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Over the last 5 years or so we have learnt much about existing and new disorders in horses from documentation of careful clinical observations and interventions and from painstaking pathological studies with special emphasis on clinicopathological correlates. Some of these disorders will be discussed elsewhere in this conference and this paper will highlight a few of these disorders through which we have added to our understanding of anatomy, physiology and clinicopathological correlates - the building-blocks for advancing equine neurology.

**ACQUIRED CERVICAL TORTICOLLIS ASSOCIATED WITH PARELAPHOSTRONGYLUS TENUIS**

The amazingly selective meanderings of these migratory nematode parasites are exemplified by the plight of *Parelaphostrongylus tenuis* in some horses that have been elegantly documented4–6. This worm has caused an acute onset of a lateral deviation of the cervical vertebrae, or scoliosis, which remained static, and was the result of an exquisitely selective, continuous, cervicothoracic, inflammatory dorsal grey column lesion. Cutaneous hypalgesia to analgesia of the neck and/or thorax and mild unilateral ataxia and paresis but with no evidence of denervation atrophy in the epaxial muscles was observed in all affected horses. The scoliosis was clearly argued to be due to loss of afferent cervical proprioceptive inputs because of the dorsal grey column lesions with some white matter involvement accounting for ataxia and weakness (Figure 1).

**VESTIBULAR SYNDROMES FOLLOWING CERVICAL NERVE ROOT LESIONS**

A rather forgotten component to the vestibular system is proprioceptive input from the cranial cervical vertebrae, ligaments and muscles.12,13 Special proprioceptive inputs from the cranial cervical vertebral ligaments and muscles pass via at least...
the C1–3 dorsal spinal nerve roots to ascend the spinal cord via the spinovestibular tract (Figure 2) to the caudal vestibular nuclei. These nuclei receive no other afferent inputs. Lesions involving these cranial cervical nerves or the vestibulospinal input to the vestibular apparatus can result in signs of vestibular disease. This certainly can be seen with symmetric lesions of the dorsal nerve roots of C1–3 when loss of balance, eye deviation and head tilt have been seen.

CERVICAL VERTEBRAL ARTICULAR ULTRASOUND AND ARTICULAR INJECTION
Cervical (peri) articular injections have become a favoured diagnostic and therapeutic tool at least in North America14,19,20. However, empirical injection of enlarged articular processes without substantive evidence that they are causing a clinical problem of neck pain alone, neck pain with ataxia and ataxia alone is to be discredited.

ELECTRODIAGNOSTICS: MAGNETIC MOTOR EVOKED POTENTIALS AND QUANTITATIVE ELECTROMYOGRAPHY
Certainly the noninvasive and reasonably innocuous testing for magnetic motor evoked potentials now has received attention in large animal neurology21 and it appears to be a very sensitive and quite specific electrophysiological test for disruption of somatic motor pathways in disease states22,23. This and the additional use of more elaborate but error prone quantitative EMG investigations24,25 should allow more accurate identification of the presence and location of conduction blocks, and thus functional lesions, in neurological disease states such as wobblers and unusual hindlimb gait abnormalities.

SCANDINAVIAN KNUCKLING HORSES
This clinical syndrome is one of varying degrees of bilateral sciatic nerve involvement, most horses showing more prominently signs of peroneal neuropathy and others showing more prominently signs of tibial neuropathy27. Occasional cases had extensor weakness also indicating femoral nerve involvement. In many cases silage was fed along with poor quality hay, or there was access to a particular feedstuff. Demyelination may be the underlying lesion compared to the axonal and myelin (fibre) degeneration seen with many bilateral stringhalt cases. Some milder cases improve but it is not certain whether this recovery is complete to allow full performance. Peripheral neurotoxins of plant or nonbiological origin would be the most likely cause of these crippling syndromes27,29,30.

EQUINE MOTOR NEURON DISEASE (EMND)
Acquired equine motor neuron disease (EMND) is a fascinating neuromuscular disorder of horses that does not appear to have existed prior to 1982 and was first described by the late John Cummings and co-workers from Cornell University in 199033. Hundreds if not thousands of horses now have been definitively diagnosed with EMND in North America and around the world.

The clinical syndrome expressed depends on the stage of the disease34–36 and is encapsulated by the listing in Table 1. A clinical truism for the syndrome is that affected horses move better than they stand.
Table 1: Proportion of major clinical signs recorded for 104 cases of EMND (34, 39).

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Occurrence %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle loss</td>
<td>100</td>
</tr>
<tr>
<td>Muscle trembling</td>
<td>95</td>
</tr>
<tr>
<td>Increased lying down</td>
<td>93</td>
</tr>
<tr>
<td>Excellent appetite</td>
<td>90</td>
</tr>
<tr>
<td>Shifting weight</td>
<td>90</td>
</tr>
<tr>
<td>Extended tail head</td>
<td>76</td>
</tr>
<tr>
<td>Lowered head posture</td>
<td>62</td>
</tr>
<tr>
<td>Retinal lesions</td>
<td>18</td>
</tr>
</tbody>
</table>

Definitive diagnosis is dependent on the post mortem demonstration of degeneration and loss of cell bodies in the ventral horn of the spinal cord and in motor nuclei in the brain stem with the exception of those supplying cranial nerves III, IV and VI. In experimental cases and in naturally-occurring cases of EMND in North America and in Europe, vitamin E deficiency has been the only consistent nutritional or toxic-related abnormality determined. Further studies are necessary to explain the development of hypovitaminosis E and EMND in horses that have adequate access to pasture. Genetic factors for alterations in amount or activity of the alpha-tocopherol transfer protein, such as the 744 del A mutation of the alpha-TTP gene operative in some forms of human hypovitaminosis E, will need exploration in this regard.

EQUINE POLYSACCHARIDE STORAGE MYOPATHY (EPSM)

Equine polysaccharide storage myopathy (EPSM) is an autosomal recessive disorder in Quarter Horse and related breeds that can result in rather exceptional susceptibility to recurrent exertional rhabdomyolysis. Recently, there has been an association of the disease with a particular microsatellite marker. However, the morphological diagnostic criteria for making the diagnosis are variable. The disease EPSM thus refers to the clinical syndrome of muscle disease, particularly rhabdomyolysis, with amylose-resistant, sarcoplasma inclusion of acid mucopolysaccharides evident on muscle biopsy sample. In distinction, where there are clinical signs of myopathy but histological evidence of no or mild myopathic changes with excess, aggregates or cores of sarcoplasmic, mostly amylose-sensitive polysaccharide (glycogen), then a distinguishing term such as polysaccharide-associated myopathy should be used. The former is seen particularly as a likely autosomal recessive trait in Quarter Horses and related breeds and in several other breeds including draught horses, whereas excess or unusual glycogen storage is seen in association with clinicopathological myopathic syndromes in a wide variety of breeds and may be present, histologically, in upwards of 50% of horses.

The clinical syndromes can likely be ameliorated in many cases with management and dietary modification to include consistent and appropriate levels of exercise and addition of <20% lipid as a source of energy and reduction of soluble carbohydrates in the animal’s diet. Dantrolene sodium may help in altering membrane Ca++ flux to reduce the outcome of myolysis in these disorders.

HYPERKALAEMIC PERIODIC PARALYSIS (HYPP)

Young-adult (2–3 years), mostly male Quarter Horse and Quarter Horse-related breeds have been reported to be affected with this autosomal dominant disease. Homozygous animals are more severely affected than heterozygotes. The owner notices intermittent episodes of muscle trembling over the body or face, sometimes with intermittent projection of the nictitating membrane, that may lead to involuntary recumbency. Other premonitory signs include yawning, lowering of the neck, swaying and disinterest in food and water. During a mild episode the horse is alert, appears distracted and reluctant to move, and may stumble as if weak. In a fulminant episode fasciculations or muscle tremor, particularly involving the flank, shoulders and neck and sometimes the face, progress to staggering, buckling, marked muscle spasms and paraplegia may precede involuntary recumbency. A severe episode, perhaps following forced exercise or KCl provocation, results in severe tremor and tetany of many muscles with recumbency and sweating. An episode may last several minutes to hours, typically less than an hour, with full and usually rapid recovery occurring.

The clinical syndrome in this inherited channelopathy is distinct but does closely resemble the acquired channelopathy induced by lolitrem-B in perennial ryegrass staggers.

STIFF HORSE SYNDROME

Recently, a stiff horse syndrome similar to stiff person syndrome has been recorded. Clinical signs appear to wax and wane and range from mild muscle stiffness to sudden and often violent muscle contractions. Generally there is an insidious onset. Between episodes the horse may appear normal although, if present, the generalised muscle stiffness may persist.
Exercise intolerance associated with mild to moderate muscle stiffness may be the only initial clinical sign. This may easily be attributed to a primary myopathy, with pain on muscle palpation, although serum muscle enzyme concentrations remain in the normal range. Components of the syndrome bear resemblance to such disorders as tetanus, equine motor neuron disease, hyperkalaemic periodic paralysis, exertional myopathies and especially the acquired channelopathies associated with the mycotoxocoses such as perennial ryegrass staggers.

The most useful diagnostic test is detection of antibodies against GAD in serum and cerebrospinal fluid and, although some cases have had high anti-GAD titres, several strongly suspected cases have been negative on this test.

The overall message really is that with the array of enigmatic movement and postural disorders encountered in equine neurology that appear to be variations on the themes of stringhalt, shivering and claudication, a broad approach to delving into possible aetiological mechanisms should be taken that includes the possibility of immune associated neurotransmitter derangements such as SPS.

GRASS SICKNESS
Grass sickness or equine dysautonomia has been described since the early 20th century and since then has had quite a devastating effect on equine populations in parts of Western Europe. Per-acute colic with gastrointestinal stasis and rupture, anorexia with mild signs of colic and ileus, to chronic cachexia covers the general spectrum of syndromes seen with this very unusual disease. Moderate tachycardia, indifference to food, difficulty swallowing, excessive salivation, depressed gastrointestinal sounds, abdominal distension and usually mild colic are very often present to varying degrees. Muscular tremor and patchy sweating may be primary signs or may reflect the dehydration, electrolyte imbalances and colic that occur. Posturing with all feet close together as a weak patient does, ptosis and especially rhinitis sicca are very distinctive signs when present.

No definitive clinical diagnostic test exists. As the clinical signs of Horner’s syndrome are symmetric, ptosis can be difficult to detect. However, a recently desorbed aid to clinical diagnosis is the observance of a rapid reversal of ptosis with 0.5 ml of 0.5% phenylephrine eye drops. The resulting marked difference in degree of ptosis and particularly in eye lash angle can be spectacular.

ATYPIICAL MYOPATHY
Several hundred cases of highly fatal, atypical myopathy or myoglobinuria have been reported in young, adult, grazing horses mostly from Europe but also North America and Australasia. Horses may be found dead or more often showing various signs of reluctance to move, stiff and short strides, apparent sedation and fine muscle tremors. They quickly become laterally recumbent and urine becomes dark with myoglobin staining although more sub-acute cases do occur. Plant, bacterial and fungal toxins have all been considered as possibilities but the cause or causes remain completely unknown. Clinicians suspecting cases are urged to log on to the atypical myopathy alert site and complete the appropriate forms in an effort to unravel the epidemiology of this dastard disease: (dominique.votion@ulg.ac.be); (http://www.ivis.org/reviews/rev/votion/chapter.asp?LA=1#forms).

COMPLEX REGIONAL PAIN SYNDROME
Cases of complex regional pain syndrome have been reported in horses in which the localised profound allodynia has been so debilitating as to prompt decisions for euthanasia. Interestingly, sometimes following a perineural anaesthetic block is performed in the limb of a horse there is a regional strip of reflex vasodilation and sweating proximal and distal to the injection site. The regional distribution of this sympathetic response outside the resulting analgesic area is similar to that seen around the trigger point of horses having complex regional pain syndrome.

FLUPHENAZINE TOXICITY
The long acting phenothiazine drugs perphenazine and fluphenazine have caused an interesting syndrome of fluctuant somnolence and compulsive activity that can consist of adopting abnormal postures and displaying incredibly frantic, repetitive movements. Thus an affected horse may stand fixated by an object and appear to watch unapparent images move, stand with the forelimbs placed well forward and the head flexed between the knees, and perform tonic repetitive movements such as incessant pawing with one limb, head swinging and pseudo-rubbing on objects. Recumbency without somnolence and seizure-like activity also occurs. Anticonvulsant and narcotic drugs are indicated to help control the signs and possibly anticholinergic drugs such as benztrapine and diphenhydramine can be considered.

GRANULOMATOUS MENINGOENCEPHALOMYELITIS (GME)
A collection of cases demonstrating disseminated, multifocal, granulomatous lesions are documented in large animal internal medicine and dermatology literature and are referred to by several terms including idiopathic generalised granulomatous...
Stringhalt, also known as springhalt and Hahnentritt (‘rooster kick’), is an anciently recorded disease that is characterised by a sudden, apparently involuntary, exaggerated flexion of one or both hindlimbs during attempted movement. The hindlimb motion may be as mild as a slightly excessive flexion to violent movements during which the fetlock or toe will contact the abdomen, thorax and occasionally the elbow with attempted strides leading to a peculiar bunny hopping and plunging gait.

The form that usually occurs as outbreaks is seen in Australia\textsuperscript{120}, New Zealand\textsuperscript{121}, United States\textsuperscript{122,123}, Chile\textsuperscript{124} and Japan\textsuperscript{125} and thus will be referred to as bilateral, plant-associated stringhalt. Usually there is symmetrical or slightly asymmetrical involvement of the pelvic limbs, with prominent distal muscle atrophy in severe cases. The thoracic limbs are also affected in severe cases with knuckling of the forelimb fetlocks, prominent extension of more proximal joints and atrophy of the distal musculature, in association with prominent stringhalt in both hindlimbs. Bilateral stringhalt has been associated with exposure to several plants notably \textit{Hypochoeris radicata}, \textit{Taraxicom officinal} and \textit{Malva parviflora} (mallow weed)\textsuperscript{120,121,123}. These are related species of flat weeds, \textit{Taraxicom officinal} being the common dandelion. It is interesting that size and age may be predisposing factors in at least bilateral stringhalt, in so far as older and taller horses tend to become affected\textsuperscript{126} in preference to smaller horses such as ponies and native Chilean breeds\textsuperscript{124}.

The pathological lesions present represent a distal axonopathy preferentially affecting large diameter axons in long nerves\textsuperscript{126,127}. This explains the muscle atrophy but there must also be selective involvement of $\gamma$-efferent fibres to account...
for the movement disorder with abnormal input via the 1a-afferent fibres to the α-efferent neurons resulting in inappropriate firing of lateral digital extensor and other muscles.

Although palliative, removing a section of the myotendinous region of the lateral digital extensor muscle relieves the syndrome quite spectacularly in many cases128,129.

**TEMPOROHYOID OSTEOARTHROPATHY**

Temporohyoid osteoarthropathy (THO) with proliferative osteopathy involving the temporal bone, temporohyoid joint and hyoid bone, is reported only in adult horses and may be sub-clinical or may result in evidence of difficulty chewing or more often neurological syndromes, notably various combinations of facial and vestibulocochlear nerve dysfunction. Some of the cases have bilateral disease as determined by endoscopic and radiomaging studies, although the clinical signs are most often unilateral130–134.

The cause of temporohyoid osteoarthropathy is unclear although to this author a traumatic origin is most plausible in most cases135 with chronic otitis media/interna accounting for a select few cases. Regardless of the aetiology of the osteoarthritis, clinical signs can occur from either the osteoarthritis itself or from fractures of the adjacent temporal bone and rarely basilar bones, due to partial or complete fusion of the joint.

Physical examination findings may include difficulty chewing, pain on external palpation of the parotid area, head shaking and behavioural problems especially when being ridden131,132,134,136. Once the joint is partly fused, sudden forced head jerking, falling, teeth floating, nasogastric intubation and sudden prolonged vocalisation can cause periarticular fractures of the petrous temporal bone resulting in combinations of an abrupt onset of facial and vestibular nerve dysfunction.

Endoscopic examination of the gullet pouch is probably superior to plain radiographic imaging in confirming the presence of the disease by revealing enlargement of the proximal stylohyoid bone due to osteoarthritis when compared to the opposite side. In acute or progressive cases having ill-defined endoscopic and plain radiographic imaging findings, gamma scintigraphy should be considered as a diagnostic aid. Monitoring brain stem auditory evoked potential recordings is a very noninvasive procedure that may assist in refining the prognosis in individual cases137 and following progress of the disease.

Several cases have improved with the passage of time only to show further signs relating to facial and vestibular nerve dysfunction in weeks to months time. These would seem to be ideal candidates for unilateral surgical disunion of the hyoid apparatus. Initial surgical disunion of the hyoid apparatus was performed by removal of a mid-shaft portion of the stylohyoid bone138. To reduce the temporary difficulties in swallowing encountered and to reduce the possibility of other real and potential complications of this surgery the technique of ceratohyoidectomy was proposed and used with success135,136.

Except with major cranial fractures and if eye problems cannot be resolved133, the outlook for survival with residual neurological deficits is quite good. Of 33 cases of temporohyoid osteoarthropathy132, 20 cases survived for which there were longer term follow up details. Of these, 70% returned to previous level of use although more than 50% of the 20 horses still had evidence of facial nerve deficits and/or vestibular dysfunction. Thus, in spite of some optimistic suggestions, if full athletic performance without neurological dysfunction is required then the prognosis with or without surgical intervention has to be far guarded for these cases.

Cases of THO have given us a better insight into the ability of horses to accommodate to vestibular dysfunction and to survive with degrees of facial paralysis.

**POST ANAESTHETIC CEREBRAL NECROSIS**

An newly defined unexpected complication of apparently routine general anaesthesia in some mature horses is diffuse and severe cerebral necrosis resulting in signs of diffuse encephalopahty immediately or some hours to days after recovery from anaesthesia139,140. There is cerebral oedema and laminar neuronal cortical necrosis, and with time gliosis and small paravascular mononuclear cuffs, most prominent in the watershed zones between major vascular supplies in the occipitoparietal lobes. These lesions are associated with generalised signs predominantly consisting of somnolence to dementia, central blindness, wandering compulsively, pushing against objects and ataxia. One patient with this tentative diagnosis that recovered showed prominent muzzle and ear twitching141, very reminiscent of patients suffering from bacterial meningitis and from West Nile viral meningoencephalitis.

There certainly must be a compromise to cerebral circulation or metabolism and circumstantially it is related to the general anaesthetic procedure, but no consistent perturbations predominate139,142.

**CONCLUDING COMMENTS**

Being a biology watcher does have its rewards in equine neurology. Over the last 5–10 years by making accurate observations, recording of findings and publishing clinical results we have a better insight into the pathophysiology of diseases, the application of better therapy and improved accuracy of diagnosis and prognosis. Hopefully this discourse on some of the interesting aspects of several equine neurological diseases will stimulate others to share their experiences.
REFERENCES AND FURTHER READING


28. Sykes, B. Neurological outbreak. [Email: ben.sykes@hyvinkaanhuvostovaara.fi]


