* - Poaceae (Gramineae) (Grass family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description
Johnson grass is a coarse drought-resistant perennial growing 3 to 8 feet (1 to 3 meters) tall, with scaly root stalks and relatively broad leaves with a prominent mid vein (Fig. 1-7A). Seeds are yellow-purple and occur in a large multi- branched panicle. Sudan grass and its hybrids are very similar in appearance but are annuals and tend to be more robust than Johnson grass, with broader leaves and thicker stems (Fig. 1-7B). The seed heads are produced terminally and, in some hybrids, contain much larger seeds than the species.

Figure 1-7A. Johnson grass (*Sorghum halapense*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-7B. Sudan grass (*Sorghum sudanense*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
Cyanogenic glycoside, dhurrin [3,4].

Note - Johnson and Sudan grasses are the most common cause of cyanide poisoning in cattle and sheep and are especially toxic when growing rapidly. Fertilization with nitrogen increases the potential for cyanide toxicity [1,11]. Regrowth of sorghums after cutting has high potential for poisoning, and there is an old saying that sorghums should not be grazed until they are above knee height. Cyanide-free hybrids of Sudan grass are available as forage crops for animal consumption. All species of sorghum may also accumulate toxic levels of nitrate, and are a common source of nitrate poisoning in cattle.
In addition to their acute cyanogenic and lathyrogenic effects, certain grain *Sorghum* species also contain tannins that can have (astringent) protein-precipitating properties. Condensed tannins impart a red color to sorghum seed that deters birds from eating the seed. Ruminants are not affected by the tannins in sorghum seed.

Poison Suckleya

Suckleya suckleyana - Chenopodiaceae (Goosefoot family)

Habitat
This small, prostrate plant grows in moist conditions preferring the edges of receding reservoirs and ponds. It also grows around the edges of irrigated fields, and where run-off water collects, it becomes a robust plant. Suckleya is found in localized areas from Montana to New Mexico.

Habitat of Poison Suckleya. *Suckleya suckleyana* - Chenopodiaceae (Goosefoot family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description
Suckleya is an annual, succulent, prostrate herbaceous plant with reddish fleshy stems 1 to 2 feet (30 to 60 cm) long (Fig. 1-8A). The leaves are alternate, triangular, or spade shaped with dentate margins and long petioles. The inconspicuous small flowers are formed in the leaf axils (Fig. 1-8B). The plants are monoecious with the male flowers at the tips of the branches and the female flowers along the remainder of the branching stems. The fruits are reddish brown and are enclosed by two papery, dark-colored scales joined at the tip.

Figure 1-8A. Poison suckleya (*Suckleya suckleyana*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-8B. Poison suckleya showing the green flowers at the leaf axils (*Suckleya suckleyana*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
Cyanogenic glycosides [23,24,64].

Note - Poisoning from suckleya varies, being troublesome in some years when cattle and sheep find it quite palatable [1,24]. This may be due to the fact that it often grows around ponds, and in years of drought, livestock eat it as something green when they come to drink and congregate in the area. In some years, large populations of suckleya may appear in flood plains. The glycoside content of the plants is quite variable depending upon the growing conditions of the plants.

Arrow Grass, Pod Grass, Goose Grass

Triglochin maritima

T. palustris - (Marsh arrow grass) Juncaginaceae (Arrow grass family)

Habitat
Arrow grass species grow throughout North America preferring alkaline soils at most elevations and flourishing in marshy ground and irrigated pastures. *T. maritima* is found mostly in the midwestern states and to the west and south; *T. striata* occurs in the southeastern states into Florida and southern California into Mexico. *T. palustris* is found in the northern states from Washington to New York and the Rocky Mountain area.

Habitat of Arrow Grass, Pod Grass, Goose Grass. *Triglochin maritima*, *T. palustris* - (Marsh arrow grass) Juncaginaceae (Arrow grass family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description
These are perennial "grasslike" plants with fleshy, half rounded, dark green leaves clumped at the base of the plant (Fig. 1-9A). Leaves are 6 to 12 inches (15 to 30 cm) long, linear, unjointed, and sheathed at the base. The flower is a pediceled raceme up to 4 feet (1.5 meters) in length that appears as an unbranched, unjoined flower spike. The individual flowers are inconspicuous and numerous, with a greenish, six-part perianth. The fruits are made up of capsules or pods of three to six cells that turn golden brown before splitting open (Fig. 1-9B).

Figure 1-9A. Arrow grass showing grass-like leaves and seed heads (*Triglochin maritima*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-9B. Arrow grass seed pods (*Triglochin maritima*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
Cyanogenic glycoside, triglochinin [18].

Note - Arrow grass is not a true grass. Its long slender grass-like leaves make it difficult to recognize in a grass meadow unless the distinctive flower and seed pods are present. The plant is most toxic when green, losing its cyanogenic potential when dried. Arrow grass has long been recognized as a poison for cattle and sheep when green, but it is generally not a problem when incorporated in hay [16].

Table 1 - 2. Plants Known to Accumulate Nitrates [92,93**]**

Botanical Name	Common Name
Ambrosia spp.	Ragweeds
Amaranthus spp.	Pigweed
Avena fatua	Wild oat grass
Chenopodium spp.	Lamb's-quarter
Cirsium arvense	Canada thistle
Convolvulus arvense	Field bindweed
Datura stramonium	Jimsonweed
Echinochloa spp.	Barnyard grass
Helianthus annuus	Sunflower
Kochia scoparia	Kochia weed
Malva spp.	Cheese weed
Melilotus spp.	Sweet clover
Polygonum spp.	Smart weed
Rumex spp.	Sorrel, curly leafed dock
Salsola kali	Russian thistle
Solanum spp.	Nightshades
Solidago spp.	Goldenrods
Sorghum halapense	Johnson grass
Crop Plants	
Avena sativa	Oats
Beta vulgaris	Sugar beets
Brassica napus	Rape
Glycine max	Soybean
Linum spp.	Flax
Medicago sativa	Alfalfa
Pennisetum glauca	Pearl millet
Secale cereale	Rye
Sorghum vulgare	Sudan grass
Triticum aestivum	Wheat
Zea mays	Corn

Plant-Associated Nitrate Poisoning

Nitrate poisoning is a universal and economically important problem for ruminants that is caused by the ingestion of plants that have accumulated toxic levels of nitrate [65-74]. Normally plants absorb nitrates from the soil converting them into plant proteins. Application of organic or inorganic nitrogenous fertilizers can result in excessive accumulation of nitrates in crop plants and common weeds. Livestock consuming these plants in quantity can develop nitrate poisoning. Plant nitrates, however, are rarely a problem for horses because their digestive system does not readily convert nitrate (NO_3) to toxic nitrite (NO_2). The effects on animal health of nitrate and its metabolites, nitrite and N-nitroso compounds, have been extensively reviewed [75]. The potential for nitrate poisoning is increased when water sources for livestock also contain high levels of nitrates [76,77]. Nitrate fertilizers are highly toxic chemicals capable of causing fatal poisoning in ruminants and horses that gain access to them accidentally. When animals consume nitrate fertilizers, the chemicals themselves cause severe gastrointestinal irritation, colic, and diarrhea.

Many common weeds, forage crops, and cereal grain plants have the potential for accumulating nitrate under specific growing conditions (Table 1 - 2). Nitrate poisoning has been reported most often in ruminants that have consumed sorghums [74,78-80]. However, sugar beet tops, turnips, kale, oats, silage, Italian rye grass, white clover, red root pigweed, and variegated thistle have also been incriminated in nitrate poisoning [78,81-86]. Nitrate levels in plants vary considerably depending on the plant species, stage of growth, water and organic content of the soil, and application of nitrogen fertilizers. Drought conditions, acidic soils, and soils deficient in sulfur, phosphorous, and molybdenum result in nitrate accumulation in plants [73,87-89]. Cool, cloudy days enhance nitrate formation in plants because the light-and warmth-dependent enzyme, nitrate reductase, is inhibited, thus allowing nitrate to accumulate in the plant [90]. Nitrate levels are therefore highest in plants at night and early morning when the nitrate-reducing enzymes are least active. Highest levels of nitrate tend to be found in the stems where nitrate reduction normally occurs, and not in the leaves [90,91]. Nitrate does not accumulate in the flowers or fruits of plants and therefore nitrate poisoning is unlikely when seeds (corn, oats, barley) are fed to livestock. Properly prepared silage from forage crops high in nitrates reduces the nitrate content by 60 percent, while there is little reduction of nitrate in dried hay [77]. The application of herbicides such as 2.4-dichlorophenoxyacetic acid (2,4-D), not only increases the nitrate content of plants, but also the palatability of the plants thereby increasing the potential for poisoning [87,90,92].

Nitrate Toxicology

There is considerable variation as to what constitutes a safe level of nitrate in animal feeds because of different factors that influence nitrate metabolism. Under normal circumstances, nitrate is reduced in the rumen in a series of steps from nitrate to nitrite, to ammonia, and eventually to microbial proteins. It is the rapid formation and absorption of large quantities of nitrite (NO_2) and not nitrate (NO_3) that causes poisoning. The rate at which nitrate is converted to highly toxic nitrite depends on the rate of adaptation of rumen microorganisms to nitrate, the rate and amount of nitrate ingested, and the amount of carbohydrate available in the rumen. Experimental data suggest that nitrate poisoning is more likely to occur in ruminants after several days of feeding forages high in nitrate [94,95]. Other investigators have demonstrated that nitrate-adapted rumen microflora more completely reduce nitrate beyond nitrite to ammonia thereby reducing the potential for poisoning [96,97]. Similarly, when carbohydrates such as corn and molasses are present in the rumen, nitrates are more rapidly converted to ammonia and microbial proteins without the accumulation of nitrite [87,96,98,99]. On the other hand, low-energy diets increase an animal's susceptibility to nitrite poisoning.

The amount of nitrate that can be safely consumed in forages (45 g nitrate/100 lb body weight) is three times greater than the amount of potassium nitrate (KNO_3) that can be given orally as a drench [87]. Similarly sheep can be fatally poisoned by a single oral dose of KNO_3, although the same dose has no ill effects when incorporated in the feed [96]. The lethal dose of nitrate given as a drench is 0.5 g KNO_3 kg body weight [83]. From this information it is apparent that nitrate produced in plants is far less toxic than the pure chemical present in fertilizer. Plants or hay containing more than 1 percent nitrate (10,000 ppm) dry matter are potentially toxic and should be fed with caution. Forages containing more than 1 percent nitrate should only be fed if the total nitrate intake can be reduced to less than 1 percent by diluting the nitrate forage with nitrate-free forages. Because nitrate is often reported in different units, care must be exercised in interpreting nitrate values. Conversion factors for nitrate and nitrite compounds are given in Table 1 - 3.

The addition of monensin to rations high in nitrate may precipitate poisoning. This has been reported in cattle fed turnips and forage high in nitrate that produced no clinical signs until monensin was given as a feed additive [100,101].

Accumulation of nitrates in water sources frequently poisons livestock [76,98,102]. Surface water and water from shallow wells is most likely to contain nitrates, especially if there is the potential for run-off water from fertilized arable land contaminating the water source. Acute nitrate poisoning resulted when cattle were given well water containing 2790 ppm of nitrate [102]. An unusual case of nitrate poisoning occurred in cattle drinking water from shallow ponds created by blasting

using the explosive mixture of ammonium nitrate fertilizer and dynamite [103]. Acceptable levels of nitrate nitrogen in water according to United States Health Service standards should not exceed 10 ppm of nitrate nitrogen (45 ppm nitrate) [104]. Water nitrate levels less than 45 ppm are also desirable for livestock, but nitrate levels up to 445 ppm (100 ppm nitrate nitrogen) can be tolerated [105,106]. Levels above 200 ppm of nitrate should be considered potentially toxic to pregnant animals [107,108]. However, it has been shown experimentally that sheep can consume water with up to 667 ppm of nitrate-nitrogen without measurable adverse effects presumably because they were on a high plane of nutrition [109]. Water containing up to 100 ppm of nitrate can be considered safe for all classes of livestock assuming that the animals are on a normal diet that does not have high levels of nitrate [98]. To be safe, both the water and the forage should be analyzed to ensure that total nitrate does not exceed potentially toxic levels.

Table 1 - 3. Conversion Factors for Nitrate and Nitrite Compounds
Nitrate ppm = Nitrate mg/kg = Nitrate mg/L
% Nitrate X 10,000 = ppm
Ppm X 0.0001 = % Nitrate
Ppm = mg/mL
Potassium/Sodium nitrate X 0.61 = Nitrate
Potassium/Sodium nitrate X 0.14 = Nitrate-nitrogen
Nitrate-nitrogen (NO-N) X 4.45 = Nitrate
Nitrate-nitrogen (NO-N) X 3.29 = Nitrite
Nitrate-nitrogen (NO-N) X 6.1 = Potassium or Sodium nitrate

Monogastric animals such as horses, pigs, and dogs are unlikely to develop nitrate poisoning from plants because they cannot readily convert nitrate to nitrite in their digestive systems. However, monogastric animals that gain access to nitrate fertilizers will eat them and develop severe gastrointestinal irritation resulting in colic and diarrhea. Horses, pigs, and ruminants are equally susceptible to nitrite poisoning should they ingest nitrite salts such as sodium or potassium nitrite [70,71,96,110]. Nitrites are also potent vasodilators and cause a rapid drop in blood pressure [111]. In general all animals are susceptible to nitrate poisoning if they consume enough of the chemical.
In all animals, the nitrite ion readily reacts with hemoglobin in red blood cells, oxidizing it to form methemoglobin, which cannot transport oxygen. When over 30 to 40 percent of hemoglobin is converted to methemoglobin, clinical signs of poisoning become apparent [95,107,111,112]. Death occurs as methemoglobin levels approach 80 percent.

Clinical Signs
The first sign of nitrate poisoning is usually the sudden death of one or more animals. If observed before death, ruminants with nitrate poisoning may exhibit drowsiness and weakness, followed by muscular tremors, increased heart and respiratory rates, staggering gait, and recumbency [65,67,78-80,86,113-116]. Signs of poisoning develop within 6 to 8 hours of the consumption of a toxic dose of nitrate [68]. Stress or forced exercise will increase the severity of clinical signs and hasten death. Examination of the mucous membranes, especially the vaginal mucous membranes, may reveal a brownish discoloration depending on the quantity of methemoglobin present. This color change can be detected in the vaginal mucous membranes when 20 percent or more methemoglobin has formed [94]. This brownish discoloration occurs well before other clinical signs become evident, suggesting vaginal color changes are a good means of detecting nitrate poisoning before severe toxicity develops [94,117]. Venous blood also has a chocolate brown discoloration. Depending on the quantity and rate of absorption of nitrite from the digestive tract, and the amount of stress to which the animal is subjected, death may occur within 2 to 10 hours [118].

Chronic Nitrate Poisoning
Sublethal doses of nitrate may induce abortion because nitrate readily crosses the placenta and causes fetal methemoglobinemia and death [119]. Severe methemoglobinemia also impairs oxygen transportation across the placenta, thus contributing to fetal hypoxia and death [94]. Fetal death and abortion may occur at any stage of gestation as a result of

the combined effects of decreased placental oxygen transport and the limited ability of the fetus to metabolize nitrite [74,77,78,80,120,121]. Abortions may also result from decreased progesterone production induced by chronic nitrate poisoning interfering with luteal production of progesterone [127].
Low levels of nitrate in the diet of cattle have also been suspected of affecting vitamin A metabolism, thyroid function, reproduction, and milk production. There are however many conflicting reports on the effects of low level nitrate poisoning. Nitrate appears to affect metabolism of carotene and vitamin A, reducing liver levels but having little effect on plasma levels [123,124]. Experimentally however, there appears to be little destruction of vitamin A in the rumen in the presence of high levels of nitrate, and nitrates do not appear to have any goitrogenic effect in cattle [125-127]. Nitrate levels in the ration exceeding 1 percent can cause a reduction in feed intake in cattle [128] but if a ration with high levels of digestible nutrients is fed concurrently, increased weight gains occur [128,129]. These findings indicate that high-carbohydrate rations increase the utilization of nitrate in the formation of protein. Numerous studies have also shown that nitrates do not affect milk production unless the levels of nitrate induce significant methemoglobinemia [128,130-133]. Low levels of nitrate accumulate in milk of animals consuming forages high in nitrate, with maximum levels attained 2 hours after ingestion of the nit- rate [122,134,135]. Reproductive efficiency, gestation length, and birth weights appear to be unaffected by low nitrate consumption [114,119].

Treatment
Animals showing signs of nitrate poisoning should be handled carefully to avoid stress or excitement that will worsen the animal's respiratory distress. The suspected nitrate food source should be removed. The preferred treatment for nitrate poisoning is methylene blue solution administered intravenously. As a reducing agent it converts methemoglobin to hemoglobin thereby restoring normal oxygen transport by the red blood cells. The recommended dose range for methylene blue is 4 to 15 mg/kg body weight administered as a 2 to 4 percent solution [73,136]. A dose of 8 mg/kg body weight intravenously has been effective in cattle [82,118,136]. In sheep, the half-life of methylene blue is about 2 hours, indicating that small doses of the drug can be repeated as needed every few minutes to reduce methemoglobinemia to the point that the animal is not in severe respiratory distress [108]. Excessive administration of methylene blue to animals other than ruminants will result in hemolytic anemia due to formation of Heinz bodies. Horses, and especially dogs and cats, are particularly susceptible to methylene blue toxicity. Animals with severe respiratory distress can be given oxygen where possible to optimize oxygen saturation of remaining hemoglobin. In severe cases, epinephrine can be administered intravenously to counter the acute hypotensive effects of the nitrite.
The administration of mineral oil (1 gallon for a 500 kg cow) orally via stomach tube will counteract the caustic effect of the nitrates on the gastrointestinal system and will speed up the passage of the nitrates. Several gallons of cold water with added oral broad-spectrum antibiotics will further decrease nitrate reduction to nitrite by rumen microorganisms. Similarly vinegar given orally via stomach tube will help prevent nitrate reduction in the rumen.

Diagnosis
Sudden deaths in ruminants grazing Sudan grass (*Sorghum* spp.), weeds or crop stubble post harvest should raise suspicion of nitrate poisoning. Confirmation should be based on the demonstration of toxic levels of nitrate in the forage, water source, rumen contents and tissues of the animal. At necropsy, the highest concentrations of nitrite are found in the heart, lungs, and kidneys. Detection of high levels of methemoglobin (greater than 40 percent of total hemoglobin) in the animal is diagnostic of nitrate poisoning. Normal levels of methemoglobin in cattle blood are in the range of 0.1 to 0.2 g/dL [138]. Because reduction of methemoglobin occurs rapidly after death, samples should be taken and submitted for analysis as soon after death as possible. Tissue and plant samples should be frozen if they cannot be analyzed immediately. If the blood sample cannot be tested immediately, it should be diluted with 1 part blood to 20 parts phosphate buffer (pH 6.6) and frozen [93].
If the animal has been dead for several hours or more, the best sample to submit for nitrate analysis is the aqueous humor from the eyes. Nitrate in the aqueous fluid is protected from autolytic changes that occur rapidly in other parts of the body after death. Good correlation with serum levels can be obtained for about 24 hours postmortem and the nitrate levels remain diagnostically significant for as long as 60 hours [136-142]. The normal level of nitrate in the ocular fluid of healthy cattle is 4 to 5 mg/L [136]. Nitrate levels in aqueous humor of 20 to 40 ppm should be considered suspect, and over 40 mg/L (40 ppm) could be considered diagnostic of nitrate poisoning if corroborating clinical signs are seen and evidence of high nitrate levels is found in the forage and/or water. Ocular fluid from an aborted fetus is useful for determining if nitrate is the cause of abortion provided the levels detected are interpreted in light of forage and water nitrate levels to which the dam would have had access.
As a general rule, levels of nitrate over 0.5 percent in forages and water levels exceeding 200 ppm are potentially hazardous to pregnant animals especially if fed continuously [107]. Forages containing in excess of 1 percent nitrate dry matter should be considered toxic [108]. Water levels of 1500 ppm or greater are potentially toxic to ruminants especially if consumed with forages high in nitrate [107,108]. Nitrate and nitrite can be assayed in forage, rumen contents, and water using the

diphenylamine test [136], ion-specific electrodes [141], and high-performance liquid chromatography [141]. Presumptive diagnosis of nitrite poisoning can be made in the field using diazotization urine test strips in the aqueous humor and peritoneal and pericardial fluids of animals suspected of nitrate poisoning [143].
Depending on the laboratory performing the test, nitrate may be reported in a variety of units that can be confusing eg: nitrate nitrogen (NO-N), ppm, NO_3 mg/kg, etc. The conversion factors are given in Table 1 - 3. It is important to convert the reported units to a standard nitrate unit that can be related to established normal values.

Prevention of Nitrate Poisoning
Nitrate poisoning can be prevented if the nitrate levels in forages are predetermined and managed accordingly. Forages such as sudan grass and sorghum hybrids, oat hay, and corn stalks should be tested especially if heavy nitrogen fertilization has been used or drought has affected the plants [88,144]. Hay containing high nitrate levels that is exposed to rain can have the nitrate leached out into the lower bales making them especially high in nitrates. It is also prudent to check the water of the animals to ensure it is not a source of nitrates that would be additive to any nitrate in the food. Contrary to popular belief, boiling water for prolonged periods does not decrease the level of nitrate [145].
Forages containing 1 percent nitrate or more should be fed cautiously to ruminants. There are several strategies that can be implemented if hay and other forages are found to contain high levels of nitrates. Ideally, hay that has more than 1 percent nitrate should be diluted with hay containing no nitrates so that the total nitrate level in the ration is below 1 percent. Feeding low-nitrate forage or hay before turning cattle onto forages containing higher levels of nitrate reduces the amount of nitrate consumed. Feeding high-nitrate forages to nonpregnant cattle eliminates the risk of abortion. Products containing nitrate-reducing bacteria (*Propionibacteria* spp.) are available commercially for feeding to ruminants before exposing them to high-nitrate forages. This enables cattle to tolerate higher nitrate consumption [146]. Increasing the total energy content of the ration also enhances the metabolism of nitrate in the rumen thereby helping ruminants tolerate higher nitrate levels in their diet. It is for this reason that cattle on a good plain of nutrition are able to consume forages that have 2 percent or more of nitrates. However, sudden changes of feed from a low energy ration to one that is high in energy and nitrates may result in high mortality because the rumen microorganisms will not have had time to adapt to the high nitrate ration. Ensuring animals are on a good plain of nutrition before introducing a forage high in nitrate reduces losses.

Common Weeds that Accumulate Nitrate

Ragweed
***Ambrosia* spp.** - Asteraceae (Sunflower family)

Habitat
The ragweeds are native annual or perennial weeds of most states west of the Missouri River. They grow in most soils in cultivated fields, roadsides, pastures, and rangeland.

Description
Giant ragweed is a rapidly growing annual that may attain heights of 8 to 10 feet (2 to 3 meters) in moist fertile soils. The stems and leaves are rough, the leaves usually being trilobed, but they also may have either no lobes or as many as five lobes (Fig. 1-10). The leaves are alternate and large and attached with a long petiole. The male flowers (uppermost) and the female flowers (lowermost) are small and produced in terminal clusters. The seeds are about 1 cm in length, each with four to five terminal spikes.

Figure 1-10. Giant ragweed (*Ambrosia trifida*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
Nitrates are readily accumulated in the young plants especially in rich fertile soils. The pollen produced from ragweed can be

a serious cause of hay fever and allergies in people and dogs.

Note - Various other members of the ragweed family also have the potential for nitrate accumulation. These include common ragweed (*A. artemisifolia*), woolly leaf bursage (*A. grayi*), and skeleton leaf bursage (*A. tomentosa*). Giant ragweed (*A. trifida*) is notorious for causing allergies in people.

Wild Oat Grass

Avena fatua - Poaceae (Grass family)

Habitat

Wild oats is a widely distributed grass, introduced from Europe, that becomes established in grain fields, pastures, and disturbed soils. It seeds are viable in the soil for at least 10 years, making it difficult to eradicate. It is considered a noxious weed in many areas.

Description

Wild oats is an annual, erect, hollow-stemmed grass that grows to 4 feet in height. It has leaf blades up to a half inch (1.5 cm) wide, with open sheaths and membranous ligules. Seedlings have leaves that twist counterclockwise. The flower is an open panicle that droops. The awn has a distinctive long bristle with a characteristic right-angle bend (Fig. 1-11). The seeds are yellow to black and about 0.5 inches (1 cm) in length.

Principal Toxin

Wild oats, like domestic oats, has the potential to accumulate significant levels of nitrate.

Note - Cultivated oats (*A. sativa*) can be differentiated from wild oats in that it has a straight bristle. Cultivated oats may accumulate toxic levels of nitrates especially if fertilized.

Figure 1-11. Wild oats showing distinctive bent awn (*Avena sativa*). - To view this image in full size go to the IVIS website at www.ivis.org . -

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Lamb's-Quarter

***Chenopodium* spp.** - Chenopodiaceae (Goosefoot family)

Habitat

Lamb's-quarter (*C. album*) is a common annual weed, introduced from Europe, and found growing throughout North America in cultivated fields, gardens, roadsides, and pastures. Nettleleaf goosefoot (*C. murale*) and netseed lamb's-quarter (*C. berlandieri*) are also common rapidly growing weeds with similar distribution and habitat.

Description

Lamb's-quarter is a variable annual, with erect branched stems, alternate leaves that often have a grayish, powdery undersurface. The basal leaves have a more coarsely serrated margin than the smaller upper leaves. The stems often have distinct red or purple stripes. Flowers are inconspicuous, gray green, and crowded at the axils and branch tips (Fig. 1-12). Large quantities of dark seeds with a "netted" surface are produced.

Figure 1-12. Lamb's-quarter (*Chenopodiun album*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxins
Lamb's-quarter is capable of accumulating significant quantities of nitrate, sulfate, and oxalates.

Canada Thistle
Cirsium arvense - Asteraceae (Sunflower family)

Habitat
Introduced from Eurasia, Canada thistle has become a widely established noxious weed. It grows readily in many soil types forming dense stands in cultivated as well as waste places. It is a prolific producer of wind-borne seeds and also reproduces from an extensive root system.

Description
Canada thistle is an erect perennial colony-forming weed with an extensive horizontal root system. Stems reach 3 to 4 feet (1 meter) in height, branching above with terminal purple thistle flowers (Fig. 1-13). Leaves are alternate, without petioles, and lance-shaped with spiny-tipped irregular lobes. Flowers are unisexual on separate plants, with purple and occasionally white, 0.5 inch (1 to 2 cm) diameter heads. The brownish seeds have a tuft of white hairs to aid in distribution by the wind.

Principal Toxin
Canada thistle is listed as a noxious weed in many states because of its invasive nature. It will accumulate nitrates and may contain high levels of sulfates when growing in sulfate-rich soils.

Figure 1-13. Canada thistle (*Cirsium arvense*). - To view this image in full size go to the IVIS website at www.ivis.org . -

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Field Bindweed
Convolvulus arvensis - Convolvulaceae (Morning glory family)

Habitat
Field bindweed was introduced from Europe and has become a noxious weed throughout North America. It adapts to almost any soil type and is very invasive, drought tolerant, and difficult to eradicate.

Description
Bindweed is a perennial, prostrate vine 2 to 4 feet (1 meter) long. It forms dense mats covered with white to pink morning glory-like flowers (Fig. 1-14). It readily twines around and up other plants or objects. Leaves are alternate, arrow shaped with pointed or rounded lobes at the base. The root system is extensive, penetrating to depths of 10 feet (3 meters) or more. The fruits are round capsules containing four brown seeds, flattened on two sides.

Figure 1-14. Field bindweed (*Convolvulus arvensis*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxins
Field bindweed will accumulate nitrates. It also contains various tropane alkaloids including pseudotropine, tropine, tropinone, and cuscohygrine [147,148]. Pseudotropine, the predominant alkaloid, is capable of affecting smooth muscle activity. Other nortropane alkaloids (calystegins) present in bindweed (*Calystegia* spp., some *Solanum* spp., and *Ipomoea* spp.) are potent glycosidase inhibitors [149].

Note - Hedge bindweed (*C. sepium*) is similar to field bindweed but has two large bracts immediately below the flower. All bindweeds are similarly toxic.

Barnyard Grass
Echinochloa crus-galli - Poaceae (Grass family)

Habitat
Barnyard grass was introduced from Europe and is widespread in North America. It is commonly found in gardens and cultivated fields; it is a noxious weed.

Description
Barnyard grass is a vigorous, annual warm-season grass, reaching 1 to 5 feet (1 to 2 meters) in height. Bases of stems are often dark purple. Leaf blades are flat, smooth, up to 1 inch (2.5 cm) broad, and with no ligules at the junction of the sheath and blade. The flower is an open panicle, reddish brown in color (Fig. 1-15). The seeds are crowded on spikelets, each with a short stiff awn. As many as 40,000 seeds may be produced by a single mature plant.

Figure 1-15. Barnyard grass seed heads (*Echinochloa crus-gali*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
Barnyard grass may accumulate toxic levels of nitrate if it is growing in fertile soils or is fertilized.

Sunflower

Helianthus annuus - Asteraceae (Sunflower family)

Habitat

Sunflowers are indigenous to North America and are common weeds of roadsides, cultivated fields, pastures, and disturbed soils.

Habitat of Sunflower. *Helianthus annuus* - Asteraceae (Sunflower family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description

Sunflowers are annuals or perennials, growing from 1 to 10 feet (1 to 3 meters) tall, with erect single to many-branched, rough stems. Leaves are alternate, rough, hairy, and heart shaped with toothed edges. The flowers are showy, with yellow ray flowers and brown or yellow disk flowers (Fig. 1-16). The seeds (achenes) vary from black to gray, and may be striped.

Figure 1-16. Sunflower (*Helianthus annuus*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin

Rapidly growing sunflowers can accumulate toxic levels of nitrate.

Kochia, Mexican Fireweed

Kochia scoparia - Chenopodiaceae (Goosefoot family)

Habitat

Kochia weed was introduced from Asia as an ornamental and now has become established as a weed in most of North America. It is versatile, growing in gardens, cultivated fields, pastures, disturbed soils, and along roadsides. It is readily grazed by livestock and can be a valuable forage when little else is available, especially in dry areas or in times of drought.

Habitat of Kochia, Mexican Fireweed. *Kochia scoparia* - Chenopodiaceae (Goosefoot family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description

Kochia is an annual growing up to 10 feet (3 meters) tall when established in fertile, moist soils (Fig. 1-17a). Stems are much branched, round, hairy, and often red tinged especially in the fall (Fig. 1-17b). Leaves are alternate, hairy especially below, lance shaped, smooth edged, and up to 2 inches (5 cm) in length. The flowers are small and are produced in dense, bracted spikes in the leaf axils (Fig. 1-17c) Seeds are brown, slightly ribbed, and produced in large quantities.

Principal Toxins

Kochia weed is capable of accumulating significant levels of nitrate as a young, rapidly growing plant. It may also accumulate oxalates and sulfates and has been responsible for causing liver disease and photosensitization in some years due to an as yet undefined toxin (see Chapter 4). The variability in the reported toxicity of kochia weed is poorly understood and is probably related to the growing conditions of the plant.

Note - Kochia weed is grown in some areas with low rainfall as a drought-tolerant forage crop for livestock without evidence of toxicity.

Figure 1-17a. Kochia weed growing in a corn field (*Kochia scoparia*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-17b. Kochia weed in flower (*Kochia scoparia*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-17c. Kochia weed immature plant (*Kochia scoparia*). - To view this image in full size go to the IVIS website at www.ivis.org . -

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Mallow, Cheese Weed

Malva neglecta - Malvaceae (Mallow family)

Habitat

Mallow is a common weed introduced from Europe that has become widespread throughout North America. It successfully establishes itself in gardens and cultivated and waste areas.

Habitat of Mallow, Cheese Weed. *Malva neglecta* - Malvaceae (Mallow family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description

Common mallow is an annual or perennial, with prostrate stems and erect branches that may reach 3 feet (1 meter) in length. Mallows have a substantial taproot. Leaves have long petioles and are rounded with prominent veins dividing the leaf into five to seven lobes. The flowers with fused petals range from white to pale lavender in color (Fig. 1-18). Fruits consist of a circle of flat-sided, brown seeds arranged like a "cheese cake".

Little mallow (*M. parviflora*) is similar in appearance but is a more upright and robust plant with 2 to 5 inch (5 to 12 cm) broad leaves, with a red spot at their base.

Principal Toxin
Mallows have the potential for accumulating toxic levels of nitrate.

Note - The plant and seeds of mallows may cause a pink coloration to egg whites when eaten by laying hens.

Figure 1-18. Mallow (*Malva* spp.). - To view this image in full size go to the IVIS website at www.ivis.org . -

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Russian Thistle, Tumble Weed

***Salsola iberica* (*S. kali*)** - Chenopodiaceae (Goosefoot family)

Habitat
Russian thistle was introduced from Russia and is now well established as a weed in much of western North America, especially in drier areas. It, however, will grow in cultivated areas, roadsides, and overgrazed rangeland. Russian thistle is the classic "tumble weed" that is encountered blowing across the rangelands of the west in the fall.

Habitat of Russian Thistle, Tumble Weed. *Salsola iberica* (*S. kali*) - Chenopodiaceae (Goosefoot family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Description
Russian thistle is a rounded, bushy, annual plant, up to 5 feet (1.5 meters) in height. Stems are often red or purple striped (Fig. 1-19a). Immature plants have soft, thin, stringlike leaves, which later shorten and become stiff and tipped with a spine (Fig. 1-19b). This makes the plant prickly to the touch. Flowers are small and green and are produced in the axils of the upper leaves, each accompanied by two spiny bracts.

Figure 1-19a. Russian thistle (*Salsola iberica*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-19b. Russian thistle young plant (*Salsola iberica*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
In fertile moist soils, Russian thistle may accumulate toxic amounts of nitrates and oxalates.

Note - Each Russian thistle plant produces thousands of seeds, which are scattered widely when blown about in the fall. The seeds can remain dormant for years, germinating when conditions are optimal for growth. Russian thistle is also an undesirable weed in sugar beet fields because it is a host plant for the sugar beet leaf hopper that transmits the virus that causes "curly top" in beets.

Plants Containing Toxic Alkaloids
Larkspur Poisoning
Larkspurs in the genus *Delphinium* cause more fatal poisoning of cattle in the western United States than any other native plant species [150,151]. As early as 1897, livestock losses to larkspur were reported in Montana and even now larkspur poisoning remains a serious threat to cattle with access to the plants [152-154] livestock losses to larkspur in the United States have been estimated to exceed $234 million annually, making larkspurs second only to the locoweeds in terms of economic losses to the livestock industry [155]. In some areas of the intermountain states, cattle losses to larkspur poisoning average 2 to 5 percent per year and may be as high as 10 percent in some year [156,157].

Larkspur, Poison Weed
***Delphinium* spp.** - Ranunculaceae (Buttercup family)

Habitat
There are at least 60 species of larkspur found throughout North America, the majority occurring in the western states. They range from Alaska and the Canadian Provinces south to Mexico [151,157]. Larkspurs grow in rich loamy soils of moist areas of the mountains and in the drier sandy soils of the plains and foothills.

Habitat of Larkspur, Poison Weed. *Delphinium* spp. - Ranunculaceae (Buttercup family). - To view this image in full size go to the IVIS website at www.ivis.org . -

Larkspur poisoning of cattle has been attributed to relatively few species, including *D. barbeyi*, *D. bicolor*, *D. geyeri*, *D. glaucescens*, *D. glaucum*, *D. nuttallianum*, *D. occidentale*, *D. tricorne*, and *D. virescens* [158]. It is probably wise, however, to assume that all larkspurs are potentially poisonous, including those cultivated as ornamentals. Larkspurs are often grouped for descriptive convenience into tall and low varieties according to their growth habit. Tall larkspurs (*D. barbeyi* and *D. occidentale*, *D. glaucescens*) (Fig. 1-20a and Fig. 1-20b) grow in deep, moist, and highly organic soils at high altitudes and often reach 7 feet in height [151,159].

Figure 1-20A. Tall larkspur (*Delphinium barbeyi*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-20B. Tall larkspur inflorescence showing flowers with characteristic spur (*Delphinium barbeyi*). - To view this image in full size go to the IVIS website at www.ivis.org . -

The tall larkspurs generally grow in montane forests, especially where snow drifts occur perennially. The plants emerge as the snows recede and once established form very long- lived dense stands. Low larkspurs (*D. nuttallianum* (Fig. 1-20c), *D. nelsoni*, and *D. virescens* (Fig. 1-20d) grow at lower elevations in drier rangeland, seldom growing more than 2 to 3 feet (0.5 to 1 meter) tall; they die in early summer as the soil dries out. Foothills larkspur (*D. geyeri*) is intermediate in its growth habit, attaining a height of 3 to 4 feet (1 meter) when in flower (Fig. 1-20e and Fig. 1-20f).

Figure 1-20C. Low larkspur (*Delphinium nuttallianum*). - To view this image in full size go to the IVIS website at www.ivis.org . -

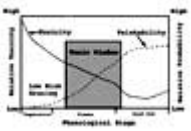
Figure 1-20D. Prairie larkspur (*Delphinium virescens*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-20E. Foothills larkspur (*Delphinium geyeri*) immature plant. - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-20F. Foothills larkspur (*Delphinium geyeri*) in bloom. - To view this image in full size go to the IVIS website at www.ivis.org . -

Description
Larkspurs are erect herbs arising from a single or clustered, often woody root stock. Indigenous species are perennials, whereas introduced species are annuals. Leaves clustered at the base of the plant are simple, alternate, petioled, palmately lobed into three to five divisions, and in some species further deeply divided. Stems are hollow. The showy flowers, generally blue to purple in color, but ranging from white to occasionally red, are produced on terminal erect racemes. Flowers have five sepals and four petals; the upper sepal and pair of petals are elongated to form a characteristic spur that protrudes backward (see Fig. 1-20d). Seed pods are erect, three to five-celled, splitting down the inside ridge to release numerous dark brown to black seeds.

Toxicity
Young rapidly growing larkspur plants are most toxic, with the highest concentration of alkaloids in the leaves. Cattle, however, appear to not eat tall larkspur until the plants initiate and elongate flower stalks [160,161]. At this stage, the alkaloid content of the plants is generally declining, although the seed pods contain high levels of alkaloids [161,162]. Tall larkspur consumption in cattle may range from virtually nothing in the preflower stage to as much as 30 percent of the animal's diet when the plant is in the flowering stage. There is a "toxic window" of time when cattle find tall larkspur increasingly palatable, and the plants contain significant total toxic alkaloids [160,161] (Graph 1-1). This window of time occurs as the tall larkspurs begin to elongate their flower stalks and until the flowers have been replaced with seed pods. Feeding studies with cattle using both fresh and dried tall larkspur showed no correlation between alkaloid concentration and palatability [160]. Sheep, however, will avoid eating the plants in the preflower stage when the alkaloid content is highest, but will readily eat the flower stalks and buds as they mature. In drought years the consumption of tall larkspur by cattle almost entirely ceases, and mortality from larkspur poisoning is lowest during droughts [160,162]. Another as yet unexplained phenomenon that contributes to tall larkspur poisoning is the glutinous consumption of the larkspur by cattle in a short period after a summer rain storm [163].



Graph 1-1. - To view this image in full size go to the IVIS website at www.ivis.org . -

The toxicity attributed to the tall larkspur species cannot be assumed to hold true for the low or foothills larkspur species. Unlike the tall larkspurs, the foothills larkspur (*D. geyeri*) is readily eaten by cattle in the early spring before it flowers, causing significant numbers ofdeaths in some years. By the time it flowers, the foothills larkspur is not consumed in any quantity presumably because cattle generally have plenty of other forage available by this stage.
Cattle are most susceptible to larkspur poisoning, but sheep and horses may also be poisoned if they eat sufficient quantity of the plants over a short period of time and are concurrently subjected to stress. Sheep are be able to tolerate about four times the amount of larkspur alkaloids that would be fatal to cattle [151]. Establishing the toxic dose of larkspur for cattle is difficult because the toxicity varies with the species, season, stage of growth, amount ingested, and duration over which the plant is eaten [164]. It has been estimated that cattle must eat 0.7 percent of their body weight of green tall larkspur in an hour to be fatally poisoned [151]. If one assumes a 1200-lb cow eats about 25 lb of forage a day, it would have to eat about 6 lb of green tall larkspur containing 5 mg/g of total toxic alkaloid to be fatally poisoned. This is about 25 percent of the cow's total daily feed intake [160]. The LD_{50} of total toxic alkaloid for tall larkspur has been shown experimentally to be between 25 and 40 mg/kg body weight [164].
Larkspurs contain many toxic and nontoxic diterpenoid alkaloids, 40 of which have been identified in the nine larkspur species most frequently associated with poisoning in cattle [158,165,166]. The alkaloids may vary in quantity depending on the species and stage of growth [150,167]. Even within a small area, certain stands of larkspur appear to be more toxic than others. These "hot spots" are well recognized by ranchers who frequently anticipate losses when cattle are herded in these areas. The alkaloid content of tall larkspurs also appears to be consistently higher in plants growing in full sun as opposed to those growing in the shade. Studies with *D. barbeyi* have shown it to be the most toxic of the larkspurs [151,159,162]. As little as 17 g/kg body weight of the green plant of *D. barbeyi* is lethal to cattle [162,168]. A rapid electrospray mass spectrometry method has been developed that may prove useful in determining the toxic alkaloid content of larkspur species at different growth stages that will facilitate the safe management of larkspur rangeland for cattle grazing [169].
To date the most toxic of the alkaloids isolated from tall larkspurs are 14-deactylnudicauline and methyllycaconitine (MLA) [158,170,171]. Although the former alkaloid is more toxic, greater than 15 times as much MLA is produced in the plant making it the most important toxic component of the tall larkspurs [161]. The foothills larkspur (*D. geyeri*) and the low larkspur (*D. nuttallianum*) contain the highly toxic alkaloid nudicauline [172]. The toxicity of the different larkspur species is, however, most likely due to the combined effects of the alkaloids present in the plants.

The alkaloids act principally at the neuromuscular junction (postsynaptic nicotinic and cholinergic receptors) causing a curare-like blockade with muscle weakness and paralysis [167,173]. The alkaloids reversibly bind to and block the action of nicotinic acetylcholine receptors at the neuromuscular junction thus competing with acetylcholine for the receptors. This effect is similar to that of nicotine and the snake toxin bungertoxin [174]. Binding affinity of the larkspur alkaloids to the cholinergic receptors varies with the tissue and among species [175]. Cholinergic receptors in cattle are possibly more susceptible to the alkaloids than are those of sheep, offering an explanation for the refractoriness of sheep to larkspur toxicity.

Clinical Signs

Sudden death in cattle is often the first indication of larkspur poisoning. Cattle frequently die within 3 to 4 hours of consuming a lethal dose of larkspur. Poisoned cattle initially show uneasiness, increased excitability, and muscle weakness that causes stiffness, staggering, and a base-wide stance [176]. The front legs may be affected first causing the animal to kneel before finally becoming recumbent. Muscle weakness may cause sudden collapse especially if the animal is stressed. Frequent attempts to stand are uncoordinated and result in rapid exhaustion. Muscle twitching, abdominal pain, regurgitation, and constipation are common clinical findings. Similar signs of poisoning occur in horses, sheep, and goats that have eaten larkspur except that vomiting is uncommon and fewer deaths are likely.

Bloat is common in larkspur poisoning because of the neuromuscular blocking effect of the alkaloids impairing eructation and the fact that the green larkspur is highly fermentable by rumen microorganisms, thereby increasing the rate of gas production in the rumen. The high protein content of larkspur may also facilitate the production of a stable foam in the rumen that enhances the severity of the bloat. Inhalation of regurgitated rumen contents in the recumbent animal will lead to fatal pneumonia. Cattle appear to be able to repeatedly eat a toxic dose of lark- spur without marked clinical signs of poisoning provided larkspur consumption is significantly decreased for 2 to 4 day intervals [177]. This appears sufficient time for metabolism and clearance of the larkspur alkaloids to occur and reduce the cumulative effect of daily larkspur consumption.

No specific postmortem findings are seen in animals that have died of larkspur poisoning. Bloat, inhalation of rumen contents, venous congestion, and mild gastrointestinal inflammation are common secondary findings. Diagnosis of larkspur poisoning is made by searching for parts of the plants in the animal's rumen and by finding evidence of the animal having grazed larkspur. It is also possible to detect microscopically the plant cell structure of *Delphinium* spp. in the feces or rumen contents that will indicate the animal had consumed the plant in the recent past [178].

Treatment

Ever since larkspurs were known to be poisonous to cattle, a variety of treatments have been advocated. Treatment myths abound in the early literature and have involved the use of a variety of compounds including atropine, potassium permanganate, turpentine, bacon fat, chewing tobacco, whiskey, and bleeding the animal from the tail vein [153,179]. Most of these early remedies have little scientific basis and have not been proven to be effective. The use of turpentine and bacon fat given orally may have helped reduce the severity of the bloat that develops with larkspur poisoning. Apparent successes with unique remedies have not considered the variability in toxicity of the larkspurs under different growing conditions, time of year, and quantity of total toxic alkaloid consumed. If less than a lethal dose of larkspur alkaloids is consumed, an animal will likely recover despite the treatment, unless severe bloat and regurgitation of rumen contents occurs while the animal is recumbent.

Anticholinesterase drugs that allow the accumulation of acetylcholine at the neuro- muscular junction by inhibiting cholinesterase are the most appropriate for the reversal of some of the effects of larkspur alkaloids. Physostigmine (0.08 mg/kg) has been effective if given intravenously to cattle about to collapse from larkspur poisoning [177]. Cattle in sternal or lateral recumbency from tall larkspur poisoning recover after treatment with physostigmine (0.4 - 0.8 mg/kg body weight) given intravenously [180]. Treatment should be repeated as needed over several hours until clinical signs have abated. Neostigmine (0.04 mg/kg) appears to be as effective in reversing some of the effects of the larkspur alkaloids but is possibly not as effective as physostigmine for treating larkspur poisoning. A formulation that has been beneficial if administered early in the course of poisoning has been the injectable mixture of physostigmine salicylate, pilocarpine hydrochloride, and strychnine sulfate [156]. Some organophosphate compounds with an anticholinesterase effect may also have potential benefit in the treatment of larkspur poisoning as they will decrease the breakdown of acetylcholine [181]. Because none of these drugs are approved for use in food-producing animals they must be administered under the supervision of a veterinarian in accordance with the regulations pertaining to the use of extra-label drugs.

An early diagnosis of larkspur poisoning is essential if treatment is to be successful. Stress and excitement of the affected animal should be avoided because it will exacerbate respiratory distress and hasten death. It is often better to quietly herd affected range cattle away from the area where larkspur is being grazed and not attempt to catch and restrain an animal to treat it. Affected animals should be kept sternal if they become recumbent. Bloat should be relieved by passing a stomach tube to remove excess rumen gas and reduce respiratory difficulty when possible.

Trocarization of the rumen to relieve the bloat may be more effective than trying to pass a stomach tube because it is less

stressful to the animal.
Acute larkspur poisoning in a range cow can resemble grass tetany (hypomagnesemia) and milk fever (hypocalcemia) especially when the affected animal is recumbent, and laboratory facilities are not readily available to differentiate these conditions. Magnesium solutions for the treatment of grass tetany are contraindicated in suspected larkspur poisoning as magnesium will exacerbate the effect of the alkaloids at the neuromuscular junction. Calcium gluconate in contrast will have a beneficial effect at the neuromuscular junction. However, calcium solutions should be administered very cautiously because of the effect of calcium on the heart.

Prevention of Larkspur Poisoning
Intuitively, cattle should be kept off of ranges containing large quantities of larkspur. However, this would eliminate vast areas of rangeland for livestock grazing, making such a management option uneconomical. By knowing the growth habits of tall larkspur, the times when it is most toxic, and when cattle like to eat the plant, it is possible to manage cattle so that they are kept away from the larkspur during a "toxic window" when chances for poisoning are highest (see Graph 1-1) [161]. Prior to this "toxic window", cattle may be grazed on the larkspur range even though tall larkspur is most toxic at this stage, because cattle find the plant unpalatable. Similarly, after the larkspur is past flowering it is relatively less toxic and more palatable. Consequently, knowing the toxicity, palatability and growth stage of tall larkspur, it is possible to make effective use of rangeland for livestock production while minimizing the risk for tall larkspur poisoning [182]. This management strategy is only valid if there is a diversity of other forages available, and the cattle are not forced into a situation where they must eat larkspur because they are without adequate food. If early season grazing of tall larkspur is used, very close attention must be paid to the eating patterns of the cattle. As soon as the tall larkspur starts to elongate its flower stalks and cattle start to eat the flower shoots, they should be moved off of the range. Early season grazing is relevant only to tall larkspur and should not be attempted with the foothills or low larkspurs that seem to be quite palatable in the early spring when they can be highly toxic.
The fact that sheep can eat larkspur without problem makes them useful biological controls for tall larkspur. Sheep if herded into larkspur stands will eat and trample the plants thereby reducing the availability of larkspur to cattle that follow the sheep [183,184]. It is doubtful, however, if sheep effectively reduce the potential for lark- spur poisoning in cattle unless large numbers of sheep are actively herded into areas where the plants are abundant.
Providing adequate calcium, phosphorus, and mineralized salts for cattle has been recommended as a preventive measure for larkspur poisoning. However, mineral supplementation of cattle grazing rangeland infested with tall larkspur had no effect in reducing the amount of larkspur consumed [185]. A balanced mineral supplement should always be provided to cattle to prevent mineral deficiencies and should not be relied on as a preventive measure for larkspur poisoning. It has been postulated that cattle may be deficient in minerals in late winter and early spring and may crave plants like foothills larkspur that are high in calcium.

Aversion to Larkspur
Cattle unfortunately do not have a natural aversion to larkspur, but they can be trained under certain management conditions to avoid eating tall larkspur. Cattle can form a strong aversion to eating larkspur if they are given intraruminal infusions of larkspur extract with lithium chloride [186-188]. Lithium is a potent irritant and emetic that induces abdominal pain that the animal associates with the last thing it was eating or was fed.
Once cattle have developed an aversion to larkspur they continue to have the aversion from year to year provided they are not exposed to cattle that are eating larkspur [187,189,191]. Socializing with cattle that are not aversed to larkspur leads to the aversed animals relearning to eat larkspur [189]. Training cattle to avoid eating larkspur can be accomplished by harvesting and feeding fresh larkspur to cattle. As soon as an animal has started eating the larkspur it is restrained and given lithium chloride (100 mg/kg body weight) via stomach tube. The subsequent abdominal discomfort is associated by the animal with the last thing it ate, namely the larkspur.
Induced aversion to eating larkspur has potential beneficial implications for some ranch enterprises. In closed herd situations where all cattle can be treated with lithium and not be exposed to non-averted cattle, larkspur aversion can be maintained in the entire herd for many years at minimal cost [191,192].

Control of Larkspur
Although it is possible to control larkspurs with herbicides, it is economically prohibitive to do so on a wide scale [155,193-195]. However, spraying of larkspur hot-spots can be effective in reducing cattle losses. The tall larkspurs can be controlled using a variety of currently available herbicides including picloram (Tordon), metsulfuron (Escort), glyphosate (Roundup) [196,197]. The most effective herbicide for all growth stages of lark- spur is picloram. All are effective because they kill the root and not just the vegetative portion of the plant as is the case with 2,4-D [196]. Surfactants enhance the efficacy of herbicides because they improve the absorption of the chemicals through the waxy surface of the leaves. The most effective

time to apply herbicides is in the early vegetative or leaf stage before the flower stalks begin to form [196]. A second application of the herbicide will eliminate any plants that survive the first application. Newer application methods such as vehicle mounted carpeted rollers apply the herbicides to tall larkspur without affecting lower growing useful forbs and use less chemical than conventional spraying methods. It should be noted that herbicides increase the alkaloid content of larkspur and therefore the plants should not be grazed after spraying until the plants have completely died off [196]. Herbicidal control of tall larkspur has additional benefit in that significant increases in the growth of grasses for up to 5 years after spraying increases the carrying capacity of the range [197].
Research is currently underway to investigate the effectiveness of insect biologic controls to control tall larkspurs. The larkspur myrid (*Hopplomachus affiguratus*), which sucks on the plants reducing plant vitality, has shown potential as an insect control [198]. Plants infected by the myrids become stunted, fail to produce flowers and seeds, and appear to be unpalatable to cattle. The success of this insect as a biologic control will depend on whether or not it can sustain itself in large numbers once transplanted to new stands of larkspur.

Aconite, Monkshood

***Aconitum* spp.** - Ranunculaceae (Buttercup family)

Habitat

Several common species of monkshood grow in North America, the most important of which include *A. columbianum* (western monkshood), *A. uncinatum* (Pennsylvania to Georgia), *A. reclinatum* (eastern states and west to Ohio), and *A. lutescens* (Idaho to New Mexico). Monkshood is generally found growing in rich, moist soils of meadows and open woods. Western monkshood (*A. columbianum*) often grows in the same areas as the tall larkspur (*Delphinium*) species found at high altitude.

Description

Monkshood plants are perennial herbaceous plants with tall leafy stems growing to 1 foot in height. The leaves are alternate, palmately lobed or parted, and similar to *Delphinium* spp. Monkshood flowers are usually deep blue-purple, but occasionally white or pale yellow, and are produced on simple racemes or panicles. The flowers are perfect, zygomorphic, with five sepals that are petal like, the upper sepal being larger and forming a characteristic helmet or hood (Fig. 1-21). The two to five petals usually are concealed within the hooded sepal. Numerous stamens and two to five pistils are present in each flower. The fruit consists of three to five pods (follicles) that spread apart when mature to release the brown seeds. Monkshood can be differentiated from larkspur, if the flowers are not present, by the fact that the stems of monkshood are not hollow like those of larkspur. Wild geranium leaves can resemble those of monkshood when they first emerge, but can be differentiated by the distinctive geranium smell to the leaves when they are crushed.

Figure 1-21. Monkshood (*Aconitum columbianum*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin

Highly toxic, diterpenoid alkaloids including aconitine, mesaconitine, napelline and hypaconitine form the principal toxins in monkshood. The mode and site of action of the alkaloids are similar to those found in *Delphinium* and *Garrya* species [199]. All species of monkshood including cultivated species (*A. napellus*) should be considered toxic to animals and humans [200]. All parts of the plant are toxic, with the roots, seeds, and new leaves being especially toxic. Although there is no extensive documentation of the toxic dose of monkshood, horses have been reported to be fatally poisoned after eating 0.075 percent of their body weight in green plant. In the western United States, most suspected cases of *Aconitum* poisoning are due to tall larkspur, which grows more abundantly in the same areas. Tall larkspur species are also more toxic than monkshood [201].

Human poisoning from monkshood is mostly due to the misuse of medicinal extracts of aconitine [202]. Occasionally poisoning occurs when the root of monkshood is mistakenly eaten for root of wild horseradish or other wild plants. The alkaloids can also be absorbed through the skin and can be hazardous to florists and those handling the plant.

Clinical Signs
Symptoms of monkshood poisoning resemble those of poisoning from larkspur (*Delphinium* spp.). Symptoms begin within a few hours of ingesting the plant, and death may occur a few hours to a few days later depending on the dose of toxic alkaloids ingested. The alkaloids primarily cause cardiac conduction disturbances and arrhythmias. Affected animals initially become restless, salivate excessively, develop muscle weakness, hypotension, and have difficulty in breathing before collapsing into lateral recumbency [2]. Bloating is a common problem in ruminants once they become recumbent.
There is no proven effective treatment for monkshood poisoning. Affected animals should be stressed as little as possible, and have a better chance of survival if they are herded away from the source of the plants without stressful attempts at treatment. Symptomatic treatment with intravenous fluids and relief of rumen bloat should be administered as necessary. Activated charcoal and osmotic laxatives orally may be helpful in preventing further absorption of alkaloids from the gastrointestinal track.

Poison Hemlock, European Hemlock Spotted Hemlock, California Fern

Conium maculatum - Apiaceae (Parsley family)

Habitat
Introduced from Europe, poison hemlock is now found throughout North America, growing along roadsides, ditches, cultivated fields, and waste areas especially where the ground is moist. It is a prolific seed producer and will form dense stands if left unchecked.

Description
Poison hemlock is a coarse, erect biennial or perennial plant 4 to 6 feet (2 meters) tall (Fig. 1-22a). The smooth, branching stems are hollow, with purple spots especially near the base (Fig. 1-22b). The root is a simple carrot-like tap root. Leaves are alternate three to four times pinnately dissected, coarsely toothed with a fernlike appearance. The terminal inflorescence is a compound flat topped, loose umbel with multiple, small, white five-petaled flowers. Fruits are gray brown ovoid, ridged, and easily separated into two parts. The plant including the root has a strong pungent (likened to mouse urine) odor that makes it generally unpalatable. Of the four known species of *Conium*, the only one in North America is *C. maculatum*.

Figure 1-22A. Poison hemlock (*Conium maculatum*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-22B. Poison hemlock showing spotted stems (*Conium maculatum*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin
At least eight piperidine alkaloids have been found in various parts of the plant [203,204]. The two predominant toxic alkaloids are coniine (mature plant and seeds), and g-coniceine (young growing plant) [203,204]. The mechanism of action of the conium alkaloids is complex because they have a profound effect in blocking spinal cord reflexes. After an initial stimulatory effect, the autonomic nervous system ganglia become depressed [205]. Large doses of alkaloid cause skeletal muscle stimulation followed by neuromuscular blockade and paralysis similar to that caused by nicotine on the central and peripheral nervous systems [3,206]. In small quantities, the alkaloids cause skeletal defects in the fetal calf if poison hemlock is grazed by pregnant cows [206-208].
The leaves and stems prior to the development of seed heads are the most toxic part of the plant. The seeds themselves are highly toxic and can be a source of poisoning when they contaminate cereal grains fed to livestock. Young plants in the first year of growth are less toxic than mature plants, and those growing in the warmer southern states appear to be more toxic than those in the northern areas [209]. Poison hemlock is toxic to a wide variety of animals including man, birds, wildlife, cattle, sheep, goats, pigs, and horses [203,206,210-219]. People are usually poisoned when they mistakenly eat hemlock for plants such as yampa (*Perideridia gairdneri*), parsley (*Petroselinum crispum*), wild anise (*Pimpenella anisum*), or wild carrot, Queen Anne's lace (*Daucus carota*) [215]. A tea made from poison hemlock was reportedly used to kill Socrates. Livestock seldom eat hemlock because of its strong odor, but they will do so if no other forage is available or if it is incorporated in hay or silage. Cattle have been fatally poisoned by eating as little 0.5 percent of their body weight of green hemlock [215]. Experimental hemlock poisoning in cattle, pigs, and sheep has been produced by a wide range of doses suggesting that there is considerable variation in the toxic alkaloid content of the plant. Cattle dosed with1 g/kg developed clinical signs, while 5.3 g/kg of green plant was lethal [207]. In sheep, repeated *Conium* doses of 10 g/kg body weight were lethal [18]. Cattle were most susceptible to pure coniine administered by stomach tube, requiring 3.3 mg/kg body weight to induce severe poisoning. Mares required 15.5 mg/kg and sheep 44.0 mg/kg of the alkaloid to induce severe poisoning [214].

Clinical Signs
Signs of poisoning are similar in all species and develop within an hour of hemlock consumption. If a lethal dose has been consumed, death from respiratory failure occurs in 2 to 3 hours. Salivation, abdominal pain, muscle tremors, and incoordination will occur initially, followed soon by difficulty in breathing, dilated pupils, weak pulse, and frequent urination and defecation [215]. Prolapse of the nictitating membrane across the cornea in cattle and pigs may cause temporary blindness. Cyanosis of the mucous membranes, respiratory paralysis, and coma without convulsions precede death [215]. Goats may recover from hemlock poisoning only to develop a strong craving for the plant, which ultimately proves fatal [204]. Pregnant animals that survive the acute toxicity may abort [215].
Poison hemlock is also teratogenic causing abnormal fetal development if it is eaten by pregnant cows between the 40th and 70th days of gestation [213]. Calves and piglets may be born with crooked legs, deformed necks and spines (torticollis, scoliosis), and cleft palates that are indistinguishable from similar deformities caused by the teratogenic effects of lupines and tobacco species [206,207,213,219,222-225]. Sows consuming poison hemlock in early gestation produce litters of piglets with congenital skeletal malformations [208,220,221]). Observations in pregnant ewes using real-time ultrasound have shown that an increase in birth defects is associated with decreased fetal movements induced by ingestion of lupines, poison hemlock, and tobacco species [226]. Lambs born to ewes fed poison hemlock from 30 to 60 days of gestation showed varying degrees of excessive carpal joint flexure and lateral deviation that corrected itself by the time the lambs were 2 months old [227]. The teratogenic and toxic effects of poison hemlock appear to be most severe in cattle with sheep being most tolerant [206]. Mares are susceptible to poison hemlock poisoning, but foals born to mares fed coniine between 45 and 75 days of gestation did not develop congenital deformities [214].
Because there is no specific treatment for hemlock poisoning, acutely poisoned animals should be given supportive treatment as necessary. Stressing the animal should be kept to a minimum. If the hemlock has been recently consumed, saline cathartics and activated charcoal are beneficial in removing the plant from the gastrointestinal tract. A dilute tannic acid solution administered via stomach tube may help to detoxify the hemlock alkaloids. All hemlock should be removed from pastures to which animals have access. Destroying the plants by mowing or with herbicides before the seed stage greatly reduces the chances of hemlock becoming an invasive weed and a problem to livestock.

Water Hemlock, Cowbane, Poison Parsnip

Cicuta douglasii
***Cicuta maculata* (Spotted water hemlock)** - Apiaceae (Parsley family)

Habitat

Water hemlocks, as the name suggests, prefer wet meadows, riverbanks, irrigation ditches, and water edges, often growing with their roots underwater. *Cicuta maculata* is found predominantly in the eastern United States; *C. douglasii* occurs more commonly in the western states (Fig. 1-23a). Water hemlocks may be found growing at altitudes as high as 8000 feet (2,438 meters) above sea level. At least eight poorly differentiated species of water hemlock occur in North America and all should be considered highly toxic [228,229].

Figure 1-23A. Water hemlock (*Cicuta douglasii*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Synonyms for water hemlock include musquash root, muskrat weed, fever root, mock-eel root, and beaver poison.

Description

Water hemlock is a stout, erect, hairless, perennial or biennial growing to a height of 4 to 6 feet (1 to 2 meters) from a condensed bundle of two to eight thick tuberous (parsnip-like) roots (Fig. 1-23b). Flowers and seeds are produced in the second year of growth. At the base of the hollow stem are a series of tightly grouped partitions that may contain an acrid, yellow fluid (Fig. 1-23c). The leaves are alternate, one to three times pinnate, the leaflets are 2 to 4 inches (3 to 10 cm) long, linear-lancelate to ovate-lancelate with toothed edges (Fig. 1-23d). The flowers are white in the form of a loose, compound umbel. The flower is supported by a whorl (involucre) of a few narrow bracts. There is also an involucel of several narrow bractlets. A disc-like swelling (stylopodium) is present at the base of the style. The fruits are oval, flattened laterally with prominent ribs.

Figure 1-23B. Water hemlock tuberous roots showing yellow fluid on cut surfaces (*Cicuta douglasii*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-23C. Water hemlock hollow stem with horizontal partitions (*Cicuta douglasii)*. - To view this image in full size go to the IVIS website at www.ivis.org . -

Figure 1-23D. Water hemlock leaf showing veins running to each notch at the leaf's margin (*Cicuta douglasii*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Several other members of the family *Apiaceae (Umbelliferae)* are also toxic to man and animals, including spotted hemlock (*Conium* spp.) and water dropwort (*Oenanthe* spp.). Cowbane (*Oxypolis fendleri*), found growing along alpine streams, closely resembles water hemlock but is a much smaller, slender plant with a few, toothed leaves. (The name hemlock is also given to the evergreen trees of the genus *Tsuga*, which are not considered toxic).

Principal Toxin

Cicutoxin ($C_{17}H_{22}O_2$), a highly unsaturated (diol), is one of the most toxic naturally occurring plant compounds known [230,231]. The alcohol derivative, cicutol ($C_{17}H_{22}O$), is relatively nontoxic [232]. The toxin is concentrated in the tuberous roots, but all parts of the plant including the fluid found in the hollow stems are toxic. The roots are highly poisonous at all times, and livestock consuming the root usually die. The roots are easily pulled up because the ground in which the plants grow is usually wet. Mature plants often have a prominent root crown that protrudes above ground making it accessible to animals even in winter. The newly emerging plant in the spring is the most toxic, whereas the mature leaves in late summer seem to have minimal toxicity to cattle that eat them. The dry stems are minimally toxic.

All animals, including humans, can be fatally poisoned by eating as little as 50 to 110 mg/kg body weight of the green water hemlock plant [228,233-237]. The lethal dose of fresh green water hemlock (*C. douglasii*) is 2 oz for adult sheep, 12 oz for adult cattle, and 8 oz for adult horses [233]. Sheep dosed with ground water hemlock tubers with 1.4, 2.8, and 6.4 g/kg of tuber developed signs ranging from mild increase in salivation, nervousness, and a few muscular tremors without seizures at the lowest dose, to seizures followed by recovery at a dose of 2.8 g/kg. Those that received 6.4 g/kg of tuber developed severe seizures and died 90 minutes after dosing [232].

Fatalities have occurred in children who have sucked on the hollow stems of water hemlock. In 1984, a river tour guide died after mistaking the tuberous roots of water hemlock for the edible root of common yampa (*Perideridia gairdneri*). The tuberous roots have also been mistaken for edible wild parsnip (*Pastinaca sativa*).

Clinical Signs

Cicutoxin is a potent neurotoxin capable of causing rapid onset of muscle tremors and violent convulsions [235]. Death often occurs in a matter of 2 to 3 hours after a lethal dose of water hemlock has been consumed. Excessive salivation, vigorous chewing movements, teeth grinding, frequent urination, and defecation are common. Depending on the quantity of toxin absorbed, animals become ataxic and uncoordinated and develop grand mal seizures [5]. During the convulsions, animals may chew off their tongue. Signs may start within an hour of eating the plant or tuberous roots and progress rapidly to convulsive seizures and lateral recumbency. Poisoned animals have dilated pupils and progress to a state of coma, before dying from respiratory paralysis and asphyxia. Death may occur in about 90 minutes after ingestion of a lethal dose [232]. If animals consume a sublethal dose, they will recover if not stressed.

Sheep that die acutely from water hemlock poisoning show no gross postmortem lesions. Because of the rapid lethal effects of the cicutoxin, pieces of the water hemlock root may be found in the esophageal groove and not in the rumen at post mortem examination. Multifocal, diffuse myocardial degeneration is characteristic in acute poisoning [232]. In less acute poisoning muscle degeneration is also seen in skeletal muscle and results from the severity of the seizures. The serum enzymes lactic dehydrogenase, aspartate transaminase, and creatine kinase markedly increase in animals that have frequent seizures of long duration [232].

Treatment

There is no specific antidote for cicutoxin. Studies in sheep have shown that the intravenous administration of sodium pentobarbital at the onset of seizures prevented lethal cardiac and skeletal muscle degeneration and resulted in complete recovery [232]. When possible, therefore, early treatment should consist of heavy sedation of poisoned animals with sodium pentobarbital to reduce the severity of the convulsions. Laxatives may be beneficial in removing the plant from the digestive system. Vomiting should be induced in dogs and people suspected of eating water hemlock. Artificial respiration should be given where possible if respiratory failure occurs. In cattle that are actually observed eating the water hemlock roots, it may be life saving to immediately perform a rumenotomy to remove the plant parts from the digestive system before the toxin is absorbed. Dilute acetic acid (vinegar) administered via stomach tube in cattle may be beneficial in neutralizing the toxin if administered very soon after the plant has been consumed.

Control of Water Hemlock

The fact that water hemlock is so poisonous makes it important to remove all water hemlock plants from livestock enclosures. The plant spreads primarily by seed which is often disseminated by water. The plant should be dug up and burned where possible. Spraying water hemlock with herbicide will kill the plant, but it should be remembered that the herbicide may make the plant more palatable before it dies off.

Copperweed

Oxytenia acerosa - Asteraceae (Composite family)

Habitat

Copperweed is an indigenous plant of the semiarid alkaline soils of southwest North America. It is often found locally in dry streambeds and canyons.

Description

Copperweed is an erect, bushy, perennial, with woody stems growing 3 to 5 feet tall (Fig. 1-24). Leaves are alternate, hairy, and irregularly divided into needle-like segments. The individual flowers are small, yellow, or white and produced in dense terminal panicles that give it the appearance of a goldenrod.

Figure 1-24. Copperweed (*Oxytenia acerosa*). - To view this image in full size go to the IVIS website at www.ivis.org . -

Principal Toxin

The toxin has not been defined. About 0.5 percent of an animal's body weight of the green plant is a lethal dose [238]. The plant remains toxic at all times, even when dry. Cattle and sheep are susceptible to poisoning and eat the plant when other forage is unavailable.

Clinical Signs

Cattle, and less often sheep, stop eating after ingesting copperweed and become markedly depressed with some animals showing nervousness. Affected animals become comatose, and die 1 to 3 days after the onset of signs. Liver and kidney degeneration occur in fatally poisoned animals [238].

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