Nigropallidal encephalomalacia was diagnosed in two horses in northern Victoria that had a history of long-term pasture access to a dense growth of *Rhaponticum repens*. The region in which the affected horses lived had received well above average rainfall for several months preceding the poisoning. Affected horses had sudden onset of subcutaneous oedema of the head, impaired prehension and mastication, dullness, lethargy and repeated chewing-like jaw movements. Diagnosis was confirmed at necropsy, with characteristic malacic lesions in the substantia nigra and globus pallidus of the brain. This is the first documented case of nigropallidal encephalomalacia in Australian horses associated with *R. repens*.

**Keywords** chewing disease; creeping knapweed; horses; nigropallidal encephalomalacia; poisoning; *Rhaponticum repens*

**Abbreviations** MRI, magnetic resonance imaging; NPEM, nigropallidal encephalomalacia

Nigropallidal encephalomalacia (NPEM), commonly known as chewing disease, is a plant poisoning of horses that causes irreversible brain damage. It has been reported in North and South America after consumption of either *Rhaponticum repens* (L.) Hidalgo, previously called *Acroptilum repens* (L.) DC or *Centaurea repens* (L.) (creeping knapweed, Russian knapweed, hardheads, hard-thistle, blueweed) or *C. solstitialis* (L.) (St Barnaby’s thistle, yellow burr, yellow star thistle), both of the daisy and thistle family (Asteraceae). The incidence of equine NPEM is rare and there is only one documented case in Australia, involving young horses grazing pastures dominated by *C. solstitialis* in the Molong district of New South Wales in 1971 and 1972. To our knowledge, poisoning of horses by *R. repens* has not been previously reported in Australia.

Clinical signs of equine NPEM include sudden onset of impaired prehension and mastication with concurrent hypertonicity of facial muscles, resulting in the mouth being held partly open with lips retracted and the occurrence of repeated chewing motions. Younger horses are more likely to be affected. Other clinical signs including lethargy, a persistent head droop, aimless walking, ataxia and tongue paresis. Affected horses are able to swallow normally if food or water reaches the back of the oropharynx. Horses may attempt to drink by placing the head deep within water troughs. There are no treatment options for this disease. Affected horses will die of starvation and dehydration if they are not euthanased. Pathology typically involves bilaterally symmetrical malacia of the globus pallidus and/or the substantia nigra regions within the thalamus. The only previous Australian case was documented in five Spring-drop foals and one 9-month-old foal with signs of lethargy, inability to graze or drink and paresis of the tongue with the lateral edges curling upwards to form an open tube.

The toxin causing equine NPEM remains uncertain. Tyramine and the sesquiterpene lactone repin have both been proposed as causative agents. The characteristics of the brain lesions in affected horses suggest that the toxin involved results in dopamine deficiency in the dopaminergic nigrostriatal pathway after an initial massive release of stored neurotransmitters into the corpus striatum. The ability of repin to induce neurotoxicity in rodents, in which reduced levels of striatal extracellular dopamine and hippocampal glutathione were seen, coupled with its vastly higher concentration within *R. repens* appears to make it the more likely of the two to be the causative toxin. *Rhaponticum repens* is native to central Russia, Turkey, Afghanistan and Mongolia. It is believed to have been introduced to Australia in the early 1900s and is a declared noxious weed in Victoria, New South Wales, Western Australia and South Australia. It is a weed of roadsides and irrigation channels and of major concern in irrigated vineyards, orchards and dryland crops. It is primarily found in areas with 300–600 mm annual rainfall and often invades livestock pastures. The plant is an erect perennial, growing to a height of 50 cm (Figure 1). Stems branch from the centre and are covered in greyish hairs when young. Leaves are greyish to silver-green, lance-shaped, 15 cm long and 5 cm wide, alternatively arranged around the stem and getting smaller as they near the top (Figure 2). The flower heads are thistle-like in appearance and up to 2.5 cm in diameter, with purple, pink or occasionally white petals. The plant is relatively hardy, with an extensive root system that is capable of sprouting new shoots as it spreads underground.

**Case reports**

Horse 1, a 2-year-old cross-bred cob colt in good body condition was presented in May 2010 to the Goulburn Valley Equine Hospital with a 1-day history of a swollen head and an inability to eat or drink. The colt was dull and depressed, but with heart rate, respiratory rate and rectal temperature all within normal limits. There was severe subcutaneous oedema of the head, particularly in the periorbital, submandibular and muzzle regions. Lymph nodes were not palpably enlarged.
No ocular or nasal discharge was noted. The jaw was seen to be held partially open with saliva running from the open lips. Oral examination revealed normal tongue tone and no lesions. All external structures of the head and neck were carefully examined and palpated, with no abnormalities detected that could explain the oedema. A definitive diagnosis at time of presentation was not achieved, but initial differential diagnoses included anaphylaxis, cellulitis, foreign body, trauma, sinusitis, strangles, purpura haemorrhagica and Hendra virus. The colt was given dexamethasone sodium phosphate 0.1mg/kg IV (Dexol 5, Bomac, Hornsby, NSW, Australia) and discharged on a 5-day course of procaine penicillin 22mg/kg IM twice daily (Bomacillin SA, Bomac) and phenylbutazone 4.4mg/kg PO daily (Bute paste, Ranvet, Botany, NSW, Australia). The owner was instructed to wash the colt’s mouth out daily and return it for re-examination if the condition had not improved by the end of the course of treatment.

Three days later a farm visit was conducted to examine horse 1 after the owner reported its condition to have deteriorated. It was found to be in poor body condition and housed in a heavily weed-infested paddock. Another horse of similar breed (horse 2) was also housed in the same paddock. Horse 1 was unable to eat or drink unassisted, but able to swallow normally when small volumes of food and water were syringed into the back of the pharynx by the owner. Heart rate, respiratory rate and rectal temperature remained within normal limits despite a persistently swollen head. The mouth was seen to be constantly held open with subtle chewing-like motions noted.

At this stage a plant poisoning was suspected. The 40-acre native pasture paddock in which the two horses were grazing was dominated by an upright weed approximately 30 cm high with small greyish-green leaves. The horses had been in this paddock for approximately 8 months prior to the onset of clinical signs. The paddock had been grazed for similar lengths of time in previous years without any problems. The weed was the only green forage within the pasture. Many plants showed evidence of being grazed, with some having small thistle-like flower heads. Two flowering plants were pressed, dried and submitted to the National Herbarium of Victoria for formal identification. The plants were confirmed as *R. repens*. A presumptive diagnosis of NPEM was made based on the presenting clinical signs and the history of long-term access to *R. repens*.

Two days later, horse 2 was presented to Goulburn Valley Equine Hospital after acute onset of inability to eat or drink, marked weight loss and intermittent unusual jaw movements. Horse 2, a 3-year-old cross-bred cob colt, was in poor body condition and had repeated rapid and seemingly involuntary chewing motions. When these chewing motions were not occurring, the mouth was held partially open. The upper lips were curled in and over the incisors. The tongue was partially protruded but had normal tone.

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**Figure 1.** *Rhaponticum repens* in dry pasture.

**Figure 2.** Flowering head of *Rhaponticum repens*. 
Both horses were euthanased with pentobarbitone sodium (325 mg/kg IV; Lethobarb, Virbac Australia, Milperra, NSW, Australia) on humane grounds because of the hopeless prognosis associated with suspected NPEM. Necropsy examination of the head of horse 1 showed extensive subcutaneous oedema, particularly in the periorbital, submandibular and muzzle regions. Ground-up feed material was seen within the back of the pharynx. No other lesions were seen. Necropsy examination of the head of horse 2 was normal. Both brains were removed whole and immersed in a 10% formalin solution for 72 h, then submitted for histopathology to the Department of Primary Industries Veterinary Diagnostic Services, Atwood, Victoria. Full necropsies were not performed. At the laboratory, lesions characteristic of nigropallidal malacia were found. The brain of horse 1 had bilaterally symmetrical focal malacia and tissue loss in the thalamus at the region of the substantia nigra (Figure 3A). Horse 2 had bilaterally symmetrical malacia and tissue loss in the rostral thalamus at the region of the globus pallidus (Figure 3B). There was also mild enlargement of the mesencephalic aqueduct of horse 1, and a small choroid plexus cholesteatoma in the third ventricle of horse 2, both unrelated and incidental findings. Histologically, the malacic regions were well-circumscribed areas of tissue loss with numerous lipid-laden phagocytes and remnant blood vessels filling the spaces. There were rare to moderately abundant axonal spheroids at the margin of the malacia, but no reaction in the adjacent tissue (Figure 4). The globus pallidus in horse 1 and the substantia nigra in horse 2 were not affected. The diagnosis of NPEM was confirmed by the characteristic gross and histological findings.

Discussion

Conditions leading to the development of NPEM must involve several weeks of access to pasture dominated by young, green plants of the known causative species before flowering. Mature plants become woody and generally are unpalatable. Horses must consume a minimum of 59–71% of body weight in *R. repens* for poisoning to occur, with the average interval from first access to development of clinical signs being 30 days. In the only other Australian case, the weather conditions leading to the poisoning event involved unseasonably good summer rainfall, which resulted in rapid growth and abundance of *C. solstitialis*, followed by a dry early winter. These conditions allowed *C. solstitialis* to dominate the pasture, resulting in it comprising a large proportion of the young horses’ diet. The weather conditions associated with the current case of NPEM were similar; the area where the affected horses lived received almost double its average rainfall for the 5 months preceding the poisoning (mean rainfall Jan–May 164.2 mm; prior to intoxication Jan–May 303.4 mm). As in the previous case, these conditions would have significantly contributed to *R. repens* becoming the dominant plant species within the paddock.

The current cases showed many of the typical clinical signs of NPEM, but with several notable differences. Horse 1 presented with a diffusely swollen head, which does not appear to have been previously reported.
in cases of equine NPEM. Whether this was a primary result of the toxin involved, or secondary to a persistently dropped head, is difficult to determine. The upper lips curling in and over the incisors, described as a ‘purse string effect’, seen in the current case has previously been reported in approximately 25% of NPEM cases related to C. solstitialis, but not specifically described in cases of R. repens poisoning.3–6 Unlike the other reported case in Australia, in the current case there was no evidence of tongue paresis or lateral curling. Both affected horses had normal tongue tone and no change in tongue contour. The paresis and curling of the tongue appears to be a particular manifestation of C. solstitialis poisoning that is not present in poisoning by R. repens. This observation is consistent with the findings of NPEM in North America.3–6

Unlike the current case, where horse 1 had malacia and tissue loss only within the substantia nigra and horse 2 had loss only within the globus pallidus, the majority of NPEM cases show bilateral lesions within both nuclei. Lesions within the substantia nigra alone have previously been reported in only 26% of cases, with globus pallidus lesions only seen in 11%.1,2 The similarity of the clinical signs in the two affected horses, despite different lesions, fits with previous suggestion that the lesions interrupt a single neural pathway, but at different levels.1,2

A presumptive diagnosis of NPEM is made based on the presence of clinical signs in conjunction with a history of long-term access to large quantities of C. solstitialis or R. repens. Definitive diagnosis is made by brain histopathology; however, a recent study has demonstrated the magnetic resonance imaging (MRI) features of NPEM.15 According to those authors, MRI enables antemortem diagnosis of the condition. However, because of the irreversible and fatal nature of the disease and the limited access to MRI, this method of diagnosis does not appear to be practical at this time. Postmortem brain examination remains the standard method of confirming a tentative clinical diagnosis of NPEM.

Conclusion

NPEM is a rare plant poisoning of horses, with only one previously documented case occurring in Australia as a result of consuming C. solstitialis. The cases reported here demonstrate that R. repens is also capable, under certain conditions, of inducing NPEM in Australian horses and care must be taken in the management of horses in regions where this weed is prevalent.

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References


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