Atypical myopathy: an update

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Atypical myopathy is an acute intoxication induced by the ingestion of hypoglycin A, a toxin contained in the seeds and seedlings of certain trees of the genus *Acer* (particularly *Acer pseudoplatanus* [sycamore] in Europe), which results in disruption of the energy metabolism. The clinical signs arise from energy depletion in the type I fibres of the postural and respiratory muscles, and lead to a specific biochemical profile that may be used to confirm a diagnosis. Since there is no cure for the condition, the emphasis is on prevention, which requires knowledge of the conditions necessary for the causative agent to exert its toxicity. This article gives an overview of atypical myopathy, discussing the mechanism involved, its aetiology and the clinical signs and management (therapeutic and prevention).

History of atypical myopathy in Europe

From sporadic cases to large outbreaks

In 1984, an apparently new equine myopathic syndrome named atypical myoglobinuria was reported (Linklater 1984). Horses kept at grass were suddenly presenting with an acute myopathic syndrome that was not induced by exertion; most of the affected animals died within a couple of days. Since then, outbreaks of this condition (which was later renamed atypical myopathy) have occurred sporadically in the autumn but, over the past decade, large series of cases have been observed repeatedly in several European countries not only in the autumn (Fig 1) but also in the spring (van Galen and others 2012a). Since autumn 2000, more than 1800 cases of atypical myopathy have been recorded throughout Europe by the Atypical Myopathy Alert Group (AMAG), an informal group set up in 2004 comprising veterinarians and researchers (Table 1).

Cases are reported on a spontaneous basis and result mainly from observations via social media and a dedicated website: www.myopathie-atypique.be. As the performance of this type of investigation does not exceed 5 per cent (Dufour 1994), it can be roughly estimated that the number of equids affected since autumn 2006 is tens of thousands.

Discovering the cause

By gathering information on cases of atypical myopathy throughout Europe via the dedicated website, knowledge about its epidemiology has grown year by year. The centralisation of cases allowed information to be obtained in real time (ie, when cases occurred), which enabled relevant samples to be collected to help determine the pathophysiological mechanism. Samples obtained at postmortem examinations showed that the myodegenerative process of atypical myopathy is selective and affects postural and respiratory muscles rather than locomotor muscles (Cassart and others 2007); histology revealed that the acute myonecrosis process (Fig 2) affects the type I fibres (ie, oxidative fibres) that are involved in lipid storage. Analyses of blood and urine samples revealed a multiple acyl-coenzyme A (CoA) dehydrogenase deficiency (MADD) that prevents affected horses using the most efficient energy source – lipids – resulting in them having to rely solely on carbohydrate metabolism (Westermann and others 2008). Identification of this metabolic defect was a key step in the discovery process since it guided the search for the aetiological agent towards toxins that cause this biochemical defect.

In addition, detailed knowledge of the epidemiology of atypical myopathy suggested that the aetiological agent had an environmental origin (Votion and others 2007, van Galen and others 2012a) and it was hypothesised that, on overgrazed pastures, horses might ingest grass contaminated with soil containing a toxin and/or eat plants that should normally not be consumed by equids. However,

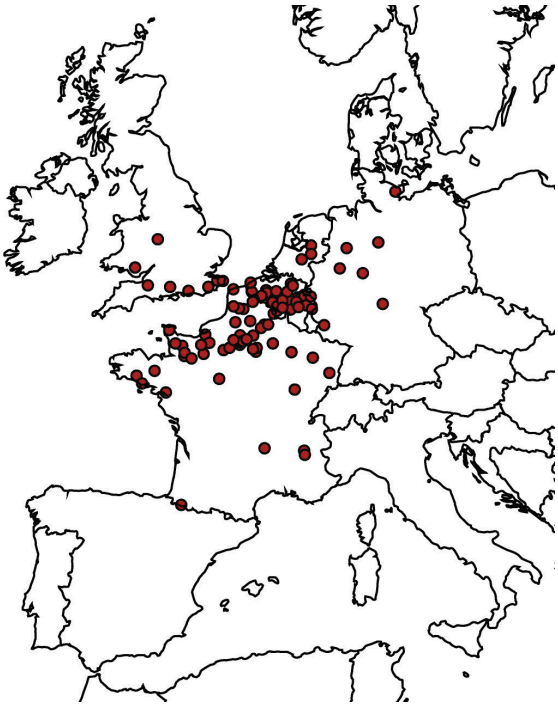

Fig 1: Distribution of atypical myopathy cases in Europe in autumn 2013 (Picture: F. Patarin)

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Table 1: Number of cases* of atypical myopathy in Europe reported to the Atypical Myopathy Alert Group from autumn 2006 to autumn 2013

	Number of cases															
	2006	2007		2008		2009		2010		2011		2012		2013		2006-2013
	Aut	Spr	Aut	Spr	Aut	Spr	Aut	Spr	Aut	Spr	Aut	Spr	Aut	Spr	Aut	
Austria	–	–	–	–	–	–	–	–	–	–	3	–	–		–	3
France	29	1	11	17	10	–	127	103	29	7	41	18	–	–	97	490
Germany	7	–	3	5	–	–	93	19	1	–	57	2	–	–	51	238
Belgium	46	7	18	6	6	–	66	10	14	2	16	–	–	–	168	359
Denmark	3	–	–	–	–	–	2	–	–	–	–	–	–	–	–	5
Luxembourg	1	–	–	–	–	–	2	–	–	–	–	–	–	–	–	3
Ireland	–	–	–	–	–	–	2	–	–	–	–	–	–	–	2	4
The Netherlands	13	–	3	–	2	–	34	6	1	–	–	–	–	–	22	81
UK	1	–	14	–	–	–	39	17	22	–	35	4	–	–	51	183
Switzerland	–	–	9	–	–	–	30	3	1	–	7	–	–	–	13	63
Spain	–	–	–	–	–	–	–	–	1	–	31	–	–	–	–	32
Czech Republic	–	–	–	–	–	–	–	–	1	–	–	–	–	–	11	12
Unknown	–	–	–	–	–	–	–	1	–	–	1	–	–	–	–	2
Total per season	100	8	58	28	18	0	395	159	70	9	191	24	0	0	415	–
Total per year	>100†	66		46		395		229		200		24		415		>1475

* Cases reported in early winter or in September were considered autumnal; when they were reported in early summer, they were included in the spring total. Data differ slightly from those previously published due to refinement in the counting

†Recording of European data started in autumn 2006; there are no official data available for spring 2006

Aut Autumn, Spr Spring

at that time, no specific plants had been implicated in the aetiology of atypical myopathy. *Ranunculus repens* and *Acer pseudoplatanus* (the familiar sycamore tree in northern Europe, Fig 3) were the only plants both present on premises surveyed in Belgium (Votion and others 2007).

The contribution of trees (in general) to the pathogenesis of the disease was eventually suggested by van Galen and others (2012a), who found trees were present on 98 per cent of European pastures on which cases of atypical myopathy occurred. Van der Kolk and others (2010) suggested that *A pseudoplatanus* leaves contaminated with an endophyte (Fig 4) had a role in the aetiology of the condition but scientific evidence for this is lacking. *Clostridium sordellii* has also been suspected of being involved (Unger-Torroledo and others 2010) but, again, evidence is lacking.

In 2006, a similar condition called seasonal pasture myopathy was recognised in the USA (Finno and others 2006); cases also exhibited a MADD-like biochemical profile (Sponseller and others 2012). Following a botanical survey, it was hypothesised that the condition was caused by ingestion of seeds from *Acer negundo* (box elder tree) (Fig 5) as these trees were present on all pastures associated with cases. Hypoglycin A – a toxin known to cause acquired MADD in people (Tanaka and others 1972) and found in the seeds of some *Acer* species (Fowden and Pratt 1973) – was found in *A negundo* seeds collected on the pastures and its metabolite, methylenecyclopropyl acetic acid (MCPA), was found in a conjugated form in the serum (ie, MCPA-carnitine) and urine (ie, MCPA-glycine) of affected animals (Valberg and others 2013).

By analysing blood samples collected over the years in Europe, it was concluded that atypical myopathy, like seasonal pasture myopathy in the USA, is highly associated with MCPA-carnitine, the toxic metabolite of hypoglycin A (Votion and others 2014). However, in Europe, the source of hypoglycin A appears to be the seeds of *A pseudoplatanus* (Unger and others 2014) in the autumn, and its seedlings in the spring (Baise and others 2015).

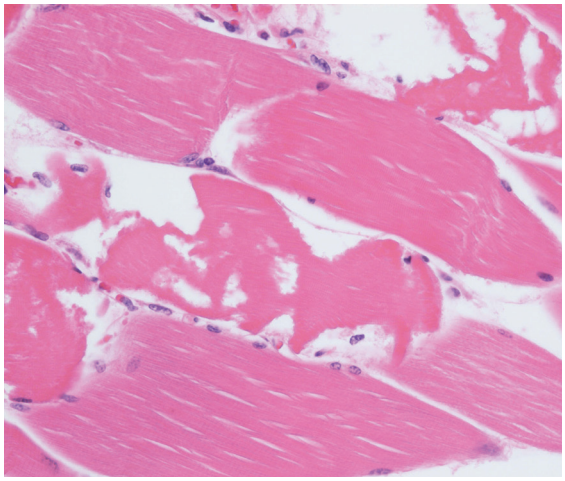

Fig 2: Multifocal and segmental necrosis in skeletal muscles (intercostal). The most specific microscopic feature of atypical myopathy is the accumulation of neutral lipid in type I muscle fibres that undergo Zenker's necrosis/ degeneration. Accumulation of neutral fat is best observed by staining frozen muscle samples that have undergone a special processing before freezing with Oil Red O; however, samples fixed in 10 per cent formol cannot be stained in this way. Haematoxylin and eosin, x 400 (Picture: D. Cassart)

Is atypical myopathy equine specific?

Although it is considered to be a species-specific disorder, other pasturing animal species might suffer from atypical myopathy. In the 1970s, an outbreak of acute myopathy of unknown origin occurred in a group of cattle kept outside in the winter (Linklater 1977). For various reasons (eg, monogastric versus polygastric digestive systems), horses may be more susceptible than other species to the phytotoxin causing the condition. Epidemiological and clinical data gathered from European outbreaks suggest that donkeys and zebras may also suffer from the condition (van Galen and others 2012a).

Toxic mechanism

Once ingested, hypoglycin A is metabolised into MCPA, a toxic compound that disrupts the energy metabolism.

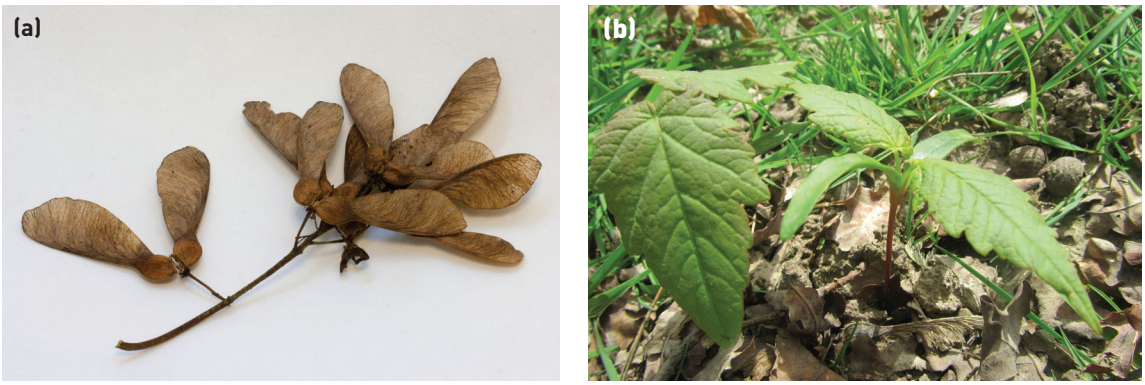

Fig 3: (a) Seeds and (b) seedlings of *Acer pseudoplatanus*, more commonly known as the sycamore tree (Picture a: L. Leinartz)

This then combines with CoA to form MCPA-CoA, which inhibits acyl-CoA dehydrogenases that are involved in the metabolism of short- and medium-chain fatty acids. MCPA-CoA also inhibits acylcarnitine-CoA transferases that are involved in the transport of long-chain fatty acids into the mitochondria, where they undergo beta-oxidation, and interferes with the amino acid metabolism (but to a lesser extent). These biochemical disorders result in the accumulation of acylcarnitines in the blood, which leads to the acquired MADD biochemical profile observed in affected animals. MCPA-carnitine is present in blood and is eliminated in urine as MCPA-glycine.

The clinical signs of atypical myopathy and seasonal pasture myopathy therefore result from energy starvation in muscle fibres whose predominant energetic pathways rely on oxidative metabolism. In resting animals, these are mainly the muscles involved in posture and breathing, and the heart muscle.

Clinical presentation and diagnosis

Affected animals initially exhibit muscle weakness and stiffness, and an inability to stand, which rapidly progresses to recumbency. They are frequently dyspnoeic, which often leads to death (74 per cent mortality rate [van Galen and others 2012a]). Cardiac signs are generally mild (slightly raised heart rate, heart murmurs).

All the clinical signs result from the massive destruction of the targeted muscle groups. However, the incidence of specific signs may vary from one year to another. For example, in autumn 2013, heart murmurs were more frequent and there was less recumbency in affected animals compared with previous years (Table 2).

A clinical diagnosis of atypical myopathy can be made based on the history, clinical signs, laboratory findings and histology of muscle specimens, as summarised in Table 3.

Management

Therapeutic measures

Atypical myopathy is often fatal and, to date, there is no specific cure. Nevertheless, a comparative study of survivors versus non-survivors demonstrated that treatment significantly increases the animal's chances of survival (van Galen and others 2012b). The main aims of therapy are to:

- Limit further muscle damage;
- Restore the circulating volume;

Fig 4: European tar spot (*Rhytisma acerinum*) on an *Acer pseudoplatanus* leaf (Picture: L. Leinartz)

- Correct acid–base and electrolyte disturbances;
- Provide energetic substrates that are usable by muscle cells;
- Provide vitamins and antioxidants; and
- Alleviate pain, if present.

These measures are largely supportive and symptomatic, but it is worth noting that the only therapeutic groups that appear to be beneficial are vitamins, antioxidants (vitamins B, C and E, and selenium) and carnitine (van Galen and others 2012b); in particular, supplementation with riboflavin (vitamin B2) might improve the compromised mitochondrial function. Since atypical myopathy severely affects the energy metabolism by blocking several steps in the aerobic mitochondrial lipid metabolism (Westermann and others 2008), nutritional support is important. Glucose infusion is recommended as well as a diet poor in lipids and rich in carbohydrates, which should be regularly offered to affected animals (except those that have dysphagia with or without oesophageal obstruction) to provide energy. As the toxic metabolite is secreted in urine, a large amount of perfusion is advised.

These general recommendations have been extensively described by van Galen and Votion (2013a, b).

Prevention

Discovery of the cause of atypical myopathy has had major implications for prevention of the condition. As well as following previous recommendations that have been widely described elsewhere (Votion 2012), it is advisable to:

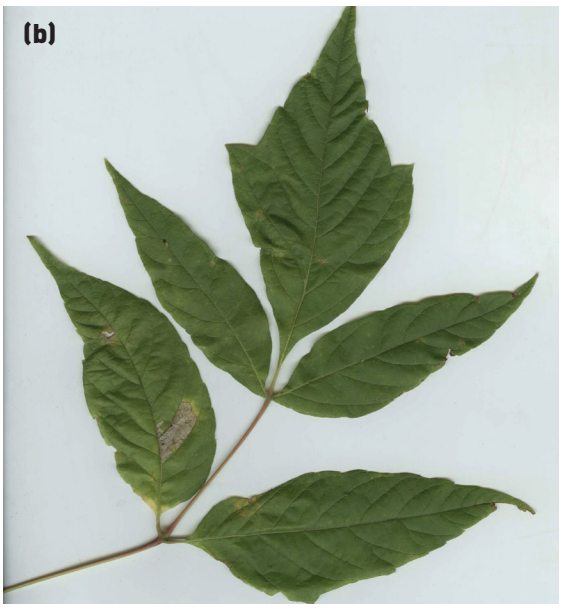

Fig 5: (a) Seeds and (b) leaves of *Acer negundo*. Unlike *Acer pseudoplatanus*, *A negundo* has pinnately compound leaves that have several leaflets (Picture b: L. Leinartz)

- Screen the pasture in early autumn to check for the presence of samaras (seeds) and, if found, the horses should be removed from the field;
- Prevent horses ingesting the toxic seedlings in the spring;
- Try to remove the aetiological agent (ie, collect the seeds and burn them), although this may not be possible if they are too abundant (Fig 6);
- Follow alert messages via the atypical myopathy website (Votion 2004) and manage horses accordingly;
- Manage pasturing time according to weather conditions.

Table 2: Main clinical signs of atypical myopathy in autumnal outbreaks in Europe

Clinical sign	Number of cases	
	Autumn 2006 to 2009 (percentage) (n = 354, N = 600)*	Autumn 2013 (percentage) (n* = 72, N = 415)†
Pigmenturia	93	96
Weakness	85	75
Stiffness	83	82
Depression	80	90
Tachycardia	79	90
Recumbency	78	63
Trembling	68	75
Sweating	64	66
Normothermia	60	61
Distended bladder on rectal palpation	58	87
Congested mucous membranes	53	58
Dyspnoea	44	68
Colic	27	24
Dysphagia	25	28
Heart murmurs	21	35

*van Galen and others (2012a)
†Unpublished preliminary data
N Total number of cases reported to the Atypical Myopathy Alert Group
n Number of cases with confirmed, or a high probability of, atypical myopathy
n* Number of files considered (very preliminary data)

Outbreaks of atypical myopathy are triggered by inclement climatic conditions, possibly by making the causal agent easily accessible for ingestion when wind or heavy rain brings vegetation to the ground.

The author is currently undertaking field studies to establish a system of risk-based prevention (probable emergence of cases based on monitoring the toxicity of seeds, which may vary during the season) rather than a system based on the observation of cases (current alert system) (Box 1).

Aetiological agent

Emerging disease

It is not known why atypical myopathy has suddenly appeared in Europe when the tree thought to be involved with the aetiology – the sycamore – has been naturalised for many decades. To prevent atypical myopathy, it is necessary to understand how the pathogenic system develops. One reason for the emergence of cases may be the observed climate changes of recent years that might increase the production of samaras (Vitasse and others 2009) and/or impair their maturation-dormancy stages (in association with a variation in the degree of toxicity). In addition, it might be hypothesised that unripe seeds contain a higher level of the toxic hypoglycin A than ripe seeds. Epidemiological investigations have highlighted the contribution of environmental factors as factors that trigger outbreaks. In particular, wind seems to predispose the onset of clinical signs. The greater severity of storms and/or the occurrence of storms earlier in the year than previously might also contribute, resulting in samaras being removed from trees at a stage of maturity when they are more toxic. However, one must keep in mind that the development of atypical myopathy is probably multifactorial.

Other possible explanations for the emergence of the disease are that an increased number of pastures border forests, that there is a greater density of *A pseudoplatanus* and/or geographical extension over time and, finally, possibly an increased susceptibility of horses following changes in their management and/or use over recent decades.

Table 3: Major factors pointing to a diagnosis of atypical myopathy

History	Clinical signs (in more than 50 per cent of cases)	Laboratory findings	Postmortem examination
Grazing horses Sudden onset of clinical signs Several animals affected in the same pasture Ongoing outbreaks (autumn and spring) Inclement weather Possible access to seeds (in autumn) or seedlings (in spring) of *Acer* species	Myoglobinuria Muscle weakness and stiffness Depressed mental state (most often with no evidence of severe pain) Recumbency Sweating Muscle tremors Congested mucous membranes Rapid deterioration of clinical signs (with increased dyspnoea)	Large increase in muscle enzyme activities in serum, in particular creatine kinase (>10,000 iu/litre; normal range 50 to 200 iu/litre) Hypocalcaemia Hyperglycaemia Hyperlipidaemia MADD phenotype* MCPA-carnitine in blood	No other evident cause of death No significant gross lesions Postural, respiratory and cardiac muscle discolourations *Histological findings* Degenerated fibres in postural and respiratory muscles Necrosis of type I fibres*

*Tests are available in a limited number of veterinary laboratories

MADD Multiple acyl-coenzyme A dehydrogenase deficiency, MCPA Methylenecyclopropyl acetic acid

Is *A pseudoplatanus* the only toxic maple tree in Europe?

For all cases of atypical myopathy recorded in autumn 2013 and spring 2014, seeds or seedings of *A pseudoplatanus* were found in the direct vicinity of the horses affected (unpublished data). However, information from cases in autumn 2013 indicate that the absence of *A pseudoplatanus* in or around fields is not a sufficient guarantee to guard from atypical myopathy: samaras were found on pastures where there were affected animals even though the closest tree was over 200 meters away.

Box 1: Ongoing research

It should be easy to fight against the cause of atypical myopathy since it is readily identifiable, but the series of cases in autumn 2013 has taught us that faced with 'the enemy', a chainsaw will be of little use because of its mode of dissemination (Fig 6). Determining the reasons for the emergence of the condition will provide a chance to slow or even halt the increase in the number of cases seen. To this end, epidemiological studies remain essential. Research, far from dying out as a result of the cause being discovered, is now taking on a new impetus.

Objectives

The aims of the research are divided into three interconnected areas:

- **Identification of the environmental conditions that are responsible for the emergence of the disease by defining precisely what affects the toxicity of *Acer* species (or other trees). This involves:**
  - **Topoclimatological studies (integration of epidemiological data using specialised software to define the interaction between biotope and the emergence of cases);**
  - **Validation of hypoglycin A assays of organic samples to define the conditions that determine the toxicity of samaras and seedlings (action of heat, cold, moisture, etc). This will help to prevent the risk of poisoning through the definition of new techniques for pasture management based on the identification of the conditions that induce the production of hypoglycin A by samaras and/or seedlings.**
- **Strengthening surveillance of atypical myopathy:**
  - **Improve the current alert system to enable information about ongoing outbreaks of atypical myopathy to be provided more quickly;**
  - **Establish a system of risk-based prevention rather than one based on the observation of cases.**
- **Improving case management through better diagnosis and more accurate assessment of prognosis; find a preventive and curative treatment based on the pathogenesis of the disease.**

Fig 6: Seeds and seedlings of *Acer pseudoplatanus* in great abundance on pasture in early spring (Picture: T. Art)

A negundo is not indigenous to Europe but tends to establish itself and was observed in the pasture of one Belgian case (Votion and others 2014). Other *Acer* species that have also been found on some pastures associated with atypical myopathy cases are *Acer platanoides* (Norway maple) and *Acer campestre* (field maple). These two trees are considered to be 'non-toxic' (Fowden and Pratt 1973, Westermann and others 2016).

The toxicity of seeds of many *Acer* species was determined in a study conducted 40 years ago (Fowden and Pratt 1973), but it did not take into account possible seasonal and annual variations in toxicity. Therefore, although the toxicity of *A pseudoplatanus* and *A negundo* has been confirmed (Fowden and Pratt 1973, Valberg and others 2013, Unger and others 2014), the innocuousness of other *Acer* species across Europe needs to be checked by hypoglycin A quantification using validated methodology.

Are maple trees the only cause of atypical myopathy in Europe?

Acer species belong to the Sapindaceae family. This contains almost 2000 species of trees and includes *Aesculus hippocastanum* (horse chestnut tree), which is very common in Europe. To the author's knowledge, no research has been conducted to determine the presence of the toxin in the seeds of European tree species other than maples.

Fraxinus excelsior (European/common ash), belonging to the Oleaceae family, was frequently found on the pastures of affected horses (Patarin and others 2011). The seeds of several members of this family contain pharmacologically active substances but hypoglycin A has not been specifically searched for in the fruits of these plants. Moreover, there are no data available on the toxicity of the leaves of plants in the Sapindaceae or Oleaceae families. Other trees and shrubs that produce samaras, such as *Corylus avellana* (common hazel, Betulaceae family), *Fagus sylvatica* (European/common beech, Fagaceae family) and *Populus* species (Salicaceae family), were also frequently present in or around the pastures associated with cases in autumn 2013 (unpublished data). Further research is needed to check the toxicity of other trees that are in close proximity to pastures where cases of atypical myopathy occur.

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References

BAISE, E., HABYARIMANA,. J. A., AMORY, H., BOEMER, F., DOUNY, C., GUSTIN, P. & OTHERS (2015) Samaras and seedlings of *Acer pseudoplatanus* are potential sources of hypoglycin A intoxication in atypical myopathy without necessarily inducing clinical signs. *Equine Veterinary Journal* doi: 10.1111/evj.12499

CASSART, D., BAISE, E., CHEREL, Y., DELGUSTE, C., ANTOINE, N., VOTION, D. & OTHERS (2007) Morphological alterations in oxidative muscles and mitochondrial structure associated with equine atypical myopathy. *Equine Veterinary Journal* **39,** 26-32

DUFOUR, B. (1994) Le questionnaire d'enquête. *Epidémiologie et Santé Animale* **25,** 101-112

FINNO, C. J., VALBERG, S. J., WÜNSCHMANN, A. & MURPHY, M. J. (2006) Seasonal pasture myopathy in horses in the midwestern United States: 14 cases (1998-2005). *Journal of the American Veterinary Medicine Association* **229,** 1134-1141

FOWDEN, L. & PRATT, H. M. (1973) Cyclopropylamino acids of the genus *Acer*: distribution and biosynthesis. *Phytochemistry* **12,** 1677-1681

LINKLATER, K. A. (1977) Acute myopathy in outwintered cattle. *Veterinary Record* **100,** 312-315

LINKLATER, K. A. (1984) Myopathy in horses and ponies. *Veterinary Record* **115,** 666

PATARIN, F., VAN GALEN, G., MARCILLAUD PITEL, C., SERTEYN, D. & VOTION, D. M. (2011) Incidences pratiques tirées des dernières séries cliniques de myopathie atypique sur le territoire français. In 37th Journée de la Recherche Equine. Paris, France. pp 65-74

SPONSELLER, B. T., VALBERG, S. J., SCHULTZ, N. E., BEDFORD, H., WONG, D. M., KERSH, K. & SHELTON, G. D. (2012) Equine multiple acyl-CoA dehydrogenase deficiency (MADD) associated with seasonal pasture myopathy in the midwestern United States. *Journal of Veterinary Internal Medicine* **26,** 1012-1018

TANAKA, K., ISSELBACHER, K. J. & SHIH, V. (1972) Isovaleric and -methylbutyric acidemias induced by hypoglycin A: mechanism of Jamaican vomiting sickness. *Science* **175,** 69-71

UNGER, L., NICHOLSON, A., JEWITT, E. M., GERBER, V., HEGEMAN, A., SWEETMAN, L. & VALBERG, S. (2014) Hypoglycin A concentrations in seeds of *Acer pseudoplatanus* trees growing on atypical myopathy-affected and control pastures. *Journal of Veterinary Internal Medicine* **28,** 1289-1293

UNGER-TORROLEDO, L., STRAUB, R., LEHMANN, A. D., GRABER, F., STAHL, C., FREY, J. & OTHERS (2010) Lethal toxin of *Clostridium sordellii* is associated with fatal equine atypical myopathy. *Veterinary Microbiology* **144,** 487-492

VALBERG, S. J., SPONSELLER, B. T., HEGEMAN, A. D., EARING, J., BENDER, J. B., MARTINSON, K. L. & OTHERS (2013) Seasonal pasture myopathy/atypical myopathy in North America associated with ingestion of hypoglycin A within seeds of the box elder tree. *Equine Veterinary Journal* **45,** 419-426

VAN DER KOLK, J. H., WIJNBERG, I. D., WESTERMANN, C. M., DORLAND, L., DE SAIN-VAN DER VELDEN, M. G., KRANENBURG, L. C. & OTHERS (2010) Equine acquired multiple acyl-CoA dehydrogenase deficiency (MADD) in 14 horses associated with ingestion of maple leaves (*Acer pseudoplatanus*) covered with European tar spot (*Rhytisma acerinum*). *Molecular Genetics and Metabolism* **101,** 289-291

VAN GALEN, G., MARCILLAUD PITEL, C., SAEGERMAN, C., PATARIN, F., AMORY, H., BAILY, J. D. & OTHERS (2012a) European outbreaks of atypical myopathy in grazing equids (2006-2009): spatiotemporal distribution, history and clinical features. *Equine Veterinary Journal* **44,** 614-620

VAN GALEN, G., SAEGERMAN, C., MARCILLAUD PITEL, C., PATARIN, F., AMORY, H., BAILY, J. D. & OTHERS (2012b) European outbreaks of atypical myopathy in grazing horses (2006-2009): determination of indicators for risk and prognostic factors. *Equine Veterinary Journal* **44,** 621-625

VAN GALEN, G. & VOTION, D. M. (2013a) Management of cases suffering from atypical myopathy: interpretations of descriptive, epidemiological and pathophysiological findings. Part 1: first aid, cardiovascular, nutritional and digestive care. *Equine Veterinary Education* **25,** 264-270

VAN GALEN, G. & VOTION, D. M. (2013b) Management of cases suffering from atypical myopathy: interpretations of descriptive, epidemiological and pathophysiological findings. Part 2: muscular, urinary, respiratory and hepatic care, and inflammatory/infectious status. *Equine Veterinary Education* **25,** 308-314

VITASSE, Y., PORTE, A. J., KREMER, A., MICHALET, R. & DELZON, S. (2009) Responses of canopy duration to temperature changes in four temperate tree species: relative contributions of spring and autumn leaf phenology. *Oecologia* **161,** 187-198

VOTION, D. M. (2004) Atypical Myopathy Alert Group (AMAG) www.myopathie-atypique.be. Accessed April 28, 2015

VOTION, D. M. (2012) The story of equine atypical myopathy: a review from the beginning to a possible end. *ISRN Veterinary Science* **2012**

VOTION, D. M., LINDEN, A., SAEGERMAN, C., ENGELS, P., ERPICUM, M., THIRY, E. & OTHERS (2007) History and clinical features of atypical myopathy in horses in Belgium (2000-2005). *Journal of Veterinary Internal Medicine* **21,** 1380-1391

VOTION, D. M., VAN GALEN, G., SWEETMAN, L., BOEMER, F., DE TULLIO, P., DOPAGNE, C. & OTHERS (2014) Identification of methylenecyclopropyl acetic acid in serum of European horses with atypical myopathy. *Equine Veterinary Journal* **46,** 146-149

WESTERMANN, C. M., DORLAND, L., VOTION, D. M., DE SAIN-VAN DER VELDEN, M. G., WIJNBERG, I. D., WANDERS, R. J. & OTHERS (2008) Acquired multiple acyl-CoA dehydrogenase deficiency in 10 horses with atypical myopathy. *Neuromuscular Disorders* **18,** 355-364

WESTERMANN, C. M., VAN LEEUWEN, R., VAN RAAMSDONK, L. W., MOL, H. G. & OTHERS (2016) Hypoglycin A concentrations in maple tree species in the Netherlands and the occurrence of atypical myopathy in horses. *Journal of Veterinary Internal Medicine* doi: 10.1111/jvim.13927

Quiz: Atypical myopathy: an update

1. A horse is found recumbent at pasture in the autumn (European outbreaks have been announced by the Atypical Myopathy Alert Group). Determination of creatine kinase (CK) activities in serum indicates CK activities > 2000 U/L and samaras of maple tree were found on pasture (see right). Can a diagnosis of atypical myopathy be concluded?

Answer:

1. No. Some laboratories do not give an exact value of the CK activities in serum when high activities are detected. Instead, they indicate that the value found is out of range. In fact, when a horse is lying down, mild to moderate elevations in serum CK activities may be observed due to muscle crushing during recumbency. Therefore, it is necessary to ask to the laboratory to dilute the serum to determine the exact CK activities level. In atypical myopathy, the value found are (usually) largely above the ones found due to recumbency; serum CK activities in atypical myopathy cases may attain hundreds of thousands or even millions of U/L. If CK activities level remains below 10,000 U/L, diagnosis of atypical myopathy is challenging.

In addition, the samaras shown in the figure are those of *Acer campestre* (field maple) and not the ones of *Acer pseudoplatanus* (sycamore tree). The samara of *Acer campestre* has two winged achenes aligned at 180°, each achene eight to 10 millimeters wide, flat, with a two centimeters wing. So their wings are almost opposite, distinguishing them from those of *Acer pseudoplatanus* held at about right angles to each other. The seeds of *Acer campestre* does not contain hypoglycin A. Currently, only *Acer negundo* (the box elder) in the US and *Acer pseudoplatanus* (the sycamore maple) in Europe are identified as causing atypical myopathy in horses.

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Notes