

Review Article

## Toxic plants affecting the nervous system of ruminants and horses in Brazil<sup>1</sup>

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**ABSTRACT.**- Riet-Correa F., Medeiros R.M.T., Pfister J.A. & Mendonça F.S. 2017. **Toxic plants affecting the nervous system of ruminants and horses in Brazil.** *Pesquisa Veterinária Brasileira* 37(12):1357-1368. Laboratório de Diagnóstico Animal, Universidade Federal Rural de Pernambuco, Rua Dom Manoel de Medeiros s/n, Dois Irmãos, Recife, PE 52171-900, Brazil. E-mail: [fabio.mendonca@pq.cnpq.br](mailto:fabio.mendonca@pq.cnpq.br)

This review updates information about neurotoxic plants affecting ruminants and equidae in Brazil. Currently in the country, there are at least 131 toxic plants belonging to 79 genera. Thirty one of these poisonous plants affect the nervous system. Swainsonine-containing plants (*Ipomoea* spp., *Turbina cordata* and *Sida carpinifolia*) cause numerous outbreaks of poisoning, mainly in goats, but cattle and horses are occasionally affected. The poisoning by *Ipomoea asarifolia*, a tremorgenic plant, is very common in sheep, goats and cattle in the Northeastern region and in the Marajo island. Poisoning by the pods of *Prosopis juliflora* are frequent in cattle in Northeastern Brazil; occasionally this poisoning affects goats and more rarely sheep. Some poisonings by plants, such as *Hybanthus calceolaria*, *Ipomoea marcellia* and *Talisia esculenta* in ruminants and *Indigofera lespedezioides* in horses were recently described and needs to be accurately investigated about its occurrence and importance. Other plants poisonings causing nervous signs in ruminants and equidae are less important, but should be considered for the differential diagnosis of neurologic diseases.

INDEX TERMS: Poisonous plants, ruminants, equines, nervous system, plant poisoning, toxic plants, Brazil.

**RESUMO.**- [Plantas tóxicas que afetam o sistema nervoso de ruminantes e equinos no Brasil.] Esta revisão tem por objetivo atualizar as informações sobre plantas neurotóxicas que afetam ruminantes e equinos no Brasil. Atualmente sabe-se que existe no país pelo menos 131 plantas tóxicas pertencentes a 79 gêneros. Trinta e uma espécies afetam o sistema nervoso. As plantas quem contém swainsonina (*Ipomoea* spp., *Turbina cordata* and *Sida carpinifolia*) causam numerosos surtos de intoxicação, principalmente em caprinos, mas bovinos e cavalos são

ocasionalmente afetados. A intoxicação por *Ipomoea asarifolia*, uma planta tremorgênica, é muito comum em ovinos, caprinos e bovinos na região Nordeste e na ilha de Marajó. A intoxicação pelas vagens de *Prosopis juliflora* é frequente em bovinos no Nordeste do Brasil; ocasionalmente são afetados caprinos e mais raramente ovinos. Algumas intoxicações por plantas, como *Hybanthus calceolaria*, *Ipomoea marcellia* e *Talisia esculenta* em ruminantes e *Indigofera lespedezioides* em equinos foram recentemente descritas e precisam ser investigadas com precisão sobre sua ocorrência e importância. Outras intoxicações por plantas que causam sinais nervosos em ruminantes e equídeos são menos importantes, todavia devem ser consideradas para o diagnóstico diferencial de doenças neurológicas.

TERMOS DE INDEXAÇÃO: Plantas tóxicas, ruminantes, equinos, sistema nervoso, intoxicação por planta, Brasil.

### INTRODUCTION

In Brazil, there are at least 131 toxic plants belonging to 79 genera and annual losses due to animal deaths related to poisonous by plants are estimated at 820,761 to 1,755.763

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cattle, 399,800 to 445,309 sheep, 52,675 to 63,292 goats, and 38,559 horses (Pessoa et al. 2013). Knowledge of the epidemiology, clinical signs and pathology of poisoning by plants causing nervous system impairment is important for the prophylaxis and control of the intoxications and also for the differential diagnosis with other important diseases affecting the nervous system, including rabies and botulism, which are very common in Brazil. This review describes and updates current information on epidemiology, clinical signs, pathology, the toxic principle, and the diagnosis of poisonous plants affecting the nervous system in ruminants and horses in Brazil. Plants that cause hepatic encephalopathy are not included in this review. Some of these plant poisoning, mainly *Senecio* spp. in cattle in Southern and *Crotalaria retusa* in horses in Northeastern region are very frequent cause of nervous signs.

## LITERATURE REVIEW

### Swainsonine-containing plants: *Ipomoea carnea* subsp. *fistulosa*, *Ipomoea riedelii*, *Ipomoea sericophylla*, *Ipomoea marcellia*, *Turbina cordata* and *Sida carpinifolia*

Intoxication by *Ipomoea carnea* subsp. *fistulosa* (Convolvulaceae) occurs frequently in goats in northeastern and on Marajó Island in northern Brazil. It has been reported in cattle in the Pantanal of Mato Grosso (Antoniassi et al. 2007) and is rarely observed in sheep (Tokarnia et al. 1960). The plant is found in flood plains or on the edge of ponds and rivers where it stays green for the entire year (Tokarnia et al. 1960, Armién et al. 2007, Oliveira et al. 2009). The intoxication by *I. riedelii*, *I. marcellia* (= *Ipomoea* aff. *verbascoidea*) and *I. sericophylla* (Convolvulaceae) affects goats in the state of Paraíba and Pernambuco during the rainy period. *T. cordata* (Convolvulaceae) causes intoxication in goats, and with less frequency in cattle and horses in the states of Bahia and Pernambuco. They produce fruit and desiccate at the start of the dry period and then sprout at the start of the rainy period. All these plants are characteristic of Brazilian Caatinga and are probably found in other northeastern States (Barbosa et al. 2006b, 2007, Dantas et al. 2007, Mendonça et al. 2012, Lima et al. 2013). *S. carpinifolia* (Malvaceae) is frequently found in wet and shaded places in all Brazilian regions, and the intoxication has been reported in the states of Rio Grande do Sul, Santa Catarina, Rio de Janeiro, and São Paulo in goats, horses, sheep, and cattle (Driemeier et al. 2000, Colodel et al. 2002a, Loretto et al. 2003, Seitz et al. 2005, Furlan et al. 2009).

A common feature in all swainsonine-containing plants is that normally goats in paddocks with good forage availability do not ingest these plants. However, when there is a shortage of forage, some animals begin to feed on swainsonine-containing plants and become habituated to eat them compulsively regardless of palatability; further, through social facilitation, these animals induce grazing cohorts to consume the plants (Armién et al. 2007, Oliveira et al. 2009, Pimentel et al. 2013). Farmers suggest that after habituation these animals consume the plants in preference to other forages. However, in an experiment to evaluate the feeding preferences of experienced and non-experienced (naïve) goats and sheep for *I. carnea*, it was observed

that experienced or naïve sheep and goats do not prefer *I. carnea* when it is offered with other foods or forages, suggesting that animals will avoid the plant and not become poisoned if other food options are available (Oliveira et al. 2015). Mean crude protein concentrations in samples of *I. carnea* collected monthly during one year at Marajo Island in Northern Brazil and Patos, in Northeastern Brazil, over a 12 month period, were  $27 \pm 0.5\%$  and  $24 \pm 0.2\%$ , respectively, which may explain why *I. carnea* becomes desirable to grazing livestock as forage becomes limited during the dry season (Cook et al. 2015).

Clinical signs include rough hair coat, depression, weight loss, difficulties in standing, ataxia, hypermetria, wide-based stance, lateral gait, intention tremors, spastic paresis or weakness (mainly in the hind legs), abnormal postural reactions, nystagmus, head tilting, depressed tongue or lip tonus, and occasionally other signs of cranial nerve impairment. Many clinical signs are exacerbated when the animals are disturbed or frightened as startled animals often lose equilibrium falling to the side or backward. In severely poisoned goats severe intention tremors or falling can be induced by simply raising the head of the animal for about 60 seconds and then suddenly releasing it (head raising test) (Tokarnia et al. 1960, Driemeier et al. 2000, Colodel et al. 2002ab, Loretto et al. 2003, Seitz et al. 2005, Barbosa et al. 2006b, Armién et al. 2007, Dantas et al. 2007).

Infertility, abortion, and birth of weak newborns which are unable to stand and suckle normally have been reported in swainsonine-containing plants (Driemeier et al. 2000, Colodel et al. 2002b, Seitz et al. 2005, Gotardo et al. 2011). Animals will eventually recover if the plant is removed from their diet at the first signs of intoxication. Also, goats showing clinical signs for less than 20-30 days can recover (Barbosa et al. 2006b, Lima et al. 2013). Permanent neuronal loss, mainly in the cerebellum, causes irreversible intoxication (Barbosa et al. 2006b) and goats with chronic non-reversible clinical signs, even at low intensity, had poor productive and reproductive performance and are highly susceptible to gastrointestinal parasites (Oliveira et al. 2011).

Generally, no gross lesions are observed, but some animals with chronic signs may show cerebellar atrophy (Oliveira et al. 2011). Histologic lesions are vacuolation of the perikaria in neurons in all regions of the nervous system, but lesions are more prominent in the Purkinje cells of the cerebellum and in neurons of the cerebellar nuclei. Axonal spheroids are observed in the granular layer of the cerebellum, cerebellar white matter, cerebellar peduncles and cerebellar nuclei. Cytoplasmic vacuolation is also observed in parenchymal cells of various organs including pancreatic acinar cells, hepatocytes, epithelial cells of the kidney, follicular epithelial cells of the thyroid gland, Kupffer cells and macrophages of the lymphatic tissues (Driemeier et al. 2000, Colodel et al. 2002a, Loretto et al. 2003, Seitz et al. 2005, Barbosa et al. 2006b, Armién et al. 2007, Dantas et al. 2007). Under electron microscopy the vacuoles observed under light microscopy correspond to dilated lysosomes surrounded by a single layered membrane. The vacuoles are empty or contain fragments or small amounts of a fine-

ly granular material. The axonal spheroids in the granular layer are filled with membrane-bound residual bodies and some mitochondria (Driemeier et al. 2000, Colodel et al. 2002a, Barbosa et al. 2006b, Armien et al. 2007).

The toxic compound of *Ipomoea* spp., *Turbina cordata* and *Sida carpinifolia* is the indolizidine alkaloid swainsonine, a well known inhibitor of lysosomal  $\alpha$ -mannosidase and Golgi mannosidase II, causing glycoprotein storage diseases (Colodel et al. 2002b, Haraguchi et al. 2003, Barbosa et al. 2006b, Mendonça et al. 2012). Calystegines B<sub>1</sub>, B<sub>2</sub>, B<sub>3</sub> and C<sub>1</sub> are also present in *I. riedelii*, *I. marcellia* and *I. carnea* (Barbosa et al. 2006b, Haraguchi et al. 2003). The toxic effects of calystegines to animals have not been determined, but they are strong inhibitors of glycosidases, mainly  $\beta$ -glucosidase and  $\alpha$ -galactosidase. Preliminary results comparing U.S. locoweeds (swainsonine only) with Brazilian-grown *Ipomoea carnea* (swainsonine and calystegines) suggests that calystegines do not add significantly to the intoxication in goats.

The concentration of swainsonine in these plants is variable. Samples of *I. riedelii* and *I. sericophylla* collected in 2002 contained 0.14% and 0.11% swainsonine, respectively; in 2003, the concentration of swainsonine was 0.01% and 0.05% for *I. riedelii* and *I. sericophylla*, respectively (Barbosa et al. 2006b). *S. carpinifolia* and *I. carnea* contained 0.006% (Colodel et al. 2002b) and 0.0029% swainsonine (Haraguchi et al. 2003), respectively. The swainsonine concentration in *T. cordata* is very variable, from less than 0.001 to 0.14% (Dantas et al. 2007). Samples of *I. marcellia*, contained swainsonine (0.017%), calystegine B<sub>1</sub> (0.16%), calystegine B<sub>2</sub> (0.05%), and calystegine C<sub>1</sub> (0.34%) (Mendonça et al. 2012). In leaves of *I. carnea* var *fastuosa* it was found 0.0029% swainsonine and 0.0045% calystegines and in flowers and seeds the concentration was nearly 10 times greater (Haraguchi et al. 2003). In 8 samples of leaves of *I. carnea* from Pará state the mean concentration of swainsonine was 0.05%±0.05 with a range from non-detected to 0.155% (Oliveira et al. 2015).

In *I. carnea* swainsonine has been shown to be produced by a fungal endophyte belonging to the Ascomycete order Chaetothyriales associated with this species (Cook et al. 2013). Swainsonine, calystegine, and crude protein amounts were determined in leaves of *I. carnea* on a monthly basis for a year in northern and northeastern Brazil. Mean swainsonine concentrations at Marajo and Patos over the 12 month period were 0.06 ±0.004% ranging from non-detected to 0.21%. At one location swainsonine concentrations were generally the highest during the rainy season or the months immediately following the rainy season. Mean calystegine concentrations at Marajo and Patos over the 12-month period were 0.03±0.0003 and 0.05±0.0003 (Cook et al. 2015).

Lima et al. (2013) produced clinical signs in goats after the ingestion of 0.8mg swainsonine/kg daily for 22-29 days. In a comparative study, daily doses of 1 and 3 mg of swainsonine induced clinical signs after 37-52 days in goats and 42-64 days in sheep, demonstrating that the difference of the frequency of the disease, which is much more common in goats is due mainly to the fact that goats consu-

me the plant more readily than sheep (Riet-Correa, unpublished data)

Clinical signs and pathology are characteristic of the intoxication. Even so, swainsonine poisoning should be differentiated from other plant-caused intoxications such as *I. asarifolia*, which causes a tremorgenic disease, and intoxication by *Solanum* spp., which also causes CNS signs in cattle. Histologic evaluation of liver biopsies can be used in the diagnosis of poisoning by swainsonine-containing plants, even in goats without clinical signs with only seven days of plant consumption. Lectin histochemistry of the liver biopsies can also be used as a supplementary diagnostic method (Rocha et al. 2016).

There is no treatment for affected animals, but if they are moved from pastures with the plants within 2 weeks after first clinical signs are noted, they will usually recover. Goats that ingest these plants for a longer period after first clinical signs will have permanent signs (Barbosa et al. 2007, Rocha et al. 2016). Affected animals develop preferences for the plant, thus they should not be reintroduced into contaminated pastures; further, through social facilitation they will induce other animals to graze the plant.

Conditioned food aversion has been used as an efficient tool to control poisoning by swainsonine-containing plants in Brazil. In controlled experiments as well as in field experiments, aversion induced with lithium chloride in goats trained previously to ingest *I. carnea* lasted until the end of the experiments, 24 and 32 months later, respectively (Oliveira et al. 2014). In experiments with *I. carnea*, in different situations, it was concluded that conditioned food aversion was effective in reducing goat consumption of this plant, but the duration of aversion depends on the time of grazing and amount of plant available; however, the aversion is quickly extinguished by social facilitation when averted animals grazed with non-averted animals (Pimentel et al. 2013). An experiment averting every goat ingesting *T. cordata* in a herd resulted in the control of the poisoning by this plant. In contrast, in another farm, aversion of goats that consumed *I. carnea* was not efficient to control poisoning. These differences seem to be due to the different environment where those plants grow: *T. cordata* grows during the raining period, with good forage availability, and disappears during the dry period. In the other hand, *I. carnea* stays green most of the year, including the dry season when there is a severe shortage of forage (Pimentel et al. 2013).

### ***Solanum bonariense*, *Solanum paniculatum* and *Solanum subinerme***

The intoxication by *Solanum bonariense* (= *Solanum fastigiatum* var. *fastigiatum*) (Solanaceae) occurs in Rio Grande do Sul. There are no seasonal differences in the frequency of the intoxication but apparently, the plant is eaten more when forage is scarce. Cattle of different breeds and all ages older than 8 months old are affected. Morbidity is 1%-20% and fatality rate is low, up to 3.4%. Usually affected cattle are slaughtered after the first clinical signs (Riet-Correa et al. 1983, Rech et al. 2006). The disease has not been reported in sheep or goats, but sheep are experimentally affected

(Zambrano et al. 1985). The intoxication by *Solanum paniculatum* was diagnosed in the state of Pernambuco (Guaraná et al. 2011) and the poisoning was produced experimentally (Barros et al. 1987, Medeiros et al. 2004, Rego et al. 2012). One feature that favors the poisoning is that after mowing the pastures *S. paniculatum* sprouts between the grasses, which probably facilitated its intake (Guaraná et al. 2011). Poisoning by *S. subinerme* occurs in the state of Roraima in northern Brazil mainly in pastures of *Brachiaria humidicola* where the plant appeared as a weed (Lima et al. 2014)

The intoxication is characterized by periodic episodes of cerebellar origin, including loss of equilibrium, extension of the neck and fore limbs, hypermetria, nystagmus, opisthotonus, wide-based stance, falling to the side or backwards, and muscular tremors. The attacks occur mainly when the animals are disturbed or frightened. Between the episodes, most cattle show no clinical signs, but some may show permanent hypermetria, extension of the head or head tilting or others abnormal positions of the head. The neurological signs can be induced by the head rising test (Riet-Correa et al. 1983, Rech et al. 2006). The disease is chronic and regression of the clinical signs does not occur or is very rare. Some cattle die because of misadventure or drowning during convulsions (Riet-Correa et al. 1983, Rech et al. 2006).

Most cases show no gross alterations, but traumatic lesions can be observed. Occasionally the cerebellum is reduced in size (Rech et al. 2006). Histologic lesions, localized in the cerebellum, are degeneration and loss of Purkinje neurons, which appeared enlarged, with a clear homogeneous perikaryon, loss of Nissl substance, and fine diffuse vacuolation. Some nuclei appeared with globular aspect or pyknotic. Later, these neurons disappear and are substituted by proliferation of the Bergman glia. Numerous axonal spheroids are observed in the granular layer and white matter of the cerebellum, and cerebellar peduncles. Wallerian-like degeneration with macrophages and vacuolation of the white matter is observed associated with the axonal spheroids (Riet-Correa et al. 1983, Rech et al. 2006, Rego et al. 2012). Vacuolation and neuron necrosis were also observed in other sites such as the obex, cerebellum peduncles, rostral and caudal colliculi, and rarely in the thalamus, basal ganglia, hippocampus and medulla oblongata (Rego et al. 2012).

Lipidic inclusions, similar to those observed in hereditary or induced lipidosis in human and animals, are observed under electron microscopy of semi-thin sections in the perikaryon, axons and dendrites of the Purkinje cells. It appears that these inclusions originate in the endoplasmic reticulum and are probably due to an interaction between the toxic compound of the plant and lipids from the affected cells forming complexes, which are not degraded (Barros et al. 1987).

The toxin(s) is unknown. Cattle have to ingest large amounts of the plant to become intoxicated, approximately 5g/kg bw of green plant daily for more than 100 days (Rego et al. 2012).

The diagnosis is based on the characteristic non-rever-

sible clinical signs and on histologic lesions. The intoxication should be differentiated from tremorgenic intoxications caused by *Ipomoea asarifolia* and *Claviceps paspali* which are transient, and with the intoxication by swainsonine-containing plants reported in cattle (*S. carpinifolia*, *Ipomoea* spp and *T. cordata*).

Lesions are not reversible and there is no treatment for affected animals. The only preventive measure is control of the plant, or altering grazing management to limit intake below a toxic threshold.

### **Tremorgenic plants: *Ipomoea asarifolia*, *Chloris virgata*, *Chloris barbata* and *Phalaris angusta***

Tremorgenic syndrome is an all-inclusive term for a group of nervous system disorders caused by indole-diterpenoid mycotoxins produced by various types of fungi on forages (Riet-Correa et al. 2013). In Brazil, excluding forages (for example *Paspalum* spp. contaminated by *Claviceps paspali* and *Cynodon dactylon* infected by *Claviceps cynodontis*), *I. asarifolia* and *Chloris* spp. are the main invasive plants of forages causing a tremorgenic syndrome (Pessoa et al. 2010).

*Ipomoea asarifolia* (Convolvulaceae) is found in the whole country, but the intoxication has been reported in sheep, goats, cattle, and buffalo in the northeastern region and on Marajó Island in the state of Pará. The disease occurs during the dry season when there is shortage of forage (Döbereiner et al. 1960, Medeiros et al. 2003, Guedes et al. 2007, Barbosa et al. 2012, Carvalho et al. 2014a). Lambs are more frequently affected. It has been demonstrated that the toxic compound is eliminated by milk affecting nursing lambs that are maintained confined while their mothers ingest *I. asarifolia* but do not show clinical signs themselves (Carvalho et al. 2014a, Chaves et al. 2016). The disease also occurs in nursing calves and lambs that remain confined while their mothers are in the field ingesting *I. asarifolia* (Carvalho et al. 2014c). This hypothesis was demonstrated in experimentally poisoned sheep and mice (Lopes et al. 2014).

Goats and sheep ingesting *I. asarifolia* at daily doses of 5 g/kg bw collected during the dry season had clinical signs after 19-31 days. The daily dose of 2.5g/kg bw did not cause clinical signs. During the rainy season the plant is less toxic, with affected animals requiring daily doses of 20 g/kg bw to cause clinical signs (Araújo et al. 2008). Cattle and buffalo show clinical signs after 1-4 daily doses of 10-20 g/kg bw (Barbosa et al. 2005).

Initial signs are slight tremors of the muscles of the head and neck or discrete head nodding, observed mainly after exercise. Later the animals have an uncoordinated gait, hypermetria, swaying when standing and wide based stance. When they are driven or startled they have severe uncoordinated movements, sideway progression and falling, sometimes into unusual positions. After a period of rest, they usually rise unassisted. In the more affected animals tremors became generalized. Generally, appetite is maintained, but weight loss occurs. Hypersensitivity to noise or movements is also observed. Severely affected animals become recumbent with generalized tremors, opisthotonus,

nystagmus, salivation, and clonic convulsions (Döbereiner et al. 1960, Medeiros et al. 2003, Barbosa et al. 2005). When the animals are moved from the pastures, clinical signs disappear in 7-15 days. Some animals died as a consequence of accidents. Others die while remaining recumbent (Döbereiner et al. 1960, Medeiros et al. 2003, Barbosa et al. 2005).

*Chloris* spp. are presumed the main cause of a disease known as staggers that occurred in cattle in the semiarid region of Pernambuco in 1956 and 1962. Pessoa et al. (2010), in the semiarid region of Paraíba, described a disease caused by *Chloris* spp. in cattle, sheep and horses with clinical signs identical to those observed in *I. asarifolia* poisoning. The outbreaks reported high morbidity rates but low mortality. When removed from the invaded pasture the animals recovered within a variable period, generally from 3-4 days to two weeks until complete recovery.

Outbreaks of intoxication by *Phalaris angusta* (Gramineae) occur in cattle in the state of Santa Catarina, in farms where there is a large amount of plant, mainly in soybean stubble or as a weed in ryegrass pastures or wheat fields (Gava et al. 1999). Clinical signs occur 10-20 days after the introduction of cattle into invaded pastures. Affected animals exhibit generalized tremors, an uncoordinated and rigid gait, and hypermetria. Intention tremors with lateral swaying of the head and neck are also observed. Clinical signs get worst when the animals are disturbed or forced to move, causing loss of equilibrium and falling. Cattle recover in 20-30 days once they are removed from the infested pastures (Gava et al. 1999). Calves ingesting diets of 50% to 100% of *P. angusta* had clinical signs 2-12 days after exposure (Sousa & Irigoyen 1999). Experimentally clinical signs are observed 2-12 days after the start of the ingestion. The plant is apparently more toxic when sprouting (Sousa & Irigoyen 1999).

No gross lesions are related to *I. asarifolia* and *Chloris* spp. Gross lesions associated with *Phalares angusta* poisoning are grey to greenish discoloration in the brain, mainly thalamus, mesencephalon and medulla oblongata. In most cases of poisoning by *I. asarifolia* and *Chloris* spp. there are no histological lesions, but some cases of poisoning by *I. asarifolia* with a more prolonged clinical manifestation period have cerebellar lesions, with degeneration and loss of Purkinje cells and presence of axonal spheroids in the granular layer (Guedes et al. 2007). Histologically, the lesions found in *P. angusta* poisoning is a yellow brownish granular pigment (ceroid-lipofuscins) observed in the perikaryon of neurons. Under electron microscopy this pigment appears as an accumulation of autofluorescent lipofuscin-like storage material in the lysosome (Gava et al. 1999).

*I. asarifolia* has been found to be associated with the presence of a symbiotic fungus, identified as *Periglandula*, which produces ergot-type alkaloids (Kucht et al. 2004, Markert et al. 2008, Steiner et al. 2011) and indole-diterpenes (Scharndl et al. 2013), suggesting that these substances, probably the indole-diterpenes, could be responsible for the clinical signs of intoxication. The toxic compound of *Chloris* spp. and *Phalaris angusta* is unknown.

The diagnosis is based on the characteristic clinical signs and the presence of *I. asarifolia* and *Chloris* spp. Ani-

mals showing clinical signs should be removed from the infected pastures.

The intoxication should be differentiated from other tremogenic diseases including intoxication by *Claviceps paspali*, *Cynodon dactylon*, *I. asarifolia*, *Chloris* spp. and *Aspergillus fumigatus* toxins in barley by-products, and also from the intoxication by *S. fastigiatum* and *S. paniculatum* and swainsonine-containing plants (*S. carpinifolia*, *Ipomoea* spp. and *T. cordata*). Poisoning by *S. fastigiatum* and diploidiosis also has some similarities with *F. augusta* poisoning. Cattle should be moved from the pastures at first sign of *Phalaris* intoxication.

### ***Halimium brasiliense***

*Halimium brasiliense* (Cistaceae) is a native plant from Uruguay, southern Brazil and Argentina that causes convulsions in sheep. The plant starts growing in April or May (autumn), flowers in October and November and sets seed in November and December. Pastures where the disease occurs are constituted by native grasses, mainly Gramineae. On infested pastures, *H. brasiliense* grows intermingled with grasses, and is consumed by sheep as they eat grasses. As it is more drought tolerant than natural grasses, it is grazed in larger amounts during drought when there is a shortage of forage. The intoxication occurs in sheep in the state of Rio Grande do Sul, and also in Uruguay in the states of Maldonado and Rocha. Sheep older than three years old of both sexes are more frequently affected. Two-year old sheep are seldom affected and clinical signs have not been observed in nursing lambs or yearling sheep. The disease is seasonal with most cases occurring from August to November, but a few cases are also observed from May to July. The frequency of the intoxication varies between farms and between years. There is also variation between different paddocks within farms. Morbidity varies between 1% and 15% but in some farms morbidity can reach 50% in years when drought conditions prevail. In farms where affected sheep are removed from the paddocks after clinical signs are first observed, the fatality rate varies between 1% and 5%, but in drought conditions on farms where this measure is not practiced, it can be as high as 35% (Riet-Correa et al. 2009).

Main clinical signs are transient seizures. The sheep appear to be normal but when disturbed or frightened they move a few meters and show epileptiform seizures. During the episodes, there are other nervous signs including muscular tremors, ventroflexion of the neck or opisthotonus, nystagmus, tetanic spasms and limb paddling movements. The duration of the seizures is from a few seconds to one minute. For a few seconds immediately after standing, the sheep show incoordination of the hind limbs, walking with short steps, or jumping. After these episodes, most affected sheep appear normal. The frequency of seizures is variable; in some cases, they appear every time the animal is disturbed while in others are more sporadic. If affected sheep continuing to eat *H. brasiliense*, the frequency of neurological episodes increases and animals lose weight. After 1-3 months, some affected sheep become recumbent and die 2-5 days later. If exposure is discontinued, most affected

sheep recover in 7-30 days. However, in a few sheep, seizures persist for at least one year. If affected sheep are not removed from the pastures they start to recover in December after *H. brasiliense* matures and sets seed. A few sheep show permanent signs in the periods between the neurological disorders, including progressive hind limb ataxia, urinary incontinence, urinary discoloration of the perineal wool, ataxia, weakness, incomplete limb extension, wobbly gait, incoordination, and difficulty in standing. Some sheep with neurological signs also show dermatitis of the ears and face, probably from photosensitization, but there are no clear evidences that those lesions are related to the nervous disease (Riet-Correa et al. 2009).

No gross lesions are observed. The main histologic lesion is the presence of vacuoles in both the brain and spinal cord, with rare axonal spheroids. Under electron microscopy, the lesions are segmental axonal swelling with degeneration and disappearance of the axonal organelles and vacuolation of the axoplasm. Dilated axons (spheroids) fulfill with vesicle-membranous bodies, membranous bodies, a few dense bodies and small vesicles interspersed in the axoplasm are also observed. A pigment identified as ceroid-lipofuscin is also present in neurons, astrocytes and macrophages. Those lesions apparently represent a novel morphologic manifestation of a toxic axonopathy (Riet-Correa et al. 2009).

The toxic compound is unknown. Sheep must ingest the plant for long periods to become intoxicated. In an experimental sheep, first clinical signs were observed after the daily ingestion of 2.117 kg of green plant for 142 days (Riet-Correa et al. 2009).

Areas with large amounts of the plant should not be grazed with sheep from May to November, or sheep grazing should be for short periods. The flock should be moved from the pastures after the clinical signs are first observed (Riet-Correa et al. 2009).

### ***Prosopis juliflora***

*Prosopis juliflora* (Leguminosae-Mimosaceae) was introduced into northeastern Brazil in the 1940's with seeds from Peru and Sudan. At that time, it was cultivated in an area of approximately 150,000 hectares in the semiarid region of Northeastern Brazil. Cultivation was discontinued because of toxicity problems, but the plant spread as a weed all over this region, mainly on riverbanks, near ponds and in other wet areas. It is a xerophilous tree with rapid growth, up to 8-12m high, which produces fruits within its second or third year. Due to their palatability and nutritional value the pods (i.e., mesquite beans) or "bran" are largely used for feeding dairy and beef cattle, sheep, goats, swine, chickens and rabbits with good nutritional and economical results (Tabosa et al. 2003). "Bran" is dry ground pods mixed with a variable amount of wheat or corn bran to facilitate the grinding of the pods. The intoxication affects cattle and, with less frequency goats. Sheep were thought to be resistant because, experimentally, they did not show clinical signs after the ingestion of the pods in concentrations of 60% and 90% in the food for one year (Riet-Correa et al. 2012). However, more recently, in a flock of 500 she-

ep consuming the pods continuously, two showed clinical signs and lesions of the poisoning one year and ten months after the start of ingestion (Almeida et al. 2017). In horses the consumption of fresh pods in areas invaded by the plant causes colic induced by the presence of phytobezoars. No neurologic disease is observed (Medeiros et al. 2012). Cattle become intoxicated after ingesting 50% of their diet containing pods for approximately 3 months (Figueiredo et al. 1995). Goats need to ingest the same amount for 7 months or more (Tabosa et al. 2000a). Before the pods were known to be toxic, outbreaks occurred mainly in cattle fed with pods or "bran" (Tabosa et al. 2003). However, knowledge about the potential toxicity has reduced incidences, such that most cases occur at the end of the dry season when forage is scarce.

First signs are decreased response of the facial skin to pinprick, difficulty in mastication of food, drooling of saliva, and decreased tone of the tongue. Later, cattle show inability to close the mouth due to a dropped jaw, reduced tone on manipulation of the mandible, difficulties in apprehending food, yawning, and inability to swallow prehended food. Other signs are tongue protrusion, excessive tongue movements, tilting the head with dropping of food from the mouth during chewing, impaired swallowing, mandibular tremors during chewing or rumination, and atrophy of the masseter muscles. Weight loss, bradycardia, and ruminal atony are also observed. If the animals have been affected for no more than 60 days they fully recover after withdrawal of the pods, but in animals affected for more time, clinical signs are not reversible due to denervation atrophy of the masseter and other muscles (Figueiredo et al. 1995, Tabosa et al. 2003, Tabosa et al. 2006, Câmara et al. 2009, Almeida et al. 2017).

In goats, clinical signs are mainly excessive and noisy rumination, salivation, atrophy of the masseter muscles, tremors of the mandible, head and lips during chewing and rumination, and weight loss (Tabosa et al. 2000ab, Lima et al. 2004). The main clinical signs in sheep are dysphagia, decreased response of the facial skin to pinprick, nystagmus, head tilting with dropping of food from the mouth during chewing, dropped jaw, droppy ears, decreased tongue tone when it was pulled out, and tongue protrusion (Almeida et al. 2017).

Gross lesions are emaciation, and reduction in size of the masseter and other masticatory muscles, which may appear yellowish due muscular atrophy (Tabosa et al. 2003, Câmara et al. 2009, Almeida et al. 2017).

*P. juliflora* intoxication is characterized by damage to mitochondria in neurons of the trigeminal and other cranial nerve nuclei. The main lesion observed in the trigeminal motor nuclei is fine vacuolation of the perikaryon of neurons, which presents a granular or spongy appearance. Cranial nerve degeneration and denervation atrophy of the muscles occurs as a consequence of the neuronal lesion. Dark distended nuclei, sometimes displaced to the margin of the perikaryon are observed in some neurons. Occasionally, ghost neurons, characterized by a pale perikaryon with dissolution of the Nissl substance and undefined borders or round cavities bordered by eosinophilic

material suggest neuronal loss. Axonal spheroids are rarely observed. Reactive astrocytes with vesicular dilated nuclei and scant eosinophilic cytoplasm are observed in low numbers within the trigeminal motor nuclei. Similar but milder lesions are present occasionally in neurons of the facial, hypoglossal and oculomotor nuclei. Wallerian-type degeneration characterized by short chains of two to five vacuoles side by side, occasionally containing eosinophilic myelin residues or some macrophages are observed in the intracranial roots of facial, hypoglossal and oculomotor nerves. Wallerian-like degeneration of variable severity is observed also in the maxillary, mandibular, hypoglossal, facial, and lingual nerves (Tabosa et al. 2000b, Tabosa et al. 2003, Lima et al. 2004, Tabosa et al. 2006, Almeida et al. 2017). In goats, there is also vacuolation of motor neurons of the motor trigeminal, facial and hypoglossal nuclei and motor neurons of the spinal cord and trigeminal ganglia (Tabosa et al. 2000b, Lima et al. 2004).

Denervation atrophy characterized by fiber size variation with fibers of decreased size and some angular fibers, abundant internal nuclei, and occasional vacuolated fibers are observed, mainly in the masticatory muscles. In advanced cases, the myofibers are substituted by fibrous or fatty tissue (Tabosa et al. 2000b, Tabosa et al. 2003, Tabosa et al. 2006, Almeida et al. 2017).

Under electron microscopy the neurons of the trigeminal nuclei have markedly swollen mitochondria, corresponding to the vacuoles observed with light microscopy. The mitochondrial cristae are displaced peripherally, and are disoriented and disintegrating. In severely affected mitochondria, the cristae are extremely shortened or absent. Intramitochondrial dense granules are absent. There is an increase in the number of lysosomes, consistent with secondary lysosomes with membranous to granular/amorphous electron-dense residual bodies (Tabosa et al. 2006).

Piperidine alkaloids (julifloricine, julifloridine, juliflorinine, juliprosopine, juliprosine, juliprosinene and others) have been identified in the pods of *P. juliflora* (Batatinha 1997, Tabosa et al. 2000ab). Some of these alkaloids are toxic to laboratory animals (Tabosa et al. 2000ab) and in cell culture (Batatinha 1997). Experiments with juliprosopine in isolated rat brain mitochondria induced uncoupling of oxidative phosphorylation in the mitochondria preventing the coupling between the electron transport and phosphorylation reactions, which is attributed to a modification of the arrangement of the inner mitochondrial membrane (Maiola et al. 2012).

In Brazil, the disease was produced experimentally in cattle ingesting food containing 50% and 100% of pods. All animals had clinical signs 3 months after the beginning of feeding. Cattle with diets of 100% pods died after 6-10 months of ingestion. Cattle ingesting 50% of their diet as pods showed less severe clinical signs than those ingesting 100%, and recovered fully 12 months after the end of the administration (Batatinha 1997). In another experiment, 3 groups of calves were fed with a ration containing 50% fresh pods, 50% dry pods, and 75% dry pods, respectively. All cattle from the three groups showed clinical signs resulting from impaired function of cranial nerves V, IX, X,

and XII, starting 45-75 days after consumption of the plant (Tabosa et al. 2000b). Goats are more resistant and need to ingest food containing 60%-90% of pods to show initial clinical signs (Tabosa et al. 2000a).

Diagnosis is made by the characteristic clinical signs and a history of ingesting *P. juliflora* pods for long periods. The feeding of pods should be suspended immediately after the first clinical signs are observed. If animals have non-reversible atrophy of the masseter muscles, they will recover clinically. Breeding cattle cannot have a diet exceeding 30% pods, nor can consumption continue beyond 6 months. Cattle to be slaughtered can ingest up to 50% pods for 3 months.

Goats can ingest similar dietary levels of pods for longer periods: 30% in the diet up to one year and 50% up to 6 months. Sheep have to eat large amounts of pods for more than one year to show clinical signs of poisoning.

### **Marsdenia spp.**

In the semiarid region of Northeastern Brazil there are at least 3 toxic species of *Marsdenia* (Asclepiadaceae): *M. hilariana*, *M. megalantha* and *M. aff. zehntneri*. *M. hilariana* and *M. aff. zehntneri* are climbing vines and *M. megalantha* is a shrub of variable growth habits (prostrate, decumbent or erect), up to 60 cm tall. The roots (tuberculi) and leaves are toxic. The leaves are occasionally eaten by hungry animals. The tubercles are palatable and if they are uprooted during plowing or exposed by other means, animals ingest them readily. The roots and the fruits of these plants are also used by farmers as poison to kill rats and dogs. The spontaneous intoxication has been diagnosed in cattle, sheep, goats, swine and horses and has been produced experimentally in sheep, goats, cattle and pigs (Pessoa et al. 2011, Geraldo Neto et al. 2013ab).

Clinically affected animals have ruminal bloat, tachycardia, muscular tremors, salivation, chewing motions, dyspnea, nystagmus, mydriasis, ataxia, lost of equilibrium, and sternal recumbence followed by lateral recumbency. Death occurs in 1-6 days. Less affected animals have nervous signs, mainly cerebellar, or stay in sternal recumbence and gradually recover over time (Pessoa et al. 2011, Geraldo Neto et al. 2013ab).

No macroscopic or histologic lesions were observed in one report of the disease (Pessoa et al. 2011) but another report describes segmental laminar neuronal necrosis and spongiosis in the telencephalic cortex and degeneration of Purkinje cells (Geraldo Neto et al. 2013ab).

The toxic compound is unknown. Experimentally doses of 5-10g/kg bw of roots or leaves cause intoxication, and higher doses are lethal (Pessoa et al. 2011). It is suggested that these species of *Marsdenia* contains a toxin similar to the steroidal oligoglycoside cynanchoside, which is found in *M. rostrata* and *Cynanchum* spp. and causes nervous signs.

Diagnosis should consider the presence of the plants or their roots. The main differential diagnosis is with rabies and botulism. There is no known treatment. The roots must be collected and eliminated when they are exposed by plowing, soil erosion, or tree growth.

### ***Erythroxylum* spp.**

*Erythroxylum argentinum* and *E. deciduum* (Erythroxylaceae) are trees up to 8 m tall, which flower in August to January and set fruit in September to February. The intoxication occurs in Rio Grande do Sul in summer (December to March) when sheep ingest berries that fall from the trees. Morbidity rate and fatality rates are variable, up to 100% (Barros et al. 2004, Colodel et al. 2004).

Clinical signs are lethargy, reluctance to move, stiff uncoordinated gait with dysmetry, staggering, and falling. The animals fall with increase frequency until they remain recumbent. A wide-based stance is assumed when standing. Severe respiratory signs are also observed including labored breathing and cyanosis. If the animals are forced to exercise strenuously they collapse and died of respiratory insufficiency. Clinical signs are manifest 8-72 hours after ingestion, but if sheep are undisturbed most recover in 3-4 days (Barros et al. 2004, Colodel et al. 2004).

At necropsy, the fruits of the plant are observed in the abomasum and rumen. Pulmonary edema, hemorrhages in the serous membranes and urinary bladder distention are also observed. Histologic lesions are not observed (Barros et al. 2004, Colodel et al. 2004).

The toxic compound is unknown. Experimentally *E. argentinum* caused clinical signs with single doses of 10 and 15g/kg bw. *E. deciduum* was less toxic causing clinical signs and death after a dose of 60g/kg bw or 3 and 4 daily doses of 20 and 17g/kg bw, respectively; single doses of 30g/kg bw and 14 daily doses of 9g/kg bw did not cause clinical signs (Barros et al. 2004, Colodel et al. 2004).

The diagnosis is based on clinical signs, presence of the plant, observation of the fruit in the abomasum or rumen, and absence of histologic lesions. There is no treatment. Affected sheep should be moved as little as possible until they recover. Sheep should be removed from pastures when trees produce fruit (Barros et al. 2004, Colodel et al. 2004).

### ***Hybanthus calceolaria***

*Hybanthus calceolaria* is a herbaceous plant found in northeastern Brazil, which causes nervous signs in cattle and probably in sheep and goats in the states of Piauí and Pernambuco. The disease occurs at the end of the rainy season with a morbidity of 4% to 66% and mortality of 2.7% to 14%. The disease was produced experimentally in cattle, only when the plant was fruiting. Other experiments in cattle and sheep failed to reproduce the disease suggesting that the plant is toxic only occasionally (Carvalho et al. 2014b).

The main clinical signs are ataxia, difficulty rising, and muscle tremors, mainly during exercise. At rest or in recumbency, the animals show myokymia, mainly in limb muscles and the masseter muscle. Corneal, facial, and swallowing reflexes may be depressed and there is a reduction in tongue tone. Anorexia, ruminal hypotony, and soft feces containing the fruits of the plant are also observed. The clinical course varies from 7 to 15 days until death occurred. However, animals that stop ingesting the plant before becoming recumbent recovered after a few days. No significant lesions are observed during necropsies or on histological

examination. The only way to control the poisoning is by removing the animals from the paddocks when the plant is seeding (Carvalho et al. 2014b).

### ***Talisia esculenta***

*Talisia esculenta* is a tree that produces pitomba, a fruit consumed by humans in several regions of Brazil. However, during the raining season, the leaves and the seeds of this plant cause nervous signs in cattle and sheep. Leaves are ingested when the trees are pruned and the animals have access to branches. Fruits that had fallen off the plant are also eaten. Seeds or leaves may be ingested when the branches bend downward under the weight of the ripe fruits allowing access to browsing animals. In some of these conditions, morbidity varies from 5% to 100% and mortality from 0 to 30% (Riet-Correa et al. 2014).

Clinical signs are severe ataxia, abnormal postural reactions, weakness and muscular tremors followed by recumbence. Other animals show hyperesthesia, hyperreflexia and severe spastic paresis with stiff limbs, especially the hind limbs, Moderate ruminal bloat, halting of rumination, decreased methylene blue reduction test, death of rumen protozoa, and constipation are also observed. Some animals died after a clinical manifestation period of nearly 24 hours, but most recover after 7-15 days. No significant necropsy or histologic lesions are found (Riet-Correa et al. 2014).

The toxic compound is unknown, but a protein named talisin with hemagglutinating activity of erythrocytes, insecticidal activity, and inhibitory effect on fungal growth has been identified in the seeds of *T. esculenta*. This protein has also been shown to induce an inflammatory response in mice and to cause a noncompetitive inhibition of trypsin. Poisoning was reproduced experimentally in sheep by the administration of 30-60 g of leaves/kg body or of 5 and 10 g of seeds/kg body weight (Riet-Correa et al. 2014).

The diagnosis of *T. esculenta* poisoning should be based on the history of ingestion of seeds or leaves of the plant, the presence of reversible nervous signs, and the absence of significant gross or histologic lesions.

### ***Ricinus communis***

*Ricinus communis* L. (Euphorbiaceae), commonly called castor bean, Palma(e) Christi or wonder tree, is an upright bushy plant that is found on every continent. The ingestion of leaves and pericarp causes nervous clinical signs while the ingestion of fruits causes digestive disease in ruminants (Albuquerque et al. 2014). *R. communis* is often cited by farmers as the cause of death, especially of cattle, in epidemiological surveys from semiarid regions of Pernambuco and Paraíba, northeastern Brazil. In cattle, spontaneous poisoning is always associated with intense hunger and, historically, poisonings have occurred in years of prolonged drought. Nevertheless, sheep (Armien et al. 1996, Aslani et al. 2007) and goats (Silva Filho et al. 2016) are also affected.

The evolution of the neurological disease is acute. First clinical signs can be observed between 3-6 hours after ingestion of the leaves. The major clinical signs con-



sist of dehydration, sialorrhoea, dyspnea, ataxia, constant chewing motions, lateral deviation of the head and neck, incoordination, staggering gait, abnormal postures, and in some cases bloat can be observed. These clinical signs persist for 2-16 hours until total recuperation or death occurs depending on the amount of leaves ingested. Gross lesions are not observed. Histologically only slight to severe vacuolization of hepatocytes is noted (Döbereiner et al. 1981).

The toxin responsible for the neurological disease caused by *R. communis* is ricin, a glycoprotein lectin found in the leaves and pericarp of the plant that is toxic to mammalian cells (Lord et al. 1994, Audi et al. 2005). Additionally, *R. communis* contains the alkaloid ricinine (Ferraz et al. 1999). The intoxication was reproduced experimentally by the administration of 10 and 20g/kg of the leaves consumed at once. At these doses the disease is generally critical or fatal (Döbereiner et al. 1981).

Prophylaxis consists of eradication of the plant or keeping ruminants away from areas where there is a severe propagation of *R. communis*. There is no specific treatment for the poisoning, but in a recent outbreak in goats, a support therapy (activated charcoal + fluid therapy + glucocorticoid) had satisfactory results (Silva Filho et al. 2016).

#### **Thiaminase-containing plants: *Equisetum* spp., *Pteridium aquilinum* and *Pteridium arachnoideum***

*Equisetum* spp. (Equisetaceae) and *Pteridium* spp. (Dennstaedtiaceae) contain the enzyme thiaminase, causing a thiamine deficiency in horses. In both cases, horses consume these plants mixed with pasture and develop a preference for the plants, eventually seeking them in pastures. Other possibilities occur during the dry season when the plants are still green or when fed with contaminated hay (Tokarnia et al. 2012).

The main clinical signs of poisoning by *Equisetum* consist of weight loss and nervous signs of drowsiness, staggers, unsteady gait, and ataxia are observed 3-6 weeks after the start of ingestion. As the signs progress, horses become emaciated and recumbent and die soon thereafter (Tokarnia et al. 2012).

All parts of the plant are toxic but the sprouts are more toxic than other parts. Horses consuming diets containing 50% or more of *Pteridium* spp. develop clinical signs (Valli 2007) that consisted in anorexia, weight loss, hindlimbs incoordination with unsteady gait, muscle tremors and it may lie down and not be able to get up (Diniz et al. 1984, Burrows & Tyrl 2001). If not treated, horses may display a crouching stance, loss of muscular control and may become uneasy and nervous due to its inability to control muscle movement. Intoxication terminates in death, following convulsions, several days to several weeks after the onset of symptoms (Burrows & Tyrl 2001).

Early identification of the symptoms is critical in the *Pteridium* spp. poisoning. If identified early, simply removing the source of the fern will lead to a full recovery. No macroscopic or histologic lesions have been reported in *Equisetum* spp. and *Pteridium* spp. poisoning. Other chronic nervous diseases such as equine protozoal myeloencephalitis from *Sarcosystis neurona*, and hepatic encephalo-

pathy due to pyrrolizidine alkaloid-containing plants, have similar clinical signs, but unlike thiaminase-containing plants toxicity, these conditions have characteristic histologic lesions.

Treatment with thiamine promotes a quick positive response (vitamin B<sub>1</sub> at 500 mg-1 gm/day - on day 1 intravenously and then intramuscularly for several days (Burrows & Tyrl 2001). If the animal is emaciated and recumbent, treatment can be ineffective (Tokarnia et al. 2012). The best method of prevention is to maintain good pastures, eliminate the plant from fields and ensure that is not present in hay.

#### ***Bambusa vulgaris***

*Bambusa vulgaris* f. *vulgaris* (Poaceae-Bambusoideae) causes intoxication in horses in Northeastern Pará, in areas where the plant is cultivated for shade. Horses ingest the plant when forage is scarce during the dry season or when it grows in *Brachiaria brizantha* pastures which are not very palatable to horses. The intoxication affects horses of different ages (Barbosa et al. 2006a).

Clinical signs are somnolence, incoordination, ataxia, standing with abducted limbs, and difficulty in turning around. Signs of impairment of cranial nerves are also observed such as paresis of the tongue, difficulty in prehending, chewing and swallowing of food, and decreased palatal and labial reflexes. Cutaneous, anal, and flexor reflexes are depressed. Blindness and head pressing are occasionally observed. The clinical course is subacute or chronic and most horses recover after being removed from the pastures (Barbosa et al. 2006a). Gross lesions are not observed. Histologically only slight edema and axonal degeneration had been reported in a few axons, mainly in the medulla oblongata (Barbosa et al. 2006a).

The active principle is unknown. The intoxication was reproduced experimentally by the administration of *B. vulgaris* leaves at daily doses of 10-31g/kg bw for 6 to 60 days. First signs appeared 24-72 hours after dosing, but clinical signs were less severe than those in the spontaneous intoxication (Barbosa et al. 2006a).

The diagnosis is based on the characteristic clinical signs in horses grazing in areas with *B. vulgaris*, and in the regression of clinical signs after consumption ceases (Barbosa et al. 2006a). To prevent the intoxication horses should be removed from pastures with *B. vulgaris*, mainly during the dry season, and from *Brachiaria brizantha* or *B. decumbens* pastures with bamboo plants because the grasses are not well accepted by horses (Barbosa et al. 2006a).

#### ***Hypochoeris radicata***

*Hypochoeris radicata* causes stringhalt (high stepping with hyperflexion of the hind limb) in horses in different countries. In Brazil, the disease has been reported from the states of Rio Grande do Sul and Paraná. It is observed during winter and spring (July to December), and up to 50% of horses have been affected (Araújo et al. 2008, Rodrigues et al. 2007). The disease was reproduced experimentally in a six-month-old horse by the daily administration of 9.8 kg of fresh plant for 50 days. First clinical signs appeared 19 days after dosing began (Araújo et al. 2008).

Clinical signs are characterized by abnormal gait with involuntary flexing of the hocks of one or both hind legs. In some horses the hyperflexion is so marked that the abdomen is kicked when walking. Affected horses have difficulty in stepping backward or circling. Left laryngeal hemiplegia (roaring) can be associated with stringhalt. Muscular atrophy can be observed in the hind limbs (Araújo et al. 2008, Rodrigues et al. 2007). Involvement of the forelimbs is also seen occasionally, taking the form of stumbling, toe-scuffing, and knuckling at the carpus (Araújo et al. 2008). Axonal degeneration in peripheral nerves and muscular atrophy are observed histologically. When removed from the pastures invaded by *H. radicata* most animals recover without treatment over a period of time that can last several months (Araújo et al. 2008, Rodrigues et al. 2007).

The disease, named Australian stringhalt, is different from classical stringhalt. The disease caused by *H. radicata* is more severe, usually bilateral, occurs in outbreaks, is seasonal, and most animals recover spontaneously. Classical stringhalt is a sporadic disease of unknown cause that has to be treated surgically because there is no spontaneous recovery (Araújo et al. 2008, Rodrigues et al. 2007).

The toxin is unknown. Treatment with phenytoin or other anticonvulsants can be of benefit. Grazing should be avoided in areas severely infested by the plant in order to prevent the disease. Horses have to be removed from the pastures immediately after clinical signs are first observed.

### *Indigofera lespedezioides*

Poisoning by *Indigofera lespedezioides* occurs in horses in the state of Roraima, Northern Brazil causing a disease similar to that caused by *I. linnaei* in Australia and *Indigofera hendecaphylla* in Florida. The plant is mostly found in the native vegetation (savanna) known as "lavrado", mainly in the borders of the forest. Most cases of poisoning occur at the end of the dry season when *I. lespedezioides* is nearly the only green vegetation available. Horses of all ages are affected and up to 10% of the horses may be affected, but mortality of 100% has been reported (Lima et al. 2012).

Main clinical signs are anorexia, sleepiness, unsteady gait, severe ataxia, weakness, stumbling, and progressive weight loss. Gait alterations are more marked in the hind limbs with the hind hooves dragging and causing excessive wear of the toes. Eye discharge and blindness are also observed. Some farmers have reported corneal opacity in affected horses. If the animals are disturbed or forced to move, nervous signs increase and the animals can fall. Abortion is commonly observed in mares. Death occurs 2–4 months after the observation of first clinical signs. If the plant consumption is interrupted, some animals may recover. No significant gross lesions are reported. Neuronal lipofuscinosis of the cerebrum, brain stem, cerebellum, and spinal cord, and Wallerian-type degeneration of some mesencephalic tracts may be observed histologically. Neuronal and axonal degeneration and lipofuscinosis are observed by electron microscopy (Lima et al. 2012).

Indospicine, ranging from 63 to 1178 mg/g, was detected in four samples of *I. lespedezioides*, and nitro toxins were detected at a concentration of 2.5 mg/g in only one

sample, suggesting that indospicine is the toxic compound responsible for the poisoning (Lima et al. 2012).

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