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9 Forage-induced Animal Disorders

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THIS chapter presents antiquality factors of forage crops that affect animal performance. A summary is given of some herbage minerals that occur in concentrations deficient or toxic to animals. Significant attention is given to organic compounds that are secondary products (1) of photosynthesis or (2) of associated organisms that alter forage quality and reduce animal performance.

MINERAL DISORDERS

Mineral element concentrations in herbage may affect animal health because low levels may lead to deficiency, because high levels may lead to toxicity, or because one mineral element interacts with another to reduce the relative availability. Herbage levels and ruminant diet requirements are given in Table 9.1.

Grass Tetany (Hypomagnesemia). Grass tetany is a magnesium (Mg) deficiency of ruminants usually associated with their grazing of cool-season grasses during spring. Next to bloat, this is probably the most important nutritional problem in grazing livestock. Annual losses in the US are estimated at $50 million to $150 million (Mayland and Sleper 1993). Grass tetany occurs in all classes of cattle (*Bos taurus* and *Bos indicus*) and sheep (*Ovis aries*) but is most prevalent among older females early in their lactation. Magnesium must be supplied daily because it is excreted in urine and milk.

Plasma Mg levels are normally 18-32 mg /L. Blood plasma or serum and urine values less than 18 mg /L are considered indicative of hypomagnesemia. Increasing concern is expressed when blood plasma or urine levels fall below 15 mg/L (Mayland 1988; Vogel et al. 1993), and the dramatic signs of tetany are evidenced at levels below 10 mg/L. Physical symptoms proceed from reduced appetite, dull appearance, and staggering gait to signs of increased nervousness, frequent urination and defecation, muscular tremors, and excitability followed by collapse, paddling of feet, coma, and death.

Grass tetany is a complex disorder. First, Mg requirements are greater for lactating than for nonlactating animals and greater for older than for younger animals. Second, there are differences among bovine breeds in susceptibility to grass tetany with Brahman (*Bos indicus*) and Brahman crossbreeds being more tolerant and European breeds being least tolerant (Greene et al. 1989). Third, many factors influence Mg concentration and availability in the herbage. The principal factor is a high level of potassium (K), which negatively affects soil Mg uptake by plants and availability of herbage Mg to animals. Also,

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TABLE 9.1. Spectrum of nutrient-element concentrations found in grass and legume herbage and a guide to herbage concentrations required by sheep and cattle

Element		Concentrations in		Herbage concentrations for	
		Grasses	Legumes	Sheep	Cattle
			(mg/g)		
Calcium	Ca	2–5	2–14	3–4	
Chlorine[a]	Cl	0.1-20.0		1	2
Magnesium	Mg	1–3	2–5	1.2	1.9[c]
Nitrogen	N	10–40	10–50	10–15	
Phosphorus	P	2–4	3–5	2.5	3.0
Potassium	K	10–30	20–37	2–6	
Silicon[a]	Si	10–40	0.5–1.5	not established	
Sodium[a]	Na	0.1–3.0	0.1–2.0	1	2
Sulfur	S	1–4	2–5	1–2	
			(μg)		
Boron	B	3–40	30–80	....	....
Cobalt	Co	0.1–0.2	0.2–0.3	0.11	0.08
Copper	Cu	3–15	3–30	5–6	7–10[d]
Fluorine[a]	F	2-20		1–2	
Iodine[a]	I	0.004–0.8		0.5	0.5[e]
Iron[b]	Fe	50–250	50–250	30	40
Manganese	Mn	20–100	20–200	25	25
Molybdenum	Mo	1–5	1–10	not established	
Selenium[a]	Se	0.01–1.0		0.03–0.7	
Zinc	Zn	15–50	15–70	25–40	

Sources: Herbage data are from the author's files, Gough et al. (1979), and Mayland (1983). Animal data are adapted from Grace (1983), Grace and Clark (1991), and NRC (1984).

[a]Not required for plant growth.

[b]Values in excess of 100–150 μg/g are often reflective of soil contamination.

[c]2 mg/g if K and N are high.

[d]Influenced by Mo and S.

[e]2 μg/g in presence of goitrogens.

low levels of readily available energy, calcium (Ca), and phosphorus (P) and high levels of organic acids, higher fatty acids, and nitrogen (N) in the herbage reduce the absorption of or retention of Mg by the animal. Forage Mg levels greater than 2.0 mg/g dry matter and a milliequivalent 0 ratio of less than 2.2 for K/(Ca + Mg) are considered safe (Grunes and Welch 1989).

Agronomic practices to reduce risk potential of tetany include splitting applications of N and K fertilizers, liming acid soils with dolomitic rather than calcitic limestone, or spraying Mg on herbage (Robinson et al. 1989). One might also use cultivars or species having high Mg and Ca and low K concentrations (Sleper et al. 1989; Moseley and Baker 1991; Mayland and Sleper 1993). Animal husbandry practices include assigning breeds and classes of livestock to pastures that are less susceptible to tetany (Greene et al. 1989). Magnesium could be supplemented through additions to herbage, drinking water, stock salt, molasses licks, or other energy sources (Robinson et al. 1989).

Nitrate Poisoning. Nitrate (NO_3^-) accumulates in plant tissue because of luxuriant uptake of soil N when plant metabolism of N is slow or even stopped. This condition is promoted by cool temperature, drought, or other physiological stress that slows growth (Wright and Davison 1964). Plant NO_3^- itself is not normally toxic to animals, but it is usually reduced to nitrite (NO_2^-) in the rumen. If the NO_2^- is not reduced further, the accumulated NO_2^- causes various intensities of methemoglobinemia that may cause acute poisoning of the animal (Wright and Davison 1964; Singer 1972; Deeb and Sloan 1975).

Intensive applications of N fertilizer to silage crops often result in appreciable amounts of NO_3^- in the herbage. During ensiling, the NO_3^- is completely or partially degraded (Spoelstra 1985). The end products are ammonia (NH_3) and nitrous oxide, with NO_2^- and nitric oxide occurring as intermediates. Silage crops containing high NO_3^- levels should be checked for NO_3^- before the ensiled crops are fed to livestock.

Silofiller's disease is an illness of farm workers caused by inhalation of nitric and nitrous oxides from fermenting forages containing high N concentrations. Good air ventilation will reduce the health hazard of these noxious gases.

The most common effect of NO_3^- poisoning is the formation of methemoglobin that occurs

when NO_2^- oxidizes the ferrous iron of blood hemoglobin to ferric iron. This produces a chocolate-brown methemoglobin that cannot release oxygen (O) to body tissue. As the toxicity intensifies, the brownish-colored blood casts a brownish discoloration to the nonpigmented areas of skin and the mucous membranes of the nose, mouth, and vulva. Clinical signs progress with staggering, rapid pulse, frequent urinating, and labored breathing, followed by collapse, coma, and death. Sublethal toxicity may be evidenced by abortion of pregnant females.

The rate and degree of NO_3^- reduction in the rumen depend on the microflora present and the energy available for continued reduction of NO_2^- to NH_3. This interaction of available energy and NO_3^- reduction results in mixed responses. Furthermore, cattle and sheep can adapt to some extent to prolonged high levels of NO_3^- feeding (Wright and Davison 1964). Sheep have been poisoned by as little as 500 μg N/g as NO_3^-, whereas in other experiments 8000 μg N/g as NO_3^- had no effect (Singer 1972). Other data show that 2000 μg N/g as NO_3^- in forage was the threshold limit for cattle (Bush et al. 1979) while no problem occurred with feeding forage containing 4600 μg N/g as NO_3^- (Davison et al. 1964).

Forages containing 3400 to 4500 μg N/g as NO_3^- should be considered potentially toxic and should be mixed with safer feeds prior to use (Wright and Davison 1964). Energy supplements will help in the complete reduction of inorganic N. Suspect forages should be tested for NO_3^- levels. Although risky, feeding additional forages low in NO_3^- would dilute the NO_3^- intake. Be aware that these test levels are reported on an elemental N basis.

Sudangrass (*Sorghum bicolor* [L.] Moench), sorghums (*Sorghum* spp.), corn (*Zea mays* L.), and small grains are often indicted in NO_3^- poisoning. These crops are often heavily fertilized and when subject to drought, frost, or other stress may accumulate large concentrations of NO_3^-. Perennial grasses generally are less of a problem because they usually receive lower levels of N fertilizer and have greater tolerance of drought and frost. Legumes fix their own N into reduced forms and do not contribute to NO_3^- poisoning.

Copper, Molybdenum, and Sulfur Interaction. Copper (Cu) deficiency significantly affects ruminant livestock production in large areas of North America (Gooneratne et al. 1989), mainly in areas where soils are naturally high in molybdenum (Mo) and sulfur (S) (Kubota and Allaway 1972). In ruminant nutrition, the two-way and three-way interactions between these three elements are unique in their complex effects on animal health. Different clinical terms describe each primary factor affecting Cu nutrition.

Sheep consuming a complete diet, low in S and Mo and with modest Cu (12-20 mg/kg dry matter), can succumb to Cu toxicity. Sheep grazing another pasture of similar Cu concentration, but high in Mo and S, will produce Cu-deficient lambs showing clinical signs of swayback disease (Suttle 1991). Copper-deficient cattle and sheep appear unthrifty and exhibit poor growth and reproduction. Copper deficiency reduces the level of melanin pigments in hair and wool so that normally dark-colored fibers will be white or grey (Grace 1983; Grace and Clark 1991). Low dietary Cu levels may limit effectiveness of the immune system in animals.

Forage plants growing on soil or peat that contain high levels of Mo will produce a scouring disease known as *molybdenosis*. In the presence of S, high intake of Mo can induce a Cu deficiency due to formation of insoluble Cu-Mo-S complexes in the digestive tract that reduce the absorption of Cu. Several pathways exist by which Cu × Mo × S interactions mediate their effect on ruminants (Suttle 1991). Most clinical signs attributed to the three-way interaction are the same as those produced by simple Cu deficiency and probably arise from impaired Cu metabolism. The tolerable risk threshold of Cu:Mo is not fixed at 3:1 but declines from 5:1 to 2:1 as pasture Mo concentrations increase from 2 to 10 μg Mo/g. Risk assessment has been only partially successful because the interactions are not yet fully understood (Suttle 1991).

Cattle are more sensitive than sheep to molybdenosis; however, sheep are more susceptible to Cu toxicity (Suttle 1991). Sheep should not be allowed to graze pastures that recently received poultry or swine manure. This manure may contain high Cu concentrations originating from the Cu salts fed to poultry or swine to control worms.

Copper-depleted animals should respond equally well to dietary Cu supplements, oral Cu boluses or pellets, and Cu injections. Copper fertilization of Cu-deficient pastures should be done carefully because the range between sufficiency and toxicity is quite small.

Selenium Deficiency and Toxicity. Herbage selenium (Se) concentrations are marginal to

severely deficient for herbivores in many areas of the world. These include the Pacific Northwest and the eastern one-third of the US (Kubota and Allaway 1972; Mayland et al. 1989). Herbage Se concentrations of 0.03 μg/g are generally adequate. However, 0.1 μg/g may be necessary when high S reduces Se availability. Climate conditions and management practices that favor large increases in forage yield may dilute Se concentrations to critical levels in herbage.

Selenium deficiency causes white muscle disease in lambs and calves. The young may be born dead or die suddenly within a few days of birth because Se intake by the gestating dam was inadequate. A delayed form of white muscle disease occurs in young animals, while a third form is identified as illthrift in animals of all ages. Injectable Se, often with vitamin E, or oral supplementation (selenized salt or Se boluses) may meet animal requirements. Selenium fertilization of soils is legal only in New Zealand and Finland.

In many semiarid areas of the world, grasses and forbs contain adequate (0.03-0.1 μg/g) to toxic (>5 μg/g) levels of Se for grazing animal requirements. These areas include desert, prairie, and plains regions of North America where Se toxicity is observed in grazing animals. Some plants growing in these areas will accumulate 100-1000 μg/g Se. Animals eating these generally unpalatable plants will likely die. Grasses, small grains, and some legumes growing on the Se-rich Cretaceous geological materials may contain 5-20 μg/g. Some animals eating this herbage may die, but most are likely to develop chronic selenosis called *alkali disease*. There is hair loss, and hoof tissues become brittle. In these instances, some animals may develop a tolerance for Se as high as 25 μg/g.

A second chronic disorder in ruminants, called "blind staggers," or polioencephalomalacia, also occurs in these areas. This disorder, while historically attributed to Se, is likely caused by excess S (Mayland, unpublished data). High sulfate levels in the drinking water and ingested herbage have led to the occurrence of blind staggers (Beke and Hironaka 1990). Changing to high-quality, low-sulfate water and forage has reduced the risk.

Under marginal levels of Se, increased S reduces the uptake of Se by plants and the bioavailability of dietary Se to animals. However, the S antagonist has not been effective against Se toxicosis. Replacing high-Se forage with low-Se forage is the most effective way of countering Se toxicity.

Cobalt, Iodine, and Zinc. Cobalt (Co) deficiencies in herbivores have been identified in the southeastern US and Atlantic seaboard states and along the Wasatch Front in Utah (Kubota and Allaway 1972). Cobalt is a metal cofactor in vitamin B_{12}, which is required in energy metabolism in ruminants. The signs of Co deficiency include a transient unthriftiness and anemia leading to extreme loss of appetite and eventually death. Two other conditions attributed to Co deficiency are ovine (sheep) white liver disease and phalaris staggers (Graham 1991). The mechanism by which oral Co supplementation prevents staggers is not understood. Pasture herbage levels of at least 0.11 and 0.08 μg Co/g will provide adequate Co for sheep and cattle, respectively. Cobalt injections or oral supplements can be given to animals. Pastures may also be fertilized with cobalt sulfate. Manganese (Mn) and iron (Fe) are antagonists to Co absorption (Grace 1983).

Plants do not require iodine (I); nevertheless, herbage in the northern half of the US is generally deficient for animal requirements. These deficiencies are noted by the occurrence of goiter in animals (Kubota and Allaway 1972). The use of iodized salt easily meets iodine needs of animals on pasture.

Zinc (Zn) concentration in pasture plants ranges from 10 to 70 μg/g but is most often in the 10-30 μg/g range. In one study, cattle grazing forage having 15-20 μg/g gained weight faster when supplemented with additional Zn (Mayland et al. 1980). Blood Zn levels were statistically higher in supplemented than in control animals, but this difference was very small and would not be useful as a diagnostic tool. There was no other obvious difference between the control and Zn-supplemented groups. More information on Zn requirements and diagnostic tests is needed.

Fluorosis and Silicosis. Plants do not require fluorine (F), but herbage generally contains 1-2 μg F/g, which is adequate for bone and tooth development in animals. At higher levels, the development of fluorosis is influenced by the age, species, dietary form, and length of exposure. Fetuses and young animals are most susceptible to excess F. Otherwise, long-term intakes of 30 μg F/g may be tolerated by ruminants before bone abnormalities appear (Underwood 1977). In areas of endemic fluorosis, plants may be contaminated by natu-

rally fluoridated dust from rock phosphate or other smelters. During manufacture of superphosphate and dicalcium phosphate, 25%-50% of the original F is lost. Excess F may also be absorbed by plants that are sprinkler irrigated with thermal groundwater. Rock phosphate supplement and naturally fluoridated drinking water are the primary dietary sources of excess F.

Grasses contain more silicon (Si) than do legumes and account for the large amount of Si ingested by grazing animals. Silicon may be needed in trace amounts by animals but is not required by herbage plants. Silicon adversely affects forage quality and may affect animal preference of plants. Silicon serves as a varnish on the cell walls, complexes microelements and reduces their availability to rumen flora, and inhibits the activity of cellulases and other digestive enzymes (Shewmaker et al. 1989). The net effect of forage Si is to reduce dry matter digestibility by 3 percentage units for each percentage unit of Si present (Van Soest and Jones 1968).

Silicon is also responsible for urolithiasis (urinary calculi or range waterbelly) in steers. Waterbelly is correlated negatively with urine volume and water intake and only weakly related to herbage Si. Management strategies in high-Si areas include stocking only heifers and providing adequate drinking water. If feasible, the Ca:P ratio in the diet should be reduced and urine acidified by supplementing animals with ammonium chloride (Stewart et al. 1991).

Soil Ingestion. Most grazing animals and some humans eat soil. The ingestion may be indirect because herbage is dusty. Nevertheless, animals may actively eat soil for unknown reasons. Ingested soil may serve as a source of minerals. In addition, soil may contain residual chemicals applied to pasture or derived from atmospheric fallout. Some soil particles are harder than tooth enamel and will cause excessive abrasion and premature loss of teeth. Ingested soil, as a possible contaminant, must also be considered in experimental pasture studies (Mayland et al. 1977).

NATURAL TOXICANTS IN FORAGES

Plants are protected against herbivory (being eaten by vertebrate and invertebrate herbivores) by many diverse physical and chemical means. Physical defenses include leaf hairs, spines, thorns, highly lignified tissue (e.g., wood), and growth habitat (e.g., prostrate form). Chemical defenses of plants include a bewildering array of often complex chemicals that are toxic or poisonous to various herbivores. These chemicals may be synthesized by the plant itself or may be produced by symbiotic or mutualistic fungi growing with the plant. The defensive chemicals produced by the plant are considered secondary compounds, as distinct from the primary compounds that are essential in plant metabolism. Secondary compounds (e.g., alkaloids) do not function directly in cellular metabolism but apparently are synthesized to serve as the plant's defensive arsenal.

Chemicals synthesized by fungi are known as *mycotoxins*, which may be produced by fungi living on or in forage plants. Mycotoxins are responsible for many disorders of grazing animals. For example, the endophytic fungi of tall fescue (*Festuca arundinacea* Schreb.) produce ergot alkaloids that cause fescue foot, summer fescue toxicosis, and reproductive disorders, while endophytes in perennial ryegrass (*Lolium perenne* L.) produce lolitrems, which cause ryegrass staggers. In the US, total livestock-related losses attributed to the tall fescue endophyte are estimated between $500 million and $1 billion a year (Ball et al. 1993). The economic impact of poisonous plants on livestock production has been reported by James et al. (1988).

Toxins of plant origin can be classified into several major categories, including alkaloids, glycosides, proteins and amino acids, and phenolics (tannins). Alkaloids are bitter substances containing N in a heterocyclic ring structure. There are hundreds of different al-

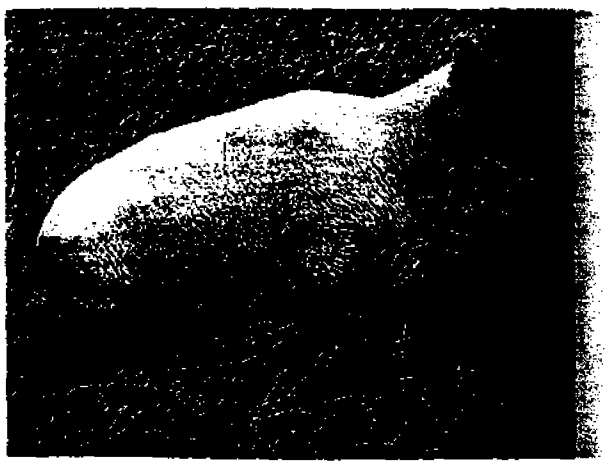

Fig. 9.1. An example of ryegrass staggers, a neurological disorder of livestock grazing endophyte-infected perennial ryegrass pastures. Lolitrem B is the major toxin involved. *Courtesy of R. E. G. Keogh.*

kaloids, which are classified according to the chemical structure of the N-containing ring(s). For example, the pyrrolizidine alkaloids in common pasture weeds (*Senecio* spp.) have a pyrrolizidine nucleus of two five-membered rings, while ergot alkaloids have an indole ring structure. Lupins (*Lupinus* spp.) contain quinolizidine alkaloids, which are based on two six-membered rings.

Glycosides are composed of a carbohydrate (sugar) portion linked to a noncarbohydrate group (the aglycone) by an ether bond. Examples are cyanogenic glycosides, glucosinolates, saponins, and coumarin glycosides. Their toxicity is associated with the aglycone, such as cyanide in cyanogenic glycosides. Glycosides are hydrolyzed by enzymatic action, releasing the aglycone. This often occurs when the plant tissue is damaged by wilting, freezing, mastication, or trampling. A good example of this is the production of toxic cyanide when forage sorghums such as sudangrass are frosted. The breakdown of cell structure releases the glycoside from storage vacuoles, allowing it to be hydrolyzed by enzymes in the cytosol and to release free cyanide.

Many toxic amino acids occur in plants. One of the best known is mimosine, a toxic amino acid in the tropical forage legume *Leucaena leucocephala* de Wit. Others include lathyrogenic amino acids in *Lathyrus* spp., indospecine in *Indigofera* spp., and the brassica anemia factor, which is caused by S-methylcysteine sulfoxide, a metabolic product of forage brassicas (*Brassica* spp.).

Phenolic compounds, which include the condensed and hydrolyzable tannins, are substances containing aromatic rings with one or more hydroxyl groups. The hydroxyl groups are chemically reactive and can react with functional groups of proteins to form indigestible complexes. The tannin-protein complexes are astringent and adversely affect feed intake. All plants contain phenolic compounds. In some cases, their type or concentration may cause negative animal responses. These include reduced feed intake and protein digestibility of birdsfoot trefoil (*Lotus cor-*

Fig. 9.2. (*a*) A steer in Australia that has been grazing on *Leucaena leucocephala* for several months. Note the loss of hair and unthrifty appearance due to the effects of mimosine, a toxic amino acid that occurs in *Leucaena*. (*b*) The same steer a few months after receiving a dose of rumen bacteria that detoxifies mimosine. These photographs illustrate quite dramatically the potential of rumen microbes to detoxify some of the natural toxins in plants. *Courtesy of R. J. Jones.*

niculatus L.) and sericea lespedeza (*Lespedeza cuneata* [Dum.-Cours.] G. Don). Oak (*Quercus* spp.) poisoning is caused by tannins in oak browse. Many tree legumes used in tropical agroforestry can contain sufficient levels of tannins to impair animal performance.

Toxins and Animal Disorders Associated with Forage Legumes. Some animal disorders are associated with forage legumes. For example, pasture bloat is a very common problem with ruminants grazing many forage legumes, such as alfalfa (*Medicago sativa* L.) and clovers (*Trifolium* spp.). Pasture bloat is caused by rapid release of cell contents of succulent, immature legume forage during rumen fermentation. The succulent material has a rapid rate of cell rupture, releasing the soluble proteins and fermentable carbohydrates. Soluble proteins are foaming agents, causing the formation of a stable foam in the rumen, which prevents eructation (belching) of rumen gases formed by the fermentation. High sugar content of lush legume forage supports a vigorous microbial population, producing large amounts of gas. The combination of vigorous gas production and presence of foaming agents produces a stable frothy foam, which blocks the esophagus, culminating in rumen distention and respiratory paralysis. Bloat can be minimized by maintaining at least 50% grass in the pasture or by giving animals access to blocks containing an antifoaming agent (e.g., poloxalene).

Some legume forages, such as birdsfoot trefoil, cicer milkvetch (*Astragalus cicer* L.), sericea lespedeza, and sainfoin (*Onobrychis viciifolia* Scop.), do not cause bloat. These plants contain tannins, which at low concentrations complex with the cytoplasmic proteins and prevent their ability to foam. However, *Lespedeza* spp. and trefoils (*Lotus* spp.) can contain sufficiently high tannin levels to inhibit animal performance by reducing feed intake and protein digestibility. Although saponins are foaming agents that occur in most bloat-producing legumes, they do not seem to have a significant role in bloat (Majak et al. 1980).

Phytoestrogens occur in many forage legumes, including alfalfa, red clover (*T. pratense* L.), subterranean clover (*T. subterraneum* L.), and other *Trifolium* spp. In clovers, the estrogenic compounds are mainly isoflavones such as formononetin, genistein, biochanin A, and diadzein, while coumestrol and other coumestans are the principal estrogens in alfalfa and medics, like black medic (*Medicago lupulina* L.).

Historically, phytoestrogens have had their greatest impact on reproduction of sheep grazing subterranean clover in Australia. "Clover disease" is characterized by a dramatic decrease in fertility of ewes, along with abnormalities of the genitalia. Since the identification of phytoestrogens as the causative agents of clover disease, Australian plant breeders have selected for and developed low-estrogen cultivars of subterranean clover. This has largely eliminated the problem of clover-induced infertility in Australia.

The phytoestrogens owe their physiological activity to their structural resemblance to endogenous estrogens, allowing them to bind to estrogen receptors and elicit an estrogen response (Adams 1989). The activity of phytoestrogens is altered by rumen fermentation. Biochanin A and genistein are converted to inactive compounds in the rumen, while formononetin is bioactivated to the more potent compounds daidzein and equol (Adams 1989).

Toxins associated with specific forage legume species will be briefly described. Further detail is provided by Cheeke and Shull (1985).

RED CLOVER (*Trifolium pratense* L.) When infected with the black patch fungus (*Rhizoctonia leguminicola* Gough & ES Elliott), red clover hay may contain the indolizidine alkaloid slaframine. Slaframine is a cholinergic agent that causes excessive salivation (clover slobbers), eye discharge, bloat, frequent urination, and watery diarrhea. These effects are due to stimulation of the autonomic nervous system. The fungal infection and potential toxicity develop most rapidly in periods of high humidity. Prompt removal of the toxic forage from livestock generally alleviates all signs of intoxication.

WHITE CLOVER (*Trifolium repens* L.). White clover may contain cyanogenic glycosides. These may have some importance in conferring resistance to slugs and other pests. The concentration of cyanogens in white clover is not sufficiently high to cause livestock poisoning but may contribute to lower midsummer palatability of the clover.

ALSIKE CLOVER (*Trifolium hybridum* L.). Poisoning from alsike clover has been reported in Canada and the northern US. It has not been conclusively proven to be caused by the clover, but circumstantial evidence strongly suggests

that it is clover caused (Nation 1991). Toxicity signs include photosensitization, neurological effects such as depression and stupor, liver damage, and contradictory effects on liver size. Sometimes, the liver is extremely enlarged, in others, it is shrunken and fibrotic.

SWEETCLOVER (*Melilotus* spp.). Sweetclover poisoning has been an important problem in North America. Sweetclover contains coumarin glycosides, which are converted by mold growth to dicoumarol. Dicoumarol is an inhibitor of vitamin K metabolism, thus causing an induced vitamin K deficiency. Sweetclover poisoning causes a pronounced susceptibility to prolonged bleeding and hemorrhaging because of the essential role of vitamin K in blood clotting. Wet, humid weather that favors mold growth during curing of sweetclover hay increases the likelihood of poisoning. Cattle are the main livestock affected.

Moldy sweetclover hay should not be fed or should be used with caution. Ammoniation of stacked hay with anhydrous ammonia reduces dicoumarol levels. Animals with signs of sweetclover poisoning are treated with injections of vitamin K. Low-coumarin cultivars of sweetclover have been developed and should be used in areas where sweetclover poisoning is a problem. Coumarin has a vanillalike odor and is responsible for the characteristic smell of sweetclover.

OTHERS. Additional forage legumes contain various toxins. As already mentioned, birdsfoot trefoil and lespedeza contain tannins. Crownvetch (*Coronilla varia* L.) contains glycosides of 3-nitropropionic acid, which are metabolized in ruminants to yield NO_2^-. Concentrations are rarely sufficient to cause NO_2^- poisoning, but the glycosides contribute to a low palatability of crownvetch. Cicer milkvetch, a minor forage legume in the northern US, has caused photosensitization in cattle and sheep (Marten et al. 1987, 1990).

The seeds of common (*Vicia sativa* L.) and hairy vetch (*V. villosa* Roth) are poisonous. They contain toxic lathyrogenic amino acids, which cause damage to the nervous system, with signs such as convulsions and paralysis. This occurs primarily in nonruminants that consume seeds as a contaminant of grain. Hairy vetch poisoning of ruminants has been reported in the US (Kerr and Edwards 1982) and South Africa (Kellerman et al. 1988). Signs include severe dermatitis, skin edema, conjunctivitis, corneal ulcers, and diarrhea. About 50% of affected animals die. The toxic agent in hairy vetch has not been identified.

Many *Lathyrus* spp. contain toxic amino acids that cause neurological problems and skeletal defects known as lathyrism. Flatpea (*L. sylvestris* L.) has potential as a forage crop for degraded soils such as reclaimed strip-mined areas. Flatpea is nearly free of toxicity, but Foster (1990) notes that "the question of flatpea toxicity must be answered conclusively before this plant can be recommended for use by livestock producers." Toxicity of flatpea hay to sheep, with typical signs of neurolathyrism, has been reported by Rasmussen et al. (1993).

Lupinus spp. contain a variety of alkaloids of the quinolizidine class. The sweet lupines such as *L. albus* L. and *L. angustifolius* L. contain low levels of various alkaloids (e.g., cytisine, sparteine, lupinine, lupanine). These cause feed refusal and neurological effects. Sheep are frequently poisoned by wild lupines on rangelands, as they avidly consume the seedpods. On rangelands in western North America, there are many species of wild lupines that are toxic to livestock. Species such as *L. sericeus* Pursh., *L. caudatus* Kellogg, and *L. argenteus* var. *tenellus* (Dougl. ex G.Don) D.Dunn (also known as *L. laxiflorus*) contain anagyrine, an alkaloid that is teratogenic in cattle. It causes crooked calf disease, if consumed by pregnant cows during days 40-70 of gestation. Severe skeletal deformations in the fetuses may occur. This teratogenic alkaloid does not occur in domesticated *Lupinus* spp.

In Australia, sweet lupines are extensively grown as a grain crop; sheep are grazed on the lupine stubble after harvest. Often the stems of lupines are infected with a fungus (*Phomopsis leptostromiformis* [Kühn] Bubak in Kab. & Bubak) that produces toxic phomopsins. These mycotoxins cause liver damage, including fatty liver and necrosis, eventually leading to liver failure and death. This condition is referred to as *lupinosis*.

Leucaena contains a toxic amino acid, mimosine. In the rumen, mimosine is converted to various metabolites, including 3,4-dihydroxypyridine (DHP). Both mimosine and DHP are toxic to ruminants, causing dermatitis and poor growth (mimosine) and goitrogenic (thyroid-inhibitory) effects. Australian researchers (Jones and Megarrity 1986) learned that Hawaiian ruminants, adapted to a leucaena diet, had mimosine-degrading rumen bacteria that eliminated the toxicity. These bacteria have now been introduced into cattle in Australia, allowing leucaena to be used as a productive source of high-protein

forage (Quirk et al. 1988). Hammond et al. (1989) in Florida also reports detoxification of mimosine by rumen microbes.

Various other tropical legumes contain toxic factors. Many *Indigofera* spp. contain the toxic amino acid indospecine (Aylward et al. 1987). The jackbean (*Canavalia ensiformis* [L.] DC) contains canavanine, an amino acid analog of arginine (Cheeke and Shull 1985). Generally, the grazing diet contains other species that dilute the effects of the toxins.

Toxins and Animal Disorders Associated with Grasses. In contrast to herbaceous plants, grasses are generally not well defended chemically. Most grasses have coevolved with grazing animals and by growth habit survive frequent defoliation. Hence, there are few intrinsic toxins in common forage grasses. More frequent are mycotoxins produced by fungi living in or on grasses. Fungi living within plant tissues or tissue spaces are called *endophytes*. Many livestock syndromes are attributed to endophyte toxins. Examples of toxins intrinsically present in grasses are the alkaloids of *Phalaris* spp., cyanogens in forage sorghums (e.g., sudangrass), and oxalates in many tropical grasses. These have been reviewed by Cheeke (1995).

PHALARIS POISONING. This poisoning produces two syndromes in livestock: a neural disorder (phalaris staggers) and a sudden death syndrome. These are disorders of both sheep and cattle consuming various *Phalaris* spp., either by grazing or as hay or other conserved feed. Phalaris poisoning has particularly been reported from Australia and New Zealand, primarily in animals grazing pastures containing *P. aquatica* L. (formerly *P. tuberosa* L.). In the US, phalaris poisoning of sheep *P. caroliniana* Walt. is associated with *P. caroliniana* Walt. (Nicholson et al. 1989) and *P. aquatica* L. (East and Higgins 1988). Reed canarygrass (*P. arundinacea* L.) poisoning of sheep has been observed in New Zealand (Simpson et al. 1969). Contamination of a sheep feedlot diet with a source of phalaris alkaloids led to an outbreak of staggers in California (Lean et al. 1989).

Phalaris staggers is characterized by convulsions and other neurological signs due to brain damage, culminating in mortality. The syndrome is caused by tryptamine alkaloids in *Phalaris* spp., which are believed to inhibit serotonin receptors in specific brain and spinal cord nuclei (Bourke et al. 1990). These tryptamine alkaloids are responsible for the low palatability of the grass and poor performance of animals on reed canarygrass pastures (Marten et al. 1976). Low-alkaloid cultivars of reed canarygrass have been developed that give improved animal productivity (Marten et al. 1981; Wittenberg et al. 1992). The cause of the phalaris sudden death syndrome has not been conclusively identified but appears not to be the tryptamine alkaloids (Bourke et al. 1988). As many as four different factors, including a cardiorespiratory toxin, thiaminase and amine cosubstrate, cyanogenic compounds, and NO_3^- compounds, have been implicated (Bourke and Carrigan 1992).

HYDROCYANIC ACID (HCN) POISONING. Forage sorghums such as sudangrass contain cyanogenic glycosides, from which free cyanide can be released by enzymatic action. The glycosides occur in epithelial cells of the plant, while the glycoside-hydrolyzing enzymes are in mesophyll cells. Damage to the plant from wilting, trampling, frost, drought stress, etc., results in the breakdown of the plant structure, causing exposure of the glycosides to the hydrolyzing enzymes and formation of free cyanide (Fig. 9.3). Cyanide causes acute respiratory inhibition by inhibiting the enzyme cytochrome oxidase. Signs of poisoning include labored breathing, excitement, gasping, convulsions, paralysis, and death.

The cyanide potential and risk of poisoning decrease as forage sorghums mature (Wheeler et al. 1990). The likelihood of acute cyanide poisoning may be greater when feeding sorghum hay than when grazing the fresh plant because of the more rapid dry matter intake. Ground and pelleted sorghum hay may be especially toxic because of the rapid rate of intake and cyanide release (Wheeler and Mulcahy 1989). Ensiling markedly reduces the cyanide risk.

Nitrogen fertilization of forage sorghums enhances the cyanide risk. Special caution is needed when livestock is grazing lush, immature forage sorghums and when frost has occurred. Laboratory analysis of the cyanide potential of sorghum hay is advisable (Wheeler and Mulcahy 1989). Cattle deaths on sorghum pastures occur most frequently in late summer or early fall, following an overnight frost.

OXALATE POISONING. Many tropical grasses contain high levels of oxalate. Upon ingestion by ruminants, the oxalate complexes dietary Ca and forms insoluble calcium oxalate. This leads to disturbances in Ca and P metabolism

Fig. 9.3. Forage sorghums like sudangrass are excellent feeds for grazing animals. However, they must be managed carefully to avoid cyanide toxicity. *Courtesy of C. Mulcahy.*

involving excessive mobilization of bone mineral. The demineralized bones become fibrotic and misshapen, causing lameness and "bighead" in horses. Ruminants are less affected, but prolonged grazing by cattle and sheep of some tropical grass species can result in severe hypocalcemia, i.e., Ca deposits in the kidneys and kidney failure. Tropical grasses that have high oxalate levels include *Setaria* spp., *Brachiaria* spp., buffelgrass (*Cenchrus ciliaris* L.), 'Pangola' digitgrass (*Digiteria eriantha* Steud.), and kikuyugrass (*Pennisetum clandestinum* Hochst. ex Chiov.). Provision of mineral supplements high in Ca to grazing animals overcomes the adverse effect of oxalates in grasses.

FACIAL ECZEMA. Many livestock poisons are caused by fungi growing on or in grass. Other organisms like nematodes, insects, and bacteria are sometimes involved. Facial eczema of grazing ruminants is a classic example of secondary or hepatogenous photosensitization, due to liver damage. Facial eczema is a major problem of sheep and cattle on perennial ryegrass pastures in New Zealand and has been reported sporadically in other countries.

The fungus *Pithomyces chartarum* (Berk. & M.A. Curtin) M.B. Ellis grows on the dead litter in ryegrass pastures and produces large numbers of spores. The spores contain a hepatotoxin, sporidesmin, which is only slowly broken down in the liver. Spores are consumed during grazing of infected pastures, which leads to sporidesmin-induced liver damage. The damaged liver is unable to metabolize phylloerythrin, a metabolite of chlorophyll, which then accumulates in the blood. Phylloerythrin is a photodynamic agent that reacts with sunlight, causing severe dermatitis of the face, udder, and other exposed areas.

There are species differences in susceptibility to sporidesmin: for example, goats are much more resistant to facial eczema than sheep, probably because of a faster rate of sporidesmin detoxification in the liver (Smith and Embling 1991).

ERGOT. Ergotism is another mycotoxicosis associated with grasses. Seed heads of many grasses are susceptible to infection with *Claviceps paspali* F Stevens & JG Hall and other *Claviceps* spp. In the US, dallisgrass (*Paspalum dilatatum* Poir.) poisoning is the major *Claviceps*-caused ergotism. Ergot alkaloids cause vasoconstriction and reduced blood supply to the extremities, resulting in sloughing of ear tips, tail, and hooves. There are also neurological effects, including hyperexcitability, incoordination, and convulsions. Ergotism can be avoided by not allowing grasses to set seed.

TALL FESCUE TOXICOSIS. Tall fescue infected with the endophytic fungus (*Acremonium*

coenophialum Morgan-Jones & Gams) is responsible for three types of livestock disorders when animals consume forage or seed. These include fescue foot, summer fescue toxicosis, and fat necrosis. Animal performance is reduced, and reproduction is impaired.

Tall fescue toxicity is caused by ergot alkaloids such as ergovaline, which is produced by the endophyte growing systemically within the plant tissues. One effect of ergovaline is the inhibition of prolactin from the pituitary gland. Physiologically, tall fescue toxicosis and its associated reproductive effects are explained by reduced prolactin levels that, via effects on brain neurotransmitters, inhibit smooth muscle contraction. Because prolactin also stimulates lactation, agalactia, i.e., lack of milk production, occurs with consumption of endophyte-infected tall fescue. This is particularly severe in horses (Porter and Thompson 1992). The problems associated with endophyte-infected tall fescue are further described in Chapter 28, Volume 1.

RYEGRASS TOXICITY. There are several livestock disorders associated with consumption of ryegrass. Besides facial eczema (already described), two other major syndromes are perennial ryegrass staggers and annual ryegrass (*L. multiflorum* Lam.) toxicity.

Perennial ryegrass staggers is caused by compounds called *tremorgens*. Affected animals exhibit various degrees of incoordination and other neurological signs (head shaking, stumbling and collapse, and severe muscle spasms), particularly when disturbed or forced to run. Even in severe cases, there are no pathological signs in nervous tissue. Affected animals usually spontaneously recover. With sheep, ryegrass staggers is primarily a problem in animal management, as affected animals are difficult to move from one pasture to another. Growth rate of the animal is also reduced (Fletcher and Barrell 1984). In Australia and New Zealand, ryegrass staggers occurs in sheep, cattle, horses, and deer. It has been reported in sheep and cattle in California (Galey et al. 1991). It also occurs in sheep grazing winter forage and stubble residue of endophyte-enhanced turf-type ryegrasses in Oregon.

The main causative agents of ryegrass staggers are a group of potent tremorgens called *lolitrems*, the most important of which is lolitrem B (Gallagher et al. 1984). Lolitrem B is a potent inhibitor of neurotransmitters in the brain. The lolitrems are produced by an endophytic fungus, *Acremonium lolii*, which is often present in perennial ryegrass. Turf cultivars of both tall fescue and perennial ryegrass are often deliberately infected with endophytes because the endophyte increases plant vigor, in part by producing ergot alkaloids (*A. coenophialum*) and tremorgens (*A. lolii*). While the presence of the endophyte is advantageous when the grass is used for turf purposes, it has negative effects on animal performance when the grass is consumed by livestock.

In Australia and South Africa, annual ryegrass toxicity is a significant disorder of livestock. It has an interesting etiology, involving annual ryegrass, a nematode, and bacteria. Although the neurological signs are superficially similar, annual ryegrass toxicity and ryegrass staggers are totally different disorders. In contrast to the temporary incoordination seen with ryegrass staggers, there is brain damage with annual ryegrass toxicity. The neurological damage is evidenced by convulsions of increasing severity that terminate in death.

Annual ryegrass toxicity is caused by corynetoxins, which are chemically similar in structure to the tunicamycin antibiotics. Corynetoxins are produced by a *Clavibacter* spp. (formerly designated *Corynebacterium* spp.). This bacterium parasitizes a nematode (*Anguina agrostis*) that infects annual ryegrass. Ryegrass is toxic only when infected with the bacteria-containing nematode. The nematodes infect the seedling shortly after germination, and the larvae are passively carried up the plant as the plant stem elongates. They invade the florets, producing a nematode gall instead of seed. When consumed by animals, corynetoxins inhibit an enzyme involved in glycoprotein synthesis, leading to defective formation of various blood components of the reticulo-endothelial system. This impairs cardiovascular function and vascular integrity, causing inadequate blood supply to the brain.

Corynetoxins have been identified in other grasses besides annual ryegrass, including *Polypogon* and *Agrostis* spp. (Finnie 1991; Bourke et al. 1992). Annual ryegrass toxicity can be avoided by not allowing animals to graze mature grass containing seed heads or by clipping pastures to prevent seed head development. In Australia, these measures are often impractical because of the extensive land areas involved.

OTHER GRASS POISONS. Kikuyu grass is a common tropical forage that is occasionally

toxic to livestock (Peet et al. 1990). Clinical signs include depression, drooling, muscle twitching, convulsions, and sham drinking (Newsholme et al. 1983). There is a loss of rumen motility and severe damage to the mucosa of the rumen and omasum. In many but not all cases, kikuyu poisoning occurs when the pasture is invaded by armyworm (*Spodoptera exempta* [Walker] [Lepidoptera, Noactuidae]). The causative agent has not been identified, and it is not conclusively known if the armyworm has a role in the toxicity.

Photosensitization of grazing animals often occurs with *Panicum* and *Brachiaria* spp. (Bridges et al. 1987; Cornick et al. 1988; Graydon et al. 1991). The condition is usually accompanied by crystals in and around the bile ducts in the liver. Miles et al. (1991) have shown that the crystals are metabolites of saponins, which are common constituents of *Panicum* spp. The crystals impair biliary excretion, leading to elevated phylloerythrin levels in the blood, causing secondary (hepatic) photosensitization, as previously described.

Toxins in Other Forages. Most common forages are legumes or grasses. A few others are sometimes used, including buckwheat (*Fagopyrum esculentum* Moench.), spineless cactus (*Opuntia* spp.), saltbush (*Atriplex* spp.), and forage brassicas such as kale (*B. oleracea* L.), rape (*B. napus* L.), cabbage (*B. oleracea* L.), and turnips (*B. rapa* L.).

Brassica spp. contain glucosinolates (goitrogens) and the brassica anemia factor. Glucosinolates are primarily of concern in the brassicas grown for seed, such as rapeseed and mustard. Forage brassicas contain a toxic amino acid, S-methylcysteine sulfoxide (SMCO), the brassica anemia factor. Ruminants often develop severe hemolytic anemia on kale or rape pastures, and growth is markedly reduced.

S-methylcysteine sulfoxide is metabolized in the rumen to dimethyl disulfide, an oxidant that destroys the red blood cell membrane. This leads to anemia, hemoglobinuria (red urine), and liver and kidney damage. Mortality frequently occurs. Because the SMCO content of brassicas increases with plant maturity, it is not advisable to graze mature brassica or to use these crops for late winter pasture in temperate areas. Avoiding the use of S and high N in fertilizer reduces SMCO levels and toxicity. Brassica anemia is reviewed by Cheeke and Shull (1985) and Smith (1980).

Buckwheat is a fast-growing, broad-leaved annual sometimes grown as a temporary pasture. Buckwheat seed and forage contain a photosensitizing agent, fagopyrin. This compound is absorbed by the body and moved to the surface of the skin, where it reacts with sunlight, causing photodermatitis (photosensitization). Light-skinned animals are particularly susceptible.

Acute bovine pulmonary emphysema may occur when cattle are moved from sparse dry pasture to lush grass, legume, or brassica pasture. The abrupt change in pasture type results in a disturbance in the rumen microbes, leading to excessive conversion of the amino acid tryptophan to a metabolite, 3-methyl indole (3-MI). The 3-MI is absorbed and is toxic to the lung tissue, causing pulmonary edema and emphysema (Carlson and Breeze 1984). The condition, also called *summer pneumonia*, may be fatal. Provision of supplementary feed before moving cattle onto lush meadows is helpful in preventing the disorder.

Animal Metabolism of Plant Toxins. Plants and animals have coevolved. As plants have developed the enzymatic means to synthesize defensive chemicals, animals have evolved detoxification mechanisms to overcome the plant defenses. The most fundamental of these are the drug-metabolizing enzyme systems of the liver, such as the cytochrome P450 system. This enzyme system (also called the *mixed function oxidase system*) oxidizes hydrophobic, nonpolar substances such as plant toxins and introduces a hydroxyl group. The hydroxyl group increases the water solubility of the compound, mainly by providing a site to react (conjugate) with other water soluble compounds such as amino acids (e.g., glycine), peptides (glutathione), and sugars (e.g., glucuronic acid). These conjugated compounds, such as glucuronides, are much less toxic and can be excreted in the urine or bile (e.g., saponin glucuronides in the bile of animals consuming *Panicum* spp.). Most differences in susceptibility among livestock species to plant toxins are due to differences in liver metabolism. Some toxins are bioactivated, or made more toxic, because of liver metabolism (e.g., aflatoxin or slaframine). The relative rates at which the active metabolites are formed and detoxified determine the extent of cellular damage.

On an evolutionary basis, browsing animals such as sheep and goats have been exposed to greater concentrations of plant toxins than

have grazing animals such as horses and cattle. As a result, these browsing species generally are more resistant to many plant toxins than are the strict grazers, and they find plants containing toxins more palatable than do cattle and horses (Cheeke 1991). Sometimes, as with pyrrolizidine alkaloids in *Senecio* spp., the resistance of sheep and goats is due to a lower rate of bioactivation of the compounds in the liver to the toxic metabolites (Cheeke 1988).

Browsing animals are better able than grazers to resist adverse effects of dietary tannins and phenolic compounds, which are common constituents of shrubs, trees, and other browse plants. For example, deer, which are browsers, have salivary tannin-binding proteins that counteract the astringent effects of tannins (Austin et al. 1989). These salivary proteins are absent in sheep and cattle. Mehansho et al. (1987) reviews the roles of salivary tannin-binding proteins as animal defenses against plant toxins. Resistance to tannin astringency would result in tannin-containing plants being more palatable to browsers than to grazers, which lack the tannin-binding proteins.

In ruminants, metabolism of toxins by rumen microbes is an important factor in altering sensitivity to plant toxins. In some cases, e.g., cyanogenic glycosides and the brassica anemia factor, the toxicity is increased by rumen fermentation. Sometimes, e.g., mimosine or oxalate toxicity, the compounds are detoxified by microbial metabolism. The toxic amino acid mimosine in *Leucaena* spp. has been of particular interest in this regard. As discussed earlier, the successful use of leucaena as a high-protein forage was not possible in Australia and many other areas until ruminants were dosed with mimosine-degrading bacteria.

QUESTIONS

1. What is the genetic potential of various forage species for increased palatability, digestibility, and bioavailability of elements like Mg, Ca, and Se?
2. What is the empirical relationship of bioavailable Cu to forage Cu, Mo, and S concentrations?
3. What affect does Si and soil ingestion have on digestive processes and bioavailability of trace elements?
4. What is the toxicity of excess S in herbage and its role in animal nutrition and health, specifically polioencephalomalacea?
5. How does the element requirement for nutrition (production functions) differ from that required for adequate immune response in animals?
6. Why do many plants contain toxic substances?
7. Why does pasture bloat occur more often with legumes than with grasses? Why are some legumes nonbloating?
8. How have the problems associated with *Leucaena leucocephala* toxicity been overcome? Does that technique have potential application with other plant toxins?
9. What are endophytes? What is the role of endophytes in perennial ryegrass staggers?
10. Under what conditions is sudangrass most toxic? How can toxicity be prevented?
11. Why do cattle, sheep, and goats differ in their susceptibility to plant toxins?

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