CASE REPORT

Pimelea trichostachya poisoning (St George disease) in horses

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A dense population of *Pimelea trichostachya* plants (Family Thymelaeaceae) in pasture poisoned a horse herd in southern inland Queensland in October–November 2005. Plant density was 2 to 45 g wet weight/m^2 (mean 16 g/m^2) from 5 to 69 plants/m^2 (mean 38 plants/m^2) representing 3 to 20% (mean 9%) of the volume of pasture on offer. Ten of 35 mares, fillies and geldings were affected. Clinical signs were loss of body weight, profound lethargy, serous nasal discharge, severe watery diarrhoea and subcutaneous oedema of the intermandibular space, chest and ventral midline. Pathological findings were anaemia, leucocytopenia, hypoproteinaemia, dilatation of the right ventricle of the heart, dilated hepatic portal veins and periportal hepatic sinusoids (*peliosis hepatis*), alimentary mucosal hyperaemia and oedema of mesenteric lymph nodes. Cattle grazing the same pasture were affected by *Pimelea* poisoning simultaneously. Removal of the horses to *Pimelea*-free pasture initiated recovery. The one other incident of this syndrome, previously only recognised in cattle in Australia, occurred in horses, in South Australia in 2002, with access to a dense *Pimelea simplex* population.

Key words: *Pimelea trichostachya*, St George disease, poisoning
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AGID	Agar gel immunodiffusion
AST	Aspartate aminotransferase
CK	Creatine kinase
EDTA	Ethylenediamine tetraacetic acid
EHV1	Equine herpesvirus 1
EIA	Equine infectious anaemia
EVA	Equine viral arteritis
GGT	Gamma glutamyltransferase
PCR	Polymerase chain reaction
PCV	Packed cell volume
VNT	Virus neutralisation test

St George disease, or Marree disease, is a chronic intoxication of cattle seen only in Australia and recognised since the 1920s[1] as a unique syndrome of circulatory failure, anaemia and diarrhoea with *peliosis hepatis*.[1–4] The disease occurs in inland southern Queensland,[1,5] north-western New South Wales,[6,7] north-eastern South Australia[8] and southern Northern Territory.[9] It is caused by the diterpene ester simplexin[10] (and probably other such compounds) usually obtained by inhalation[3] or involuntary ingestion[3,7] of fine hairs or dead fragments of the annual herbaceous Australian native plants *Pimelea trichostachya, P simplex* subspecies *simplex, P simplex* subspecies *continua* or *P elongata* of the Family Thymelaeaceae.[11] Isolated cases due to shrubby perennial *Pimelea* species are known.[12,13] Dosing *Pimelea* extracts intravenously to cattle[3] and testing such extracts on bovine pulmonary vein preparations in organ baths[14] demonstrated that sustained contraction of the highly muscular bovine pulmonary venules explained the pulmonary venous hypertension that is the most prominent of the effects of these plants in cattle. The lack of such thick smooth muscle coats in the pulmonary venules of horses was thought to prevent the syndrome developing in that species,[3] however, horses are susceptible to *Pimelea* toxins if they are forced to eat the plants, succumbing to acute severe alimentary tract irritation. There are rare records of such poisonings of horses by *Pimelea decora* in northern Queensland[15] and *Pimelea prostrata* in New Zealand.[16] Recently, horses exposed to *Pimelea simplex* near Marree in north-eastern South Australia were reported as having severe oedema of the head, neck and brisket and the characteristic *peliosis hepatis* liver lesion seen in cattle.[17] We report here the St George-Marree disease syndrome in horses exposed to a dense population of *P trichostachya* in the Maranoa district of southern inland Queensland.

Case report

History

A herd of 35 Australian Stockhorses comprising locally-bred and introduced mares, fillies and geldings were grazed about 100 km south-south-west of Roma, Queensland. The improved pastures consisted of a good coverage of *Cenchrus ciliaris* (buffel grass) and native grass species on red sandy loam in partly-cleared open woodland previously dominated by *Eucalyptus populnea* (poplar box). Other prominent plants in the area grazed were *P trichostachya* (flax weed, rice flower), *Acacia aneura* (mulga), *Geijera parviflora* (wilga), *Ventilago viminalis* (supplejack),

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Eremophila mitchellii (false sandalwood), *Alstonia constricta* (bitter bark), *Ipomoea* sp Q6 aff *calobra* (weir vine), *Sclerolaena birchii* (galvanised burr) and *Eremophila maculata* (spotted fuchsia). Illness with significant loss of body weight was first seen in the horses by their owners in early October 2005, approximately 15 months after their introduction to the paddock in July 2004. Cattle on the same pastures had had signs typical of St George disease since October 2004. Two newborn (day-old) foals from affected mares died, followed by two adults that had severe loss of weight, one with diarrhoea. The first veterinary examination was on 14 November 2005, about 6 weeks after signs were first noticed. At this time, 10 horses were affected. There was no evidence that the horses had eaten *P trichostachya* – partly-eaten plants bitten off above ground level were not seen and no horse was directly observed eating the plants. After this examination, supplementary feed consisting of lucerne (*Medicago sativa*) hay provided without restriction and a mixture of powdered molasses, a commercial phosphorus supplement (Phosmix®), salt and copra was provided daily. One horse was necropsied on 21 November. A second veterinary examination of affected horses was carried out on 29 November 2005. Two mares and a gelding were moved to a property free of *Pimelea* plants in Roma and the rest of the herd was moved to a property near Augathella about 200 km WNW of Roma with very small numbers of *Pimelea* plants in its pastures in late December 2005.

Clinical signs

On 14 November, the 10 affected horses were in poor body condition. Nine horses had severe watery diarrhoea, and three had serous nasal discharges and profound lethargy (Horses 1, 2 and 3). Three horses (Horses 1, 6 and 10) had subcutaneous oedema in the intermandibular space, chest and ventral midline. One gelding (Horse 5) had extensive oedematous swelling of the ventral midline that included the sheath. Horse 1 had oedematous swelling of the lips. Horses 3, 4 and 5 had the most severe diarrhoea. Horse 7 had no diarrhoea, but had a dry cough and an enlarged right submandibular lymph node. No horse had oedema of the limbs. Jugular veins did not appear distended, and nor was there a prominent jugular pulse. No abnormalities were detected on thoracic auscultation of four more tractable horses (1, 3, 5 and 8). Their clinical signs were so severe that exercising them to assess their cardiac function was not practical. Rectal temperatures of these four horses ranged from 37.1 to 39.1°C. On 29 November, the horses' body condition and degree of lethargy had worsened, but the severity of the diarrhoea had lessened.

After being removed from contact with *P trichostachya*, the clinical signs of all surviving horses lessened in intensity and resolved over the following 6 weeks.

Necropsy findings

On the morning of 21 November 2005, Horse 1 was found recumbent with signs of colic (sweating, pawing at the ground, attempting to roll) and was killed by cranial gunshot. Necropsy 2 hours after death revealed a large amount of oedema subcutaneously and within the fascial planes of the neck and chest muscles. The liver was engorged with blood, dark red and friable. Kidneys were congested. The heart appeared slightly enlarged, with thickening of the left ventricular wall and distension of the right ventricle. The mucosal surface of the intestines had extensive areas of diffuse erythema. Recognisable alimentary tract contents comprised mostly *Medicago sativa* (lucerne). The mesenteric lymph nodes were enlarged and oedematous with massive oedema of the caecal lymph nodes, swelling them to about four times their normal size.

Laboratory examinations

Jugular blood was collected on 14 November 2005 from Horses 1 to 8, on 21 November from the horse to be necropsied (Horse 1) and on 29 November from Horses 2 to 5 and 9 to 11, into lithium heparin for plasma biochemical analyses, and into EDTA for haematological examination. Results of clinical biochemistry and haematology assays that revealed abnormalities are given in Table 1. All results for GGT, creatinine and erythrocyte indicies were within reference ranges. Anaemia was present in three horses (Horses 1, 5 and 6), with values for haemoglobin, PCV and erythrocyte counts below the reference ranges. Horse 2 had low haemoglobin and erythrocyte count values, Horse 7 had low haemoglobin and PCV values and Horses 3 and 4 had low haemoglobin values. Leucocytopenia occurred in three horses (Horses 1, 3 and 5). Hypoproteinaemia was detected in five horses (Horses 1, 2, 3, 5 and 6).

Jugular blood was collected for serum on 14 November from Horses 1 to 8 and tested by PCR for EHV1 antigen and AGID for EIA antibodies. On 29 November blood from Horses 2 to 5 was collected and serum subsequently tested by AGID for EIA antibodies and VNT for EVA antibodies. No antigen or antibodies were detected. Serum from Horse 1 collected at necropsy was also negative on AGID for EIA antibodies. The jugular blood samples in lithium heparin collected on 14 November from Horses 1 to 8 were cultured for viruses in equine dermis cells; no virus was isolated.

Faecal samples from the rectums of Horses 3, 4, 6 and 8 on 14 November and of Horses 2, 4 and 9 to 11 on 29 November, were examined for strongyle eggs and cultured for *Salmonella*. Large intestinal contents collected at necropsy of Horse 1 was also cultured for *Salmonella*. Faeces collected on 14 November from Horse 6 contained 1200 nematode eggs/g (92% *Cyathostomum* sp on larval differentiation), but those from Horses 3, 8 and 4 had insignificant nematode egg numbers, as did faeces collected on 29 November from Horses 2, 4, 9, 10 and 11. No *Salmonella* was detected in any sample cultured.

Sections of formalin-fixed liver, kidney, lung, heart, lymph node, stomach, intestines and spinal cord from Horse 1 were stained with haematoxylin and eosin and examined by light microscopy. The lung and intestinal mucosal blood vessels were moderately congested. Hepatic portal veins were markedly congested and dilated throughout the liver. The periportal hepatic sinusoids were similarly congested and dilated, consistent with *peliosis hepatis* (Figure 1). No significant abnormalities were detected in the other tissues.

Table 1. Biochemistry and haematology values measured in horses exposed to *Pimelea trichostachya*[a] and correlated with clinical signs observed.

Variable/Clinical sign	Reference ranges	Horse															
		1		2		3		4		5		6	7	8	9	10	11
November date sampled and observed		14	21	14	29	14	29	14	29	14	29	14	14	14	29	29	29
Total protein	60–90 g/L	**54.4**	**55.6**	**58.5**	**53.5**	59.9	**56.8**	59.9	60.0	**55.7**	**53.8**	**56.1**	66.5	66.6			
Albumin	25–40 g/L	**24.2**	**24.1**	29.8	29.3	28.7	29.5	25.6	28.7	28.7	28.7	28.6	31.4	32.8			
Globulin	30–45 g/L	30.2	31.5	**28.7**	**24.2**	31.2	**27.3**	34.3	31.3	**27.0**	**25.1**	**27.5**	35.1	33.8			
A/G ratio	0.4–0.9	0.80	0.77	**1.04**	**1.21**	**0.92**	**1.08**	0.75	**0.92**	**1.06**	**1.14**	**1.04**	0.89	**0.97**			
Calcium	2.8–3.5 mmol/L	2.8	**2.69**	2.97	3.09	3.09	3.15	2.9	3.07	2.96	2.92	2.8	**2.57**	3.16			
Magnesium	0.65–1.30 mmol/L	0.70	0.97	0.80	0.75	0.79	**0.63**	0.84	0.76	0.68	**0.56**	0.89	0.89	**1.33**			
Total bilirubin	3–43 µmol/L	24	**46**	32	23	29	21	17	14	25	25	37	23	19			
Urea	4.0–9.5 mmol/L	**10.5**	**16.9**	8.1	9.3	6.7	8.5	7.7	7.3	6.9	**10**	5.6	6.8	5.8			
AST	120–340 IU/L	176	**865**	175	190	200	194	166	209	178	151	182	233	172			
CK	30–190 IU/L	160	**31600**	258	305	133	131	163	208	284	144	238	213	215			
Haemoglobin	11–19 g/dL	**10.4**	**6.8**	12.1	**10.8**	**10.8**	**10.4**	11.5	**10.4**	**10.1**	**8.8**	**9.9**	**10.0**	13.0			
Packed cell volume	32–52%	**31**	**21**	37	33	33	33	35	33	**31**	**27**	**29**	**31**	39			
Erythrocyte count	6.5–12.0 × 10^{12}/L	7.3	**4.91**	6.89	**6.21**	7.09	6.88	8.56	7.77	7.12	**6.29**	**5.89**	7.5	7.56			
Leucocyte count	5.5–12.0 × 10^{9}/L	5.7	**3.9**	6.6	5.9	**4.5**	**3.2**	5.6	6.9	**4.8**	**4.1**	7.7	10.0	9.9			
Fibrinogen	0.1–0.4 g/dL	0.3	0.2	**0.6**	**0.5**	**0.7**	0.4	0.2	0.4	0.4	0.4	**0.6**	0.2	0.4			
Poor body condition		+	++	+	++	+	++	+	++	+	++	+	+	+			
Diarrhoea		++	+	++	+	+++	+	+++	+	+++	+	++	++	++			
Nasal discharge		+		+		+											
Subcutaneous oedema		++	++							++	+	+			+		
Profound lethargy		+	+	+		+											

A/G ratio-albumin/globulin ratio; AST-aspartate aminotransferase; CK-Creatine kinase. [a]Results given in bold indicate deviations from reference ranges.

Plant observations

Plants collected from the vicinity of the affected horses were identified as *Pimelea trichostachya* (Queensland Herbarium voucher AQ767897). The density of these plants in the horse paddock was estimated on 17 January 2006 by counting and weighing all *P trichostachya* plants in each of 10 squares of 1 m^2 area marked out along a line across the paddock. This yielded densities of between 2 and 45 g wet weight/m^2 (mean 16 g/m^2) and between 5 and 69 plants/m^2 (mean 38 plants/m^2). The mean weight of each plant was calculated as 0.43 g (range for individual squares 0.15 to 0.88 g); individual plants were not weighed. At the same time, *P trichostachya* as a proportion of the total volume of plants in each area was estimated by visual inspection to be between 3 and 20% (mean 9%).

Discussion

The clinical syndrome and liver pathology (*peliosis hepatis*) in this incident were consistent with the effects of *Pimelea* plants on the cardiovascular system of cattle. The simultaneous occurrence of the syndrome in cattle grazing the same pastures confirmed the toxicity of the plants to which the horses were exposed. The recovery of the surviving horses after their exposure to *Pimelea* plants was prevented or significantly lessened supports this diagnosis. Only one previous record of poisoning of horses by *Pimelea* plants includes evidence of chronically compromised circulatory function, the hitherto spectacularly unique effect of the intoxication in cattle. Before the report of the equine case in South Australia,[17] no such occurrence had been reported in horses, despite the many horses in the endemic St George-Marree disease areas of Queensland, New South Wales and South Australia. Our cases further confirm that *Pimelea* poisoning involving the circulatory system can affect horses, despite their relatively less muscular pulmonary venules.[3] Experimentally, *peliosis hepatis* has been induced in mice dosed with alcoholic extracts of *Pimelea trichostachya* at between 0.1 and 0.2% of their diet,[18] implying that species other than cattle are susceptible to this effect of *Pimelea* poisoning. The anaemia, leucocytopenia and hypoproteinaemia seen in our horses have all been reported in affected cattle also.[2,4,7] The anaemia was non-regenerative and consistent with the effect of the hypervolaemia reported in cattle.[18] Hypervolaemia may be a more significant cause of circulatory dysfunction in horses than in cattle, given the

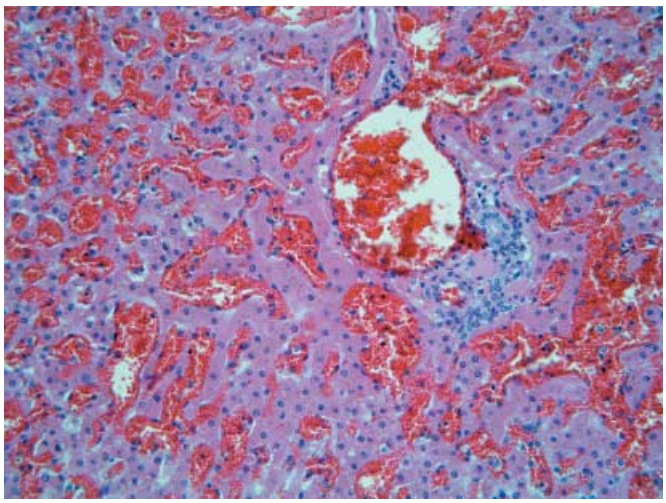

Figure 1. Equine *Pimelea trichostachya* poisoning. Dilated and congested portal vein and periportal sinusoids (*peliosis hepatis*) in the liver of an affected horse (Horse 1). Haematoxylin and eosin stain.

difference in the muscle thickness of their pulmonary venules. The degree of hypoproteinaemia was thought insufficient to explain the oedema in these horses. Leucocytopenia, but neither anaemia nor hypoproteinaemia, was detected in three of the horses affected by *Pimelea simplex* poisoning in South Australia in 2002 (K Clift, personal communication). The intermuscular and mesenteric lymph node oedema seen at necropsy of Horse 1 are not features of *Pimelea* poisoning of cattle.

Features common to our cases and previously reported poisonings of horses by *Pimelea* species (other than *P simplex*) and *Daphne* species (Family Thymelaeaceae) were colic, diarrhoea and lethargy. *Pimelea decora* poisoning was suspected to cause colic in horses in northern Queensland and experimental feeding of two horses produced colic and profuse watery diarrhoea with death within 24 hours.[15] Hyperaemia, haemorrhage and necrosis of the alimentary tract mucosa, and haemorrhages in the spleen and adrenal glands and beneath the endocardium, were the only necropsy findings. No liver lesions were reported grossly or microscopically. *Pimelea prostrata* poisoning of horses in New Zealand induced profound lethargy, stomatitis, colic, profuse watery diarrhoea, and jaundice lasting 5 days, with oesophagitis, gastritis and hyperaemia of the intestinal mucosa at necropsy of one.[16] Iatrogenic *Daphne* species poisoning induced intense colic and diarrhoea, with lethargy between evacuations.[19]

It is tempting to suggest that the intense prolonged exposure of the horses in our cases to *P trichostachya* plants was the underlying reason for its occurrence. Limited studies of *P trichostachya* plant densities have revealed that greater than 10 plants/m^2 are required for St George disease to occur in cattle, and that densities of up to 44 plants/m^2 have been measured in association with the bovine disease.[20] The greatest *P trichostachya* density in our case exceeded this. Because the *P trichostachya* plant density measurements were done about 2 months after the horses were first inspected, we consider the results to be an underestimate of the amount of *P trichostachya* to which the horses were first exposed. This is because these plants are annual herbs that usually die and disintegrate after flowering and the measurements were done at the time of year when they are usually senescent. In cattle, 2 to 3 weeks usually elapse after exposure to toxic concentrations of *Pimelea* plants before subcutaneous oedema is noticed.[3] The time of onset of this sign in the horses in this incident appeared to exceed that for cattle by several months.

This and the South Australian incident[17] considered together strongly suggest that graziers with cattle affected by *Pimelea* poisoning can no longer afford to be complacent about the health of horses grazing the same pastures.

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