

Neurologic disease putatively associated with ingestion of *Solanum viarum* in goats

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- ▶ Consumption of *Solanum* spp by ruminants has been associated with development of neurologic signs consistent with diffuse cerebellar disease.
- ▶ Cytoplasmic vacuolation of Purkinje cells within the cerebellum has been described as the pathophysiological change resulting from consumption of *Solanum* spp.

A herd of 50 Nubian-cross goats, composed of weanling (ages, 6 to 10 months) and adult male and female goats, was placed on a property in central Florida between the beginning of April and the end of June. The farm consisted of 28 acres of unimproved woodlands and approximately 2 acres of cleared land. Livestock had not grazed the property for approximately 8 months before placement of the goats. There was no history of neurologic disease among cattle kept on the same range during the preceding 15 years.

Six months after placement of the goats, an adult doe was noticed to have ataxia and head tremors. During a period of several weeks, the goat's condition progressively worsened until it became recumbent, unable to rise, and was euthanatized. Subsequently, during a period of 2 to 3 months, 5 more goats, all suckling or weanling kids (ages, 4 to 9 months), developed similar clinical signs. All affected goats initially developed fine head tremors and, during a period of weeks, became increasingly ataxic to the point of recumbency and either died or were euthanatized. Approximately 8 months after placement of the goats on the property, 7 pregnant does were removed from the main herd and placed in a small fenced pasture for supplemental feeding during the final stages of gestation. Two of the kids born to those does developed head tremors at 1 and 2 months of age.

Goats were able to browse over the full range of the property. In addition, they received a commercial pelleted feed^a formulated for lactating does, a mineral supplement for cattle, and free-choice coastal bermuda hay during the winter months. Inspection of the plants growing on the property revealed the presence of snake plant (*Sansevieria* spp), night-blooming cereus (*Cereus* spp), climbing hempweed (*Mikania cordifolia*), Caesar

weed (*Urena lobata*), wild coffee (*Psychotria nervosa*), tropical soda apple (*Solanum viarum*), slender buttonwood (*Spermacoce* spp), Matt's palm (*Blechnum brownii*), camphor tree (*Cinnamomum camphora*), tea weed (*Sida acuta*), prairie iris (*Iris hexagona*), and sour orange (*Citrus aurantium*).

The goats drank water from a creek that collected runoff from a nearby citrus grove and from a large plastic container that was filled periodically with well water. There was a similar container in the maternity enclosure. Routine veterinary care consisted of administration of ivermectin every 40 to 60 days for intestinal parasites. The attending veterinarian was involved in examining and treating all of the affected goats, including testing for antibodies against caprine arthritis-encephalitis virus (CAE) and providing supplements (oral administration of selenium and injections of thiamine). None of the affected goats tested positive for CAE nor did any medical treatment improve the neurologic signs.

After the occurrence of these cases, 3 weanling kids were brought to the Veterinary Medical Teaching Hospital (VMTH), including a 9-month-old male that had been affected for 2 months and a 2-month-old male and 3-month-old female, both of which developed neurologic signs 2 to 3 weeks prior to evaluation. All 3 goats were in adequate condition, bright, alert, and responsive. With the exception of neurologic findings, results of physical examinations were unremarkable. The goats appeared hyperresponsive to auditory and tactile stimuli. Continuous fine head tremors were exacerbated by attempts to drink water or eat. In addition, there were occasional single spasms of the whole body. The goats had a wide-based posture at rest and walked in a jerky, dysmetric fashion. In comparison with clinically normal goats of the same age, affected goats were mildly to moderately weak when tested by pressure over the withers and rump. In the 2 younger kids, positional horizontal nystagmus could be induced, crossed extensor reflexes were evident in hind limbs and were similar to those of age-matched clinically normal kids, and menace responses were reduced, although vision appeared to be present. When blindfolded, the affected goats became disoriented, swept their heads horizontally from side to side, and within several minutes fell over and remained in lateral recumbency without moving. Removal of the blindfold immediately returned the goat's ability to orient itself.

Hemogram values were within reference ranges except for mild to moderate anemia (PCV, 22 to 28%; reference range, 27 to 45%). Results of serum biochemical analyses and CSF analyses were within reference

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ranges. Plasma cholinesterase activities in affected and clinically normal goats were below the level of detection in our laboratory. Typical acetylcholinesterase activity values in goats have been reported in the range of 4.2 to 5.6 $\mu\text{mol}/\text{min}/\text{mL}$ in blood and 0.60 to 1.00 $\mu\text{mol}/\text{min}/\text{mL}$ in plasma.¹ The range of detectable concentrations in our laboratory is 0.20 to 12.5 $\mu\text{mol}/\text{min}/\text{mL}$ in plasma; thus, the assay's sensitivity of detection may have precluded accurate measurement of plasma cholinesterase activity in these goats.

Brain stem auditory-evoked responses were tested on a single affected goat by stimulating both sides of the brainstem and calculating the mean responses. In brief, subdermal recording electrodes¹ were placed below the external ear canal of the ear to be tested (negative electrode), close to the tragus, and at the vertex (positive electrode). The ground electrode was placed below the contralateral ear canal. Recordings of the waves were made at 100 dB sound pressure with a stimulus created with an alternating click at a speed of 10/s. The masking noise was set at 30 dB less than the stimulus and applied to the contralateral ear. The responses were recorded at an amplifier sensitivity of 10.0 μV per division. The analysis time base was 10 milliseconds; low and high filters were set at 100 Hz and 2 kHz, respectively, with an automatic artifact rejection built in. Both ears were examined, and mean value of 1,024 stimulations was determined. Four peaks were identified in all recordings and identified as I, II, III, and V. Interpeak latencies were calculated for I-III (the approximate time required for the electrical activity generated in the cochlear nerve to reach the pons) and I-V (the approximate time to reach the mesencephalon). With the exception of the V:I amplitude ratios, substantial asymmetry was not detected for any of the measured variables. Although the ratio for the right side was approximately twice that of the left, the left side ratio was considered normal because it was > 0.5 .² Likewise, the right side ratio was within reference limits.

Electroencephalography also was performed on the same affected goat without sedation. In brief, subdermal recording electrodes^b were placed to conform to a standard 8-channel referential montage and were situated over the surface of the frontal and occipital lobes on the right and left sides and the vertex of the cranium. The recording was made at a standard speed of 30 mm/s, with a vertical calibration of 5 $\mu\text{V}/\text{mm}$. Frequency filters were set at 0.5 Hz (low end) and 15 Hz (high end). Wave patterns, frequencies, and amplitudes were measured in attempts to quantify abnormalities. With the exception of the frontal-vertex channels, sharp waves with high amplitude and arrhythmic patterns were detected in all channels. These waves had mean amplitude of 60 μV , which is high, compared with other species.³ However, in previous studies⁴ performed in alert goats, wave frequencies from 1 to 15 Hz and waveform amplitudes ranging from 10 to 100 μV were reported. Although the waveform frequencies and amplitudes were within reference limits, the arrhythmic patterns were suggestive of diffuse cortical abnormality.

On the basis of the physical and neurologic findings, diffuse cerebellar dysfunction with possible involvement of vestibular nuclei, proprioceptive, and motor tracts of

the brainstem, spinal cord, or both was suspected. Potential causes that were considered included tremorgenic mycotoxins, annual ryegrass toxicosis, *Phalaris* spp toxicosis, CAE, heavy metal toxicosis (including chronic methylmercury toxicosis), chronic organophosphate toxicosis, acquired mannosidosis (eg, *Astragalus* spp toxicosis), verminous encephalomyelitis (*Parelaphostrongylus tenuis*), polioencephalomalacia, enzootic ataxia associated with copper deficiency, and cerebellar-vestibular disease associated with other unknown toxic plants. Congenital and inherited storage diseases such as β -mannosidosis were not considered likely, because the affected goats ranged in age from nursing kids to mature adults. Furthermore, the original goats were of mixed breeds and generally were unrelated.

The goats were maintained in the hospital on a balanced diet of concentrate feed and free-choice timothy-alfalfa hay. Clinical signs did not appear to change during a 30-day period of observation. One goat was relocated to a privately owned farm for long-term follow up. The remaining 2 goats were euthanatized, and complete postmortem examinations were performed. Gross abnormalities were not found except for *Haemonchus contortus* in the abomasum. Blood, kidney, and liver samples were submitted for detection of arsenic, copper, lead, zinc, selenium, and mercury; analyte concentrations were within reference ranges in all fluid and tissue samples.

Evaluation of H&E-stained sections of the brains revealed substantial lesions throughout the cerebellum, cerebellar peduncles, and associated brainstem. Many Purkinje cells and neurons within the cerebellar nuclei had finely vacuolated cytoplasm or were necrotic (Fig 1). Numerous spheroids were at the junction between the Purkinje cells and the granular layer, and Wallerian degeneration was evident in the folial white matter. Vacuolated neurons, glial cells, and spheroids were also prominent within the cerebellar nuclei, which were moderately depleted of neurons (Fig 2). The lesions varied in severity, and the 8- to 10-month-old kid was most severely affected. Histologic examination of non-neural tissues did not reveal any important lesions.

Heavy metal toxicosis and copper deficiency were

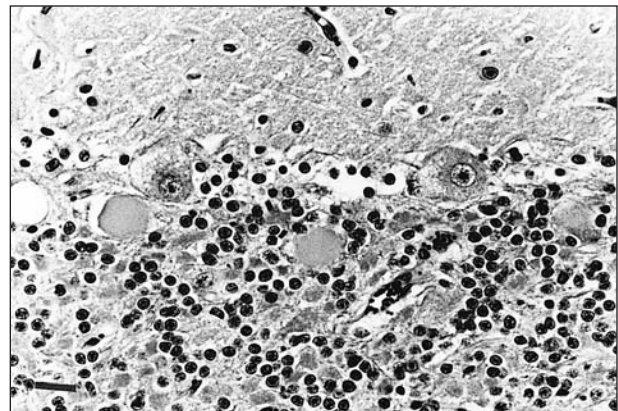


Figure 1—Photomicrograph of a section of the cerebellum of a goat with neurologic disease putatively associated with ingestion of *Solanum viarum*. Notice Purkinje cells with vacuolation of the perikaryon. Two axonal spheroids are also evident. H&E stain; bar = 20 μm .

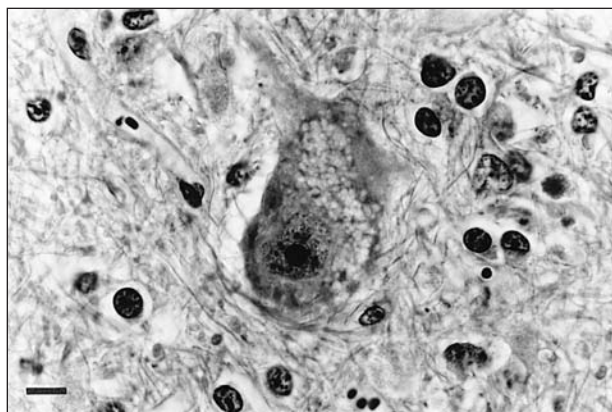


Figure 2—Photomicrograph of the nucleus of a cerebellar neuron of the goat in Figure 1. Notice that the nucleus is distended by numerous small cytoplasmic vacuoles. H&E stain; bar = 10 μ m.

ruled out on the basis of blood and tissue concentrations within reference ranges. Additionally, CAE was unlikely because of the negative serologic results and the absence of polysynovitis and respiratory tract disease in the herd. The persistence of clinical signs for several weeks after removal of the goats from the pasture reduced the likelihood that tremorgenic mycotoxins (ie, perennial ryegrass, *Paspalum* spp, or bermuda grass staggers) were responsible for the clinical signs. *Phalaris* spp and annual ryegrass were not present in the goats' environment and were excluded as possible causes. Chronic organophosphate toxicosis remained a consideration, although serum cholinesterase data were inconclusive. It has been reported that chronic organophosphate toxicosis is not primarily associated with suppression of blood cholinesterase activity but may be related to depletion of neuronal esterase, which affects myelin and neuronal metabolism.⁷ Because it is a primary demyelinating disease, symmetric axonal degeneration within the central and peripheral nervous systems is common. Affected animals typically have hind limb paresis (dog-sitting) or tetraparesis. Histologic examination of the spinal cord did not reveal axonal degeneration consistent with organophosphate toxicosis. Likewise, polioencephalomalacia was ruled out because of the absence of gross and histologic lesions within the CNS and the lack of response to thiamine administration. Verminous encephalomyelitis caused by *P tenuis* was considered because of whitetail deer on the property and a wet, low-lying environment conducive to the survival of the intermediate gastropod host. However, cytologic examination of CSF and absence of migrating larvae throughout the CNS eliminated this diagnosis. Acquired mannosidosis has been associated with the ingestion of various alkaloid-containing plants including *Astragalus*, *Oxytropis*, and *Delphinium* spp. Ingestion of these toxic alkaloids inactivates mannosidase in neurons and other cells resulting in an accumulation of mannose-rich substances within lysosomes and neurovisceral dysfunction. *Astragalus* spp and *Oxytropis* spp do not grow in Florida, and *Delphinium* spp were not identified on the property.

In contrast to the widespread cellular vacuolation

associated with acquired mannosidosis, the histologic lesions in the kids were suggestive of a storage disease restricted to the cerebellum. The histologic and clinical findings closely resembled conditions that were associated with ingestion of *Solanum* spp (not including *S viarum* [tropical soda apple]) in cattle⁶⁻⁸ and goats.⁹ Neurologic disease was reported in cattle in South Africa that were grazing *S kwebense*. Affected cattle were hypersensitive to stimuli and severely ataxic. Histologic evaluation revealed vacuolar degeneration and necrosis of Purkinje cells. A similar syndrome in cattle in Texas was associated with ingestion of *S dimidiatum*. Calves fed the plant developed clinical signs consistent with cerebellar dysfunction, including staggering and incoordination. The primary histologic lesion was degeneration and loss of Purkinje cells. Ingestion of *S fastigiatum* var *fastigiatum* was suspected to cause recurrent seizures, opisthotonus, nystagmus, and ataxia in cattle, with vacuolation, degeneration, and axonal spheroids in Purkinje cells. Goats feeding on *S cinereum* in Australia developed a degenerative cerebellar disorder with signs that included variable forelimb and hind limb paresis, wide-based stance, incoordinated gait, disturbed equilibrium, head and neck tremors, and nystagmus. The histologic lesions were restricted to the cerebellum and included cytoplasmic vacuolar degeneration and loss of Purkinje cells.

Solanum cinereum has not been identified in North America; however, there was evidence on the property investigated here of a large amount of *S viarum* (tropical soda apple), much of which had been consumed by the goats. There was striking similarity between the findings reported in goats and cattle that ingested a variety of *Solanum* spp and the goats reported here that ingested *S viarum* in central Florida. On the basis of these observations, we hypothesized that ingestion of *S viarum* caused the neurologic disorder observed in these goats. Tropical soda apple is a common weed in South America, Honduras, and Mexico, was introduced into Florida during the past decade, and is now known to exist throughout the southeastern United States and Puerto Rico.¹⁰ This plant is solely responsible for the loss of large tracts of grazing land in central Florida because of its vigorous growth and shading out of pasture species. Interestingly, the use of goats to control the spread of tropical soda apple has been proposed by local agriculturists unaware of the potential for debilitating neurologic disease in these animals. However, although the plant has existed in the United States for more than 10 years, to our knowledge, this is the first report of neurologic disease in animals consuming the plant. The stems and leaves are covered with large thorns that preclude it from the diet of most other herbivores, and the plant produces a globular fruit that is approximately 1 inch in diameter and yellow when mature. Goats consume the stems, leaves, and fruit, whereas other ruminants appear to prefer the fruits alone. It remains to be determined whether the toxic elements are in the stems and leaves or in the fruit. This may explain the lack of documented neurologic disease in ruminants feeding on the fruit alone versus those consuming the entire plant. The endemic nature of tropical soda apple in North and South

America enhances the likelihood of future reports of neurologic disease in animals that consume the plant.

^aWalpole Feed & Supply, Okeechobee, Fla.

^bGrass Instruments Co, Quincy, Mass.

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