BRACKEN FERN POISONING

Bracken fern (*Pteridium aquilinum*) is found throughout the world and is among the five most numerous vascular plants in the world. Because the species includes numerous subspecies and varieties, plant size varies, with frond lengths ranging from 0.5 to 4.5 m.

Bracken fern is a perennial, with erect deciduous fronds that remain green until they are killed by frost or drought. It spreads primarily through dense rhizome networks, and it can dominate plant communities, especially those that are burned or disturbed. Bracken fern can be found in a diversity of sites, but it is most common in semi-shaded, well-drained, open woodlands.

A variety of syndromes have been associated with bracken fern poisoning. These syndromes are largely determined by the dose and duration of exposure and the species of the poisoned animal.

Enzootic Hematuria

Enzootic hematuria, the most common form of bracken fern poisoning, primarily affects cattle and less frequently affects sheep. It is characterized by **intermittent hematuria** and **anemia**. Poisoning most often occurs during late summer when other feed is scarce, or when animals are fed hay containing bracken fern. Poisoning requires prolonged exposures because affected livestock must ingest bracken fern for several weeks to years before disease develops.

Affected cattle are weak, rapidly lose weight, and develop fever (106°–110°F [41°–43°C]). Calves often have difficulty breathing, with pale mucosal membranes. Hemorrhages vary from minor mucosal petechia to effusive bleeding, and, at times, large blood clots may be passed in the feces. Coagulation is prolonged, and bleeding may be pronounced and excessive even at small wounds such as insect bites or other minor scratches.

Once animals develop clinical disease, poisoning is almost always fatal. Postmortem examinations usually reveal multiple hemorrhages or bruises throughout the carcass. There may also be necrotic and hemorrhagic ulcers in the GI tract. The bladder mucosa often contains small hemorrhages, dilated vessels, or vascular, fibrous, or epithelial neoplasms. Other neoplasms in the upper GI tract of cattle and other species have also been reported. In most cases, mixtures of hemorrhagic and neoplastic lesions are found.

Bracken Staggers

Bracken fern poisoning in monogastric animals was first recognized as a neurologic disease when **horses consumed contaminated hay**. Typical poisoning requires relatively high doses of long duration, such as feeding hay with 20%–25% bracken fern contamination for 3+ months. **Equine bracken staggers is characterized by anorexia, weight loss, incoordination, and a crouching stance while arching the back and neck and standing with feet placed wide apart.** When forced to move, trembling muscles are noted. In severe cases, tachycardia and arrhythmias may occur, and death (usually 2–10 days after onset) is preceded by convulsions, clonic spasms, and opisthotonos. Poisoning has been attributed to bracken fern thiaminases, because clinical disease is similar to vitamin B1 deficiency. Most animals respond with thiamine therapy.

Thiamine deficiency is generally not a problem in ruminants because the vitamin is synthesized in the rumen; however, altered thiamine metabolism and polioencephalomalacia in sheep poisoned with bracken fern and rock fern (*Cheilanthes sieberi*) have been reported in Australia.

Although not all bracken fern toxins have been completely characterized, the primary cause of enzootic hematuria has been attributed to **ptaquiloside**, 'a norsesquiterpene glucoside'. Other toxic and potentially carcinogenic toxins include quercetin, isoquercetin, ptesculentoside, caudatoside, astragalin, and various tannins.

Ptaquiloside is a potent radiomimetic compound that initially damages the bone marrow and later is carcinogenic (primarily producing urinary tract neoplasia in ruminants). Both the hemorrhagic syndrome and uroepithelial neoplasms have been reproduced experimentally with bracken fern and ptaquiloside. High ptaquiloside doses for a few months duration produce the characteristic hemorrhagic disease. This has been attributed to ptaquiloside's radiomimetic damage to proliferating bone marrow stem cells. This is characterized by depletion of bone marrow megakaryocytes followed by both leukocytic and erythrocytic hypoplasia. The resulting leukogram is often a mixed response. In the initial phase of poisoning there is often pronounced monocytosis followed by granulocytopenia and thrombocytopenia. Final phases include marked thrombocytopenia with anemia, leukopenia, and hypergammaglobulinemia. Urinalysis generally includes hematuria and proteinuria. Affected animals have both an increased susceptibility to infection and a tendency for spontaneous bleeding.

Bright Blindness

A less common presentation of ptaquiloside toxicity is called bright blindness. It is seen clinically as tapetal hyperreflectivity that is **most commonly reported in sheep in parts of England and Wales**. Affected sheep are permanently blind and adopt a characteristic alert attitude. The pupils respond poorly to light, and funduscopic examination in advanced disease is characterized by narrowing of arteries and veins and a pale tapetum nigrum with fine cracks and spots of gray. Histologically, the lesion is seen as severe atrophy of the retinal rods, cones, and outer nuclear layer that is most pronounced in the tapetal portion of the retina.

NITRATE AND NITRITE POISONING

Nitrate poisoning (toxicosis) in animals (especially ruminants) results from excess consumption of nitrates from plants or water or via ingestion of nitrate-containing fertilizers. The nitrate ion (NO_3^-) is reduced to nitrite ion (NO_2^-), which is rapidly absorbed and leads to the formation of methemoglobin, which inhibits oxygen transport. This results in dyspnea, cyanotic mucous membranes, weakness; and, if severe, death due to anoxia. Ruminants are more susceptible because rumen flora can rapidly reduce nitrates to nitrites. Methylene blue, administered IV, will reverse the methemoglobinemia and may be effective as a treatment with supportive care. Ocular fluid specimens are most appropriate sample for postmortem, with laboratory testing of suspected sources of nitrate exposure.

Etiology:

Crops that readily concentrate nitrate include cereal grasses (especially oats, millet, and rye), corn (maize), sunflower, and sorghums. Weeds that commonly have high nitrate concentrations include pigweed, lamb's-quarter, thistle, Jimson weed, fireweed (*Kochia*), smartweed, dock, and Johnson grass. Anhydrous ammonia and nitrate fertilizers and soils naturally high in nitrogen tend to increase nitrate content in forage.

Sign:

Brown, cyanotic mucous membranes develop rapidly as methemoglobinemia exceeds 50%. Dyspnea, tachypnea, anxiety, and frequent urination are common. Some monogastric animals, usually because of excess nitrate exposure from nonplant sources, exhibit salivation, vomiting,

diarrhea, abdominal pain, and gastric hemorrhage. Affected animals may die suddenly without appearing ill, with terminal anoxic convulsions within 1 hour; or after a clinical course of 12–24 hours or longer. Acute, lethal toxicoses almost always result from development of ≥80% methemoglobinemia.

In certain conditions, adverse effects may not be apparent until animals have been eating nitrate-containing forages for days to weeks. Some animals that develop marked dyspnea recover but then develop interstitial pulmonary emphysema and have continued signs of respiratory distress; most of these animals recover fully within 10–14 days. Abortion and stillbirths may be seen in some cattle 5–14 days after excessive nitrate/nitrite exposure; however, this is likely only in cows that have survived an initial acute ≥50% methemoglobinemia for 6–12 hours or longer.

LESIONS:

Blood that contains methemoglobin usually has a chocolate-brown color, although dark red hues may also be evident. There may be pinpoint or larger hemorrhages (petechiae, ecchymoses) on serosal surfaces. Ascites has been reported in stillborn calves, as well as edema and hemorrhage in the lungs and gastrointestinal tract of neonatal calves with excessive maternal nitrate exposure. However, dark brown discoloration evident in moribund or recently dead animals is not pathognomonic, and other causes of methemoglobin must be considered. If necropsy is postponed too long, the brown discoloration may disappear, with conversion of methemoglobin back to Hgb.

SALT TOXICOSIS

Excessive sodium chloride intake can lead to salt toxicosis, also known as **hypernatremia** or as **water deprivation–sodium ion intoxication**. Salt toxicosis is unlikely to occur as long as sodium-regulating mechanisms are intact and fresh drinking water is available.

Salt toxicosis has historically been more common in **swine** (the most susceptible species), **cattle, and poultry**, there are also adverse effects reported in dogs.

Animals can tolerate high concentrations of salt or sodium in the diet if they have continuous access to fresh water. Salt toxicosis is often directly related to water consumption and can be reduced notably or abolished completely in production animals by means of appropriate management of factors such as mechanical failure of waterers, overcrowding, unpalatable medicated water, new surroundings, or frozen water sources.

Mechanism of Action

As serum sodium concentration increases, water moves along the osmotic gradient out of the interstitium and intracellular fluid into the extracellular fluid. Rapid development of hypernatremia results in cerebral dehydration and neuronal cell shrinkage, with the brain then pulling away from the calvarium, which disrupts the blood supply to the brain and can cause tearing of vessels and hemorrhage. To prevent excess water loss to the extracellular fluid, cells of the brain increase their intracellular osmolarity through the generation of idiogenic osmoles. Sodium diffuses passively across the blood–brain barrier and eventually redistributes into neural tissues; however, high intracellular sodium concentrations inhibit energy-dependent pathways for transporting sodium out. With changes in cellular osmolarity in chronic water deprivation, once water access is restored, due to a rapid decrease in serum sodium concentration, intracellular water influx into neurons along the osmotic gradient can lead to cerebral edema.

Clinical Findings

In pigs, early signs (rarely seen) may be increased thirst, pruritus, and constipation. Affected pigs may be blind, deaf, and oblivious to their surroundings; they will not eat, drink, or respond to external stimuli. They may wander aimlessly, bump into objects, circle, or pivot around a single limb. After 1–5 days of limited water intake, intermittent seizures occur with the pig sitting on its

haunches, jerking its head backward and upward, and finally falling on its side in clonic-tonic seizures and opisthotonos. Terminally, pigs may lie on their sides, paddling in a coma, and die within a few to 48 hours.

In cattle, signs of acute salt toxicosis involve the GI tract and CNS. Salivation, increased thirst, vomiting (regurgitation), signs of abdominal pain, and diarrhea are followed by ataxia, circling, blindness, seizures, and partial paralysis. Cattle sometimes display belligerent and aggressive behavior. A sequela of salt toxicosis in cattle is dragging of hind feet while walking or, in more severe cases, knuckling of the fetlock joint.

In poultry and other birds, clinical signs include increased thirst, dyspnea, fluid discharge from the beak, weakness, diarrhea, and leg paralysis.

Lesions

Postmortem examination after salt toxicity may reveal some degree of gastric irritation, including ulceration and hemorrhages. The content of the GI tract may be abnormally dry. Histopathologic lesions may be limited to the brain and include cerebral edema and inflammation of the meninges. During the first 48 hours, swine develop eosinopenia, eosinophilic cuffs around vessels in the cerebral cortex and adjacent meninges, and cerebral edema or necrosis. After 3–4 days, eosinophilic cuffs are usually no longer present. Cattle do not develop eosinophilic cuffs but can have edema of the skeletal muscles as well as hydropericardium. Chickens can also have hydropericardium.

In acute cases, no gross lesions may be present in any species

GOSSYPOL POISONING

Gossypol is produced naturally by the glands of the cotton plant. Although all animals are susceptible to gossypol toxicity, monogastrics, preruminants, immature ruminants, and poultry are affected most frequently. Affected animals may show cardiac failure and sudden death; hepatotoxicosis; liver necrosis secondary to congestive heart failure; hematologic effects, including anemia and increased RBC fragility; reproductive effects (including decreased libido and spermatogenesis in males; irregular cycling, disrupted pregnancy, and embryonic death in females; and green coloration of egg yolks and decreased hatchability in chickens); thumping in swine; and cardiotoxicosis in dogs. Treatment requires removal of the gossypol source, usually the feed, and supportive care.

Gossypol toxicosis—usually chronic, cumulative, and sometimes insidious—follows consumption of cottonseed or cottonseed products containing excess free gossypol. It is of most concern in domestic production animals, and pre-ruminants or immature ruminants & pigs, and poultry appear to be most affected; mature ruminants are more resistant to gossypol's toxic effects. However, gossypol toxicity can affect high-producing dairy cows with high feed intake, dairy goats, and other mature ruminants fed excess gossypol for long periods. It has also been reported in dogs fed diets containing cottonseed meal or housed on cottonseed bedding.

Etiology

Gossypol, the predominant pigment and probably the major toxic ingredient in the cotton plant (*Gossypium* spp). Gossypol is found in cottonseed as both protein-bound and free forms; only the free form is toxic.

Lipid-soluble gossypol is readily absorbed from the GI tract. It is highly protein-bound to amino acids, especially lysine, and to dietary iron. gossypol renders many amino acids unavailable for absorption.

SIGNS:

Hepatotoxicosis can be a primary effect from direct damage to hepatocytes. Gossypol inhibits glutathione-S-transferase, impairing the liver's ability to metabolize xenobiotic compounds.

Hematologic effects include anemia with reduced numbers of RBCs and increased RBC fragility, decreased oxygen release from oxyhemoglobin, and reduced oxygen-carrying capacity of blood with lowered Hgb and PCV values due to complexing of iron by gossypol.

Reproductive effects include decreased spermatogenesis, as well as sperm abnormalities (which are reversible) resulting from enzyme inhibition of steroid synthesis in testicular Leydig cells and extensive damage to germinal epithelium. Effects in females may include irregular cycling, luteolytic disruption of pregnancy, and direct embryotoxicosis.

Prolonged exposure can cause acute heart failure resulting from cardiac necrosis. Also, a form of cardiac conduction failure similar to hyperkalemic heart failure can result in sudden death.

LESIONS:

At postmortem, gross examination may show an enlarged, flaccid, streaked, and mottled heart with pale myocardial streaking; enlarged and dilated ventricles, and valvular edema may be evident.

Skeletal muscles may also be pale.

A froth-filled trachea and edematous, congested lungs are common, with interstitial pulmonary edema and markedly edematous interlobular septa.

Generalized icterus (jaundice) and an enlarged, congested, mottled or golden, friable "nutmeg" liver with distinct lobular patterns may be evident.

The kidneys, spleen, and other splanchnic organs may be congested, possibly with petechiae; mild renal tubular nephrosis may be present. Hemoglobinuria and edema and hyperemia of the visceral mucosa may develop.

SORGHUM POISONING IN HORSES

Sorghum species are **drought-tolerant plants** with a high nutritional value related to protein, fiber, calcium, potassium, phosphorus, and antioxidant content. Unfortunately, the plants may produce **neuropathic and teratogenic manifestations** if consumed by animals.

The syndrome is reported almost exclusively in horses, although a similar disease has been reported in sheep and cattle. The syndrome develops in horses after they have grazed for weeks to months on hybrid **Sudan Grass** pastures, and axonal degeneration and myelo-malacia in the spinal cord and cerebellum develop. In Ruminants, it is often seen associated with feeding of Jwar (*Sorghum vulgare*).

Sorghum poisoning is characterized by **caudal ataxia or incoordination** due to spinal cord lesions, **cystitis**, **urinary incontinence** (which predisposes both male and female horses to cystitis), and **alopecia on the hind legs** due to urine scalding. The loss of urinary bladder function is related to axonal degeneration of spinal cord neurons. Incoordination may progress to irreversible flaccid paralysis. Deformities of the fetal musculoskeletal system (ankylosis or arthrogryposis) and abortion may occur during late pregnancy.

Sweet Clover Poisoning

Etiology & Pathogenesis:

Sweet clover (*Melilotus officinalis* and *M. alba*) at many places is used for preparation of hay or silage for feeding cattle. Damp conditions caused stacks of hay to mold and spoil. During the process of spoiling, the **coumarins** in sweet clover are converted to **toxic dicumarol,** a potent vitamin K antagonist and anticoagulant.

Weathered, large round bales, particularly the outer portions, usually contain the highest concentrations of dicumarol. When toxic hay or silage is consumed for several weeks, dicumarol alters proenzymes required for synthesis of prothrombin, resulting in hypoprothrombinemia (by preventing formation of the active enzyme). It probably also interferes with synthesis of factor VII and other vitamin K–dependent coagulation factors. **Dicumarol concentrations of 20–30 mg/kg** of hay ingested throughout several weeks are usually required to cause poisoning in cattle.

CLINICAL SIGNS of sweet clover poisoning are related to **hemorrhages that result from faulty blood coagulation**. It is a fatal hemorrhagic disease leading to uncontrollable hemorrhages that were generally fatal (differentiation needed from Anthrax). Because dermal pigmentation and hair can obscure small hemorrhages, the first indication of dicumarol poisoning is often death of one or more animals. However, with closer observation, poisoned animals may be stiff or lame due to bleeding into the muscles and joints.

(i) Faulty blood coagulation and (ii) prolonged blood clotting times are observed with sweet clover poisoning.

Important Differential Diagnosis:

Sweet clover poisoning is **normally a herd problem** affecting numerous animals, which contrasts sharply with diseases that affect individual animals, such as **anthrax, blackleg, pasteurellosis, bracken fern poisoning, and aplastic anemia**.

Rodenticide poisoning would be a likely alternative differential diagnosis for hemorrhagic disease involving many animals.

STRYCHNINE TOXICOSIS

Strychnine is an indole alkaloid obtained from the seeds of the tree *Strychnos nux-vomica*, native to India and southeast Asia. strychnine has been used as a pesticide to control rats, moles, and coyotes. Strychnine is highly toxic to most domestic animals.

Strychnine is a pesticide that typically causes toxicosis in companion and production animals by accidental ingestion or malicious poisoning. Onset of toxicosis is rapid and results in agitation, stiff gait, tremors, and seizures, leading to respiratory arrest and death.

Strychnine is ionized in the acidic pH of the stomach and then rapidly absorbed in the small intestine. Strychnine is metabolized in the liver and highest concentrations of strychnine in the body are found in the blood, liver, and kidneys.

Pathogenesis / Mechanism:

Strychnine competitively and reversibly inhibits the **inhibitory neurotransmitter glycine** at postsynaptic neuronal sites in the spinal cord and medulla. This results in unchecked reflex stimulation of motor neurons affecting all the striated muscles. Because the extensor muscles are relatively more powerful than the flexor muscles, they predominate to produce generalized rigidity and tonic-clonic seizures.

Signs / Lesions:

Extensor rigidity causes the animal to assume a sawhorse stance with splayed, stiff legs. Severe tetanic seizures may appear spontaneously or may be initiated by stimuli such as touch, sound, or a sudden bright light. The mucous membranes become cyanotic and the pupils dilated. Rhabdomyolysis and secondary renal failure may occur due to prolonged muscle activity. Hyperthermia (40°–41°C [104°–106°F]) due to stiffness and seizures often occurs in dogs.

Animals dying from strychnine toxicosis have **rapid rigor mortis**.

LEAD POISONING

Young animals, pica, and greater accessibility to lead disposal (contaminated used oil and battery, lead-based paints, contaminated foliage growing near smelters) are key risk factors associated with Lead toxicosis.

Absorbed lead enters the blood, soft tissues, reticulum and eventually redistributes to the bone.

Lead has a profound effect on sulfhydryl-containing enzymes, the thiol content of erythrocytes, antioxidant defenses, and tissues rich in mitochondria, which is reflected in the clinical syndrome.

Signs:

The prominent clinical signs are associated with the GI and nervous systems. In cattle, clinical signs include ataxia, blindness, salivation, spastic twitching of eyelids, jaw champing, bruxism, muscle tremors, and convulsions.

Impairment of the swallowing reflexes frequently contributes to development of aspiration pneumonia. Embryotoxicity and poor semen quality may contribute to infertility.

In horses also, lead poisoning produces chronic syndrome characterized by weight loss, colic, laryngeal or pharyngeal paralysis (roaring), and dysphagia that frequently results in aspiration pneumonia.

Lesions

In animals that die from acute lead poisoning, oil or flakes of paint or battery may be evident in the GI tract. The caustic action of lead salts causes **gastroenteritis**.

In the nervous system, edema, congestion of the cerebral cortex, and flattening of the cortical gyri are present. With histologic analysis, endothelial swelling, laminar cortical necrosis, and edema of the white matter may be evident. Tubular necrosis in kidneys; Osteoporosis; Placentitis and accumulation of lead in the fetus may result in abortion.

Diagnosis:

Tentative diagnosis based on neurologic and gastrointestinal manifestations.

Hematologic abnormalities, which are indicative, not confirmatory of lead poisoning, include anemia, **basophilic stippling, metarubricytosis**, and hypochromia.

COPPER POISONING

Sheep are most frequently affected animal. In various breeds of dogs, notably Bedlington Terriers, an inherited sensitivity to copper toxicosis similar to Wilson disease in humans has been identified. Acute and Chronic copper poisoning (toxicosis) can affect animals.

Primary chronic copper toxicosis occurs most commonly in **sheep** when excessive amounts of copper are ingested over a prolonged period. The disease remains subclinical until copper that accumulates in the liver is released in massive amounts into the bloodstream.

Subsequently, Serum copper concentrations increase acutely, causing lipid peroxidation and intravascular hemolysis.

Decreased concentrations of molybdenum or sulfate in the fodder or diet also increases copper absorption and copper toxicity.

Signs

Acute copper toxicosis causes **severe gastroenteritis** characterized by anorexia, signs of abdominal pain, diarrhea, dehydration, and shock. Hemolysis and hemoglobinuria may develop after 3 days or so.

The sudden onset of clinical signs in **Chronic copper poisoning** is associated with a hemolytic crisis. Clinical signs include depression, recumbency, rumen stasis, anorexia, thirst, dyspnea, pale mucous membranes, hemoglobinuria, and jaundice. During the hemolytic crisis, laboratory testing will often indicate **methemoglobinemia, hemoglobinemia, and decreases in PCV** and blood glutathione concentration.

Lesions

Acute copper poisoning produces **severe gastroenteritis**, with erosions and ulcerations in the ABOMASUM of ruminants. Icterus develops in animals that survive >24 hours.

Tissues discolored by icterus and methemoglobin are characteristic of chronic poisoning. Swollen, **gunmetal-colored kidneys**, **port-wine-colored urine**, and **enlarged spleen with dark brown-black parenchyma** are manifestations of the hemolytic crisis. The liver is enlarged, friable with centrilobular hepatic necrosis and renal tubular necrosis is also evident.

Other diagnoses to be ruled out may include bacillary hemoglobinuria, leptospirosis, babesiosis and postparturient hemoglobinuria. Molybdenum tissue concentrations should also be determined.