Poisonous native range plants

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Plant poisoning is a common problem throughout North America, causing significant economic losses not only through death loss, but through the costs associated with reproductive loss, poor growth rates, herbicides, etc. Through good pasture management, recognizing toxic plants, and by understanding the effects of toxins on animals, plant poisoning can be largely avoided. Plants contain a variety of toxic compounds that help to deter herbivores and insects from eating them. A classic example of this is milkweed (*Asclepias* species) that contains a milky sap that is an irritant and therefore distasteful, and is also poisonous. Other compounds found in plants that may be toxic to animals are normal components of plants essential for plant growth. Nitrates and cyanogenic glycosides, for example, are found in a wide variety of plants and are essential in the formation of plant protein. Yet another reason some plants such as locoweed (*Astragalus* and *Oxytropis* species) are poisonous is that they have developed a mutually beneficial relationship with specific fungi (endophytes) that, when growing in the plant, produce a toxic alkaloid poisonous to horses and livestock.

There are numerous native range plants that are potentially poisonous to livestock, but rarely is an animal poisoned by eating a few mouthfuls of these plants. This famous quote by Paracelsus summarizes it best. "All things are poison and nothing is without poison; only the dose makes that a thing is no poison." In other words, "the dose makes the poison" Paracelsus (1493-1541). Livestock poisoning occurs most often when rangeland is overgrazed and animals are forced to eat whatever is available. Feeding hay that is full of weeds can have similar repercussions.

Plants with the potential to cause sudden death

Plants causing sudden or acute death do so within a few hours of the onset of clinical signs, and the animals are often found dead before anything is noticeably wrong. Fortunately, there are relatively few plants capable of causing acute death. Native plants that can cause sudden death in animals include water hemlock, some species of milkweed, death camas, larkspur, and choke cherry. Poison hemlock is an invasive weed that, if eaten before it matures, can cause fatalities.

Water Hemlock – *Cicuta* spp.

There are two species of *Cicuta* in the family Apiaceae that are native to the temperate areas of North America. These perennial herbaceous plants prefer wet/marshy environments, growing up to 4-6 feet at maturity. Water hemlock has hollow, compartmentalized stems. Leaves are compound, alternate, pinnate with leaflets 5-8 cm long and 1-2 cm wide, with the leaf veins ending in the notches of the toothed leaf edges. The flowers are compound and umbellate with many small, white flowers. The tuberous roots when cut exude a pungent yellowish fluid that is highly toxic.

The potential for water hemlock poisoning is high in livestock and horses grazing pastures that have marshy areas, or where animals have access to stream or river banks where the plants tend to grow. Animals find water hemlock palatable, especially the new leaves in the spring.

The roots and seeds of water hemlock contain highly toxic cicutoxin. At least 11 C17-polyacetylenes have been isolated from water hemlock. These compounds act as gamma-aminobutyric acid (GABA)

antagonists in the central nervous system, causing nerve depolarization, leading to severe seizures, respiratory failure and death. The new leaves in the spring are the most toxic, whereas the mature leaves and dry stems are minimally toxic. Horses and livestock are most likely to be poisoned by water hemlock when grazing in marshy areas and along river and stream banks. Cicutoxin is rapidly absorbed through the skin and mucous membranes of the mouth and digestive tract to the extent that the tuberous root parts are often still present in the esophagus at necropsy. The lethal dose of water hemlock roots is less than 0.5% body weight.

Poison or Spotted Hemlock – *Conium maculatum*

Poison hemlock is native to Europe, Asia and North Africa, and has become a common invasive weed in North and South America commonly found growing in pastures, along roadsides and disturbed sites and waste areas. Poison hemlock causes acute fatal poisoning of humans and domestic animals, although horses are less susceptible. The plant is also teratogenic, causing fetal deformities if grazed by pregnant animals in early gestation.

Poison hemlock is an erect biennial or perennial growing 4 to 6 feet tall. The hairless, branching stems are hollow, with purple spots or streaks especially near the base. The leaves are alternate, three to four times pinnately dissected, coarsely toothed with a fern-like appearance. The terminal inflorescence is a compound, flat topped, loose umbel of multiple, small, white flowers with 5 petals. The plant has a carrot-like tap root.

Poison hemlock contains many piperidine alkaloids including coniine, and gamma-coniceine, that act on the central nervous system nicotinic acetylcholine receptors, blocking the neuromuscular junction in a manner similar to curare. The alkaloids are present in all parts of the green plant, and are reduced as the plant matures and dries. However, hay containing large quantities of poison hemlock can cause significant death loss. A lethal dose of the green plant for cattle ranges from 0.2-0.5% of their body weight. The quantity of alkaloids present in poison hemlock varies considerably with growing conditions. Horses may show colic episodes in addition to symptoms of ataxia, incoordination, muscular weakness, respiratory paralysis, prostration and death seen in other species.

An entirely different syndrome occurs when pregnant animals consume *Conium maculatum* during the first trimester of pregnancy. The pregnant animal is usually unaffected, but the developing fetus may be born with a variety of malformations, including arthrogryposis and cleft palate.

Plants Containing Cyanogenic Glycosides

Choke Cherries – *Prunus virginiana*
The genus Prunus contains more than 200 species, and many hybrids and varieties that have the potential to cause cyanide poisoning in livestock and occasionally horses. The concentration of cyanogenic glycosides in plants varies with the stage of growth, time of year, soil mineral and moisture content, and plant stressors such as drought and frost damage. Cool moist growing conditions enhance the conversion of nitrate to amino acids and cyanogenic glycosides instead of plant protein.

Arrow Grass – *Triglochin maritima*

Cyanogenic glycosides in plants are broken down by two plant enzymes to release hydrogen cyanide (HCN, prussic acid). This process is facilitated by a neutral or slightly alkaline pH, while in acidic conditions the enzymes are inhibited. This explains why ruminants with an alkaline stomach suffer from cyanide poisoning, while horses and pigs with highly acidic stomach contents are not nearly as susceptible to HCN poisoning from plants.

The lethal dose of new leaves from choke cherry (*Prunus* spp.) and service berry (*Amelanchier* spp.) is in the range of 1.0 to 4.0 g of plant material per kg body weight. In general, plant material containing more than 200ppm (20mg/100g of plant) of cyanogenic glycosides has potential for poisoning. The HCN reacts

with ferric iron (Fe^{+++}) in the cytochrome oxidase in the red blood cells to immediately stop cellular respiration. The formation of the cyanide-cytochrome oxidase complex prevents the release of oxygen from the red blood cells, thus causing cellular anoxia and death.

Sudden death of an animal may be the only observed sign of acute cyanide poisoning. Early signs of poisoning include difficulty in breathing, including open mouth breathing, staggering and collapse. Frequent urination and paddling may also be observed prior to death. Any stress on the animal will hasten death. The mucous membranes may be bright red/pink and venous blood cherry-red in color, but as the animal becomes deprived of oxygen, cyanosis is likely to develop.

Sorghum Poisoning

Although horses are rarely fatally poisoned by plants containing cyanogenic compounds, horses, cattle and sheep can develop a syndrome of posterior ataxia and urinary incontinence after consuming sorghum hay for a period of weeks. Degeneration of the white matter of the spinal cord due to the chronic exposure of nitrile compounds in the sorghum results in hind leg ataxia, tail paralysis, and urinary bladder paralysis leading to incontinence. Loss of rectal tone can result in fecal impaction. The degenerative changes in the nerves are irreversible. Fetal limb deformities have been reported in foals and calves whose dams are fed sorghums during pregnancy.

Milkweed – *Asclepias* **species**

Milkweeds belong to the genus *Asclepias* in the family Apocynaceae, with over a hundred species of *Asclepias* in North America occurring in a variety of habitats. Relatively few species of milkweed are a problem to animals. Most poisoning from milkweeds has occurred in sheep, goats, cattle, horses, and domestic fowl, especially when other forages are scarce or milkweeds are incorporated into hay.

Milkweeds are erect or decumbent, branched or unbranched perennial herbs that have either broad leaves (3-6 inches wide) or narrow linear leaves less than 0.5 inch wide, arranged either alternately or in whorls. Most species contain a milky sap or latex. The flowers are produced in terminal or axillary umbels, the color of the flowers varying among species from greenish white to orange and red. The characteristic follicle or seed pod contains many seeds, each with a tuft of silky white hairs that aid in their wind-borne dispersal.

Milkweeds contain a variety of toxins that either affect the heart and digestive system or the nervous system. In general, the most poisonous of the milkweeds are those with narrow leaves. The more toxic milkweeds include western whorled milkweed (*A.subverticillata*), woollypod milkweed (*A. eriocarpa*), and Mexican whorled milkweed (*A. fascicularis*). The principle toxins in the narrow leafed milkweeds are cardenolides that affect the heart and digestive tract (Joubert 1989). The primary effect of the cardenolides is to inhibit Na+/K+-ATPase, thus affecting the transport of Na^+ and K^+ across cell membranes and causing profound effects on heart function. Some species of narrow leafed milkweeds contain compounds that affect the nervous system with no cardiotoxic effects. The highest concentration of the cardenolides is found in the milky sap, but all parts of the plant are toxic. Milkweeds remain toxic when dried, and therefore are a high risk to animals eating the dried plants in hay. As little as 1.0 kg of green milkweed plant material is lethal to an adult horse. Milkweeds are poisonous when green or dried in hay.

Animals may be found dead without any prior symptoms in severe cases. Clinical signs usually start about 12 hours after consumption of the milkweed and are characterized by marked depression, labored and slow respirations. Horses may show colic and diarrhea. Heart irregularity is not common despite the fact that the cardenolides act like digitalis. The neurotoxic effects of the narrow leafed milkweeds are

characterized by muscular tremors, staggering gait, a weak, rapid pulse, and dilated pupils. After frequent attempts to rise, animals eventually become recumbent with violent seizures and respiratory failure.

Whenever sudden death is the presenting sign, plants such as water hemlock, poison hemlock, milkweeds, and choke cherry should be considered. Ornamental plants such as yew and oleander should also be considered in a differential diagnosis of sudden death.

Death Camas
There are 13 species of death camas (*Zigadenus* spp.) native to North America. Animals that are most commonly poisoned by death camas include sheep, cattle, horses, and alpacas. Deer and other wild ruminants may be more tolerant of the toxic effects of death camas. Human poisoning has occurred when the death camas bulbs were mistaken for plants such as onions (*Allium* spp.) or camas lily (*Camassia quamash*).
Death camas is a perennial, hairless, grass-like plant with linear, V-shaped, parallel-veined leaves arising from an onion-like bulb. (The leaves are not hollow like those of onions, nor do they have an onion odor.) The inflorescence, a terminal raceme or panicle, has small, perfect, greenish-white to yellow flowers.

All parts of the plant are toxic, especially the new growth and the bulbs. The steroidal alkaloids act by binding to Na^+ channels that allows increased movement of Na^+, K^+ and Ca^{2+} through cell membranes. Death results from central respiratory paralysis.

Recent research has shown that the simultaneous consumption of low larkspur *(Delphinium nuttallianum)* and death camas that grow in the same habitat and time of year will have an additive effect, thereby increasing the toxic effects of zygacine.

Most livestock poisoning occurs in the springtime when the succulent shoots of the death camas emerge before the grasses and other plants, thus making it palatable to hungry animals. Rarely are the bulbs consumed by animals, as the bulb is usually 6-8 inches underground.

Sheep show signs of poisoning after eating as little as 0.5 lb of the green plants: excessive salivation, vomiting, muscular weakness, ataxia, dyspnea and staggering gait leading to recumbency and prostration. Convulsions, coma, and death occur rapidly in sheep eating 2 to 2.5 lbs of green plant per 100 lbs body weight.

There is no specific treatment for death camas poisoning. Supportive therapy with intravenous electrolytes to counter the hypotension and bradycardia induced by the alkaloids is indicated, and activated charcoal via stomach tube can reduce the absorption of the alkaloids.

Larkspur – *Delphinium* spp.
Larkspurs (*Delphinium* species) are a major cause of fatal plant poisoning of cattle in the western United States, with an estimated annual cost exceeding $234 million. Cattle losses to larkspur poisoning range from 2-10% per year in the western states. There are at least 60 species of larkspur found throughout North America, with most cattle poisoning attributed to *D. barbeyi, D. bicolor, D. geyeri, D. glaucescens, D. glaucum, D. nuttallianum, D. occidentale, D. tricorne, and D. virescens*. However, all larkspurs are potentially poisonous. Larkspurs are often grouped into tall and low varieties according to their growth habit. Tall larkspurs (*D. barbeyi, D. occidentale,* and *D. glaucum*) grow in deep, moist, highly organic soils at high altitudes in montane forests, often reaching 7 feet in height. The plants emerge as snows recede and form perennial, dense stands. Low larkspurs (*D. nutallianum*, *D. nelsoni*, *D. andersonii* and *D. virescens)* grow at lower elevations in drier rangeland, seldom exceeding 2-3 feet in height. Foothills larkspur (*D. geyeri*) is intermediate in its growth habit, attaining a height of 3 to 4 feet when in flower.

Delphinium species, members of the Ranunculaceae (buttercup) family, are generally erect perennials with hollow stems and basally clustered, alternate, palmate lobed leaves. Depending on the species, the plants range in height from 8 inches to 6 feet. The flowers are produced in racemes, generally blue to purple or white in color, each with five sepals and four petals; the upper sepal and pair of petals are elongated to form a characteristic spur that protrudes behind the petals. The seed pods are three to five-celled, and when ripe, split open to release numerous dark brown seeds.

Larkspurs contain many toxic and nontoxic norditerpenoid alkaloids, 40 of which have been identified in the nine larkspur species most frequently associated with poisoning in cattle. Young rapidly growing larkspur plants have the highest concentration of alkaloids in their leaves. The most toxic alkaloids are 14-deactylnudicauline and methyllycaconitine (MLA). The foothills larkspur (*D. geyeri*) and the low larkspur (*D. nutallianum*) contain a different highly toxic alkaloid nudicauline. The toxicity of the different larkspur species is most likely due to the combined effects of the alkaloids present in the plants. The alkaloids act on the postsynaptic nicotinic and cholinergic receptors at the neuromuscular junction, causing muscle weakness and paralysis. The action of the larkspur alkaloids on the cholinergic receptors varies among species; cattle are more susceptible to the alkaloids, while sheep are refractory to larkspur poisoning. Fatalities in animals are increased when other plant alkaloids such as those in death camas (*Zygadenus* spp.) are eaten concurrently.

Cattle are most susceptible to larkspur poisoning, while sheep tolerate about five times the amount of larkspur alkaloids that would be fatal to cattle. Horses are rarely affected by larkspur unless they are in a situation where they eat sufficient quantities of the plant and are then stressed. Although there is little documentation of larkspur poisoning in goats or camelids, they are more than likely to be affected, especially if subjected to stress. The amount of tall larkspur that a cow must eat to be fatally poisoned depends on the amount and combination of alkaloids present in the plant. It has been shown that the total concentration of anthranoyllycoctonine (MSAL)-type alkaloids and 7, 8-methylenedioxylycoctonine (MDL)-type alkaloids should be determined when assessing the relative toxicity of tall larkspur populations.

Larkspur is palatable to cattle, especially during a 'toxic window' in the plants' growth cycle when the plants are initiating flower spikes and until the plants go to seed.

Sudden death in cattle is often the first indication of larkspur poisoning noticed by the owner. Cattle frequently die within 3 to 4 hours of consuming a lethal dose of larkspur. Poisoned cattle initially show nervousness, increased excitability, muscle tremors, stiffness, staggering, and a base-wide stance. The fore limbs may be affected first, causing the animal to kneel before 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, rumen bloat and constipation are common clinical findings. Similar milder signs of poisoning occur in horses, sheep, and goats that have eaten larkspur, and fewer deaths are likely.

Bloat is common in larkspur poisoning due to the rumen microorganisms rapidly fermenting the green plant, thereby increasing the rate of gas production in the rumen, and because of the neuromuscular blocking effect of the alkaloids impairing eructation. Cattle frequently die within 3 to 4 hours of consuming a lethal dose of larkspur, with bloat often being the immediate cause of death**.**

Specific gross postmortem lesions are absent 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 larkspur in the animal's rumen, from the history, and by finding evidence of the animal having access to

larkspur. Fresh rumen contents or feces can be submitted to diagnostic laboratories for microscopic identification of the characteristic plant cell structure of larkspurs.

It is important to avoid stressing an animal poisoned by larkspur, as this will frequently cause death. Rumen bloat in a down animal should be treated before doing anything else! The animal should be placed in sternal recumbency, and if necessary, the bloat relieved by passing a stomach tube or by trocarization of the rumen. Physostigmine (0.04 to 0.08 mg/kg body weight) is effective if given intravenously to cattle in the early staggering phase of larkspur poisoning. Treatment should be repeated as needed until clinical signs have ceased. Neostigmine is an alternative, readily available anticholinesterase effective in reversing some of the effects of the larkspur alkaloids. Neostigmine (0.02 to 0.04 mg/kg) administered intramuscularly is less stressful. Relapse of clinical signs will require repeated doses of physostigmine or neostigmine.

Research has shown the alkaloid content of tall larkspur species is highest preflowering, while the palatability of the plants increases as flower spikes are initiated, and declines after seed pods are mature. Knowing this "toxic window" in the life cycle of tall larkspurs when cattle find tall larkspur increasingly palatable, and the plants contain significant levels of toxic alkaloids, it is possible to move cattle from the larkspur areas, and return them once the larkspur has formed seed pods. The alkaloid content of the plants declines after seed pod formation, although the seed contain high levels of alkaloids. Sheep 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. Large bands of sheep can therefore be used as biological controls to reduce the biomass of larkspur before cattle are introduced to the larkspur rangelands.

Selective use of certain herbicides can be used to control large stands of larkspur, thereby reducing the risk to cattle. Herbicides that have been shown to be effective in controlling tall larkspur include metsulfuron, picloram, while 2,4-D is effective in controlling preflowering low larkspur species. Since herbicides can increase the palatability of larkspur, livestock should not be allowed to graze the plants until they are brown and dried.

Locoweeds, vetches, milk vetches – *Astragalus* and *Oxytropis* spp.

The term locoweed refers to members of the genera *Astragalus* and *Oxytropis* in the family Fabaceae. Locoweeds are found predominantly in western North America. At least 2000 species of *Astragalus* are found globally; however, relatively few are known to be toxic. A few species of locoweed have long been recognized as important poisonous plants affecting horses and livestock, causing more overall economic losses to the livestock industry than any other group of plants.

There are at least 401 species and 207 varieties of *Astragalus,* and 22 species of *Oxytropis* in the United States, Canada and Mexico. Locoweed populations vary with the amount of rainfall, and in times of drought become virtually non-existent. However, the soil seed bank of many *Oxytropis* and *Astragalus* species can be viable for at least 50 years, germinating when sufficient moisture is present.

Astragalus species (milkvetches) can be annuals or perennials, with erect or sprawling stems. The leaves are generally pinnate with as many as 20 leaflets, with a terminal leaflet. The flowers are pea-like and are produced on stems (racemes) arising from leaf axils. Each flower has 5 fused sepals and 5 petals ranging in color from white to blue to purple. The keels are usually rounded and not beaked. The fruits are leguminous pods of varying shape and size, each pod containing many seeds.

Oxytropis species (point locoweed, poison vetch) are perennials, arising from a taproot, and unlike the *Astragalus,* are stemless and do not branch. Leaves are pinnately compound with up to 41 leaflets, one of which is terminal. Flowers are pea-like and are produced on stalks above the leaves. Each flower has 5

fused sepals and 5 petals, the keel usually having a distinct beak. Color ranges from white to yellow and shades of pink and purple. Seeds are produced in cylindrical, pea-like pods.

Those species that are most often associated with locoism include *Astragalus emoryanus, A. lentigenosus, A. mollissimus, A. missouriensis, A. nothoxys, A. pubentissimus, A. wootonii, Oxytropis besseyi, O. campestri, O. lambertii,* and *O. sericea*. Some species of *Astragalus* can produce toxicity through the accumulation of selenium, or they may contain other neurotoxins called nitrotoxins. Some species (*Astragalus cicer* and A. *nuttalianus*) are not toxic and have been introduced as useful forages for livestock.

Locoism:
Some 21 species of *Astragalus* and *Oxytropis* contain the toxic alkaloid swainsonine produced by an endophytic fungus *Undifilum oxytropis* (previously called *Embellisia oxytropis*). The endophyte has a mutually beneficial association with locoweeds; the infected plants are unaffected by the endophyte and the plants benefit from the presence of a toxin that helps deter herbivory. *Astragalus* and *Oxytropis* species that do not have the endophyte do not contain swainsonine, and therefore are not toxic. The highest concentrations of swainsonine are generally found in *Astragalus wootonii* (0.37%), *A. lentigenosus* and *A. mollissimus* (0.16-0.18%), and *Oxytropis sericea* (0.04%).

Horses are particularly susceptible to locoweed poisoning, but cattle, sheep, goats, deer and elk are commonly affected. Animals find locoweeds palatable and will graze the green plants readily in the spring before the grasses emerge from dormancy. Swainsonine is an indolizidine alkaloid that inhibits the cellular enzymes alpha-mannosidase and mannosidases II that are essential in the metabolism of complex glycoproteins, and result in the accumulation of intracellular oligosaccharides. In essence, swainsonine induces a lysosomal storage disease that is very similar to bovine congenital mannosidosis. The accumulation of the oligosaccharides in cells and the production of abnormal glycoproteins in cells affect the function of many organs, especially the brain and reproductive organs.

Swainsonine is readily absorbed from the rumen and intestinal tract, and is distributed to all tissues including the brain, reproductive organs and the fetus in utero. Swainsonine is also passed through the milk of lactating animals and will affect the suckling young. Swainsonine has a short half-life in the blood in the order of 20 hours, which means it is undetectable in about 5 days.

Nitrotoxin Poisoning from Astragalus species – 'Cracker Heels':
Of the many species of *Astragalus* in North America, about half contain nitrotoxins and not swainsonine. The two most common nitrotoxins found in these plants are 3-nitropropionic acid (3-NPA), and miserotoxin, 3-nitropropanol (3-NPOH). Both compounds are usually not present in the same plant, but a few species such as *Astragalus emoryanus* may contain both swainsonine and nitrotoxins. All livestock and horses are susceptible to nitrotoxin poisoning, cattle being the most commonly affected. The nitrotoxin content of milk vetches varies with the species and the stage of growth, being highest during the flower and seed pod stage. Cattle fed emory milkvetch at the rate of 2.2 g dry weight per kg body weight daily develop signs of poisoning in 3-4 days.

Once absorbed from the gastrointestinal tract, 3-NPOH is converted to 3-NPA in the liver (Muir et al. 1984). The 3-NPA appears to be the primary neurotoxin that causes irreversible inhibition of mitochondrial succinic dehydrogenase, which ultimately blocks cellular energy, causing basal ganglia and myelin degeneration, resulting in neurological clinical signs. In cattle, after eating the nitrotoxin-containing *Astragalus* for a week or more, weakness, ataxia, muscle tremors, and depression, progress to recumbency and death. The hindquarters of the animal are usually most severely affected, resulting in a wobbly gait and clicking together of the hooves as the animal walks – giving the syndrome the name "cracker heels."

Signs of Locoism:
Horses exhibit the most distinctive signs of locoism, characterized by changes in normal behavior including marked depression, drowsiness, blindness, abnormal gaits, marked difficult in walking and backing-up. Abnormal attempts at chewing food and spastic jaw movements may be observed.

Handling affected horses tends to produce marked abnormal behavior, especially if the horse is led by a halter. Affected horses show unpredictable behavior such as rearing on hind legs and falling over backwards, and periods of sudden and extreme excitement. Riding locoed horses is dangerous. If clinical signs associated with locoweed poisoning are recognized early and the horse removed from the locoweed, clinical improvement will occur, but it may take many months for the residual abnormal behavior to resolve.

Locoed cattle may show minimal neurological signs as compared to horses. Cattle are generally depressed, eat poorly and loose body condition. Some cattle may have difficulty in eating, with exaggerated chewing movements. Excessive head shaking is common. Some locoed cattle become aggressive when handled or processed through a chute. The greatest impact of locoweed on cattle is on the reproductive system. Irregular estrus cycles, fetal resorption, abortions, weak calves at birth, poor suckling ability, and congenitally deformed calves with arthrogryposis and contracted tendons are common in pregnant cows. Congenital deformities may also be attributed to other toxic plants including lupine (*Lupinus* spp.), poison hemlock (*Conium maculatum*) and tobacco (*Nicotiana* spp.). In some cases, hydrops amnion is marked and ultimately causes abortion, uterine infection and a poor prognosis for future fertility. Bulls may show decreased libido, abnormal spermatogenesis, decreased sperm mobility and increased number of sperm abnormalities that decrease fertility.

Cattle ranged at high altitude and grazing locoweed are also predisposed to developing congestive right heart failure (high mountain disease). There is also a higher incidence of disease, and a poor response to vaccines because of the compromised immune system.

Locoed sheep and goats show relatively mild signs as compared to affected cattle. Loss of direction and flocking instincts, increased nervousness, high stepping gaits with head held high, and occasionally aggressiveness may be seen. Over time, weight loss, weakness, loss of wool and recumbency precede death. Rams show decreased fertility and semen quality.

Diagnosis of locoweed poisoning if the plants have been eaten for a period of several weeks is based on the histological findings of cytoplasmic vacuolization in cells of many tissues including the brain and spinal cord, thymus, lymph nodes, lungs, liver, intestines, kidneys and reproductive organs. Elevations in serum aspartate aminotransferase and alkaline phosphatase, with decreases in serum iron, transferrin and thyroid hormones can be seen in locoed animals. Vacuoles in the cytoplasm of peripheral lymphocytes in the early stages of locoweed poisoning are unique to locoweed toxicity. However, once animals stop eating locoweed, the vacuoles in the cells disappear after a few weeks. Vacuolation throughout the central and peripheral nervous system is characteristic. In horses the degenerated Purkinge cells are replaced by glial cells, which possibly explains the permanent nature of the disease in horses.

Prevention:
Horses and livestock should not be allowed access to locoweeds in the early spring when other forages are unavailable. Since locoweeds are palatable and nutritious and animals will eat them readily, it is important to keep animals out of the locoweed until there are other grasses available for them to eat. Establishing safe or locoweed-free pastures or areas where animals can be moved to while locoweed is most palatable – in its pre-flowering stage and up to when it is in bloom – is an effective strategy. Locoweed-free pastures can be created and maintained through the judicious use of herbicides

At the end of the growing season, the dried locoweed stems remain toxic and a source of poisoning if there is little else to eat. Late summer rains may also encourage new growth that can enhance the palatability of the locoweed. Overgrazing or overstocking pastures will increase the potential for locoweed poisoning. Livestock should be closely observed on a regular basis to identify animals that preferentially eat locoweed and remove them from the herd. It is well known that through a process of social facilitation, animals that eat locoweeds teach other animals to do the same. This simple management practice can keep the number of animals in a herd that eat locoweed to a minimum.

Effective herbicides for control of locoweeds include clopyralid, picloram, and metsulfuron. All herbicides should be applied according to manufacturer's recommendations.

Groundsel – *Senecio* spp.
In general, *Senecio* are recognizable by the single layer of touching, but not overlapping, greenish bracts surrounding the yellow ray flowers. *Senecio* spp. have alternate leaves, varying from lanceolate to ovate, dentate and often irregularly and deeply pinnately divided. The composite flower heads are flattened terminal clusters with showy yellow ray flowers. Each seed has a tuft of white hairs that aids in wind dissemination.

Pyrrolizidine alkaloids (PA) are the principal toxins in senecios. The quantity of alkaloid in Senecio spp. varies with the species and stage of growth, the young pre-flowering plant being most toxic. Horses and cattle are most frequently affected after eating small quantities of Senecio over a period of 3 weeks or more. As an estimation, it requires a dose of 2% of an animal's body weight of dry plants over a 3-week period to cause poisoning. The cumulative effects of PAs on the liver may take 6 or more months to reach the point where 80% or more of the liver is affected and clinical signs of liver disease become evident.

In addition to the groundsels, Hound's tongue (*Cynoglossum officinale*), Blue weed (*Echium vulgare*) and Rattlepod (*Crotolaria spp.*) are important sources of pyrrolizidine alkaloid poisoning.

At least 350 separate PAs have been identified in plants, with about half of them being toxic to the liver and lungs, and some are carcinogenic. Horses and cattle are most susceptible to the toxic effects of the PAs, while sheep and goats are resistant to poisoning from PAs because their livers slowly metabolize the PAs to the toxic reactive pyrroles. The small ruminant rumen is more efficient in degrading PAs through microbial action. The susceptibility to PAs for various animals are: pigs =1, chickens =5, cattle and horses =14, and sheep and goats =200.

Generally, the highest concentrations of PAs are in the flowers and seeds, but all parts of the plants contain the alkaloids at all stages of growth. The pyrrolizidine alkaloids are metabolized by liver oxidases and P450 enzymes into reactive pyrroles, which are potent alkylating agents that react with cell nucleic acids and proteins inhibiting mitosis, and leading to hepatotoxicity and genotoxicity (Li et al. 2011). Typically PAs cause cellular swelling of hepatocytes, megalocytosis, bile duct proliferation and fibrosis, resulting in liver failure.

Horses and cattle are most commonly affected by plants containing PAs when they are forced to eat the plants when other forages are scarce or pastures are heavily invaded by these plants. Weedy hay can also be the source of PAs, and if fed for prolonged periods, will result in the cumulative toxicity of the PAs. The PA retain toxicity in hay for many months but in silage there is some degradation.

Of the 1500 or more species of Senecio occurring worldwide, at least 70 species are present in North America. The genus *Senecio* is very varied, with some being annuals, perennials, vines, shrubs and small trees. Some have very succulent leaves and bulbous stems. The diversity of the genus has resulted in some of the *Senecio* being moved to a different genus, *Packera.*

In general, the plants have erect, branching stems arising from fibrous roots. The leaves are varied but are simple, alternate, some with smooth edges, others toothed, lobed or pinnate. Flowers are usually produced at the ends of branches in clusters, with distinct ray flowers, and many disc flowers in the center. Flower color is generally yellow, but some species are white, a few orang-red. The seeds are cylindrical achenes surmounted by a pappus of white hairs that facilitate wind dispersal.

Habitat and Distribution:
Native *Senecio* species are adapted to a wide range of ecological zones ranging from high altitude mountainous ranges to prairies, and throughout most states. Introduced species such as *Senecio jacobaea* and *S. vulgaris* have spread across North America, becoming invasive weeds especially in the West Coast states. Disturbed sites, waste places, and roadsides are often common sites for the *Senecio* species.

Principle toxin:
Multiple pyrrolizidine alkaloids have been identified in *Senecio* species, the most toxic of which is seneciocine. Both the free base and the N-oxides of the alkaloids are toxic. Not all species of Senecio or *Packera* contain toxic levels of pyrrolizidine alkaloids. At least 25 *Senecio* species in North America are known to contain Pas. The most common toxic species of *Senecio* present in North America include both native (*Senecio flaccidus, S.integerrimus, S. plattensis, S. ridellii, S. spartioides, S. aureus,* and *S.glabellus*) and introduced noxious species (*S. jacobaea, S, vulgaris,* and *S.madagascariensis).* The *Senecio* species that have caused the most problems to livestock include *S. flaccidus, S. ridelli, S. jacobaea* and *S. vulgaris.*

Generally it requires an animal to eat 25-50% of its body weight in green Tansy ragwort over a period of months before extensive liver damage occurs to produce clinical signs of poisoning. Cattle can be fatally poisoned by feeding as little as 0.2 lb. dry weight of *S. jacobaea* per day for 4 weeks, while sheep and goats require 200-300% of their body weight in green tansy ragwort to be fatally poisoned.

Lupinus **spp. – Lupines**

As a large genus of at least 200 species and many hundreds of subspecies or varieties in the family Fabaceae, lupines are found throughout North America. The native species grow in a variety of habitats ranging from high altitude forests to the plains, often growing in rocky, poorly fertile soils. Nebraska lupine (*Lupinus plattensis*) is common from Montana to Texas.

Lupinus spp. are annuals or perennials, with erect branching stems. Leaves are palmate, with long petioles, and up to 17 leaflets. Flowers are produced in terminal spikes, with 5 showy petals, the banner petal being most prominent, the lower petals forming a distinct keel. Petal color varies from blue to purple, to white or yellow or red, depending on the species and what hybrid. Numerous seeds are produced in typical leguminous pods.

Lupines contain a variety of different alkaloids, some of which are neurotoxic and others cause birth defects (teratogens). In North America most livestock losses are associated with the neurotoxic and teratogenic effects of lupines. In Australia, Spain and other countries that grow lupines for their seeds, the most common problem is a liver disease of sheep and occasionally cattle and horses that graze lupine stubble after the seed is harvested. Lupinosis is the name given to a syndrome associated with the mycotoxins Phomopsin A, B, C produced by the fungus *Diaportha toxica* growing in the stems of lupines. Phomopsins are hepatotoxic in a similar way to pyrrolizidine alkaloids found in *Senecio* spp., *Crotolaria* spp., *Cynoglossum* spp., and various other genera.

Clinical Signs:
Sheep are most commonly affected with lupinosis, but cattle and occasionally horses grazing lupine stubble can develop signs of lupinosis. Affected sheep initially have poor growth weights, and tend to lag

behind the flock as it moves. As the disease progresses, the animals show severe weight loss, icterus, and some show signs of hepatic encephalopathy. Liver enzymes are markedly elevated. Switching the sheep from the dry stubble to green grass can precipitate photosensitization in the sheep. In addition to the liver toxicity of the phomopsins, sheep also develop muscle degeneration. Cattle show similar signs relating to liver disease, but have two phases of the disease: initially a fatty liver syndrome, followed by liver fibrosis.

Selected References

Water Hemlock and Poison Hemlock

Frank, B.S., W.B. Michelson, K.E. Panter, et al. 1995. Ingestion of Poison Hemlock (*Conium maculatum*). Western J Med. 163: 573–574.

Galey, F.D., Holstege, D.M., Fisher, E.G. 1992.Toxicosis in dairy cattle exposed to poison hemlock (*Conium maculatum*) in hay: isolation of Conium alkaloids in plants, hay, and urine. *Journal Veterinary Diagnostic Investigation. 4:60-64.*

Panter, K.E., R.F. Keeler, D.C. Baker. 1988. Toxicoses in livestock from the hemlocks (*Conium* and *Cicuta* spp.). J Animal Sci. 66:2407-2413.

Panter, E., Bunch, D., Keeler, F. 1988 Maternal and fetal toxicity of poison hemlock (*Conium maculatum*) in sheep. *American Journal Veterinary Research* 49, 281–283.

Panter, K.E., Gardner, D.R., Stegelmeier, B.L. et al. 2011. Water hemlock poisoning in cattle: Ingestion of immature *Cicuta maculata* seed as the probable cause. *Toxicon*. 57;157-161.

Reynolds, T. 2005. Hemlock alkaloids from Socrates to poison aloes. *Phytochemistry*.66:1399-1406.

Vetter, J. 2004. Review. Poison hemlock (*Conium maculatum* L.). *Food Chem Toxicol*. 42, 1373−1382.

Prunus species – Cyanide Poisoning
Burrows, G.E., R.J. Tyrl . 2001. *Prunus*. Pages 1063-1065 In: Toxic Plants of North America. (eds G.E Burrows, and R..J. Tyrl) Iowa State University Press, Ames Iowa. 1063-1065.

Knight, A.P., R.G. Walter. 2001. A Guide to Plant Poisoning of Animals in North America. Jackson, Wyoming: Teton New Media, 194-197, 1-14.

Majak,W., R.E. McDiarmid, W.J. Hall. 1981. The cyanide potential of Saskatoon service berry (*Amelanchier alnifolia*) and choke cherry (*Prunus virginiana*). Can J An Sci 61:681.

Arrow Grass
Majak W., McDiarmid R.E., Hall J.W., Van Ryswyk A.L. 1980. : Seasonal variation in the cyanide potential of arrow grass (*Triglochin maritima*). Can J Plant Sci. 60:1235–1241

Milkweeds
Burrows, G.E., R.J. Tyrl . 2001. *Asclepiadaceae*. Pages 125-146 In: Toxic Plants of North America. (eds G.E Burrows, and R..J. Tyrl). Iowa State University Press, Ames Iowa.

Smith, R.A., Scharko, P., Bolin, D., et al. 2000. Intoxication of sheep exposed to Ozark milkweed (*Asclepias viridis* Walter). Vet and Human Toxicol 42:349-350.

Death Camas
Collet, S., Grotelueschen, D., Smith, R., et al. 1996. Deaths of 23 adult cows attributed to intoxication by the alkaloids of *Zigadenus venosus* (meadow death camas). *Agricultural. Practice* 17:5–9.

Smith, R.A., Lewis, D. 1991. Death camas poisoning in cattle. *Veterinary & Human. Toxicology*. 33:615–616.

Larkspur
Green, B.T., Welch, K.D., Gardner, D.R., Stegelmeier, B.L., et al. 2012 Toxicokinetics of norditerpenoid alkaloids from low larkspur (*Delphinium andersonii*) orally administered to cattle. *American Journal of Veterinary Research* 73, 1318-1324.

Green, B.T., Welch, K.D., Gardner, D.R., et al. 2009 Serum elimination profiles of methyllycaconitine and deltaline in cattle following oral administration of larkspur (*Delphinium barbeyi*). *American Journal of Veterinary Research* 70:926-931.

Pfister, J.A., Gardner, D.R., Panter, K.E.,et al 1999 Larkspur (*Delphinium* spp.) poisoning in livestock. *Journal of Natural Toxins* 8:81-94.

Pfister, J.A., Ralphs, M.H., Gardner, D.R., et al 2002. Management of three toxic *Delphinium* species based on alkaloid concentrations. *Biochemical Systematics and Ecology* 30. 129–138.

Pfister, J.A., Gardner, D.R., Stegelmeier, B.L., et al 2003. Kimberly Hackett, Glen Secrist Catastrophic cattle loss to low larkspur (*Delphinium nuttallianum*) in Idaho. *Veterinary and Human Toxicology* 45:137-139.

Welch, K.D., Green, B.T., Gardner, D.R.., et al. 2012. The effect of 7, 8-methylenedioxylycoctonine-type diterpenoid alkaloids on the toxicity of tall larkspur (*Delphinium* spp.) in cattle. *Journal Animal Science* 90: 2394-2401.

Locoweeds
Cook, D., D.R. Gardner, M.H. Ralphs, et al. 2009a. Swainsonine concentrations and endophyte amounts of *Undifilum oxytropis* in different plant parts of *Oxytropis sericea*. *Journal of Chemical Ecology* 35:1272-1278.

James, L.F., Hartley, W.J., Nielsen, D., et al. (1986) Locoweed (Oxytropis sericea) poisoning and congestive heart failure in cattle. *Journal of the American Veterinary Medical Association.* 189:1549-1556.

Pryor, B.M., R. Creamer, R.A. Shoemaker, et al. (2009) *Undifilum*, a new genus for endophytic *Embellisia oxytropis* and parasitic *Helmintosporiuim bornmuelleri* on legumes. *Botany* 87:178-194.

Ralphs, M.H., Stegelmeier, B.L. (2011). Locoweed toxicity, ecology, control and management. *International Journal of Poisonous Plant Research*. 1:47-64.

Ralphs, M.H., R. Creamer, D. Baucom, et al. (2008) Relationship between the endophyte *Embellisia* spp. and the toxic alkaloid swainsonine in major locoweed species (*Astragalus* and *Oxytropis*). *Journal of Chemical Ecology* 34:32-38.

Stegelmeier, B.L., S.T. Lee, L.F. James, et al. (2007). The comparative pathology of locoweed poisoning in livestock, wildlife and rodents. (eds. K.E. Panter, T.L. Wierenga, and J.A. Pfister) Poisonous Plants: Global Research and Solutions , pp. 359-365. CAB International, Wallingford, U.K

Welsh, S.L, Ralphs, M.H., Panter. K.E., (2007). Locoweeds of North America: taxonomy and toxicity. In K.E. Panter, T.L. Wierenga, and J.A. Pfister, eds., *Poisonous Plants: Global Research and Solutions*, pp. 20-29. CAB International, Wallingford, U.K.

Groundsel, Senecio
Giles, C.J. 1983. Outbreak of ragwort (Senecio jacobea) poisoning in horses. Equine Vet J.15:248-250.

Stegelmeier, B.L., Edgar, J.A., Colegate, S.M., et al. 1999. Pyrrolizidine alkaloid plants, metabolism and toxicity. *Journal of Natural Toxins.* 8:95-116.

Lupine

Burrows, G.E., Tyrl, R.J. (2001d) *Lupinus.* In: *Toxic plants of North America*. (eds. G.E. Burrows & R. J. Tyrl) pp. 576-584. Iowa State University Press, Ames, Iowa.

Panter, K.E., T.D. Bunch, R.F. Keeler, et al. 1990. Multiple congenital contractures (MCC) and cleft palate induced in goats by ingestion of piperidine alkaloid-containing plants: reduction in fetal movement as the probable cause. J Toxicol and Clin Toxicol. 28: 2869–2883.

Livestock poisoning associated with cultivated crops

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Nitrate Poisoning

Nitrate poisoning has been reported in ruminants that have consumed sorghums, sugar beet tops, turnips, kale, oats, corn silage and corn stalks, Italian rye grass, white clover, red rooted pigweed, and a variety of thistles and other common weeds. Plants containing high levels of nitrate cause poisoning most commonly in cattle, occasionally in small ruminants, and rarely, if ever, in horses, because the equine digestive system does not readily convert nitrate (NO_3) to the toxic nitrite (NO_2).

Normally plants absorb nitrates from the soil and convert them into plant proteins. Application of organic or inorganic nitrogenous fertilizers can result in excessive accumulation of nitrates in crop plants and common weeds. Nitrate levels in plants vary considerably depending on the plant species, stage of growth, water and organic content of the soil, and whether nitrogen fertilizers have been applied. Drought conditions, acidic soils, and soils deficient in sulfur, phosphorous and molybdenum result in nitrate accumulation in plants. 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. Nitrate levels are therefore highest in plants at night and early morning when the nitrate-reducing enzymes are least active. Highest levels of nitrate are found in the stems where nitrate reduction normally occurs, and not in the leaves, flowers or seeds.

Silage from forage crops high in nitrates will reduce the nitrate content by 60%, while there is little reduction of nitrate in dried hay. 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. The potential for nitrate poisoning is increased when water sources for livestock also contain high levels of nitrates.

Normally nitrates are 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 from the rumen 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. Nitrate poisoning is more likely to occur in ruminants after several days of feeding forages high in nitrate. 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, thereby reducing the potential for poisoning. Conversely, low-energy diets increase an animal's susceptibility to nitrite poisoning. Plants or hay containing more than 1% nitrate (10,000 ppm) dry matter are potentially toxic and should be fed with caution. Forages containing more than 1% nitrate should only be fed if the total nitrate intake can be reduced to less than 1% by diluting the nitrate forage with low-nitrate forages. Since nitrate levels are often reported in different units, care must be exercised in interpreting nitrate values provided by different laboratories.

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

Accumulation of nitrates in water sources frequently poisons livestock. Surface water and water from shallow wells are most likely to contain nitrates, especially if there is the potential for run-off water from fertilized arable land. 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. Above 200 ppm nitrate, pregnant animals can abort. Livestock can consume higher levels of nitrate feed if they are on a high-energy ration. The presence of monensin in rations high in nitrate may precipitate poisoning.

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 develop severe gastrointestinal irritation resulting in colic and diarrhea.

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 40% of hemoglobin is converted to methemoglobin, clinical signs of poisoning become apparent. Death occurs as methemoglobin levels approach 80%.

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. Signs of poisoning develop within 6 to 8 hours of the consumption of a toxic dose of nitrate. 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. Venous blood also has a chocolate brown discoloration.

Sublethal doses of nitrate may induce abortion because nitrate readily crosses the placenta and can cause fetal methemoglobinemia and death. Severe methemoglobinemia also impairs oxygen transportation across the placenta, thus contributing to fetal hypoxia and death. Abortions may also result from decreased progesterone production induced by chronic nitrate poisoning interfering with luteal production of progesterone.

Low levels of nitrate in the diet of cattle have also been suspected of affecting vitamin A metabolism, thyroid function, reproduction, and milk production. However, there are many conflicting reports on the effects of low level nitrate poisoning. Numerous studies have also shown that nitrates do not affect milk production unless the levels of nitrate induce significant methemoglobinemia. Reproductive efficiency, gestation length, and birth weights appear to be unaffected by low nitrate consumption.

Livestock 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 4-15 mg/kg body weight administered as a 2-4% solution.

Confirmation of nitrate poisoning should be based on the detection of toxic levels of nitrate in the forage, water source, rumen contents and tissues of the animal. Levels of nitrate in the eyeball of 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.

Levels of nitrate over 0.5% in forages and water levels exceeding 200 ppm are potentially hazardous to pregnant animals, especially if fed continuously. Forages containing in excess of 1% nitrate dry matter should be considered toxic. Water levels of 1500 ppm or greater are potentially toxic to ruminants, especially if consumed with forages high in nitrate. Nitrate and nitrite can be assessed in forage, rumen contents, and water using the diphenylamine test

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. Forages containing 1% 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% nitrate should be diluted with hay containing no nitrates so that the total nitrate level in the ration is below 1%. Feeding low-nitrate hay before turning cattle onto forages containing higher levels of nitrate reduces the amount of nitrate consumed. 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% or more of nitrates. Ensuring animals are on a good plain of nutrition before introducing a forage high in nitrate reduces losses

Plant Induced Cyanide Poisoning

At least 2000 plant species are known to contain cyanogenic glycosides with the potential to produce Hydrogen Cyanide (HCN) poisoning.

Plants Associated with Cyanide Poisoning in Animals

BOTANICAL NAME	COMMON NAME
Acacia spp.	Catclaw, acacia
Amelanchier alnifolia	Service, June, or Saskatoon berry
Cercocarpus montanum	Mountain mahogany
Cynodon spp.	Star grass
Glyceria grandis	Tall manna grass
Linum spp.	Flax
Lotus spp.	Bird's foot trefoil
Prunus spp.	Choke-cherry, pin cherry
Sambuccus spp.	Elderberry
Sorghum spp.	Johnson, Sudan grass
Sorghastrum nutans	Indian grass
Suckleya suckleyana	Poison suckleya
Trifolium repens	White clover
Triglochin maritima	Arrow grass
Vicia sativa	Common vetch
Zea mays	Corn,

Cyanide poisoning of livestock is most commonly associated with Johnson grass (Sorghum halapense), Sudan grass (Sorghum vulgare), and other forage sorghums. Choke-cherries (Prunus spp.), service berry (Amelanchier alnifolia), and arrow grass (Triglochin spp.) are less frequent but long recognized sources of cyanide poisoning. Cyanogenic glycosides in the leaves and stems of plants are not toxic unless acted on by the plant or rumen microorganism enzymes to form HCN. Enzymatic conversion of the glycosides is enhanced when plant cells are damaged or stressed, as occurs when the plant is chewed, crushed, wilted, frozen, or subjected to drought. The young rapidly growing portion of the plant and the seeds contain the highest concentrations of cyanogenic glycosides. Drying or ensiling the plants decreases their cyanogenic potential

New growth, time of year, soil mineral and moisture content, and time of day can increase the cyanogenic potential of plants. 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. Nitrate fertilization, therefore, has the potential to increase the cyanogenic glycoside content of plants. Frost and drought conditions may also increase cyanogenesis in some plant species. Application of herbicides (2, 4-dichlorophenoxyacetic acid [2, 4-D]) can also increase the cyanogenetic glycoside content of plants. Selective breeding of certain sorghum varieties has produced hybrids that have low cyanide content, which has greatly increased the safety of feeding sorghums 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. Water drunk after animals have eaten cyanogenic plants enhances the hydrolysis of the glycosides. Cattle 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 exclusively a grass, hay or alfalfa diet. Horses have an acidic stomach (pH 2-4) that reduces the rate of cyanide production in their digestive systems, and therefore rarely suffer from plant-induced HCN poisoning.

Hydrogen cyanide (HCN) is highly poisonous to all animals because it rapidly inactivates cellular respiration, thereby causing death. 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 in hemoglobin, thereby inhibiting or preventing cellular respiration.

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. When large quantities of cyanide are rapidly absorbed and the body's detoxification mechanisms are overwhelmed, cyanide poisoning occurs. However, if plenty of other plant material and carbohydrates are present in the stomach, formation and absorption of HCN may be slowed, allowing animals to tolerate higher doses of the HCN.

Chronic cyanide poisoning is a neurotoxicity resulting from nitrile compounds in Sorghum grasses that causes osteolathyrism in animals, especially horses. Musculoskeletal deformities in foals and calves have been associated with pregnant mares and cows that chronically eat Sudan grass (*Sorghum sudanense*) or sorghum hybrids containing low levels of cyanogenic glycosides. In addition to limb deformities, calves also develop severe degeneration of the spinal cord and brain. Affected animals develop hindquarter weakness, urinary incontinence and cystitis resulting from lower spinal cord degeneration. 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. Thyroid gland enlargement is also seen in animals caused by the formation of thiocyanate, which inhibits the intrathyroidal transfer of iodine and elevates the concentration of thyroid-stimulating hormone. Pregnant ewes grazing star grass (Cynodon spp.) have developed goiter because of the presence of cyanide in the grass.

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. 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. 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.

Diagnosis of HCN poisoning is difficult because HCN 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. 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.

Treatment of cyanide poisoning is accomplished by injecting sodium nitrite and sodium thiosulfate intravenously. A recommended treatment for cyanide poisoning is the intravenous administration of a mixture of 1 mL of 20% sodium nitrite and 3 mL of 20% sodium thiosulfate. This dose is given intravenously per 100 lbs of body weight. The dose may be repeated in a few minutes if the animal does not respond. A gallon of vinegar diluted in 3 to 5 gallons of water given via stomach tube will help acidify the rumen and reduce the production of HCN.

Selenium Poisoning

Cover Crops
Buckwheat - *Fagoypyrum esculentum*
Buckwheat is often cultivated as a cover crop or for its seeds, and is a problem to horses and livestock that graze it. The toxin in the plant is a natural pigment called fagopyrin, present in the green, and to a lesser extent, the dry plant. Once absorbed from the intestinal tract, fagopyrin accumulates in the blood and can fluoresce when exposed to sunlight in any white-skinned areas where there is no protective skin pigment. The fluorescing pigment damages the blood vessels in the skin, causing cell death and ultimately sloughing of the white-skinned areas. Unlike the photosensitivity produced by groundsel (*Senecio* spp.) and other plants containing pyrrolizidine alkaloids where liver damage is present and irreversible, buckwheat causes no liver damage, and animals recover once removed from the buckwheat.

Alsike Clover – *Trifolium hybridum*
Alsike clover is a perennial legume that is commonly grown for livestock consumption in northern regions of North America. Two disease syndromes have been reported in horses and occasionally cattle grazing alsike clover. The first is an irreversible liver disease often accompanied by neurologic disturbances and referred to as alsike clover poisoning. The second syndrome is one of photosensitivity without apparent concurrent liver disease, and is referred to as trifoliosis (dew poisoning). The specific toxins responsible for either of these syndromes have not been determined. Since the disease is sporadic in occurrence and often follows wet humid conditions, the toxicity may be caused by a mycotoxin produced by a fungus growing on the clover. Horses with alsike clover poisoning typically develop signs of liver failure including weight loss, jaundice, depression, aimless wandering and walking in circles. Significant elevations of specific liver enzymes are usually present and are indicative of severe liver disease. The neurologic findings in affected horses are possibly due to hepatic encephalopathy caused by the failing liver. The appearance of photosensitivity can be attributed to the accumulation of phylloerythrin in the horse's circulation as a result of liver failure (Colon *et al*. 1996). The main lesion found in horses with alsike clover poisoning is a grossly enlarged, fibrotic liver, with marked bile duct proliferation.

Sweet Clover Poisoning – *Melilotus officinalis*

Commonly grown in the northwestern United States as a forage for livestock, yellow sweet clover in itself is not poisonous. However, if it becomes moldy, a variety of different fungi growing on sweet clover is capable of converting coumarin in the plant to dicoumarol, a potent anticoagulant. Sweet clover poisoning is clinically identical to warfarin poisoning, a common rodenticide. Moldy sweet clover poisoning is most commonly encountered in cattle, but occasionally horses and other livestock are susceptible to the effects of dicoumarol. Sheep are quite resistant to the toxic effects of dicoumarol. Signs of poisoning may not appear for up to 3 weeks after feeding moldy sweet clover hay, and depend on the quantity of dicoumarol consumed. Poisoning is likely to occur when dicoumarol levels exceed 10 mg/kg of hay. Hay containing dicoumarol levels of 10 to 20 mg/kg of feed can be fed for 100 days before poisoning develops. Feeds containing 60 to 70 mg/kg of feed can cause poisoning in as little as 21 days. Dicoumarol has strong anticoagulant properties that interfere with the production of vitamin K that results in failure of the blood to coagulate, resulting in internal and external hemorrhaging. Calves are usually more severely affected than adult cattle, and dicoumarol can cross the placenta to affect the newborn calf. Sweet clover, being a legume, can also cause acute rumen bloat in cattle, especially if it is lush and leafy.

Animals with sweet clover poisoning are initially weak and depressed. The sudden appearance of subcutaneous swellings, bleeding from the nose, and black tarry feces are common in sweet clover poisoning. Subcutaneous hematomas, especially ventrally and over areas that are easily traumatized, frequently develop. Hemarthrosis is often seen in the carpal and hock joints. Lameness due to massive intramuscular hemorrhage can be the primary presenting sign, and a swollen leg can resemble blackleg, a severe myositis caused by Clostridium chauvoei. Hemorrhaging may be observed in the anterior chamber of the eye, and hemorrhages may be seen in the mucous membranes. Vaginal hemorrhaging may be a presenting sign in dairy cattle with sweet clover poisoning. Fatal hemorrhaging in cows at calving is a common occurrence. Signs of anemia including pale mucous membranes and a rapid weak pulse are consistent with sweet clover poisoning. Affected animals are afebrile and maintain a good appetite. Mortality is usually high. Sweet clover poisoning should be suspected when hemorrhaging is excessive after surgical procedures such as castration and dehorning. Prothrombin times should be determined if animals have been eating sweet clover and surgery is contemplated. Prothrombin times above 40 seconds suggest decreased clotting ability.

The concentration of dicoumarol tends to be higher in large round bales where the hay is more likely to have a higher moisture content. Dicoumarol-containing sweet clover may be fed to livestock as long as it does not constitute more than 25% of the animals' total diet, but feeding any moldy feed is not recommended. Sweet clover hay containing less than 20 μg/g is safe to feed to cattle. Concentrations of dicoumarol exceeding 50 μg/g are toxic and will severely affect an animal's blood clotting ability after 3 weeks of feeding the affected hay. To prevent the risk of moldy sweet clover poisoning, sweet clover hay or haylage should not be fed for at least 3 weeks before parturition or elective surgery such as castration, dehorning or tail docking. Selected varieties of sweet clover containing very low levels of coumarin can be fed even if moldy. Properly cured sweet clover silage is low in dicoumarol because dicoumarol-producing fungi require oxygen.

Affected animals should be treated with whole blood transfusions as necessary at the rate of 10 ml/kg body weight. Ideally, 1 mg/lb body weight of vitamin K1 should be injected to restore prothrombin time to normal within 24 hours. However, the cost may be prohibitive and synthetic vitamin K3 (menadione sodium bisulfite), although less effective, can be used. Treatment with large doses of vitamin K3 (1 mg/kg body weight) continued for 4 to 6 days is therapeutic.

Chronic Selenium Poisoning

Selenium-rich soils are generally alkaline and exist in areas with low rainfall where there is minimal leaching of selenium from the soil. In North America, selenium is most abundant in the cretaceous shales and glacial deposits of the Great Plains. Plant uptake of selenium is variable and depends on the chemical form of selenium, soil pH, temperature, moisture, and the species and stage of plant growth. Some plants require selenium for normal growth and are capable of accumulating 10 times the amount of selenium that is present in the soil. Such plants may contain up to 10,000 ppm dry matter of selenium. Obligate accumulator plants with 25 ppm or more of selenium may cause acute poisoning, but are generally distasteful and not eaten by animals unless they are especially hungry. Recognition of selenium-accumulating plants or indicator plants, therefore, provides a means of identifying seleniferous soils and the potential for selenium poisoning of livestock kept in these areas. Other plants known as secondary or facultative accumulators will bind selenium in its organic forms if it is present in the soil, but do not require selenium for growth. Crop plants and pasture grasses growing in seleniferous soils will accumulate toxic quantities of selenium. Phytogenic selenium poisoning is likely to occur after plants containing 5-40 ppm selenium have been consumed for several months. High selenium content of water will compound a forage selenium toxicity problem by adding to the animal's total selenium intake.

Excess selenium in an animal's diet inhibits cellular enzyme reactions, especially those involving sulfur-containing amino acids. This effect of selenium on sulfur alters the metabolism of sulfur-containing amino acids (methionine, cystine), thereby affecting cell division and growth, and causes degeneration and necrosis of the cells that form keratin, the primary protein in hair and hoof. By replacing sulfur in the keratin molecule, selenium weakens the keratin structurally at the site selenium site. Consequently, the hair and hoof wall tend to fracture at this site when subjected to mechanical stresses.

Horses are more susceptible to chronic selenium toxicity than are cattle and sheep. Some animals such as pronghorn antelopes appear capable of consuming diets high in selenium (15 ppm) for long periods without ill effect. Individual animal susceptibility, the chemical form of selenium present, and the bioavailability of selenium as a result of the interaction with other elements such as sulfur, copper, or arsenic present in the diet, are important in the development of selenium poisoning. Chronic Selenosis (Alkali Disease) is a disease of horses, cattle, pigs, sheep, and poultry that consume forages or cereal crops grown in seleniferous soils and that have accumulated toxic levels of selenium. Plants with 5-50 ppm selenium are most likely to cause chronic selenosis. Animals that consume greater than 50 ppm, or are inadvertently injected with an overdose of selenium, develop acute selenium poisoning. The signs of acute selenium poisoning are quite different from those of chronic selenosis, and are characterized by sudden death from cardiac insufficiency, and pulmonary congestion and edema.

Obligate Selenium Accumulator Plants
Milk vetches (*Astragalus* spp.)
Golden rods (*Solidago* spp.)
Woody aster (*Xylorhiza* spp.)
Princes plume (*Stanleya pinnata*)

Secondary Selenium Accumulators
Acacia (*Acacia* spp.)
Sages (*Artemisia* spp.)
Asters (*Aster* spp.)
Saltbrush (*Atriplex* spp.)
Paintbrush (*Castilleja* spp.)
Beard tongue (*Penstemon* spp.)

Gumweed (*Grindelia* spp.)
Western wheat grass *(Pascopyrum smithii*)

Chronic selenium poisoning causes lameness, and the long hairs of the tail and mane tend to break off at the same place, giving the animal a "bob" tail and "roached" mane, respectively. Lameness is due to abnormal hoof wall growth in all feet, which results in rapid uneven growth, circular ridges and subsequent cracking of the hoof wall. Some horses may slough the hoof wall entirely. Cattle will show similar defective hoof growth, but rarely loose the hoof wall. Sheep do not seem to develop as severe lesions as cattle and horses, but show marked reduction in fertility when grazing on selenium-rich pastures. Chronic selenium poisoning has also been associated with reduced reproductive performance, anemia, liver cirrhosis, heart atrophy, and degeneration of bones and joints in horses and cattle.

A diagnosis of selenium poisoning is best confirmed by submitting samples of hay, forages, water, serum, and liver for analysis. Western wheat grass accumulates selenium more readily than other common grasses, and is therefore useful to submit for selenium analysis. Forage selenium levels greater than 5 ppm should be considered potentially toxic. Blood levels of 1-4 ppm are indicative of chronic selenium poisoning. Liver and kidney levels greater than 4 ppm are indicative of selenium toxicosis. High tissue levels of selenium may take up to a year to return to normal after the animal has been removed from the source of the selenium. In chronic selenosis, levels of selenium in the tissues may be low, but hair and hoof samples retain high concentrations. Hair and hoof wall samples collected at the site where the hair is broken and where the hoof wall is cracked are useful in determining historical levels of selenium. Hoofwall containing 8-20 ppm of selenium is indicative of chronic selenosis. Similarly, hair samples containing in excess of 5-10 ppm selenium indicate excessive selenium levels capable of causing toxicity.

Treatment of chronic selenium poisoning depends on early recognition of signs and the removal of livestock from the source of the excess selenium. Recovery from chronic selenium poisoning will occur in time if the animal is fed a diet low in selenium and high in sulfur-containing amino acids. Feeding a high-protein diet with adequate copper levels counteracts the effects of selenium on sulfur-containing amino acids. Feeding good-quality alfalfa hay, provided it is low in selenium, is helpful in providing adequate sulfur to counteract selenium in the diet. Alfalfa typically has low selenium levels (0.15-0.69 ppm), but can accumulate toxic levels (22 ppm) when growing in selenium-rich soils. Adequate levels of copper in the diet has a protective effect against selenium poisoning. Attention should be given to careful and regular trimming the deformed, overgrown hooves to avoid permanent lameness.

Grass Staggers
Reed canary grass (*Phalaris arundinacea*) is a highly adaptive coarse grass well adapted to wet environments that is native to Europe and Asia. It is now widely distributed throughout the northern states. It is common along road ditches, lowland areas, wetlands, shores and irrigation ditches.

Reed canary grass contains tryptamine alkaloids that produce neurologic signs characterized by "staggers," hopping gait, weakness, hind limb paresis progressing to lateral recumbency, and death within a few days. Clinical signs may not appear until the grass has been grazed for a period of time, or may not appear for weeks after the animals have been removed from the reed canary grass pasture.

Selected References

Nitrate Poisoning
Pickerel, J.A., F.W. Oehme, S.R. Hichman, 1991. Drought increases forage nitrate and cyanide. Vet and Human Toxicol 33:247–251.

Brunning-Fann CS, Kaneene JB: 1993.The effects of nitrate, nitrite, and N-nitroso compounds on animal health. Veterinary & Human Toxicology 35:237–253.

Slenning B,D., Galey F,D., Anderson M. 1991. Forage related nitrate toxicoses possibly confounded by non-protein nitrogen and monensin in the diet used at a dairy heifer replacement operation. J Am Vet Med Assoc, 98:867–870.

http://www.ext.colostate.edu/pubs/livestk/01610.html
http://www.uaex.edu/publications/pdf/fsa-3024.pdf

Cyanide Poisoning
Pritchard, J.T., J.L.Voss, 1967. Fetal ankylosis in horses associated with hybrid Sudan pasture. J Am Vet Med Assoc 150:871–873.
Seaman, J.T., M.G. Smeal, J.C. Wright, 1981. The possible association of a sorghum (*Sorghum sudanense*) hybrid as a cause of developmental defects in calves. Australian Vet J 57:351–352.

Van Kampen, K.R. 1970. Sudan grass and sorghum poisoning of horses: a possible lathyrogenic disease. *Journal of the American Veterinary Medical Association*. 156:629-630.

Vetter, J. 2000. Plant cyanogenic glycosides. *Toxicon.* 38:11-36.

Alsike Clover Poisoning
Colon, J.L., C.A. Jackson, F. Del Piero. 1996. Hepatic dysfunction and photodermatitis secondary to alsike clover poisoning. Compendium of Continuing Education 18:1022–1029.

Nation, P.N. 1991. Hepatic disease in Alberta horses: a retrospective study of "alsike clover poisoning" (1973–1988). Can Vet J 32:602–607.

Nation, P. N. 1989 Alsike clover poisoning: a review. *Canadian Veterinary J*. 30: 410-415.

Yellow Sweet Clover Poisoning
Puschner B, Galey FD, Holstege DM, et al. 1998: Sweet clover poisoning in dairy cattle in California. J Am Vet Med Assoc, 212:857–859

Selenium Toxicity
Raisbeck MF, O'Toole D, Belden EL, Waggoner JW: Chronic selenosis in ruminants. InToxic Plants and Other Natural Toxicants. Garland T, Barr AC, Eds. New York: CAB International; 1998:389-396

Phalaris grass
Binder, E.M., Blodgett, D.J., Currin, J.F., et al. 2010. *Phalaris arundinacea* (reed canarygrass) grass staggers in beef cattle. *Journal of Veterinary Diagnostic Investigation*. 22:802-805.

Johnstone, L.K., I.G. Mayhew, L.R. Fletcher LR. 2012. Clinical expression of lolitrem B (perennial ryegrass) intoxication in horses. Equine Vet J. 44:304-309.