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## Plants Affecting the Blood (16-Jun-2003)

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### Table of Contents

#### Onion Poisoning

*Plants* - *Allium* spp. (Habitat, Description, Principal Toxins, Clinical Signs, Treatment)

#### Brassica Poisoning

**Glucosinolate Poisoning** (Clinical Signs, Treatment, Preventive Measures)

#### Red Maple Poisoning

*Plants* - *Acer Rubrum* (Habitat, Description, Principal Toxins, Clinical Signs, Treatment)

#### Yellow Sweet Clover Poisoning

*Plants* - *Melilotus Officinalis*, Bracken Fern, Brake Fern, Eagle Fern  
 (Habitat, Description, Principal Toxins, Clinical Signs, Treatment)

#### Bracken Fern Poisoning

##### Principal Toxins

##### Clinical Signs of Bracken Fern Poisoning in Cattle and Sheep

##### Bracken Fern Poisoning in Sheep

##### Bracken Fern Poisoning in Horses

##### Bracken Fern Poisoning in People

A variety of plants contain compounds that damage red blood cell (RBCs) metabolism and cell membrane integrity causing them to be removed from the circulation by the spleen. As a result, the excess hemoglobin from the damaged RBCs is filtered by the kidneys causing hemoglobinuria. If present in large quantity, the hemoglobin causes the urine to become red or dark brown in color. Plants that contain toxic compounds capable of affecting the RBCs include onions (*Allium* spp.); common crop plants such as kale, rape, turnips (*Brassica* spp.); and red maple (*Acer rubrum*). Red colored urine may also be encountered with hairy vetch (*Vicia villosa*) poisoning. In cattle, plants such as bracken fern (*Pteridium aquilinum*), and sweet clover (*Melilotus officinalis*) inhibit normal blood clotting with resulting hemorrhage into the urinary system (hematuria). Bracken fern is also capable of inducing the formation of urinary bladder tumors in cattle which may cause red-colored urine.

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### Onion Poisoning

*Allium* spp.

*A. cepa* - Domesticated onion

*A. canadensis* - Wild onion

*A. validum* - Wild onion Liliaceae (Lily family)

### Habitat

Wild onions are usually found in moist meadows, open hillsides, and in sandy bottomlands throughout North America.



Habitat of *Allium* spp. - Wild onion Liliaceae (Lily family). - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

### Description

Onions are herbaceous plants with bulbs and narrowly linear leaves that smell of "onion" The leaves are sheathing, usually basal, and hollow. The stem is simple and erect with a terminal umbel subtended by two or three membranous bracts. The six- parted flowers may be white, purple, pink, or green and are borne on slender pedicels (Fig.5-1). All parts of the plant smell of onion if crushed.



Figure 5-1. Wild onion (*Allium*) spp. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

### Principal Toxin

An alkaloid, N-propyl disulphide, present in both cultivated and wild onions, chives, and garlic, affects the enzyme, glucose-6-phosphate dehydrogenase in RBCs thereby interfering with the hexose monophosphate pathway [1,2]. Oxidation of hemoglobin results because there is insufficient phosphate dehydrogenase or glutathione to protect the RBCs from oxidative injury [1]. The oxidized hemoglobin precipitates in the RBCs to form Heinz bodies. The cells containing Heinz bodies are removed by the spleen with the resulting anemia being proportional to the number of Heinz bodies formed and the rate at which the spleen removes the damaged cells. Cattle are the most susceptible to onion poisoning; horses and dogs are intermediate; and sheep and goats are the most resistant [3-8]. Pregnant ewes are able to eat a diet consisting of 90 to 100 percent cull onions without developing a severe anemia as would cattle on a ration with more than 25 percent dry matter of onions. The sheep's adaptation to onions appears to be related to the ability of the animal's rumen microflora to rapidly change to a population of organisms capable of reducing the sulfide in the onions [9]. Sheep are therefore able to metabolize the sulfide in the rumen more effectively than can cattle, thus preventing a progressive Heinz body anemia from developing.

Dog breeds such as Akitas and Shibas with high erythrocyte levels of reduced glutathione and potassium are especially susceptible to the hemolytic effects of oxidants such as N-propyl disulfide [10]. Dogs may also be poisoned after eating quantities of onion even after the plants are cooked [11].

The severity of Heinz body anemia that develops will vary with the quantity and the rate at which onions are consumed and the species of animal. Diets containing more than 25 percent dry matter of onion have the potential to cause clinical signs of anemia. Calves 6 to 12 months old consuming 8 to 15 kg/day of onions for 5 days develop characteristic Heinz body anemia [12]. The formation of Heinz bodies in sufficient numbers to cause anemia and hemoglobinuria may occur within 1 to 3 weeks of eating onions. Small numbers of Heinz bodies will be formed in cattle even though the amount of onion consumed may be less than that necessary to induce anemia.

### Clinical Signs

Most onion poisoning is associated with the feeding of cull domestic onions to animals. It is rare to encounter poisoning from wild onions. The first noticeable sign of onion poisoning is often the presence of dark red-brown urine (hemoglobinuria). Affected animals have pale mucous membranes and a fast, weak pulse; they may stagger and collapse as a result of anemia. There is frequently a distinct odor of onion on the breath, feces, urine, and milk of poisoned animals. In severely anemic animals, additional stress and heavy parasite infestations may be sufficient to cause death of the animal. Lactating animals eating onions may have an onion flavor to their milk making it undesirable for human consumption. The onion flavor

disappears from the milk after the lactating animal has been off of onions for 24 hours.

### Treatment

Animals that are anemic from onion poisoning should not be stressed, and onion feeding should be discontinued. Whole blood transfusions may be necessary in severely anemic animals. Sheep being fed onions rarely require any treatment even though they are anemic because they adapt to an onion diet and do not develop a progressive Heinz body anemia that is fatal [9].

Cull onions can be a valuable food source for livestock in onion-growing areas. Up to 25 percent dry matter of onions and can be successfully fed to cattle in a balanced ration [12]. The onions should be chopped and well mixed in cattle rations to avoid choking the animals. Sheep are able to eat far higher quantities of onion than cattle without detriment, although weight gains in feeder lambs on diets containing more than 50 percent dry matter of onions tend to be reduced [9]. Because cull onions consist of about 90 percent water, the total caloric intake necessary for growth will be limited due to the limited capacity of the rumen. Growth rates and milk production in cows may therefore be reduced if onions comprise the bulk of an animal's diet.

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### Brassica Poisoning

Members of the Brassicaceae (*Cruciferae*), especially those grown as crop plants (turnips, kale, rape, cabbage, cauliflower, broccoli, and brussels sprouts) contain a variety of toxic compounds that have different effects on animals that eat them [13-18]. Glucosinolates and sulfur-containing amino acids in these plants cause signs of poisoning ranging from goiter, hypothyroidism, blindness, diarrhea, red-colored urine, and pulmonary emphysema. These compounds are found in greatest quantity in the young green plant and in the seeds. However, signs of poisoning produced depends on the glucosinolate unique to the particular brassica or mustard. Hemolytic anemia occurs in cattle due to the presence of the compound S-methyl-L-cystein sulfoxide (SMCO), a sulfur-containing amino acid unique to the family Brassicaceae [19] is converted in the rumen to dimethyl disulphide that oxidizes hemoglobin in a similar manner to N-propyl disulphide, a closely allied compound found in onions. The denatured hemoglobin is detectable as Heinz bodies in the RBCs that are removed from circulation by the spleen's reticuloendothelial system. Hemolysis of the cells also occurs as a result of oxidative damage to the cell membranes that result in the hemoglobinuria seen in affected animals. The severity of poisoning is greatest in cattle that are fed kale (*B. oleracea*), rape (*B. napus*), and turnips (*B. campestris*) grown as forage crops; sheep appear to be less susceptible [19].

Cattle grazing various brassicas including turnips, rape, and canola may experience up to a 10 percent death loss as a result of bloat and acute pulmonary emphysema [18]. Green turnip tops are a rich source of tryptophan that is converted in the rumen to 3-methyl-4-hydroxy-5-methylfuran-2(1H)-one (a 3-substituted furan). The bioactivated furans bind with the protein of type I cells of the lung airways, causing acute pulmonary emphysema and edema. If the animal survives the acute stage, rapid proliferation of cells in the lungs (type II alveolar cells) decrease normal air exchange and cause death from an interstitial or proliferative pneumonia. Other plants that contain similar 3-substituted furans capable of causing acute pulmonary emphysema and edema in cattle include perilla mint (*Perilla frutescens*) (Fig.5-2), and sweet potato (*Ipomoea batata*).



Figure 5-2. Perilla, or purple mint (*Perilla frutescens*). - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

The toxicity of the turnip tops is markedly reduced after they have been frozen. The turnips themselves are relatively low in tryptophan and are more likely the cause of thiamine deficiency induced polyencephalomalacia a disease characterized by blindness, depression, and death [18]. Cattle may concurrently develop hemolytic anemia that can be overlooked in the

presence of the other accompanying diseases. Nitrate poisoning may also result from feeding turnips and other brassicas.

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### **Glucosinolate Poisoning**

*Brassica* spp. contain various glucosinolates that can cause goiter and hypothyroidism, poor growth rates, and reproductive failure [20]. Glucosinolates are the precursors of active metabolites such as isothiocyanates and nitriles, irritants that can cause colic and diarrhea [21]. Glucosinolate levels are highest in seeds of brassicas, especially of the mustards, and it is for this reason that caution should be exercised when feeding rape seed meal to animals [20]. Decreased feed consumption, poor growth rates, and decreased milk production have been credited to the feeding of high levels of rape seed [22]. Acute fatal poisoning of cattle characterized by severe edema of the forestomachs and abomasum has been reported following consumption of large quantities of discarded mustard seed [23,24]. The irritant effects of the isothiocyanates presumably causes vascular damage and edema of the stomachs [23,24].

### **Clinical Signs**

If cattle are given sudden access to turnip fields after being on relatively dry, high roughage diets, they may develop nonfrothy bloat and acute respiratory distress as a result of pulmonary emphysema and edema [18]. Panting, open-mouthed breathing, coughing, and frothing at the mouth are typical of acute pulmonary emphysema. Mortality is usually high in animals with the acute respiratory involvement. Blindness and marked depression due to polioencephalomalacia may develop in some cattle after about a week of eating turnips. As with onion poisoning, cattle consuming brassicas develop hemoglobinuria, hematuria, and jaundice depending on the quantity of brassica consumed [1]. Cattle become progressively weaker and may eventually die from severe anemia unless they are removed from the source of the plants. Death of anemic animals can be accelerated by stress and by concurrent parasitic diseases that may worsen the anemia. Lactating cows fed *Brassica* spp. may also have off- flavored milk due to the presence of glucosinolates.

Tansy mustard (*Descurainia pinnata*), a member of the Brassica family and a common weed throughout North America, is sporadically associated with a syndrome in cattle characterized by photosensitization involving the nonpigmented skin around the face, neck, and udder (see Chapter 4) [26]. Feeding trials with tansy mustard, however, have been unsuccessful in creating the disease, suggesting other factors are involved [26]. Symptoms of poisoning appear to coincide with years in which timely rainfall results in lush growth of tansy mustard. Blindness, protrusion of the tongue, and difficulty in eating suggestive of polioencephalomalacia have also been associated with cattle forced to eat nothing but tansy mustard.

### **Treatment**

When possible the affected cattle should be removed from the source of the brassica and provided a good-quality roughage diet. Severely anemic animals should be carefully handled to avoid stress. Blood transfusions may be lifesaving in animals that are severely anemic. For similar reasons, animals with pulmonary emphysema should be handled very carefully. Large doses of corticosteroids and diuretics, and oxygen therapy, if available and practical, may help reduce the acute lung edema and emphysema in the early stages of poisoning.

Cattle showing signs of blindness should be injected with large doses of thiamin (10 mg/kg body weight intravenously every 3 to 4 hours for 2 to 3 days). Corticosteroids may be beneficial in reducing brain edema. Rehydrating severely affected animals with large volumes of oral fluids and providing a good-quality grass/alfalfa hay is beneficial in treating animals with brassica poisoning.

### **Preventive Measures**

In situations where brassicas and mustards are intended for cattle forage, problems with bloat and pulmonary emphysema can be reduced by gradually introducing the animals to the new food source. Waiting until after a hard freeze will markedly reduce the risk of acute pulmonary emphysema. To reduce the rapid consumption of the turnip tops, cattle should be fed a good-quality roughage beforehand so as to limit turnip intake. Feeding a few pounds of grain per head per day, along with roughages such as corn stalks prior to the turnips works well in some circumstances. The use of antibiotics such as monensin and lasalocid are also effective in reducing the conversion of tryptophan to 3-methylindole, the instigator of pulmonary emphysema. Additionally the antibiotics reduce rumen lactic acidosis and subsequent thiamin deficiency. Monensin can be administered as part of the grain or as a component of a liquid mineral/protein supplement [18].

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## Red Maple Poisoning

*Acer rubrum* *Aceraceae* - (Maple family)

### Habitat

Red maple trees are common throughout most of eastern North America and south to Florida and Texas. They adapt to moist or dry areas and are often planted as ornamental trees for their striking fall colors.



Habitat of Red Maple. *Acer rubrum* *Aceraceae* - Maple family. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

### Description

These large trees attain heights of 100 feet (30 meters) at maturity (Fig. 5-3A). Leaves have three to five lobes and are simple, opposite with red petiole, shiny green topside and white/gray underside (Fig. 5-3B). Leaves turn bright red in the fall. Dense clusters of red flowers appear before leaves, the male and female flowers being on separate trees. Fruits are red in color and have two wings 0.75 to 1 inch (2 to 2.5 cm) long.



Figure 5-3A. Red maple tree (*Acer rubrum*). - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -



Figure 5-3B. Red maple leaves (*A. rubrum*). - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

### Principal Toxin

An unidentified toxin with oxidant properties is present in the wilted or dried leaves of red maples [27-30]. Only the red maple (*A. rubrum*) and possibly closely related hybrids are known to be toxic. Horses, ponies, and zebras appear to be the only animals affected by the toxin in red maples [27,28,31]. The toxin causes oxidant damage to hemoglobin resulting in the precipitation of the oxidized hemoglobin as Heinz bodies in the RBCs. Damage apparently also occurs to the RBC membranes, which results in hemolytic anemia [28]. Poisoning is especially likely in the fall or after a storm when leaves of fallen branches become accessible to horses [32]. The fresh green leaves apparently are not toxic, but once dried they may remain toxic for up to 30 days. The bark from red maple trees is also toxic. Fatal poisoning of ponies fed 3.0 kg of dried red maple leaves occurred in 1 to 5 days [32]. As little as 1.5 kg of dried red maple leaves will induce formation of Heinz bodies and anemia [32].

### Clinical Signs

After they eat relatively small amounts of dried red maple leaves, horses exhibit clinical signs within 1 to 2 days. Poisoning is characterized by an acute hemolytic anemia that causes weakness, increased respiratory and heart rates, cyanosis, icterus, and a red-brown coloration of the urine [27-30]. Pregnant mares may abort without showing signs of hemolytic anemia [32]. Blood changes include a marked reduction in the hematocrit, methemoglobinemia, Heinz bodies in the erythrocytes, and depletion of erythrocyte glutathione, the product essential to maintain hemoglobin in its reduced state [28,30]. Serum aspartate aminotransferase, sorbitol dehydrogenase, protein, and bilirubin blood levels are usually elevated [28-30].

A diagnosis of red maple poisoning can generally be made when horses develop an acute hemolytic anemia, with Heinz body

formation, and evidence indicates that they have had access to and have eaten wilted or dried red maple leaves. The prognosis is always guarded to poor for horses with red maple poisoning because of the rapid development of intravascular hemolysis, coagulopathy, precipitation of hemoglobin in the kidneys, and vascular thrombosis [32,34]. Postmortem examination of horses fatally poisoned by red maple leaves reveals pale organ color due to the anemia, hemorrhages on serosal surfaces, and splenic enlargement [32]. In acutely poisoned horses, there may be dark brown blood and brownish discoloration of tissues due to the severe methemoglobinemia [32]. In the acute case, there is often evidence of liver lipidosis and necrosis [31,32].

### Treatment

Affected horses should be denied further access to red maple leaves and blood transfusions given as necessary. Administration of intravenous fluids is of benefit in preventing dehydration and maintaining kidney function [30]. Concurrent use of large doses of vitamin C (ascorbic acid) are also of benefit [35]. Methylene blue advocated for the treatment of erythrocyte oxidant damage should be used with caution in horses. Methylene blue is contraindicated if Heinz bodies are already formed because it induces Heinz body formation. The dosage of methylene blue should not exceed 8 mg/kg body weight and should be administered slowly intravenously as a 1 percent solution.

Prevention of red maple poisoning is best accomplished by maintaining a good feeding program for horses and removing red maple leaves and fallen branches from horse pens. It is inadvisable to plant red maple trees in or closely surrounding horse enclosures.

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## Yellow Sweet Clover

*Melilotus officinalis*

*M. alba* (White sweet clover) - Fabaceae (Legume family)

### Habitat

Yellow sweet clover is commonly grown in the northwestern United States and western Canada as a forage for livestock. It has, however, become established as a drought-tolerant weed and grows wild over much of the continent especially along roadsides and waste areas.



Habitat of Yellow Sweet Clover. *Melilotus officinalis* - Fabaceae (Legume family). - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

### Description

As biennials, both species grow to 5 feet (1.5 meters) in height and have compound leaves with three leaflets that have serrated edges, with the terminal leaflet on a stalk. The pea-like yellow flowers are produced in axillary racemes up to 5 inches (12 to 13 cm) in length (Fig. 5-4A). White sweet clover is very similar except for its white flowers (Fig. 5-4B). Smooth yellow seeds are produced in pods 0.2 to 0.3 cm (2 to 3 mm) long.



Figure 5-4A. Yellow sweet clover (*Melilotus officinalis*). - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -



Figure 5-4B. White sweet clover (*Melilotus alba*). - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

### Principal Toxin

Yellow sweet clover in itself is not poisonous. If, however, it becomes moldy, a variety of different fungi including *Penicillium* and *Aspergillus*, and *Mucor* spp. growing on sweet clover are capable of converting coumarin in the plant to dicoumarol (dicoumarin or dihydroxycoumarin), a potent anticoagulant [36,37]. Other plants containing coumarin and melilotin include sweet vernal grass (*Anthoxanthum odoratum*), *Lespedeza stipulacea* and other species of melilotus (melilot). It is the coumarin in grass that is responsible for the smell of freshly cut hay [37,38]. 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 [39-44]. Sheep appear quite resistant to the toxic effects of dicoumarol [41,42,44,45]. 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 [45]. 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 [45].

Dicoumarol has strong anticoagulant properties that interferes with the production of vitamin K and therefore affects vitamin K- dependent coagulation factors VII, IX, and X and prothrombin. The rate of depletion of these factors is directly related to the duration and amount of dicoumarol ingested, usually over a period of several weeks. Affected animals, unable to synthesize these factors, fail to stabilize fibrin necessary for normal clotting of blood with resulting internal and external hemorrhaging. Calves are usually more severely affected than adult cattle, and dicoumarol can cross the placenta to affect the newborn calf [46].

Sweet clover, being a legume, can also cause acute rumen bloat in cattle, especially if it is lush and leafy, and cattle are not accustomed to it. Like alfalfa, sweet clover produces a frothy bloat that can cause high mortality unless treated early.

### Clinical Signs

Early signs of sweet clover poisoning are not easily recognized because affected animals may only appear weak and depressed. The sudden appearance of subcutaneous swellings, bleeding from the nose, and melena are common in sweet clover poisoning. Subcutaneous hematomas, especially ventrally and over areas that are easily traumatized, frequently develop. These fluctuant swellings are painless and are not hot to the touch, thus differentiating them from abscesses. Hematomas in the mesentery with resulting colic may also develop [38]. 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* [37]. 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 [43]. Fatal hemorrhaging in cows at calving is a common occurrence [41]. Abdominocentesis often reveals intra-abdominal hemorrhage. The hemorrhagic syndrome of sweet clover poisoning has been likened to hemorrhagic septicemia due to *Pasteurella hemolytica* infections without the signs of inflammation [47]. Signs of anemia including pale mucous membranes and a rapid weak pulse are a consistent finding in 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. Before any surgical procedures are performed, it is important to ensure that animals have not been fed sweet

clover in the last month. 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. Blood prothrombin, activated partial thromboplastin times, and clotting times are markedly increased from their normal values of 9 to 12 seconds, 30 to 45 seconds, and 3 to 15 minutes, respectively.

Improperly cured or spoiled sweet clover hay and haylage is not always toxic, but should only be used for animal feed after it has been tested for the presence of dicoumarol. In one survey of 272 cured sweet clover hay samples, over one-third contained more than 10 mg/kg of dicoumarol (range, 0 to 164.7 mg/kg) [48]. The concentration of dicoumarol tends to be higher in large round bales where the hay is more likely to have a higher moisture content [38]. Dicoumarol-containing sweet clover may be fed to livestock as long as it does not constitute more than 25 percent of the animals' total diet, although 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 [52]. 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. There are select varieties of sweet clover that contain very low levels of coumarin and, therefore, hay from these varieties is safe, even if moldy [49]. Properly cured sweet clover silage is low in dicoumarol because dicoumarol-producing fungi require oxygen.

### Treatment

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 wt of vitamin K<sub>1</sub> should be injected to restore prothrombin time to normal within 24 hours [50,51]. However, the cost may be prohibitive and vitamin K<sub>3</sub> (menadione sodium bisulfite) although less effective is often administered [5]. Beneficial results can be obtained if treatment with large doses of vitamin K<sub>3</sub> is continued for 4 to 6 days [40,50]. Supplementing the ration with vitamin K<sub>3</sub> where dicoumarol is present is not effective in preventing poisoning [52]. If vitamin K<sub>3</sub> is given parenterally, the dosage should be 1 mg/kg body weight and should not exceed 2 mg/kg body weight. Greater than 2 mg/kg of vitamin K<sub>3</sub> administered parenterally greatly increases the risk of vitamin K renal toxicosis, especially in horses [50].

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## Bracken Fern, Brake Fern, Eagle Fern

*Pteridium aquilinum* - Polypodiaceae (Fern family)

### Habitat

Bracken fern is found throughout the United States and has been associated with poisoning in cattle, sheep, pigs, horses, and humans [53,54]. In North America bracken fern is commonly found in the eastern, intermountain and western states, from Canada to Mexico. Its growth in the midwestern states is sparse. Bracken fern prefers to grow in moist open woodlands with sandy soils, often forming dense stands following clear-cutting or burning of forests. It will grow in relatively dry soils, and because of its prolific root system spreads rapidly to form dense monocultures to the exclusion of any other plants.



Habitat of Bracken Fern, Brake Fern, Eagle Fern. *Pteridium aquilinum* - Polypodiaceae (Fern family). -  
To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

Bracken fern is also found in many parts of the world with the majority of animal poisoning reported in England and Europe [53,54].

### Description

Bracken fern is a perennial fern with a black, horizontal branching root system often extending for several meters. Leaves arise directly from the rhizome, are broadly triangular, up to 6.5 feet (2 meters) in height, bipinnately compound, and heavily haired on the underside (Fig. 5-5A). The characteristic brown reproductive spores are produced under the rolled edge of the leaflets in late summer Fig. 5-5B.



Figure 5-5A. Bracken fern (*Pteridium aquilinum*). - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -



Figure 5-5B. Spores lining the underside of bracken fern leaflets. - To view this image in full size go to the IVIS website at [www.ivis.org](http://www.ivis.org) . -

### **Bracken Fern Poisoning**

Bracken fern has been associated with a variety of syndromes in animals, the best recognized of which include:

- Thiamin deficiency
- Retinal degeneration and blindness
- Hemorrhaging and bone marrow destruction (thrombocytopenia)
- Urinary bladder cancer (enzootic hematuria)
- Digestive tract cancers

In the interest of continuity, all the syndromes of bracken fern poisoning will be discussed in this chapter and only mentioned in subsequent chapters on plants causing digestive and urinary system diseases.

### **Principal Toxins**

Bracken fern contains an enzyme thiaminase, which splits the essential vitamin thiamin (B<sub>1</sub>) into its two inactive components pyrimidine and thiazole [55]. Thiamin is essential in energy metabolism, especially in the conversion of pyruvate to acetyl-coenzyme A, and the oxidation of  $\alpha$ -ketoglutarate to succinylcoenzyme A in the citric acid cycle [55]. Horses and pigs are most susceptible to the effects of thiaminase. Ruminants are rarely affected because they produce ample thiamin in the rumen [56-59]. Horses have to consume a diet containing 3 to 5 percent bracken fern for at least 30 days before clinical signs appear [60]. Sheep can be experimentally poisoned if they are fed large quantities of bracken fern for prolonged periods [61]. Affected animals develop a thiamin deficiency that is characterized by central nervous system depression and polyencephalomalacia. A similar thiaminase enzyme is also found in other plants including horsetail (*Equisetum arvense*), the Australian nardoo fern (*Marsilea drummondii*), and the rock fern (*Cheilanthes sieberi*) [62,63].

Bracken fern and rock ferns (*Cheilanthes* spp.) also contain ptaquiloside, a norsesquiterpene glycoside that has carcinogenic and bone marrow depressant activity [64-69]. All species of bracken fern should probably be considered toxic because at least *P. aquilinum*, *P. esculentum*, and *P. revolutum* are known to be toxic [70-72]. The root rhizome is the most toxic part of the plant; the leaves are poisonous whether green or dried. The concentration of ptaquiloside varies in bracken fern depending on its geographic distribution. In one survey of 77 samples from plants collected worldwide, 43 percent had ptaquiloside concentrations of over 1000  $\mu\text{g/g}$  bracken [73]. Some bracken fern samples from Australia have had as high as 12,000  $\mu\text{g}$  ptaquiloside/g of plant [73]. Ptaquiloside is transferred through the milk of animals eating bracken fern and

consequently has the potential of affecting the suckling young [73]. In addition to ptaquiloside, bracken fern also contains various pterosides, the toxicity of which have not been determined [55,75].

Cattle appear to be the most susceptible to the effects of ptaquiloside; sheep are minimally affected, and horses are resistant [75]. The newly emerging fiddleheads and fronds of bracken fern are five times as toxic as the mature fronds and are quite palatable to cattle if other forage is scarce. In general, cattle have to eat their weight in bracken fern over several months to develop disease. If large quantities of fern are eaten in a short period, cattle develop an acute, usually fatal, hemorrhagic disease due to severe bone marrow destruction probably induced by ptaquiloside [76]. Long-term consumption of bracken fern leads to the development of tumors in the urinary bladder (enzootic hematuria or red water disease) [72] and possibly other parts of the digestive tract [77-79]. The susceptibility of cattle to the carcinogenic effects of ptaquiloside is possibly due to the fact they generally have alkaline urine. Under alkaline conditions, ptaquiloside is converted to the active carcinogen dienone that alkylates DNA leading to tumor formation [75].

In cattle evidence suggests that bracken fern may predispose papilloma (wart) type 4 virus to produce malignant tumors in the mouth, esophagus, and rumen. The compound quercetin found in bracken fern acts as a cocarcinogen with the papilloma virus to produce the tumor [79-83]. A variety of different tumors in people have been associated with carcinogens in bracken fern [84-86].

### **Clinical Signs of Bracken Fern Poisoning in Cattle and Sheep**

Bracken fern poisoning in cattle and sheep may present in various forms depending on the quantity and duration of consumption of the plant [53,83,87,88]. In acute poisoning, cattle develop severe bone marrow depression that decreases blood platelets (thrombocytopenia) and produces anemia and leukopenia. The clinical signs that appear after animals have eaten the plant 1 to 2 months include depression and hemorrhages on the mucous membranes of the nose and mouth. Hemorrhaging may occur from the nose, mouth, and vagina. The anterior chamber of the eyes may fill with blood (hyphema). Hemorrhagic diarrhea, melena, and red urine (hematuria) are indicative of hemorrhaging into the digestive and urinary tracts [87]. Anemia results both from blood loss and bone marrow depression. Affected animals may have a high temperature due to secondary bacterial infection resulting from the severely depleted bone marrow and decreased circulating neutrophils. Mortality is very high in animals whose leukocyte count is below 2000/ $\mu$ L and platelet count less than 50,000/ $\mu$ L.

### **Enzootic Hematuria of Cattle**

Enzootic hematuria (red water disease) occurs worldwide in cattle wherever bracken fern is grazed [72,87]. Ptaquiloside is the primary carcinogen in bracken fern, and has been shown experimentally to produce cancer of the urinary bladder if cattle consume bracken fern for extended periods [64,71,74,80,88-91]. Small polyp-like tumors develop in the bladder and form bleeding tumor masses (hemangiomas) that result in the formation of red urine (hematuria).

Cattle with enzootic hematuria are often first noticed when voiding red-colored urine, which over time leads to severe blood loss and anemia. There is no effective treatment for the bladder tumors, and usually the animal will die from severe anemia or local tumor invasion of the tissue around the bladder. A variety of tumor types including hemangiomas, hemangiosarcomas, papillomas, fibromas, adenomas, and transitional cell carcinomas have been associated with bracken fern carcinogenicity [72,92,93].

### **Treatment**

Early treatment with blood transfusions and bone marrow stimulants may be beneficial [87]. Batyl alcohol has been used as a bone marrow stimulant in cattle, but it is not consistently effective when thrombocytes and leukocytes are severely depleted [88]. Cattle have also been treated effectively before severe bone marrow depletion has occurred by administering protamine sulfate and blood intravenously [89]. Protamine sulfate is a heparin antagonist and therefore will counteract the increase in heparin that may occur in bracken fern poisoning. Broad-spectrum antibiotics are indicated to help protect the animal against secondary bacterial infections that may develop as a result of bone marrow depletion.

Diagnosis of bracken fern poisoning should be based on the history of the fern being eaten for an extended period of time, a hemorrhagic syndrome caused by bone marrow depletion resulting in thrombocytopenia, and leukopenia. At postmortem examination, there is usually diffuse hemorrhaging involving multiple organs.

### **Bracken Fern Poisoning in Sheep**

"Bright blindness" of sheep is a syndrome of retinal degeneration and blindness associated with grazing of bracken fern in England [94,95]. The disease has been produced experimentally in sheep by feeding them a diet of 50 percent bracken fern for a period of 63 weeks [75]. The blind sheep have a dilated pupil that reflects light from the depigmented retina giving the syndrome its name. The exact cause of the retinal depigmentation is not known, and blindness is permanent.

### **Bracken Fern Poisoning in Horses**

Bracken fern poisoning in horses is uncommon. When encountered it is characterized by a nervous system disease resulting from depletion of thiamin, a vitamin essential for normal energy metabolism [53,94]. Affected horses refuse to eat and consequently lose weight. Depression, muscle tremors, uncoordinated gait, especially of the hind legs and paralysis are typical of bracken fern poisoning. Horses may show colic, constipation, hemoglobinuria, severe anemia, elevated temperature, and rapid heart rate [96].

Diagnosis of bracken fern poisoning should be based on evidence that horses have eaten the fern, the clinical signs, and the animal's response to thiamin therapy. Elevated serum pyruvic acid levels (normal 2 to 3 µg/dL) and decreased thiamin levels (normal 8 to 10 µg/dL) are helpful in confirming the diagnosis. Bracken fern poisoning in horses should be differentiated from viral encephalitis and hepatic encephalopathy, which have similar clinical signs.

### **Treatment**

Horses with thiamin deficiency should be treated with intravenous thiamin, 5 mg/kg body weight. This dose should be repeated intramuscularly for several days. Horses should be provided with a balanced diet that is free of bracken fern.

### **Bracken Fern Poisoning in People**

The young bracken fern shoots (fiddleheads) have for years been considered a delicacy in many Asian countries. A strong correlation appears to exist between the chronic consumption of bracken fern shoots and the high incidence of stomach cancer, especially in Japan [84,85]. Cooking and treating bracken fern by boiling in an alkaline solution reduces but does not eliminate the carcinogenic properties of bracken fern [86]. Because good evidence also indicates that bracken fern causes tumors in the esophagus, stomach, and intestine of animals, it is recommended that people do not eat bracken fern under any circumstances.

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