POISONOUS WEEDS IN HAY CROPS

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ABSTRACT

In California, the most common and costly cause of poisonings from weeds in hay are the plants which contain pyrrolizidine alkaloids (PAs). The two plants which are most commonly found in alfalfa hay and which contain the PAs are fiddleneck (*Amsinckiia intermedia*) and common groundsel (*Senecio vulgaris*). Horses are the most sensitive companion animal species to the toxic effects of the PAs, and they are commonly fed alfalfa hay. The PAs induce liver damage by being activated during liver metabolism. The toxic metabolites produce damage which is cumulative, and can occur over a long exposure time. The capacity of the liver to sustain considerable damage before showing adverse effects, often makes it difficult to confirm the source of exposure because signs of toxicity may be delayed in onset. There are no cures or antidotes for PA poisoning, thus prevention is the key.

PYRROLIZIDINE ALKALOIDS

Pyrrolizidine alkaloid poisoning has been reported in all parts of the world. Poisoning of livestock was first reported in South Africa in the early 1900's. In California the most prominent plants involved are fiddleneck, tansy ragwort and common groundsel. Pyrrolizidine alkaloid content of these plants ranges from less than 0.5% up to 1.2% dry weight. Comfrey, which is used as an animal feed and human herbal remedy, also contains small quantities of PA's. Plant parts ranked in decreasing concentration of PA's are: flowers and seeds > leaves > stems > roots. The plants contain PA's at all stages of growth. The PA's are resistant to heat, and also maintain their toxicity in dried plant material and hay. The PA's toxic action is principally exerted on the liver, and depending on the animal species, the kidney and lungs may also be affected but to a lesser extent than the liver. Pyrrolizidine alkaloids are activated by liver metabolism to toxic pyrrole metabolites which have been shown to be carcinogenic, mutagenic, and embryotoxic. Most of the toxic effects of the PA's can be traced to their destructive effect on liver cells, and thus the clinical signs and symptoms of PA intoxication are those of progressive liver failure.

Pyrrolizidine alkaloids produce very characteristic pathological changes in the structure of the liver. The characteristic hepatic lesion of PA toxicity is hemorrhagic centrilobular necrosis without inflammation, occlusion of the central veins, sinusoid distension, and megalocytosis (enlarged cells). The severity of the changes reflect the degree of damage. Extensive fibrosis (cirrhosis) may be seen in the liver of patients that recover from acute PA poisoning and patients that have had chronic exposure to PA's. In humans this disease has been called venoocclusive disease (VOC) and no other known toxin produces this histopathological picture.

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PYRROLIZIDINE ALKALOID POISONING OF ANIMALS

Horses are the most sensitive species to the toxic effects of PA's, followed by cattle, pigs and chickens which are less sensitive, and sheep, goats and turkeys which are the least sensitive. The young of all species are more sensitive than are adults. Numerous feeding trials have been conducted using cattle, sheep, goats and horses, and the results of these trials, although somewhat confusing, indicate that the PA's produce a classical time-dose-response toxicity picture. Thus high doses of PA's fed over a period of a few days will produce toxicity in a short period of time whereas low doses fed over a longer period will produce a very similar but much delayed toxicity. There is presumably a no effect level for PA plants and it is probably less than 5% of the total ration. One of the more resistant species, the goat, has to consume a quantity of tansy ragwort at least equal to its body weight in order to be poisoned.

The clinical signs of PA poisoning in animals vary from species to species. In cattle, common signs are: dull haircoat, dry muzzle, lack of conditioning, photosensitization, diarrhea with tenesmus (straining), rectal prolapse, depression and death. In horses the neurological signs predominate, and they gradually lose condition, become anoretic, depressed, and wander aimlessly (Walk-about Disease). In sheep, acute deaths are rare but the liver damage produced by the PAs often predispose sheep to copper toxicity. In goats the clinical picture is similar to that seen in cattle. The amount of plant material that must be ingested in order to produce serious toxicity is dependent on the species, the period of consumption and the alkaloid content of the plants. Estimates range from 5-10% of body weight for cattle and horses to more than 100% for sheep and goats. Smaller amounts may depress production without producing observable signs.

The degree of liver damage produced by the PAs can be assessed by measuring certain serum enzyme activities. Some of the enzymes which have been useful in predicting the degree of PA induced liver damage are: glutamate dehydrogenase, alkaline phosphatase, sorbitol dehydrogenase, gama-glutamyl transpeptidase, and lactate dehydrogenase. These enzymes are released when the liver cells are damaged and increased enzymatic activity in blood serum is indicative of cellular damage. A study at the Veterinary Medical Teaching Hospital at the University of California at Davis done during the 1980's looked at the effects of PAs on plasma amino acid patterns in the horse. The ratios of various amino acids were followed during PA intoxication in horses. Changes in the amino acid pattern have been used in human medicine as markers of hepatic damage and it has been proposed that these changes in amino acid ratios in the serum may be responsible for some of the toxic effects seen in hepatic failure. A more recent experimental approach to the treatment of hepatic failure involves restoration of normal amino acid balance in the plasma. Because serum enzyme levels and amino acid levels are non-specific markers of hepatic damage, definitive diagnosis of PA intoxication requires microscopic examination of biopsy or necropsy material. At necropsy, the liver is small, pale, firm and may have a nutmeg appearance. The gall bladder is almost always full and very distended. Edema of the gastrointestinal tract (especially the abomasum) may also be seen. Jaundice, ascites and

petechial (paintbrush) hemorrhages are more variable findings. The discovery of the characteristic histopathological changes in liver structure produced by the PAs can be used to make a definitive diagnosis. Treatment of PA induced liver damage is supportive because there are currently no specific antidotes. In many cases diagnosis of PA intoxication occurs post mortem, but if the diagnosis is made in time and feeding of PAs is discontinued, the animals may recover due to the liver's reserve capacity and ability to regenerate.

SUMMARY

Prevention is the best "cure" for PA intoxication. In veterinary species, preventing exposure to PA containing plants often means preventing the growth of the plants in forage. Because fiddleneck and groundsel are principally spring seasonal plants, most problems are associated with first cut hay. Most animals find PA plants unpalatable and will not eat them if better forage is available, but they will ingest toxic amounts of PA plants if they have nothing better. Animals can't select PA plants out of cubes or pellets and last year, hay containing PA plants was made into a pelleted feed which was responsible for losses in a feed lot in southern California. In Oregon, ranchers have used sheep to clear the Tansy ragwort from their pastures. Apparently there were no problems in these sheep however in feeding trials, liver damage in sheep was often not seen until after 2 seasons of exposure.

Diagnosis of PA poisoning can be confirmed by chemical analysis of feed and tissue samples (which contain PA adducts). Suspect problems should be referred to the California Veterinary Diagnostic Laboratory Services Toxicology section.