ics. Clin Toxicol 26:189-197, 1988.
3. McLauchlan GA: Acute mercury poisoning. Anaesthesia 46:110-112, 1991.
4. Gerstner HB, Huff JE: Selected case histories and epidemiologic examples of human mercury poisoning. Clin Toxicol 11:131-150, 1977.
5. Murphy MJ, Culliford EJ, Parsons V: A case of poisoning with mercuric chloride. Rescuscitation 7:35-44, 1979.
6. Giunta F, DiLandro D, Chiaranda M et al: Severe acute poisoning from the ingestion of a permanent wave solution of mercuric chloride. Hum Toxicol 2:243-246, 1983.
7. Worth DP, Davidson AM, Lewins AM et al: Haemodialysis and charcoal haemoperfusion in acute inorganic mercury poisoning. Postgrad Med J 60:636-638, 1984.
8. Toet AE, Dijk AV, Savelkoul TJF et al: Mercury kinetics in a case of severe mercuric chloride poisoning treated with dimercapto-1-propane sulphonate (DMPS). Hum Exp Toxicol 13:11-16, 1994.
9. Sastry KV, Sharma K: Mercury induced haematological and biochemical anomalies in Ophiocehoalus (Channa) punctatus. Toxicol Let 5:245-249, 1980.
10. Sastry KV, Gupta PK: Chronic mercuric chloride intoxication in the digestive system of Channa punctatus. J Environ Pathol Toxicol 2:443-446, 1973.

Beef Cattle Losses After Grazing *Lupinus argenteus* (Silvery Lupine)

KE Panter PhD
USDA-ARS Poisonous Plant Research Laboratory, 1150 E 1400 N Logan, UT 84341

HF Mayland PhD
USDA-ARS Northwest Irrigation and Soils Research Laboratory, Kimberly, ID

DR Gardner PhD
USDA-ARS Poisonous Plant Research Laboratory, 1150 E 1400 N Logan, UT 84341

G Shewmaker PhD
USDA-ARS Northwest Irrigation and Soils Research Laboratory, Kimberly, ID

ABSTRACT. Ten yearling steers weighing 270-360 kg died acutely after eating early seed pod stage *Lupinus argenteus* (silvery lupine) containing high levels of piperidine alkaloids, including ammodendrine and N-methylammodendrine. Reduced availability of quality feed from range moderately depleted of quality grasses appeared a major factor in causing the cattle to graze lupine. Proximate analysis of whole plant, seed pods and seed showed high levels of crude protein ranging from 16.4 to 48 % for whole plant and seed. Alkaloid analysis of the whole plant and individual plant parts such as seed and seed pods (30-40 % seed shatter) showed total alkaloid levels ranging from 0.70 to 2.5 % (0.70-2.5 mg/100 mg plant) dry weight. Ammodendrine levels ranged from 0.24% in seed pods with >70% seed loss to 1.35 % in early growth plant with no seed. N-methylammodendrine levels ranged from 0.38 % in seed pods with >70 % seed shatter to 1.04 % in pure seed. Other minor alkaloids totaled 0.08 % in seed pods with >70 % seed shatter to 0.60 % in early growth plant before seed pod formation. These cattle ate an estimated 1.8 g/kg dry weight (486 g to 648 g) of lupine in 24 h. This appears the first report of acute death in cattle associated with piperidine alkaloid-containing *Lupinus argenteus*.

Lupines, depending on alkaloid composition and concentration, are toxic and/or teratogenic to livestock. Most toxicoses resulting in death from lupine ingestion have been reported in sheep and occurred extensively in the late 1800's and early 1900's (1). During this period sheep ranchers relied on lupine as important forage for summer grazing and winter hay. Much of the wild hay cut in Montana had lupine as an important component and it often contained 50% or more lupine. In the winter of 1898-1899 in the Judith Basin area of Montana, 3,600 sheep of a band of 7,000 died from eating lupine hay. Between 1897 and 1900 over 2,800 sheep from a flock of about 12,000 died after grazing lupine. In Livingston, MT, 1,900 sheep of 3,000 died in 1 flock after eating *Lupinus cyaneus* seed pods. In most field-grazing cases the losses were attributed to eating lupine pods before seed shatter occurred. *Lupinus sericeus, L cyaneus* and *L leucophyllus* were reported to cause most of the poisoning. Even though no alkaloid analysis was done at that time we now know that *L sericeus* and *L leucophyllus* contain predominantly quinolizidine alkaloids (2). Alkaloid analysis of *L cyaneus* is apparently not known.

Chesnut and Wilcox (1) reported that cattle and horses readily ate lupines during immature stages whereas sheep generally did not eat lupine in spring and summer but grazed it in early fall when in seed pod stage; they readily ate it in hay. Cattle losses from lupine were not reported, although 4 horses were reported poisoned by lupine and 3 of those died (1).

Although sheep losses were extensive in the late 1800's and early 1900's, relatively few losses have been reported recently. This reduced incidence of poisoning in sheep is the result of multiple factors including reduced numbers of sheep on western ranges, better understanding and knowledge of lupine toxicity because of research, changes in feeding and grazing practices, and improved range management practices utilizing herbicides and grazing strategies. The few reported cases of cattle poisoning are likely due to different grazing habits of cattle vs sheep (grazers vs browsers), but may also be attributed to different management practices for these 2 livestock species (eg cattle are allowed to range freely whereas sheep are often grazed in bands with large numbers of animals con-

Table 1. Alkaloid composition of *Lupinus argenteus* based on plant parts and stage of growth. Values are mg of alkaloid per 100 mg of dry plant.

Plant Sample	Total Alkaloid	Ammodendrine	N-methyl Ammodendrine	Other Alkaloids
Regrowth Plant	1.00	0.27	0.53	0.20
Plant, Flower	2.50	1.35	0.55	0.60
Plant, <10% pods	1.40	0.54	0.53	0.33
Plant, 10-20% pods	1.70	0.77	0.58	0.35
Seed Pods, 30-40% shatter	1.00	0.37	0.48	0.15
Seed Pods, >70% shatter	0.70	0.24	0.38	0.08
Seeds	1.80	0.41	1.41	0.35

centrated in smaller areas where poisonous plants may be prevalent).

The most common syndrome associated with lupine in recent years (since the early 1960's) is referred to as "crooked calf disease", which results from maternal ingestion of teratogenic lupines (those containing anagyrine) during susceptible periods of gestation (3-7). Although toxicoses have been observed in association with crooked calf disease, death losses in adult cattle eating the plants have not been extensively reported. However, losses in newborn calves from the induced skeletal defects and/or cleft palates born to cows that ate lupines have been extensive (6-9). Even though knowledge, research and management recommendations are available to reduce or avoid losses from crooked calf disease (10), there are still frequent reports of large outbreaks of crooked calf disease (10, 11). One of the most recent outbreaks resulted in the loss of over 4000 calves in 1 county in Washington State (Tom Platt, personal communication, 1997). These calves were either destroyed because of the malformations or died as a result of their deformities and/or dystocia. The incidence of C-sections in cows was also higher and many cows died or were culled because of lupine. Over the last several years reports to the Poisonous Plant Research Lab in Logan, UT, of lupine-induced crooked calf disease have increased, suggesting that lupine poisonings have increased on western rangelands for various reasons; eg environmental, reduced use of herbicides on public lands, changes in management. The available management recommendations to reduce crooked calf disease are apparently not being fully utilized for unknown reasons (Tom Platt, Randy Mills, Clive Gay, personal communications, 1996-1998).

The lupines commonly associated with crooked calf disease are those containing the quinolizidine alkaloids, specifically anagyrine (2), and include the species *L sericeus, L caudatus,* (6, 7) *L laxiflorus* (4) and *L sulphureus* (9). *Lupinus latifolius* was implicated in dog and human malformations when milk from goats eating this lupine was ingested by mothers during early pregnancy (11).

While most lupines predominantly contain quinolizidine alkaloids, a few contain high levels of toxic piperidine alkaloids and some contain both (12). The toxic and teratogenic effects of 2 piperidine alkaloid-containing lupines, *L formosus* and *L arbustus*, have been demonstrated (13-15). Ammodendrine and N-methylammodendrine possess similar toxicity (16), and both are believed to be teratogenic in cattle and goats (13-15). Based on structural characteristics, N-acetylhystrine is believed to possess teratogenic activity and is more toxic than either ammodendrine or N-methylammodendrine (16). Other piperidine alkaloids from *Conium maculatum* and *Nicotiana glauca* are structurally similar and have been demonstrated to cause identical birth defects in sheep, goats, cattle and pigs (16-18).

Clinical signs of toxicoses in cattle are similar with all these piperidine-containing plants and include protrusion of the nictitating ocular membranes, irregular gait, modest tremors, excessive salivation, muscular weakness and occasional temporary, and involuntary sternal recumbency after exertion (13, 17). Death usually results from respiratory failure. Lupine-induced fetal toxicity (reduction in fetal activity and death) has been observed by ultrasound in cattle and goats (14, 15, 19).

CASE REPORT

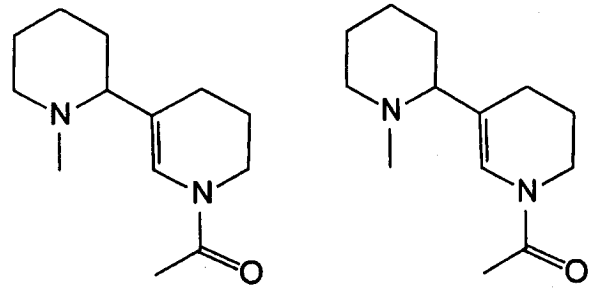
Case History

About 600 stocker steers and heifers (270-360 kg) were grazed on 3-4 sections of non-irrigated land near Twin Falls, ID. The pasture was native range having some crested wheatgrass, poa, annual mustard, rabbit brush, goatsbeard and lupine (*Lupinus argenteus*). The cattle did not graze the lupine until the grasses and goatsbeard were depleted. Ten animals died acutely while other animals showed moderate to slight signs of toxicity. The exact number of animals affected was undetermined. Cattle were observed grazing the lupine, and subsequent to the deaths most of the lupine plants had been grazed. The lupine was in the early pod stage of growth which is consistent with the phenological stage of plant development when initiation of grazing of other poisonous plants such as locoweed (20), larkspur (21) and lupine (9) has been noted.

Necropsies of dead calves were not done and blood or tissue samples were not collected for diagnostic examination. However, surviving cattle were immediately moved to new pastures, and no further losses were reported.

Chemical Analysis

A single plant specimen with flowers and seed pods was collected through the fence in an ungrazed pasture 2 d after



N-methylammodendrine Ammodendrine

Figure 1. Structure of the N-methylammodendrine and ammodendrine, predominant piperidine alkaloids in Lupinus argenteus.

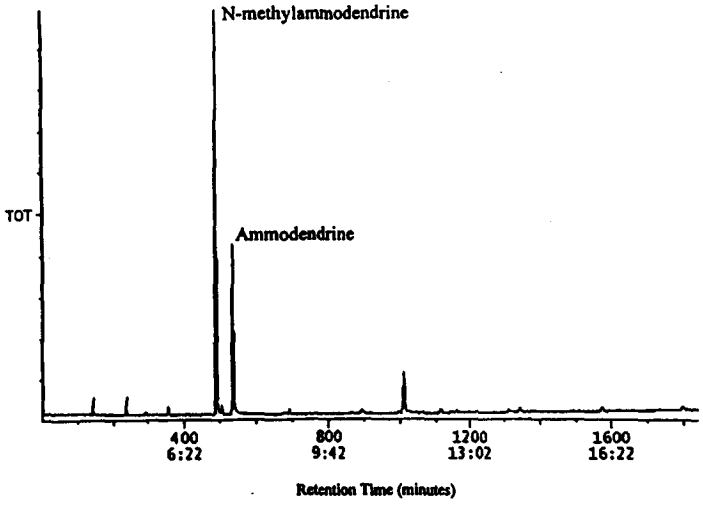


Figure 2. GC chromatogram of the piperidine alkaloids in Lupinus argenteus.

the deaths occurred and identified by the Intermountain Herbarium in Logan, UT as *L argenteus*. A second plant sample of regrowth lupine was collected in the grazed pasture 2 w after the poisoning. Whole plant, including early seed pods, flowers, leaves and stems, was air dried and ground in a Wiley mill to pass a 2 mm screen. Duplicate extractions using 100 mg of finely ground plant material were done according to established protocols (22).

Both plant samples were analyzed and total alkaloid quantified by weighing the alkaloid extract. Percent area under the peaks of the GC chromatogram was used to calculate individual alkaloid quantities from the total alkaloids extracted. Major alkaloid peaks were identified by GC/MS (gas chromatography/mass spectrometry). Standard samples of *L formosus* (a piperidine alkaloid-containing lupine) and *L caudatus* (a quinolizidine alkaloid-containing lupine) were analyzed with the putative samples for alkaloid profile and concentration comparison.

Analytical Results

Chemical analysis of the lupine samples had the same alkaloid profile and relatively high levels of 2 piperidine alkaloid toxins, ammodendrine and N-methylammodendrine (Table 1, Fig 1). Total and individual alkaloid composition varied depending on plant part analyzed. A composite sample of whole plant contained 1 % (1 mg/100 mg) total alkaloid, of which 53 % (528 µg) was N-methyl- ammodendrine, 27 % (272 µg) was ammodendrine, and the remaining 20 % (200 µg) had approximately 6 other minor unidentified alkaloids (Fig 2).

This lupine contained significant nutrient qualities (Table 2). Crude protein of whole plant was equal to mature alfalfa hay (16.4 %) and seed pods (30-40 % seed shatter) and pure seed contained 19.4 % and 48 % crude protein, respectively. The plant and seed were also a good source of essential minerals.

DISCUSSION

Reports of lupine toxicoses in cattle resulting in death have been infrequent over the last 25 y but the number of calls reporting crooked calves have dramatically increased since 1994 (9). Coincidentally, 2 cases of acute poisoning and death losses in cattle have been reported recently (this report and 1 from California; Dr Frank Galey, personal communication, 1999). The reasons for the increased incidence of crooked calf disease and these 2 toxicoses are unknown; however, they may be related to multiple factors such as weather/environmental conditions, increased lupine proliferation, reduced use of herbicides on public lands, reduced sheep numbers (browsers) on these ranges, and/or changes in management strategies. Some losses may also be due to a lack of awareness of lupines' potential toxicity.

We believe this to be the first report in which death losses have occurred in cattle from grazing lupines (*L argenteus*) containing predominantly piperidine alkaloids, specifically ammodendrine and N-methylammodendrine.

Recent research in our laboratory demonstrated that feeding *L arbustus* containing predominantly ammodendrine in multiple doses as high as 1.5 g/kg/dose 2 x daily over 10 d to 2 pregnant cows did not cause outward clinical toxicosis. However, fetal death occurred in 1 cow after 5 d at that dose, and the other calf had moderate contracture limb defects at term birth (15). The single dose of 1.5 g/kg of the arbustus plant contained 17.1 mg/kg of total alkaloid, of which 14.25 mg/kg was ammodendrine with only trace amounts of N-methylammodendrine. After repeated doses over 5 and 10 d, respectively, the resulting blood plasma alkaloid maximums were 2.4 µg/ml of ammodendrine and 0.15 µg/ml of N-methylammodendrine. These maximum concentrations occurred between 4 and 8 h after the final dose and declined rapidly to baseline by 30 and 14 h, respectively, for ammodendrine and N-methyl- ammodendrine. The plasma elimination half-lives were 8-10 h for ammodendrine and about 4 h for N-methylammodendrine (15). Based on the ammodendrine and N-methylammodendrine experimentally fed to these 2 cows and the relative concentration of alkaloid in *L argenteus* in this field case compared to *L arbustus*, we speculate that the amount of plant ingested by these yearlings exceeded 1.8 g/kg (1-2 lbs/head) grazed over a 12-24 h period.

Table 2. Proximate analysis of *Lupinus argenteus* samples[1].

	Whole Plant regrowth (no seed)	Seed Pods (30-40% shatter)	Seeds
Moisture%	9.3	11.4	---
Dry matter %	90.7	88.6	100
Crude Prot. %	16.4	19.4	48.0
Acid Det. Fib.%	31.7	27.7	---
Minerals			
Ca%	0.99	0.33	0.31
P%	0.17	0.18	0.55
K%	0.92	1.07	0.75
Mg%	0.32	0.20	0.21
Na-ppm	41.0	35.0	53.0
S%	0.10	0.12	0.31
Al-ppm	270	54	111
B-ppm	34.5	28.7	23.4
Cu-ppm	5.0	6.2	7.9
Fe-ppm	270	79	175
Mn-ppm	69.6	45.4	40.7
Sr-ppm	48.4	16.8	9.4
Zn-ppm	12.9	14.3	29.3

[1]Proximate analyis was done at Utah State University Plant and Feed Analysis Laboratory, Logan Utah 84341.

Toxicity studies in mice demonstrated individual toxicity of ammodendrine and N-methylammodendrine (iv LD_{50} of 134 and 110 mg/kg, respectively) (16).

While the focus of lupine research in the western US over the last 25-30 y has been on the teratogenic alkaloids as opposed to alkaloids that may be overtly toxic, there has been little effort to identify which alkaloids are most toxic. The most toxic alkaloids may not be those that exhibit teratogenesis and vice versa. Likewise, while variable susceptibility in toxicoses between ruminant species has been known for many years, the teratogenic variability of some of these alkaloids has just recently become apparent (13, 14). For example, sheep have recently been shown to exhibit a resistance to the teratogenic effects of piperidine alkaloids from *Nicotiana glauca,* yet show a similar susceptibility to the toxic effects when compared to goats (16, 23). Conversely, sheep and goats are both resistant to the toxic and teratogenic effects of the quinolizidine alkaloids found in most lupines while cattle are susceptible (13, 14).

Risk from lupine toxicoses is present on many ranges where lupines are prevalent even though animals appear not to graze them most of the time. While crooked calf disease appears the most important economic problem from lupines, acute cattle deaths from grazing lupines can happen, as demonstrated in this paper. Thus, several management practices will help reduce losses: avoid overgrazing (which forces animals to graze less desirable plant species; avoid grazing lupine pastures when lupine plants are in the seed pod stage; to prevent teratogenesis, reduce grazing lupine pastures during susceptible periods of gestation, ie 40-100 days gestation in cattle; control heavy infestations with herbicide treatments; and manage ranges for maximum grass production.

ACKNOWLEGEMENTS

The authors thank Terrie Wierenga for technical support and the Intermountain Herbarium, Utah State University, Logan, UT, for plant identification.

REFERENCES

1. Chesnut VK, Wilcox EV: The Stock-Poisoning Plants of Montana. USDA-Division of Botany, Bulletin No. 26:100-110, 1901.
2. Keeler RF: Lupin alkaloids from teratogenic and nonteratogenic lupins. III. Identification of anagyrine as the probable teratogen by feeding trials. J Toxicol Environ Health 1:887-889, 1976.
3. Palotay JL: "Crooked calves." Western Vet 6:16-20, 1959.
4. Wagnon KA: Lupine poisoning as a possible factor in congenital deformities in cattle. J Range Manage 13:89-91, 1960.
5. Binns W, James LF: 1961, A congenital deformity in calves, similar to "crooked calf disease," has been experimentally produced by feeding heifers lupine and lead. Proc Western Sec Amer Soc Anim Prod 12, LXVI:1-3.
6. Shupe JL, James LF, Binns W: Observations on crooked calf disease. J Am Vet Med Assoc 151:191-197, 1967.
7. Shupe JL, Binns W, James LF et al: Lupine, a cause of crooked calf disease. J Am Vet Med Assoc 151:198-203, 1967.
8. Shupe JL, James LF, Binns W et al: Cleft palate in cattle. The Cleft Palate J 1:346-354, 1968.
9. Panter KE, Gardner DR, Gay CC et al: Observations of *Lupinus sulphureus*-induced "Crooked Calf Disease" in a fall calving herd. J Range Management 50:587-592, 1997.
10. Keeler RF, James LF, Shupe JL et al: Lupine-induced crooked calf disease and a management method to reduce incidence. J Range Manage 30:97-102, 1977.
11. Kilgore WW, Crosby DG, Craigmill AL et al: Toxic plants as possible human teratogens. Calif Agr 35:6, 1981.
12. Majak W, Keller WJ, Duan Z et al: Alkaloid distribution in two species of *Lupinus* in central British Columbia. Phytochem 36:883-885, 1994.
13. Keeler RF, Panter KE: Piperidine alkaloid composition and relation to crooked calf disease-inducing potential of *Lupinus formosus.* Teratology 40:423-432, 1989.
14. Panter KE, Gardner DR, Molyneux RJ: Comparison of toxic and teratogenic effects of *Lupinus formosus, L. arbustus* and *L. caudatus* in goats. J Nat Toxins 3:83-93, 1994.
15. Panter KE, Gardner DR, Molyneux RJ: Teratogenic and fetotoxic effects of two piperidine alkaloid-containing lupines (*L. formosus* and *L. arbustus*) in cows. J Nat Toxins 7:131-140, 1998.
16. Panter KE, James LF, Gardner DR: Lupines, poison-hemlock and *Nicotiana* spp: Toxicity and teratogenicity in livestock. J Nat Toxins 8:117-134, 1999.
17. Keeler RF, Balls LD: Teratogenic effects in cattle of *Conium maculatum* and *Conium* alkaloids and analogs. Clin Toxicol 12:49-64, 1978.
18. Panter KE, James LF: Alkaloid toxicants and teratogens of plant origin. In Gustine DL, Flores HE eds: Phytochemicals and Health. American Society of Plant Physiologists, Rockville, MD: 145-154, 1995.
19. Panter KE, Bunch TD, Keeler RF et al: Multiple congenital contractures (MCC) and cleft palate induced in goats by ingestion of piperidine alkaloid-containing plants. Reduction in fetal movement as the probable cause. Clin Toxicol 28:69-83, 1990.
20. Ralphs MH: Cattle grazing white locoweed: Influence of grazing pressure and palatability associated with phenological growth stage. J Range Manage 40:330-332, 1987
21. Pfister JA, Manners GD, Ralphs MH et al: Effects of phenology, site, and rumen fill on tall larkspur consumption by cattle. J Range Manage 41:509-514, 1988.
22. Gardner DR, Panter KE: Ammodendrine and related piperidine alkaloid levels in the blood plasma of cattle sheep and goats fed *Lupinus formosus.* J Nat Toxins 3:107-116, 1994.
23. Panter KE, Weinzweig, J, Gardner DR et al: Comparison of cleft palate induction by *Nicotiana glauca* in goats and sheep. Teratology 61:203-210, 2000.

A dog is utterly sincere. He cannot pretend. From a dog's point of view, some human beings are more responsive and likeable than others, and a dog cannot act in any way patronizing to those he doesn't like.

The fact that people do not have to be suspicious of a dog's reactions to them is in itself an enormous measure of potential mental health. You may question many of the people in your life, but you don't question your dog.

Your dog has not an ounce of deceit in his soul. To be able to relate without having to doubt, to be able to love without having to fear rejection, is a source of comfort the less fortunate non-dog-lovers cannot begin to imagine.

A smile costs nothing but creates much. It enriches those who receive without impoverishing those who give. It happens in a flash and the memory of it sometimes lasts forever. None are so rich they can get along without it and none so poor but both are richer for its benefits. It creates happiness in the home, fosters good will in a business and is the countersign of friends. It is rest to the weary, daylight to the discouraged, sunshine to the sad and nature's best antidote for trouble. Yet it cannot be bought, begged, borrowed or stolen, for it is something that is no earthly good to anybody until it is given away. Nobody needs a smile so much as those whohave none left to give.