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Literature Review

Introduction

Shivers (also called ‘shivering’) is a chronic hind limb movement disorder or neuromuscular disease that has been reported to affect horses for over a century [1-3]. The prevalence of Shivers appears to vary widely depending on the textbook consulted; some texts report that the disease is as ‘common as dirt’[4], especially amongst Draft breeds [1, 2, 5-11], and others comment that the disease is now ‘rare’ in North America where Drafts are no longer worked but more common in Europe where Draft-work is still prevalent [8]. Commonly affected Draft breeds include (but not exclusively confined to) Belgian Draft Horses, Clydesdales and Shires [5, 6, 12]. Other breeds afflicted by Shivers include, more commonly, Thoroughbreds, Warmbloods and Gypsy Vanners (cob-type), and less commonly hunters, light harness horses and Quarter Horses [4, 5, 8, 10-18]. Shivers is reported in ponies but only rarely [2, 4]. Age at the time clinical signs develop can be difficult to pin-point due to the insidious nature of the signs, however signs have been reported from one year of age [1, 2, 4, 19]. Signs of Shivers are more likely to develop as the horse begins its working life, according to some authors [1, 2, 8]. In addition, Shivers signs have been reported to occur in geldings predominantly, although this is speculated to be because they were the gender of choice for ‘town-work’ in the early 20th century [2].
The etiology of Shivers has not been thoroughly studied to-date [4, 6, 9, 11], although the disease has been recognized for over one hundred years [1, 2]. A diagnosis of Shivers can be difficult to make as it is based entirely on the demonstration of classical gait changes induced by turning the horse, asking the horse to walk backwards and by manually lifting of the limb [13]. Shivers historically has been confused with Stringhalt, hock pain, fibrotic myopathy and upward fixation of the patella as the signs of these can overlap with one another [1, 2, 8, 11, 20]. Where Shivers is correctly diagnosed, there is also no epidemiological data available to guide veterinarians on possible therapies or progression of the disease, although many texts do report cases progress and that Shivers has a guarded prognosis [1, 2, 4-6, 8-11, 14, 20, 21].

**Clinical Signs**

*Nineteenth Century:* Two of the earliest reports of Shivers are from Harrison (1903) [2] and Williams (1886) [1] and these describe similar signs under the heading ‘Shivering’. These texts describe signs occurring predominantly in the hind limbs, with rare involvement of the forelimbs [1, 2]. Classic cases manifested themselves when a horse was asked to back-up or turn suddenly or occasionally when they stopped to drink at a water trough [1, 2]. The signs reported included difficulty in getting the horse to back-up, raised croup or arched back and rigid hindquarter muscles with marked fasciculations (hence the name; Shivering) [1, 2]. Periodically the hind limbs were reported to be hyperflexed at the hock, suspended for a while with the limb abducted before being replaced to the floor [1, 2]. The classic cases also appear to have marked dorsal-ventral
‘pumping’-like action of the tail as the horse was asked to walk backwards [1, 2]. In these early texts, signs often appeared to worsen during periods of stress, when offered water from a trough, and where there was concurrent systemic illness [1, 2]. These two early texts also comment that early, or non-classical cases can be difficult to diagnose as the clinical signs were often noted to be non-specific and seen infrequently [1, 2].

A French text published during the same era [22] described very similar signs of Shivers under the heading of ‘Springhalt’ (Springhalt and Stringhalt were used interchangeably during the early 20th century [23]). These horses were reported to show ‘extreme flexion of the legs in a spasmodic manner’ during backwards walking and ‘marked abduction at the time flexion occurs’ [22]. The picture below was labeled as a horse with ‘Springhalt’ [22], however the hyperflexion and abduction is more consistent with signs of Shivering [1, 2]. Other texts, published in the same time period describe Springhalt/Stringhalt as hyperflexion of the hind limbs occurring during forwards walking predominantly [23, 24]. This may demonstrate a regional difference in naming hind limb movement disorders around the early 20th century.
Twentieth century: During the 20\textsuperscript{th} century, the clinical definition of Shivers altered slightly with some texts including difficulty backing, muscle fasciculations over the hindquarters and tail quivering without mention of hind limb hyperflexion or abduction [19], and with others reporting mainly hyperflexion and abduction signs in the hind limbs as a sign of Shivers [1, 2]. Leeney (1921) described Shivering as displayed when the horse was asked to back up and resulted in ‘spasmodic rigidity’ of the hind limbs and ‘backing is a great difficulty’. This author makes no mention of hyperflexion or abduction of the limbs [19]. Leeney also commented that the tail would rise when the
horse was ‘suddenly called upon to move’, which is consistent with the older texts [1, 2]. In contrast Adam (1960) [21] reported that a horse with Shivers ‘jerks a hind foot from the ground and holds it in a flexed position abducted from the body’ when asked to walk backwards. Tail elevation and quivering was also reported. Facial twitching and rare forelimb signs were also mentioned [21]. Two other book chapters published in the 1960’s report similar hyperflexion of the hind limbs, induced by backwards walking, being the main clinical sign attributed to Shivers in horses [4, 20].

In 1972, one author described a combination of tail quivering, hindquarter muscle twitching, reluctance to back-up and hyperflexion (with abduction) as a consistent definition of Shivers in horses. The ‘Shivering’ section in ‘Equine Medicine and Surgery’ [8] describes Shivers as being a condition that affects the muscles over the hind limbs and the tail. The classical form is characterized by tail elevation with ‘spasmodic jerks and muscles of the hind limbs are tense and trembling’ as the horse is moved backwards. The more the horse moves backwards ‘the more difficult the movement becomes’ and ‘in advanced cases the affected animal may be unable to move backward more than a few paces’ [8]. The chapter goes on to describe that hyperflexion of the limb can also accompany the tail elevation and hindquarter muscle fasciculations, on some individuals. This text also describes a rare form of Shivers that can afflict the forelimbs, whereby the limb is ‘thrust forward in to fill extension’ or ‘flexed and abducted’ as the proximal musculature fasciculates when the limb is manually lifted. This rare form is reported in various other texts too [2, 8, 11, 21]. One other commonly reported sign of Shivers involves quivering of the facial muscles (facial chorea), especially those involving the
commissures of lips and the eyelids [8, 13]. These areas will twitch and the eyes blink rapidly [1, 2] as the horse is asked to back up, turn or in some cases when the horse has its hind feet manually lifted. Choreic movements over the neck have also been reported [13, 25]. Although these texts describe forelimb signs as a separate condition, that can afflict horses with Shivers, many horses with Shivers were described as showing increased extensor tone of the forelimbs induced by backing up or during manual lifting of the hind limbs which ceased once the horse moved forwards [13].

Within the last 20-30 years several lameness and neurological texts have included descriptions of Shivers [7, 9, 11, 15, 17, 25-29]. The descriptions in these texts vary from sparse [9, 26-29] to very detailed [7, 11, 15, 17]. The descriptions of Shivers from this time period are an amalgamation of previous reports and clinical experience [7, 11, 26, 29]. Hind limb muscle fasciculations and tail elevation, induced by backwards walking, was deemed the most common clinical signs seen in mild cases of Shivers by one author in 1983 (more severe cases can ‘flex a limb and abduct it’) [15], however by 2009 this author had expanded the definition to say the muscle fasciculations noted with Shivers were a ‘repetitive myoclonus’, and that ‘occasionally, when backed-up, the affected horse overflexes a pelvic limb’ [26]. Mayhew (1989, 2009) fails to mention any hyperflexion of the hind limbs in either of his recent texts, commenting that the Shivers gait, induced by backwards walking, is ‘spastic’ in nature [9, 29]. This is mirrored in other texts published around that time [27, 28]. A detailed description of Shivers in a recent lameness texts describes a combination of hyperflexion with abduction during some steps when walking backwards, and during other steps, a more spastic, hyperextensive type gait with tail
The muscle fasciculations or tail elevation noted by others [9, 15, 19, 28].

Twenty first century: There have only been a few articles published in peer-reviewed journals regarding Shivers [5, 6, 12-14, 17, 30] in the last 30 years. Bilateral muscle fasciculations, gluteal muscle tremors, refusal to back-up and a hopping gait when forced to back were reported in a 1 year old Clydesdale gelding diagnosed with Shivers [5]. An 11-year-old thoroughbred mare was reported to show signs of hyperflexion and abduction of the left hind limb, with associated muscle fasciculations and tail elevation at rest with difficulty backing up [14]. This mare also showed unilateral forelimb rigidity and a reduced foot flight without proprioceptive deficits or weakness. The author concluded the hind limb hyperflexion signs were consistent with a diagnosis of Shivers and forelimbs signs could be associated with radial nerve involvement [14]. A recent epidemiological study addressing myopathies in Warmblood horses, specified Shivers as ‘reluctance to back-up or pick up the hind legs, hyperflexion and abduction of the rear limbs with delayed placement on the ground, tail hike and trembling’ [30] defined from a review article by Baird (2006) [13]. A case series involving two Belgian Draft Horses (BDH’s) described progressive signs of hyperflexion and abduction of the hind limbs when standing still, backing up or manual lifting of the hind limbs in these horses but also remarked that horse 1 ‘was hesitant to back, and the hind feet were sometimes dragged along the floor while backing’ [6]. This could be consistent with other Shivers reports
that describe Shivers signs to predominantly involve difficulty backing with muscle fasciculations over the hind limbs and tail elevation induced with backwards walking, or lifting the limbs manually [1, 2, 15, 19]. Both of theses horses had amylase-resistant polysaccharide in muscle biopsies consistent with Polysaccharide Storage Myopathy (PSSM). PSSM could have accounted for the additional signs that the two horses would display; fine body tremors, weakness, ‘cramping’ episodes and significant muscle atrophy of the hind-quarter’s musculature [6]. The most recent paper describing Shivers in 19 BDH’s defined Shivers as ‘fasciculations of the hindquarter musculature and tail and exaggerated flexion of the hind limbs when the horse was induced to back up’ [12]. Of the 19 horses reported in this paper 11 showed signs of weakness and as such there was a significant association between a diagnosis of Shivers and the horse being weak [12]. In this same article PSSM was diagnosed in 37 horses, and only 6 horses had both PSSM and Shivers. There was no significant association between the diagnosis of PSSM and weakness being seen (although other papers have suggested that weakness is a common sign of PSSM [31-34]) [12].

A clear diagnosis of Shivers can be made where the horse shows a combination of the following signs; hyperflexion and abduction of the hind limbs, hind limb muscle fasciculations and tail head quivering when backed up or during manual lifting of the hind limbs and the horse is normal when walking forwards. However, a few reports comment that early cases of Shivers can be difficult to discern [2, 11, 20, 21].
More detailed Shivers descriptions explain that the muscle groups that appear to fasciculate the most include the quadriceps, biceps, and semimembranosis/tendinosis muscles [1, 5, 6, 11, 19]. In less advanced cases signs of hyperflexion and abduction of the hind limbs, induced by backing-up or turning, are usually intermittent but as the disease progresses these horses can become very difficult to back or manually lift their limbs [8, 11, 13, 25]. More advanced cases are also reported to develop muscle atrophy of the hindquarters [1, 8, 10, 13, 33] and associated weakness [12]. These horses can become impossible to back-up and for the farrier to work on their hind feet [1, 2, 20]. Affected horses tend to sleep standing up, so signs of sleep deprivation and wounds on the dorsal surface of the fetlock can be seen [4].

**Diagnosis**

At present there is no known etiology of Shivers, as such there is no definitive ante or post mortem test available to confirm the diagnosis [4-8, 11, 21, 25]. Thus, a diagnosis of Shivers is based entirely on upon physical examination findings and elimination of other disorders. One author [2] described using the following physical examination technique to maximize chances of inducing signs of Shivers;

1. See the horse in his stall or box, and observe if he ‘cocks’ his tail or leg. Make him move over to one side, and then to the other.

2. Sharply back him and turn him to both sides, and note how he lifts his legs.

3. Take up each of his legs, one after the other, hold them up for a few seconds, and see that there is no unusual difficulty in raising them, and that he does not shiver.
4. Offer him water to drink, and observe if he ‘cocks’ his tail or leg.’

Based on the suggestion that Shivers is caused by PSSM, a muscle biopsy has been recommended as part of the diagnostic protocol for Shivers. Findings in muscle biopsies of Shivers horses, however, are inconsistent [6, 12, 25, 26]. Muscle biopsies (gluteal and semimembranosis/tendinosis) taken from two Draft breed horses with Shivers signs [6] showed evidence of atrophy of all fiber types, amylase resistant inclusions (consistent with a ‘complex polysaccharide) and some muscles having areas of glycogen depletion. These changes were interpreted as being consistent with Equine Polysaccharide Storage Myopathy (EPSM) [6]. However, glycogen depletion was the main finding in a muscle biopsy from a 1-year-old Clydesdale horse diagnosed with a Shivers-gait [5] and amylase-resistant polysaccharide was not a consistent finding in biopsies of 19 draft horses with Shivers in another study [12]. Thus a muscle biopsy is not a definitive test for Shivers in horses.

Elevations in the activity of muscle enzymes, creatine kinase (CK) and aspartate transferase (AST) in serum do not appear to be useful to diagnosis Shivers [13]. Firshman et al. (2005) did not find differences in serum CK and AST activity between Belgian horses with and without Shivers [12]. The same study also investigated serum selenium and vitamin E concentrations, as a possible marker for Shivers disease, however they also showed no differences between horses with and without Shivers [12].
CSF analysis has only been reported on one horse with Shivers signs, and this showed a mildly elevated protein level (0.41g/l; no reference range given) [14].

Electromyography rarely has been performed on horses with Shivers [5, 36]. Fibrillation potentials were noted in one young Clydesdale gelding that had predominantly signs of rigidity, tail quivering and muscle twitching over the hindquarters when backing up [5]. Dr Baird, however, found no abnormalities on EMG of horses with Shivers signs (personal communication).

Based on postmortem studies conducted to date there are no pathognomonic lesions in the central nervous system of Shivers horses. The studies published never include more than 2-3 cases [6, 14, 37, 38]. No consistent lesions on H&E staining of the central or peripheral nervous systems are reported [6, 14, 37, 38] [15, 26]. One study of a thoroughbred mare with Shivers [14], reported a leukomyelomalacia between C3-C4, and ‘cavitated myelin in the dorsal and ventral funiculi’ diffusely through the cervical spine. Thoracic spinal cord also had ‘non-specific lymphocytic infiltration’ and meningeal hemorrhage. These lesions could not be attributed to any one causative agent or underlying pathophysiology. Interestingly one of the earliest post mortem studies conducted on older horses [38] followed by one of 3 horses 2-5 years old [37] laid the cause of Shivers firmly with osteoarthritic lesions of the vertebral column. The author speculated that these arthritic boney changes applied ‘pressure effects on the roots of the nerves going to form the lumbo-sacral plexus’ [38], [37]. The older horses had ‘marked congestion involving the roots of the lumbar nerves’ [37], whereas the younger horses
only had mildly edematous sciatic nerves [38]. No lesions were noted in the brain or spinal column proper in these two studies [37, 38]. The author also reported a high level of osteoarthritis in these horses’ hock joints and although the horses were not lame, the suggestion was made that there could be a link between hock osteoarthritis and Shivers signs developing [37].

**Possible Etiologies**

As described above there really is no known cause of Shivers. There is has been much speculation as to whether PSSM and Shivers are related diseases [6, 12, 26, 39]. Two studies have found that muscle biopsies form Draft horses with signs of Shivers had decreased glycogen stores in the gluteal muscles, while one study found abnormal polysaccharide [5, 6]. The decreased glycogen stores were postulated to be due to localized muscle cramping and weakness in Shivers horses [5, 6]. The glycogen content in the gastrocnemius muscle of a thoroughbred mare with Shivers signs was normal [14]. Interestingly in the Belgian horses diagnosed with PSSM and Shivers, the PSSM ‘severity’ diagnosed by muscle biopsy had little correlation to the severity of clinical signs of Shivers [6]. In a 2005 paper [12] 103 Belgian horses were examined 19 horses had Shivers signs, 37 horses had evidence of PSSM on muscle biopsy and only 6 horses had both PSSM and Shivers. The paper concluded that there was no significant association between Shivers and PSSM and commented that ‘the power of this analysis was such that there was an 83% chance of detecting a significant association if one truly existed’. The mean glycogen content for PSSM-only horses was also significantly higher
than the Shivers-only horses (207.4 ± 56.4 mmol/kg vs 121.6 ± 35.9 mmol/kg), thus supporting the lack of association between the two diseases. The findings in this paper support Sullins (2002) observations that it is difficult to attribute Shivers to a glycogen-storage disease as many normal Draft horses have muscle glycogen abnormalities noted on biopsy [40]. In a study of myopathies in Warmblood horses, referring veterinarians reported Shivers signs in 15% of horses with (11/62) and without (9/60) PSSM [18].

Other etiologies postulated to cause Shivers include genetic, neurologic, trauma, toxins or infectious disease [13]. Many older and newer papers/books describe families of related horses all with signs consistent with a diagnosis of Shivers [1, 2, 8, 10, 11, 19, 24-26, 28, 35]. In the United Kingdom, Shivers is considered a heritable condition, and there are reports of related Belgian Draft Horses showing high rates of Shivers, so a genetic component cannot be excluded [12, 13]. This being said a simple mendelian inheritance pattern has not been presented for Shivers, and a combination of genetics, and environmental factors are likely necessary to induce the disease phenotype [13]. Many texts warn against breeding horses with signs of Shivers due to the belief there is a heritable component [1, 2, 4, 8, 10, 26, 37].

There are several reports that signs of Shivers have manifested after a systemic infection or traumatic event [1, 2, 8, 20]. Specific infectious agents include Streptococcus equi, influenza, [1, 2, 8, 20] and Chorioptic mange [29]. These inciting causes are all different, however as ‘stress’ appears to worsen signs of Shivers in some reports [10, 13, 35] it seems plausible that a severe systemic disease could make signs more pronounced to
owners. One author commented that he had never encountered a Shiverer that did not also have concurrent osteoarthritis of the spine and other joints [37, 38], although, the examined horses showed no signs of lameness. A postulation between arthritis and peripheral nerve compression was made [37, 38].

Toxin ingestion, in the form of ‘Lathyrism’, is known to induce a Stringhalt-like gait in horses when ingested in large enough quantities [9]. Ingestion of other plants has also been attributed to cause Stringhalt signs, such as Hypochaeris radicata [41, 42]. As there can be overlap in clinical signs attributed to Shivers and Stringhalt [1, 7, 14, 17, 22, 25, 35, 40, 43], especially in mild cases a toxin cause seems plausible, however there are no reports of toxin ingestion being associated with onset of classical Shivers signs, or any ‘outbreaks’ of Shivers occurring, unlike Stringhalt [43-49].

Many authors speculate a neurological cause to Shivers [4, 10, 11, 14, 25-27, 29, 37]. An abnormality associated with neurotransmitter production or signaling has been postulated by one author [29]. Another reported that ‘the etiology is unknown but…is likely to involve an alteration in the feedback loop between 1a-afferent and gamma-efferent fibers in muscle spindles [25]. Myoclonus, as a cause of the repeated muscle tremoring, has also been suggested [26], whereby the authors decided to class Shivers as an equine episodic repetitive myoclonus, until further studies are performed. Compression of peripheral nerves of the lumbosacral plexus was proposed in the 1930’s by one author but was not found to be a repeatable abnormality, with age appearing to appearing to be a significant confounding factor [37, 38].
Necropsy studies have failed to pinpoint not only a possible pathological lesion associated with Shivers [4, 6, 14, 26, 37, 38], but there is still much controversy over where a lesion may be located within the nervous system. In a recent review article they state that ‘lesions in the sensory or motor pathways anywhere from the brain stem to the affected muscles and associated joint and tendon sensory receptors potentially could initiate the abnormal muscle tone and movements observed in shivers’ [13]. A detailed clinical and pathology study is needed to pinpoint the exact cause of Shivers.

**Differential Diagnosis**

A recent review article stated, that ‘the diagnosis of a characteristic case of Shivers seldom presents a problem’ [13]. However there are many cases, especially the earlier ones, that do not show characteristic signs and so the diagnosis of these can be very challenging [2, 11, 20, 21]. An incorrect diagnosis can lead to an inaccurate treatment plan and prognosis.

The hind limb movement and musculoskeletal disorders that are commonly confused with Shivers include stringhalt, upward fixation of the patella, fibrotic myopathy and Stiff Horse Syndrome [4, 7, 11, 22, 25, 26, 29]. Hock arthritis and Chorioptic mange have both been reported to produce intermittent mild hyperflexion of the hock in Draft horses [7, 29, 37]. Equine Motor Neuron Disease (EMND) is a consideration where there is severe muscle atrophy and signs of weakness, however this disease doesn’t reportedly produce any hind limb abnormalities consisting of hyperflexion and abduction [50-53]. Muscle
fasciculations are a common feature of EMND [50-53]. Equine protozoal myelitis (EPM) has also been known to cause gait abnormalities (more similar to Stringhalt, than Shivers) [29], however case reports of horses with Shivers signs have been ‘negative’ for EPM [6, 14].

Stringhalt (historically called Springhalt as well) is a distal axonopathy, which preferentially affects the longest peripheral nerves [25]. Symptoms of Stringhalt classically are described as marked hyperflexion of the hock and stifle of one or both hind limbs occurring during forwards walking [7, 11, 25, 54, 55]. Stringhalt has been attributed to two main etiologies historically, leading to different ‘categories’ Stringhalt:

1. True or Australian Stringhalt: results from ingestion of toxic plants (such as Hypochaeris radicata), although the exact toxin is not known and theses cases can be unilateral but are often bilateral. These cases are usually acute onset and can occur in outbreaks after horses are turned out to pasture during the spring and summer months [41, 43, 54-56]. Cases of Australian Stringhalt have been reported in Europe, North and South America [41, 42, 44-46, 48, 49, 57].

2. False or Acquired Stringhalt: results from hock arthritis, trauma to the hock or inflammation elsewhere in the limb. These typically are unilateral and can have a history of lameness, and orthopedic examination reveals pathology elsewhere in the affected limb [7, 43, 58, 59]. Signs can show months after the traumatic event [43].

There is one neurological text that attributes Stringhalt-signs to EPM in rare cases [29].
Although Australian Stringhalt signs are classically described as hyperflexion of the hind limb(s) during forwards walking, clinically, there can be variation between affect individuals. With this in mind, Huntington et al. (1989) [43] reported a clinical scale from 1-5 describing signs that may be seen with increasing severity of Australian Stringhalt:

Grade 1 - Only noticeable when horse was backed, turned or stressed.

Grade 2 - Slight jerkiness when horse moved off at walk or trot. This was more obvious when backed or turned sharply and hyperflexion was sometimes exhibited when the hind limb was picked up.

Grade 3 - Moderate hyperflexion was noted when walking or trotting, especially when moving off or pulling up. Canter was disjointed, but hind limb did not hit abdomen. Some difficulty was seen on backing and turning.

Grade 4 - Severe hyperflexion with hind limb hitting abdomen seen at rest, walk or faster gaits. Could not move backwards and had difficulty turning. Hyperflexion was often shown at rest and the horse was unable to trot.

Grade 5 - Moved only with plunging, bunny-hopping motion. Hind limb was held hyperflexed for seconds.’

Grades one and two of Stringhalt could easily be confused with Shivers. As signs of Stringhalt become more pronounced (grade 3+) there are clear differences between Shivers and Stringhalt; consistent forward walking signs of hyperflexion are not seen with Shivers nor do the hind limbs contact the abdomen during walking or trotting with Shivers. A review article looking at Australian Stringhalt also commented that ‘the onset
of the disease is often sudden’ and ‘in some cases the gait becomes normal with exercise’ [54]. Severe cases are not able to rise and chronic, severe cases can show significant hind-quarter muscle atrophy and weakness [54]. Concurrent damage to the left recurrent laryngeal nerve causing Recurrent Laryngeal Neuropathy (RLN; Roaring) is common amongst horses with Australian Stringhalt [25].

The clinical diagnosis of Stringhalt can be supported by classical clinical signs [25], geographical location (where the toxic plants have been identified) [44-46, 48, 49, 57], increased EMG activities when the animal is standing [25, 60], and biopsies of the long digital extensor muscle and superficial peroneal nerve [61]. These biopsies showed fiber atrophy and axonal degeneration and demyelination respectively [61].

A surgical therapy, for Stringhalt that is trauma-related, has been reported as transection of the long digital extensor tendon [58, 59]. There is variable success rates reported with this technique [7, 9, 58, 59]. Numerous Australian Stringhalt cases have been reported to improve with time [54] and removal of the horse from the toxic plants involved, although some horses do continue to show residual gait abnormalities. Phenytoin has been used in some cases of Australian Stringhalt, as has symptomatic relief with muscle relaxants [54, 56, 62]. Botox therapy has also been tried as a treatment in two horses with Acquired Stringhalt [60]. Kinematic analysis of the 2 treated horses showed only subtle improvements in the Stringhalt gait after Botox therapy; this may have been due to the ‘relatively low dose’ of Botox utilized here to minimize toxicity effects [60].
Stringhalt cases, unlike Shivers cases, have been reported to recover from their gait abnormalities over a period of months (presumably due to toxin removal from their diet, and time for the nerves to heal). However in certain cases their signs are so severe that the horse is unable to ambulate, or is found down and not able to rise. These cases are usually subjected to humane euthanasia [54].

Stiff Horse Syndrome (SHS) was recently described in horses from Belgium [25, 63-65]. These horses showed intermittent stiffness and contractions of the lumbosacral muscles and hind end muscles, producing a lordotic appearance in some individuals [25, 65]. Sudden, startling of affected horses induces severe, generalized muscle contractions leading to the horse being immobilized on the spot. In milder cases a stiff gait was seen for a few strides, which recovered as time progresses, but if sudden stress was applied severe signs were easily induced. Weakness and muscle atrophy are not seen with this disease [25, 65]. Neurological examinations of these horses are normal, as are routine clinical pathology tests. EMG during an attack shows ‘continuous motor unit activity’ [65]. In humans, an autoimmune disease is reportedly caused by a reduction in release of the inhibitory neurotransmitter GABA in the CNS due to production of autoantibodies against glutamic acid decarboxylase (GAD) [64, 65]. GAD converts GABA to an active form. Detectable levels of GAD-autoantibodies were present in the serum and CSF of affected horses [64].

Upward fixation of the patella is an acquired, musculoskeletal disorder [7, 29]. The medial patellar ligament becomes fixed over the medial trochlear ridge of the femur. The
limb is then stuck in extension until the patella is released and the limb then flexes rapidly. This can resemble Stringhalt if it occurs with forwards walking or Shivers and Stringhalt if it occurs with backwards walking [7]. The hoof may be dragged along the floor for a time before the leg is flexed or the sole may be dragged if the limb was in a weight-bearing stance at the start of the stride [7, 29]. Both of these conditions can be uni or bilateral and Warmbloods and Thoroughbreds appear to be predisposed [7].

Fibrotic myopathy results from a traumatic tearing of the semimembranosis/tendinosis muscles, often as a result of sliding stops in reining or getting caught in a tether [66, 67]. The scarification of these muscles results in a very characteristic ‘goose stepping’ gait at the walk, and a slapping sound associated with every stride [7]. Technically, the fibrosed muscle produces a shortened cranial swing phase with an abrupt stop to the phase and a very short caudal phase as the limb is slapped to the floor [66, 67]. The fibrosis of the muscle(s) is often palpable and is visible on ultrasound of the area. The problem can be unilateral or bilateral depending on the insult.

**Treatment and Progression of Shivers**

Shivers is reported to a chronic progressive disorder [1, 2, 4, 6, 8-10, 14, 15, 17, 19-21, 25-29, 35, 37, 38]. However, progression can be very variable, with many horses maintaining the ‘status-quo’ for a significant period of time (however this time course is extremely inconsistent), until their signs rapidly progress [8, 20, 26]. One report describes mildly affected jumping and hunting horses being able to continue their working life for ‘several seasons, but they gradually lose their ability to clear obstacles’ [8]. The same
author also reported resting a horse with Shivers can reduce the frequency of clinical signs, whereas the converse is true with heavy work [8]. At present there are no proven therapies that can alleviate the signs of Shivers once they begin [1, 2, 4, 6-11, 15, 17, 19-21, 25, 28, 29, 35, 38, 40]. One report calls treatment ‘valueless’ in cases of Shivers [20].

There are many reports that indicate that dietary manipulation in cases that have concurrent myopathies (such as PSSM) may improve some of the signs of weakness, muscle fasciculations and atrophy [6, 18, 32-34]. However others report that dietary manipulation, in horses affected with Shivers-alone, does not result in any significant improvements to the Shivers signs. Anecdotally, providing a calm stable routine for the horse with low level exercise and turnout is the best way to reduce the severity of the signs, however this doesn’t eliminate or slow progression of signs in some horses [13].

It is easy to see from this literature review that there is a lack of epidemiological data regarding Shivers, and also no one consistent definition, making a diagnosis for practitioners very difficult. This could lead to incorrect advice on treatment and prognosis. In addition, the inability to consistently phenotype horses for Shivers hampers further efforts by investigators to determine the etiology of Shivers.

**Hypothesis:**

The hypothesis for this thesis is that there are a variety of movement disorders in horses that have previously been loosely classified as Shivers. A clearer definition of the Shivers phenotype will be obtained by detailed subjective and objective (kinematic) evaluation of horses previously diagnosed with Shivers and other pelvic limb movement disorders.
Furthermore, important clinical information for practicing veterinarians can be obtained through a large-scale epidemiological study of Shivers horses.

The aims of this thesis are:

1. To develop a clinical definition of Shivers through a thorough evaluation of a large number of clinical cases
2. To objectively define the pattern of hind limb movement of Shivers compared to Stringhalt horses using video analysis
3. To determine if there is an association between the breed, height or gender of horses afflicted with Shivers and if there are management practices associated with the presence or alleviation of clinical signs.
Chapter 1

Characterization of hind limb movement in horses

Introduction

Lameness and proprioceptive deficits, which are identified by a thorough lameness and neurologic examination, account for the majority of gait abnormalities in horses. There are, however, other ill-defined equine movement disorders in horses such as Shivers, Stringhalt, intermittent upward fixation of the patella, and fibrotic myopathy that can be difficult to diagnose [1-3]. After excluding lameness and abnormal proprioception, a diagnosis of these disorders is based on clinical impression because few if any specific diagnostic tests for Stringhalt and Shivers exist [1, 3, 4]. Clear guidelines that distinguish Shivers, Stringhalt, upward fixation of the patella and other potential movement disorders are lacking and definitions found in textbooks frequently overlap [1, 5]. For example, both Shivers and mild cases of Stringhalt are described as causing hyperflexion of the hind limbs when horses walk backwards or turn without affecting forward walking [3, 6]. Furthermore, Shivers is described in some cases as causing excessive hind limb flexion upon walking backwards [5, 7, 8] and in other cases as reluctance or inability to walk backwards [9-11]. Many owners of horses, whose only clinical sign is reluctance to manually hold up a hind limb, believe their horse has Shivers. The lack of research into the pathophysiology of movement disorders such as Shivers and Stringhalt makes an evidence based diagnosis difficult. A standardized approach to evaluating movement
disorders in horses with clear diagnostic criteria for Shivers and other movement disorders like Stringhalt would be an important advance in understanding movement disorders in horses.

Videos submitted as part of an epidemiological study of Shivers (see Chapter 2), owners submitted a collection of videos of horses with potential movement disorders. In these videos, horses performed a standardized exam consisting of walking forwards at least 10 strides, turning sharply in both directions, walking backwards and lifting the hind limbs manually. The purpose of the present study was to use these videos to develop a subjective classification scheme for Shivers and compare this to other hind limb movement disorders such as Australian stringhalt. A second aim was to develop a simple objective means to compare forwards and backwards gaits in Shivers, Stringhalt, fibrotic myopathy and upward fixation of the patella.

Materials and Methods

Subjective analysis of movement in Shivers horses

Case selection: Owners of horses potentially affected by Shivers submitted videos to the Neuromuscular Diagnostic Laboratory (NMDL) as part of an epidemiologic survey (http://www.cvm.umn.edu/umec/shivers/home.html). Owners were directed to upload a video of their horse being led in hand, walking forwards, walking backwards, turning
sharply (to the left and right) and when manual holding up each limb for a minimum of ten seconds. Videos were reviewed and those that did not include a clear complete evaluation were discarded.

**Subjective video analysis:** Videos were assessed by one of the authors (Alex Draper) for the presence of forwards or backwards walking abnormalities and any issues with manually lifting any of the limbs. When walking backwards and forwards, horse’s hind limb movements were classified as; normal, unilaterally or bilaterally abnormal, consistently or intermittently abnormal, abducted, hyperflexed or hyperextended during the swing phase. In addition, when manually lifting a hind limb, presence of hyperflexion, hyperextension, abduction or inability to lift the limbs was noted. The presence of facial grimacing, tail elevation, fore limb stretching and muscle fasciculations were noted if observed, but could not consistently be evaluated in each video.

**Objective video analysis of Shivers and other hind limb movement disorders**

**Case Selection:** Videos of Shivers cases captured by owners from the first aim along with additional submissions provided by Dr John Baird were screened for suitability for quantitative analysis. The criteria for selection was that horses were captured walking forwards and backwards on a flat surface for several strides with horses close to a 90 degree angle from the camera. Normal Warmblood, Thoroughbred and Belgian Draft horse videos submitted by owners and by Dr John Baird were used as a control group. For comparison, videos of bilateral Stringhalt, fibrotic myopathy, and upward fixation of
the patella were obtained from the following author’s archives (Stephanie Valberg, John Baird, Troy Trumble and Robert MacKay). The number of fibrotic myopathy and upward fixation of the patella were small (2 each) and cases were used for graphic but not statistical comparison.

**Video analysis:** A simple video analysis was performed that allowed frame-by-frame capture in iMovie (Apple, Cupertino CA USA). A more advanced kinematic analysis was not applied as videos were taken by owners-in-the-field and they could not be completely standardized. Forwards and backwards walking of each horse were evaluated separately. One representative forward stride of the most severely affected hind limb that was closest to the camera was analyzed when the horse was as close to a 90 degree angle to the camera as possible. A stride unit was defined as the frame beginning when the sole was in contact with the ground and ending with the frame when the sole was on the ground in the same stance position (Figure 1). Using the time scale in iMovie, frames that represented 0, 0.25, 0.50, 0.66, 0.75, 0.88, 0.97 and 1 of the stride unit were selected for analysis. In each frame, 2 parallel horizontal lines were drawn, one at the level of the ground (determined from stance phase of the ipsilateral forelimb) and one at the level of the sternum. The maximal vertical displacement (VDmax) was determined in each frame and defined by the distance from the ground line to the horizontal sternal line. For each frame, the vertical displacement (VDx) of the hind limb was measured as the distance between the ground line and the toe of the hind limb closest to the camera (Figure 2). The VDx measurement was replicated 3 times and an average used for measurement at each fraction of a stride unit. The vertical displacement was calculated as a percentage using
the equation \( \frac{VDx}{VD_{max}} \times 100 \). The \( VD_{peak} \) for a stride unit was calculated as the highest measured \( VDx \). The duration of each stride unit (stride time) was obtained from the time bar of iMovie. Vertical displacement (%) versus fraction of the stride unit was plotted and the area under the curve (AUC) was calculated individually (using the trapezoid method).

**Statistical Analysis:** After subjective analysis of all videos, clear groups of movement disorders were apparent within the Shivers horses. Horses were divided into these groups for purposes of video analysis. Comparisons were made among normal horses and each of the Shivers groups. The mean and the standard deviation for the AUC, \( VD_{peak} \) and stride time were calculated per group. The AUC, \( VD_{peak} \) and stride time were compared using a one-way ANOVA amongst the groups for forwards and backwards walking. All post-hoc tests were performed using a Tukey test. All analyses were performed using Microsoft Excel and R-Project for Statistical Computing. \( P \) was set at < 0.05.

**Results**

**Subjective analysis of movement in Shivers horses**

**Video submissions:** Seventy videos of potential Shivers cases were submitted by owners and 16 videos were excluded because of quality.
**Classification of Shivers hind limb movement:** After reviewing the videos, there was a large group of horses in which the only abnormality was difficulty manually lifting the hind limbs (n=21), and this group was termed standing-hyperflexion (standing-HF). In addition, there were 2 horses that manually lifted their limbs normally, walked backwards normally but had an intermittent hyperflexion of one or both hind limbs during forwards walking. This small group was not consistent with a definition of Shivers from previous literature [3, 7, 8] and was subjectively defined as having a hitch in forward walking (Table 1). The remaining horses all had difficulty manually lifting the hind limbs as well the following signs. These horses could be divided into, three clear groups; 1) horses with hyperflexion when walking backwards (n=21) and normal forward walking, 2) horses with hyperextension when walking backwards (n=6) and normal forward walking, 3) horses with abnormal backwards gaits and intermittently abnormal forwards gait (n=4). These distinctions were utilized to develop a classification scheme for describing abnormal movement in horses with Shivers (Table 1).

**Hitch:** One 17-year-old Belgian Draft Horse gelding and one 3 year old Oldenburg gelding sporadically hyperflexed one hind limb when calmly walking forwards. The hitch in stride was sporadically present, in one hind limb in the Belgian, in both hind limbs in the Oldenburg and disappeared at more animated forward gaits. Backwards walking and manually lifting of the hind limbs were normal.

**Standing hyperflexion (Standing-HF):** In 21 horses the only abnormality was prolonged hyperflexion of one or both hind limb(s) when manually lifted. Forward and
backward walking was normal. Two female and 19 males with a mean age of 12.4 ±4.7 yrs (range; 6-23 yrs) and of a range of breeds were included in this group (Table 1). Six horses had signs bilaterally and 15 had unilateral signs (9/15; right hind and 6/15; left hind). In addition to hyperflexion when manually lifted, the hind limb was abducted in 19/21 horses.

**Shivers-hyperflexion (Shivers-HF):** Twenty one horses showed signs of hind limb hyperflexion when walking backwards and manually lifting the hind limb with normal forwards walking. Breeds were largely Warmblood, Thoroughbreds and Drafts (Table 1), and there were 3 females and 19 males with a mean age of 13.7±4.2 yrs (range; 7-22 yrs). Signs were bilateral in all cases although one hind limb could be more severely affected than the other. During hyperflexion, the hind limb was abducted and the affected limb would pause in the hyperflexed state before quickly returning to the ground. Upon backing, the tail head was elevated in all but 5 horses. Additional signs seen during backwards walking in some cases included muscle fasciculations over the hindquarters and facial chorea (twitching and involuntary contraction of the facial, upper eyelid and lip commissure muscles). In eight of the horses, hyperflexion of one hind limb during backwards walking instigated a 2 beat pace or 4-beat backward gait instead of the normal 2-beat contralateral footfall. Manual lifting of a hind limb induced hyperflexion, and in some cases abduction, of that limb, in all horses.

**Shivers hyperextension (Shivers-HE):** Five male and 1 female horse (Clydesdales, a Shire and Thoroughbred (Table 1) with a mean age of 9.5±4.7 yrs (range; 4-16 yrs)
showed hyperextension upon backward walking. Forwards walking was normal. During the backwards stride, the hind limbs were placed with an extended hock farther caudally than seemed natural often landing toe first. All horses extended both forelimbs at the initiation of backwards walking which, when combined with hind limb hyperextension, resulted in a stretched saw-horse appearance. After a few contralateral 2 beat backwards strides, horses became reluctant to back and 5/6 horses could not complete more than 2-3 strides backwards. The tail head was elevated and croup steeply sloped during backward walking in all horses. Facial chorea was a consistent finding during backwards locomotion. Muscle fasciculations over the hindquarters were seen in 4/6 horses. Manual lifting of the hind limbs was not possible in four of the horses, and two horses would quickly flex the limb slightly, before replacing the limb to the floor quickly. This meant the owners were not able to pick out their hind feet or have farriery work conducted on any of these horses.

**Shivers forward hyperflexion (Shivers-FHF):** Four Warmbloods and Thoroughbred male horses (Table 1) ranging in age; 10-19 yrs old (mean 15.0 ±4.2 yrs) had abnormal manual lifting of the limb as well as backwards and forwards walking. These horses had previously shown signs consistent with Shivers-HF and progressed over at least one year (1-3 year range) to show marked hyperflexion and abduction of both hind limbs at almost every stride during backward walking. A notable pause occurred with hyperflexion before returning the limb to the ground. At times, one hind limb was in the swing phase when the opposite hind limb was paused in hyperflexion, leaving both hind limbs off the ground and the horse solely bearing weight on their forelimbs for a short time. At the
initiation of forwards walking, marked hyperflexion with abduction of hind limbs occurred for the first few strides and when turning. After two or three such strides the horses walked normally unless a change occurred in surface, direction, speed of walking or if a distraction occurred. Tail head elevation was noted in all horses as they walked forwards initially, and when walking backwards. Extreme difficulty with manual leg lifting was present to the point where they either refused to pick up a hind limb or if they did lift the limb they moved away from the handler and slammed the foot down rapidly.

**Quantitative Video Analysis**

There were 18 high quality videos of Shivers horses that fit the selection criteria for video analysis (5 Shivers-HF, 5 Shivers-HE, 4 Shivers-FHF, 4 controls). To increase the number of videos analyzed, an additional ten Shivers videos (5 HF and 5 HE), 4 control videos and 6 Stringhalt videos were obtained from the archives of John Baird, Robert MacKay and Troy Trumble.

**Signalment:** Control horses consisted of 4 Belgian Draft Horses, 1 Percheron, 3 Warmbloods, and 1 Quarter Horse with a mean age of 16.5±5.2 yrs, comprising 4 males and 5 females. Shivers-HF consisted of 4 Belgian Draft Horses, 1 Shire, 2 Warmbloods, 2 Thoroughbreds and 1 Thoroughbred/Warmblood cross with a mean of 12.1±5.7 yrs, comprising 6 males and 4 females. Shivers–HE consisted of 7 Belgian Draft Horses, 1 Clydesdale, 1 Shire, 1 Draft/Warmblood cross with a mean age of 14.5 ± 2.5 yrs,
comprising 6 males and 4 females. Shivers-FHF consisted of the same horses in the subjective analysis.

**Stringhalt:** Stringhalt horses consisted of 3 males and 4 female horses including 5 Thoroughbreds and 2 Warmbloods of unknown age. Bilateral Stringhalt cases were from Australian horses believed to have ingested *Hypochaeris radicata*. Hindlimb hyperflexion without abduction occurred during the swing phase of every forward stride with normal forelimb movement. During backwards walking, excessive hyperflexion of the hind limbs occurred during every stride. During some strides in both forward and backward walking the affected limb would pause hyperflexed before returning to the ground. No facial chorea or marked tail head elevation were apparent in these horses. All horses were graded a III or IV on the Huntington Grading Scale (see Literature Review).

**Fibrotic myopathy and upward fixation of the patella:** The horses with fibrotic myopathy were both Quarter Horses and horses with upward fixation of the patella consisted of a Paint horse and a Quarter Horse. One unilateral and one bilateral case of hind limb fibrotic myopathy (confirmed by ultrasonography) exhibited an abrupt end to the cranial swing phase of the affected hind limb. Backwards walking was performed in one case and was normal.

In one case of upward fixation of the patella, the stifle and hock were in marked extension and the toe dragged along the floor at the beginning of the stride until the limb underwent quick, flexion. The abnormal gait in this horse was provoked if the horse was turned in a tight circle, walked backwards and when rising from lying down. Other
walking strides were normal. In the other case, signs were similar to the first case when walking forwards for a few strides and when turning (stifle and hock were held in marked extension and the sole of the foot dragged along the floor at the beginning of the stride until the limb underwent quick, flexion). This horse showed similar signs when backwards walking. Signs were abated after a few strides walking forwards and backwards.

**Quantitative Analyses of Forward walking:** AUC, VD peak and stride time did not differ amongst controls, Shivers-HE, Shivers-HF horses (Table 2). Shivers-FHF horses, however, had larger AUC, higher VDpeak and longer stride times than controls, Shivers-HE, Shivers-HF horses as well as stringhalt horses (Table 2). Stringhalt horses had greater AUC and VDpeak than controls, Shivers-HE, Shivers-HF horses but a smaller AUC than Shivers-FHF horses (Table 2).

**Quantitative Analysis of Backward walking:** AUC, VD peak and stride time did not differ between controls and Shivers-HE horses (Table 3). Shivers-HF horses had larger AUC and higher VD peaks than control and Shivers-HF horses but stride times were similar. Shivers-FHF horses had larger AUC and higher VDpeak but similar stride times to controls, Shivers-HE, Shivers-HF horses (Table 3). Stringhalt horses had similar AUC to Shivers-FHF but higher AUC than controls and Shivers-HF and Shivers-HE horses (Table 3). VDpeak in Stringhalt horses was similar to Shivers-FHF and Shiver-HE horses but greater than controls and Shivers-HE. Mean stride times for Stringhalt horses were
similar to Shivers-HF but larger than for controls, Shivers-HE, Shivers-HF horses (Table 3).

**Fibrotic Myopathy:** Descriptive analysis showed that the VDpeak for the forwards walking stride of two horses with fibrotic myopathy occurred at the very end of the swing phase (27% and 10% in horse 1 and 2 respectively) at values slightly higher than control horses (Figure 5). To complete the stride, the foot was rapidly returned to the ground to complete the swing phase. Backward walking appeared normal in the one video where it was present.

**Upward Fixation of the Patellar:** Descriptive analysis for both horses showed that the VD peak was delayed due to a lengthened stance phase with the swing phase occurring between 0.88 and 0.97 of a stride unit during backwards walking for both horses and during forwards walking for one horse. The VDpeak was comparable to the controls during forwards and backwards walking (Figure 5).

**Discussion**

The purpose of the present study was to develop a simple clinical means to classify abnormal hind limb movement associated with Shivers and to distinguish this from other hind limb movement disorders in horses. Both subjective and objective means were utilized, however, objective measures were made from owners videos that could not be completely standardized. To account for this, a large number of videos were only assessed subjectively and a select few were used for objective analysis. Parallax errors
were possible, as measures could not be taken to ensure horse were 90 degrees to the camera. To counteract this, frames were only selected for analysis in which the horse appeared parallel to the camera and a control group was filmed by horse owners in a similar fashion. Errors in measurement were likely similar across the spectrum of movement disorders and control horses analyzed. Ideally a standardized kinematic analysis of Shivers horses would be performed, however, it would be extremely difficult to assemble a large number of Shivers horses at one site that had the necessary gait analysis equipment. While the results obtained should be interpreted with caution, the subjective and objective assessments used could serve as general guides to the differences in movement among Shivers, stringhalt and other movement disorders.

Previous literature dating back to the 19th century provides a wide variety of descriptions of abnormal movements for Shivers [3, 5, 7-27] In one of the earliest articles addressing Shivers the signs were described as “difficulty in getting a horse to back-up, a raised croup or arched back, rigid hind-quarter muscles, and quivering hind limbs raised from the floor” [26]In more recent literature, the hallmark signs of Shivers is usually marked hyperflexion and abduction of a hind limb during backing up or turning [1, 3, 7, 8, 15, 28, 29]. The results of the present study indicate that in some cases of Shivers walking backwards is characterized by rigidity, decreased hock flexion and great reluctance to move backwards (Shivers-HE), whereas in other cases (Shivers-HF), hyperflexion and often abduction of the hind limbs occurs. For Shivers-HE, no quantitative difference in the AUC, VDpeak or stride time was seen in forwards or backwards locomotion when
compared to controls. In contrast, during backwards locomotion, Shivers-HF had a greater AUC over a stride unit compared to control horses and Shivers-HE.

The term Shivers arises from the clonic-tonic muscle contractions that occur in the hind limbs during backward movement [9, 26, 27, 30]. The origin of the muscle clonus is as yet unknown, as neither peripheral nor central nervous system pathology has been found in the limited number of studies available [11, 22, 23, 31]. It is possible that physiologic dysfunction occurs within the interneurons in the spinal cord in Shivers horses when walking backwards and, depending on which pool of interneurons is primarily affected, excessive hind limb flexion or extension occurs [32]. Alternatively, Shivers-HF and Shivers-HE could represent different neurologic conditions. It is interesting to note that Shivers-HE horses also showed extension of their forelimbs when asked to back-up and that both Shivers-HE and HF horses were unable to maintain a contralateral two beat pattern during backward walking. Thus, Shivers may not only represent dysregulation of flexors and extensors within a hind limb but may also represent dysregulation of backward movement amongst all four limbs.

While forwards walking was normal in both Shivers-HF and -HE, some horses showed intermittent hyperflexion and prolonged stride times during forwards walking. These horses, termed Shivers-FHF, subjectively seemed to get stuck in peak hyperflexion and precariously, the opposite hind limb could start its swing phase when both hind limbs were in the air. Based on a chronic history of Shivers-HF and greater AUC in Shivers-FHF horses compared to Shivers-HF, this appears to be a more advanced case of Shivers-
HF. Dysregulation of flexor and extensor hind limb muscles within and across limbs could have progressed to a point where it not only severely impacted backwards walking but now also intermittently impacted the initiation of forwards walking or turning. While horses with Shivers-FHF seemed disabled at a walk, historically Shivers-FHF horses in the present study had competed successful in dressage and three day eventing without evidence of gait abnormalities at the trot, canter and over fences. Thus it is quite remarkable that a movement disorder can have such strong impact on backwards walking and intermittent forward walking yet not impact complex conscious locomotion such as trotting, cantering and jumping.

Stringhalt is an important differential diagnosis for Shivers-FHF particularly since they appeared identical during backwards walking in video analyses. Distinguishing features, however, during forwards walking were shorter stride times and abrupt hyperflexion early in the stride in Stringhalt compared to Shivers FHF horses. Further, Stringhalt horses showed consistent hyperflexion with almost every forward stride, whereas hyperflexion was an intermittent occurrence in Shivers-FHF. These findings are in agreement with at kinematic analysis of Stringhalt [11]. In contrast to Shivers, Australian Stringhalt is often acute in onset and is the result of a peripheral neuropathy following ingestion of *Hypochaeris radicata* [20]. Traumatic injuries to the hind limb and other peripheral neuropathies and can also present as stringhalt [4].

The cases of both Shivers-FHF and Stringhalt in the present study were quite severe and may not truly reflect the difficulty of trying to establish an early diagnosis of either
disorder. Mild cases of Australian stringhalt may only show signs of hind limb flexion when walking backwards and manual lifting of the limbs [6]. Differentiation from Shivers in such cases would require information on acute or chronic onset [33], seasonality and geographic location [1, 33, 34]. The sole sign of hind limb hyperflexion when manually lifting the limb was not considered to be pathognomonic for Shivers in the present study. Horses were afflicted either unilaterally or bilaterally and signs could easily have had been behavioral or related to neuropathic or musculoskeletal pain. In discussing cases with owners, signs did not ever appear to progressing to affect walking backwards. Thus, it is the authors’ recommendation that signs of hyperflexion solely apparent with manual lifting of the limb not be considered diagnostic for Shivers.

Another mild movement disorder in the present study did not fit this definition of Shivers. This disorder was termed a hitch and was characterized by intermittent hind limb hyperflexion with forward walking without affecting backwards walking. Unlike Shivers and Stringhalt, it disappeared rather than temporarily worsened with excitement [3, 6]. It would appear that a hitch is distinct from Shivers and that there are a variety of movement disorders in horses that remain to be characterized.

Other differential diagnoses for Stringhalt and Shivers include fibrotic myopathy and upward fixation of the patella [1, 3, 35, 36]. Video analyses of the 2 horses with fibrotic myopathy showed a slightly longer hind limb stance phase during forwards walking with the highest trajectory (VDpeak) occurring very close to the end of the swing phase. Unlike Shivers, backwards walking and manual lifting of the limb appeared to be
unaffected in the one fibrotic myopathy case where backwards walking was recorded. The altered hind limb movement of horses with patellar fixation was variable depending on whether upward fixation occurred in the caudal swing phase or during the stance phase [1, 37]. Once the patellar disengaged, the stride showed a similar swing phase trajectory to control horses and, unlike Shivers, manual lifting of the limb was unaffected by upward patellar fixation. Thus, both fibrotic myopathy and patellar fixation show normal manual lifting of the hind limbs. Fibrotic myopathy cases have a consistent characteristic forward stride with normal backwards locomotion whereas upward fixation of the patellar cases had characteristic signs during forwards and backwards walking.

In conclusion, evaluation of horses for movement disorders should include, in addition to a complete lameness and neurological evaluation, walking horses forwards and backwards for at least 10 strides, turning sharply and manual lifting each limb. Since the pathophysiologic basis for movement disorders like Shivers is unknown, a diagnosis is currently based on clinical signs. Based on the results of this study, the authors suggest that a clinical definition of Shivers include chronic difficulty backing characterized by either excessive hind limb hyperflexion or excessive hind limb rigidity or extension. Advanced cases of Shivers will in addition, show intermittent hyperflexion of the hind limbs at the initiation of forwards walking or when turning. While backwards walking is very similar between Shivers and Stringhalt, the chronicity and intermittency with which forwards walking is affected in advanced Shivers cases distinguish this disorder from Stringhalt. The sole sign of hyperflexion of the hind limb with manually lifting was considered insufficient for a diagnosis of Shivers (Standing-HF).
Table 1: Summary of hind limb movement during manually lifting of the limb, walking backwards and walking forwards from reviewing videos of horses previously diagnosed with Shivers or Stringhalt

<table>
<thead>
<tr>
<th>Classification</th>
<th>N</th>
<th>Breeds</th>
<th>Manual Lifting</th>
<th>Backwards Walking</th>
<th>Forwards Walking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hitch</td>
<td>2</td>
<td>1 WB, 1 Draft</td>
<td>Normal</td>
<td>Normal</td>
<td>Hyperflexion, Intermittent</td>
</tr>
<tr>
<td>Standing-HF</td>
<td>21</td>
<td>14 WB, 3 Draft, 2 TB, 2 QH</td>
<td>Hyperflexion</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Shivers-HF</td>
<td>21</td>
<td>9 WB, 5 Drafts, 5 TB, 1 Cross-breed, 1 Unknown</td>
<td>Hyperflexion</td>
<td>Hyperflexion, Intermittent, Abduction</td>
<td>Normal</td>
</tr>
<tr>
<td>Shivers-HE</td>
<td>6</td>
<td>1 WB, 5 Draft</td>
<td>Hyperextension</td>
<td>Hyperextension, Consistent</td>
<td>Normal</td>
</tr>
<tr>
<td>Shivers-FHF</td>
<td>4</td>
<td>1 WB, 3 TB</td>
<td>Hyperflexion</td>
<td>Hyperflexion, Consistent, Abduction</td>
<td>Hyperflexion, Intermittent</td>
</tr>
<tr>
<td>Stringhalt</td>
<td>7</td>
<td>2 WB, 5 TB</td>
<td>Normal to hyperflexion</td>
<td>Hyperflexion, Consistent</td>
<td>Hyperflexion, Consistent</td>
</tr>
</tbody>
</table>

HF = hyperflexion, HE = hyperextension, FHF = forward hyperflexion
Breeds: WB = Warmblood, Draft = of a Draft breed type, TB = Thoroughbred
Table 2: Mean area under the curve (AUC), peak vertical displacement (VDpeak), fraction of stride unit when VDpeak occurred and stride duration during forwards walking in controls and horses with movement disorders

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>AUC (cm²)</th>
<th>VDpeak (%)</th>
<th>Fraction of stride unit at VDpeak</th>
<th>Stride Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>9</td>
<td>2.74±0.67a</td>
<td>10.32±3.30a</td>
<td>0.75</td>
<td>1.28±0.15a</td>
</tr>
<tr>
<td>Shivers - HF</td>
<td>10</td>
<td>2.82±1.54a</td>
<td>10.64±4.77a</td>
<td>0.75</td>
<td>1.45±0.25a</td>
</tr>
<tr>
<td>Shivers - HE</td>
<td>10</td>
<td>2.14±0.76a</td>
<td>8.81±4.24a</td>
<td>0.75</td>
<td>1.29±0.15a</td>
</tr>
<tr>
<td>Shivers- FHF</td>
<td>4</td>
<td>19.32±4.54b</td>
<td>69.50±8.61b</td>
<td>0.88</td>
<td>2.43±0.53b</td>
</tr>
<tr>
<td>Stringhalt</td>
<td>7</td>
<td>9.21±5.80c</td>
<td>38.17±20.36c</td>
<td>0.75</td>
<td>1.63±0.77a</td>
</tr>
</tbody>
</table>

Different letters represent significant differences (p<0.05) within columns
HF= hyperflexion, HE = hyperextension, FHF = forward hyperflexion

Table 3: Mean area under the curve (AUC), peak vertical displacement (VDpeak), fraction of stride unit when VDpeak occurred and stride duration during backwards walking in controls and horses with movement disorders

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>AUC (cm²)</th>
<th>VDpeak (%)</th>
<th>Fraction of stride unit at VDpeak</th>
<th>Stride Time (s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>9</td>
<td>2.44±0.92a</td>
<td>10.68±6.02a</td>
<td>0.75</td>
<td>1.52±0.23a</td>
</tr>
<tr>
<td>Shivers - HF</td>
<td>10</td>
<td>7.51±3.02b</td>
<td>28.73±13.27c</td>
<td>0.75</td>
<td>1.68±0.54a</td>
</tr>
<tr>
<td>Shivers - HE</td>
<td>10</td>
<td>1.50±0.57a</td>
<td>7.99±2.10a</td>
<td>0.75</td>
<td>1.17±0.47a</td>
</tr>
<tr>
<td>Shivers- FHF</td>
<td>4</td>
<td>17.74±2.79c</td>
<td>59.10±16.73b</td>
<td>0.75</td>
<td>1.88±0.51a,b</td>
</tr>
<tr>
<td>Stringhalt</td>
<td>7</td>
<td>12.23±7.03b,c</td>
<td>46.42±21.78b,c</td>
<td>0.75</td>
<td>2.82±1.33b</td>
</tr>
</tbody>
</table>

Different letters represent significant differences (p<0.05) within columns
HF= hyperflexion, HE = hyperextension, FHF = forward hyperflexion
Figure 1: Demonstration of frame by frame video capture of a horse walking backwards during one stride unit. The right hind limb closest to the camera is analyzed for vertical displacement of the hoof during each fraction of the stride unit.
Figure 2: Method of calculation of maximum vertical displacement (VD_{max}) and vertical displacement (VD_{x}) of the left hind limb from each video frame. Measurements were made using a desktop ruler (iRule). VD_{max} was defined as the distance between the sternum and the ground (orange arrow). VD_{x} was defined as the distance between the ground at the heel and dorsum of the left hind hoof (green arrow). The percentage vertical displacement was defined as (VD_{x}/VD_{max}) \times 100.
**Figure 3:** The mean vertical displacement per fraction of a stride unit during backwards walking for control horses, horses with Shivers with hyperflexion (Shivers-HF), Shivers horses with hyperextension (Shivers-HE), Shivers horses with forward hyperflexion (Shivers-FHF) and Stringhalt horses.

Significant differences in area-under-curve (AUC) were recorded between Control/Shivers-HE and the Shivers-HF, Shivers-FHF and Stringhalt groups. The Shivers-FHF and Shivers-HF groups’ AUC were also significantly different.
Figure 4: The mean vertical displacement per fraction of a stride unit during forwards walking for control horses, horses with Shivers with hyperflexion (Shivers-HF), Shivers horses with hyperextension (Shivers-HE), Shivers horses with forward hyperflexion (Shivers-FHF) and Stringhalt horses.

Significant differences in area-under-curve (AUC) were recorded between Control/Shivers-HE/Shivers-HF and the Shivers-FHF and Stringhalt groups. The Shivers-FHF and Stringhalt groups’ AUC were also significantly different.
**Figure 5**: The mean vertical displacement per fraction of a stride unit during forwards walking for control horses, horses with Fibrotic Myopathy and one horse with upward fixation of the patellar (UFoP).
Chapter 2

Epidemiology of Shivers in Horses

Introduction

Shivers is an equine postural and movement disorder characterised by abduction, hypertonic flexion or extension and muscle tremors in the pelvic limbs induced by movement, especially walking backwards and with manual lifting of a limb [1, 2]. It can be unilateral or bilateral. Shivers signs can be intermittent and regarded only as a nuisance for farriers, whereas in other cases it progresses to a total inability to have the hind feet manually picked up, exaggerated limb flexion even when standing still or for the first few strides when walking forwards and serious impairment of performance [1]. Other movement disorders such as Stringhalt and fibrotic myopathy are clinically distinct from Shivers, however there is often confusion when distinguishing one from another as diagnosis is based on physical examination findings alone and overlapping signs may occur [1]. Shivers is an age-old disease, described “as common as dirt’ by a comparative neuropathology text from 1962 [3], however, most neurology textbooks [2, 4] only refer to Shivers in passing, and there has been limited research performed regarding the disease [1, 5].

Very little is known about the etiology of Shivers with the total body of contemporary English literature encompassing 4 peer-reviewed papers and a case-report [1, 5-8]. It has been proposed to have origins in both the musculoskeletal [7] as well as the central or
peripheral nervous system [2]. Remarkably, only one histopathologic study of the nervous system of Shivers horses has been published and this involved only two Belgian Draft horses using basic H&E light microscopy techniques [7]. No histologic lesions were identified in the nervous system, although polysaccharide storage myopathy (PSSM) was identified in skeletal muscle [7]. A subsequent study discounted PSSM as the sole basis for Shivers noting that two thirds of Belgian Draft horses with Shivers in the study of 103 horses lacked evidence of PSSM [5]. Trauma, particularly a fall and osteoarthritis, are proposed causes [5] as are infectious disease leading to neurologic damage [1]. A genetic basis was proposed in 1964 in Great Britain [9].

Individual case reports and reviews indicate that Shivers commonly affects Warmblood and Draft horse breeds and their crosses, carriage horses, Thoroughbreds and less frequently other lighter breeds [1]. Veterinarians have difficulty advising clients because there is no comprehensive information published regarding signalment, precipitating factors, age of onset, progression of signs, effective management and therapeutic strategies for Shivers. The variable progression of this disease makes recommendations during pre-purchase examination of horses suspected as suffering from Shivers challenging. An epidemiologic study thus is needed to define the disease, determine risk factors for Shivers and to provide information on which to base diagnosis, prognosis and management decisions.
The aims of this study was to report the signalment, age of onset of signs, management of horses with Shivers, management practices that could be associated with presence, progression or regression of clinical signs of Shivers.

**Materials and Methods**

**Case Selection:** Potential cases of Shivers were solicited through advertisements in national and international horse magazines and owners were directed to a web-based, closed-ended questionnaire on the University of Minnesota Equine Centre (UMEC) website (http://www.cvm.umn.edu/umec/shivers/home.html) (Appendix 1). Owners were asked to mail or upload a video of their horse being led in hand, walking forwards (FW), walking backwards (BW), circling (to the left and right) and while manual lifting of each limb for a minimum of ten seconds occurred. If questionnaires were incomplete or illegible they were not included in the analysis.

**Case definition:** The clinical definition of Shivers was established in Chapter 1. In brief the definition was; normal forwards walking and intermittent hypertonic flexion (Shivers-HF) or prolonged hypertonic extension (Shivers-HE) of the hind limbs induced by BW and by manual lifting of the hind limbs. Forward hyperflexion Shivers (Shivers-FHF) was defined as the same criteria for Shivers plus intermittent hypertonic flexion of a hind limb during FW, seen when the horse changed direction or after a period of standing still.
Cases were divided into three groups: 1) Confirmed Shivers (Confirmed S; both Shivers-HF and Shivers-HE) where horses were examined by one of the authors (Alex Draper or Stephanie Valberg) in person or by viewing the submitted video: 2) Suspected Shivers (Suspected S) where cases were diagnosed based on owner-reported clinical signs without video analysis or veterinary examination: and 3) Shivers-FHF for which cases were diagnosed based on owner-reported clinical signs or by veterinary examination from one of the authors (Alex Draper or Stephanie Valberg).

**Control Group:** The owners of the Confirmed S horses were asked to complete an additional questionnaire for 2-3 unaffected horses. The Control horses were not all owned by the owners of Confirmed S cases but were free of signs of Shivers or other movement disorders, were older than 4 years, and lived in close geographical proximity to the Shivers-affected horse. The case-controls were not age-matched. The Control questionnaire ([http://www.cvm.umn.edu/umec/shivers/home.html](http://www.cvm.umn.edu/umec/shivers/home.html)) was web-based and consisting of closed-ended questions pertaining to signalment, diet, use, previous illnesses or trauma and regular drug administration (Appendix 2).

**Epidemiological Survey:** The web-based questionnaire ([http://www.cvm.umn.edu/umec/shivers/home.html](http://www.cvm.umn.edu/umec/shivers/home.html)) included contact details and location, closed ended questions for signalment (breed, date of birth, height, gender, body condition) as well as specific clinical signs, precipitating factors, diet and management. The use of the horse was recorded and grouped as pleasure (pleasure/trail or retired), competition (dressage, hunter/jumper, showing, eventing or racing) or Draft work (farm
labour or carriage/pulling). Three breed groupings were established; 1) Draft, 2) combined Thoroughbred (TB) and Warmblood (WB) including their crosses and 3) Other (Connemara, Welsh breeds, Quarter Horses, Standardbreds, Saddlebreds, Tennessee Walking horses, Missouri Fox Trotters, Paint, Morgan and ‘mixed breed’).

Clinical Signs: The age when clinical signs of Shivers were first observed was recorded. The presence of perceived reduced strength, exercise intolerance, unexplained lameness, abnormal forward and backwards walking, difficulty with the farrier or with manual lifting of the hind limbs, forelimb involvement, twitching of the face or muzzle, muscle atrophy and muscle quivering were documented using closed ended questions and a comment box for additional information. Progression of clinical signs of Shivers was classified as improving, worsening or remaining static.

Precipitating factors: Factors that have been considered to possibly precipitate signs of Shivers such as aeroplane travel, major surgery, illness requiring hospitalisation or stall rest, abuse, neglect, trailer accident and long distance road transportation (>6hrs) were reported for the year preceding and subsequent to signs of Shivers developing. Neurological, gastrointestinal, endocrine and lameness problems were also recorded. Any deterioration in clinical signs following these potentially precipitating factors or illnesses were recorded as a percent from 0, 10, 25, 50 or 75%.

Diet and management: Current dietary information was recorded in terms of type of forage, commercial ration and weight of commercial ration fed per day. Supplements
added to the horses’ diet were classed as no supplements, selenium, vitamin E, joint supplement, mineral block, salt block, vitamin and mineral, electrolytes, hoof care, putative calming compounds and probiotic.

*Diet, management and activity changes:* Dietary and supplement therapies undertaken by owners were reported. Management changes including removal of hind-shoes or no farrier work on the hind limbs. Activity changes were described as either an increase or decrease in the following categories; riding/training, pulling/labour or turnout. Improvements in Shivers clinical signs associated with any such dietary, management or activity changes were reported as 0, 10, 25, 50 or 75%.

*Treatments:* Owners were also asked to list which treatments they had tried to alleviate signs of Shivers and if they had any effect. The following list of treatments was provided; acupuncture, chiropractics, herbs, flunixin meglumine, phenylbutazone, tranquilizers, muscle relaxers and phenytoin. A comments box was provided for additional treatments tried and any observed effects.

**Statistical Analysis:** Data was entered into a spreadsheet and all analyses were performed using R-Project for Statistical Computing. Categorical data from the Confirmed S, Suspected S and Shivers-FHF groups were compared by signalment, use, diet, stall time, age of onset, disease progression, previous trauma, clinical signs and treatments. The Confirmed S, Suspected S and Shivers-FHF groups’ data were either
compared using a One-way ANOVA (if continuous) or a Pearson’s Chi-square test or the Fischer’s Exact test (if categorical).

To compare the Confirmed S data to the Control horses, a Pearson’s Chi-square test or the Fischer’s Exact test was used where appropriate. Height was not normally distributed (Shapiro-Wilk Normality test) and so Confirmed S and Control data were compared by the Wilcoxon two-sample test. Breed, gender, height, use and stall time within the Confirmed S and Control groups were included in the multivariate logistic regression model to control for potential confounding influences. Significance was set at $P<0.05$.

**Results**

**Forward Hyperflexion, Confirmed and Suspected Shivers**

**Horses:** Questionnaires were completed for 305 horses and 70 videos were received. Based on the case definition, 157 horses were diagnosed with Shivers with 27 Confirmed S, 67 Suspected S and 63 Shivers-FHF. The majority of excluded horses showed an array of other gait abnormalities or difficulties solely involving holding up a limb. Nine of 157 horses were examined at UMEC (8 with Shivers-HF or Shivers-HE and 1 with Shivers-FHF).

*Signalment:* The mean age and height ($\geq 16.3$ hands in all three groups) were not significantly different among FHF, Confirmed and Suspected Shivers groups (Table 4).
The Shivers-FHF group contained more TB and WB breeds and fewer horses of Draft or Other breeds than the Confirmed S and Suspected S (p=0.01) groups (Table 4). A similarly high proportion of males to females (4:1) existed in all S groups (Table 4). In the three groups, the BCS of most horses was described as ideal or underweight. There was no significant difference in the age-of-onset amongst the three Shivers groups. The most commonly reported age-of-onset within each affected group was as follows; Shivers-FHF 2-4 years (40% - 25/63), Confirmed S 2-4 years (44% - 12/27) and Suspected 5-7 years (37% - 25/67).

**Management:** Use was not significantly different among the Shivers groups. Dressage was reported as the most common use in Shivers-FHF (21/63) and Confirmed S (8/27) groups, whereas pleasure/trail use was most common in Suspected S (24/67) cases. There was a bimodal distribution of stall time reported in all three affected groups with most owners reporting either <1hr/day or 8-12hr/day stall times.

**Clinical Signs of Shivers:** There was no significant difference amongst the three affected groups for any of the reported clinical signs. The most commonly reported signs were muscle twitching and muscle atrophy (Table 4). The Shivers-FHF group tended (p=0.07) to have reduced strength reported more frequently than in the other two Shivers groups (Table 4). Unexplained lameness and exercise intolerance were the least common clinical signs in all three groups. A high proportion of horses in all groups were difficult to shoe particularly involving the hind limbs (Table 4). Fifty-nine percent of all affected horses were reported to demonstrate tail-head elevation when backwards walking. Interestingly,
19% of horses in all three Shivers groups showed twitching of their face, lips or eyes during backwards walking (Table 4).

*Frequency and Progression of Shivers:* Frequency of clinical signs of Shivers occurred similarly across groups, with signs occurring most commonly on a daily basis as opposed to less frequently [Shivers-FHF 84% (53/63), Confirmed S 93% (25/27) and Suspected S 82% (55/67) signs occurring daily]. Fewer than 12% of horses in all three Shivers groups had signs less frequently than weekly. Most horses showed a progressive worsening of clinical signs over time (Table 4). Shivers-FHF (29%: 18/63) and Suspected S (37%: 25/67) groups had more horses whose clinical signs remained static over time compared to the Confirmed S group (7%: 2/27) (p=0.007). Six percent of Shivers-FHF (4/63), 11% of Confirmed S (3/27) and 16% of Suspected S (11/67) showed improvement in Shivers signs over time. Improvement was commonly reported after the horse was removed from a possible precipitating environmental factor or after recovery from a traumatic experience. No horse was reported to have a total resolution of signs. There was no significant effect of breed or type of precipitating factors on the progression of signs. Long distance transportation was the most commonly reported precipitating factor among the three affected groups, both preceding and occurring within 1 year of Shivers signs [Preceding: Shivers-FHF 10% (6/63), Confirmed S 15% (4/27) and Suspected S 13% (9/67) and within 1 year: Shivers-FHF 19% (12/63), Confirmed S 19% (5/27) and Suspected S 19% (13/67)]. Where any precipitating factors were experienced across all three affected-groups, 13-70% reported worsening, 24-40% reported no change and 3-7%
reported improvement in clinical signs. There was no significant difference in the illnesses noted among the three groups.

*Diet:* Amongst all three Shivers-affected groups mixed pasture or grass hay was the most commonly used forage type. The amount of concentrate feed fed per day was similar in all three Shivers groups. The percentage of horses that received concentrate feed daily, per group was: Shivers-FHF 38% (24/63), Confirmed S 48% (13/27) and Suspected S 37% (25/67). More Suspected S horses received supplementary dietary fat than the other two groups (p=0.03) [Shivers-FHF 33% (33/63), Confirmed S 22% (6/27) and Suspected S 46% (31/67)]. Significantly more Suspected S horses received hay cubes (p=0.0476) and significantly less received low starch/high fat feed (Re-leve) (p=0.01) compared to the other 2 affected groups. Also, significantly more Confirmed S horses received oats (p=0.01) compared to the other two groups. There were no other significant differences between the affected groups with regard to diet.

The most frequently reported categories of supplement given were vitamin E [Shivers-FHF 31.7% (20/63), Confirmed S 37% (10/27) and Suspected S 39% (26/67)], selenium [Shivers-FHF 16% (10/63), Confirmed S 22% (6/27) and Suspected S 34% (23/67)], a mineral or salt block [Shivers-FHF 86% (54/63), Confirmed S 82% (22/27) and Suspected S 100% (67/67)] and a joint supplement [Shivers-FHF 25% (16/63), Confirmed S 26% (7/27) and Suspected S 33% (22/67)]. The only difference was that significantly more Suspected S horses received selenium than the Confirmed S or Shivers-FHF groups (p=0.027).
Therapeutic Strategies Employed Following Shivers Diagnosis

Diet: The most commonly reported dietary changes, implemented after Shivers signs started in all three affected groups, were an increase in proportions of forage, fat/oil, vitamin E and selenium (Table 5) and a combination of increasing fat/oil and decreasing the simple sugars fed (oats, corn, sweetfeed). The highest percentage of horses that were reported to show improvement in signs was 48% of horses (across all Shivers horses) that received more fat/oil or forage. Increasing proportions of vitamin E or selenium resulted in 42% (all Shivers groups) showing an improvement (Table 5). Of those owners that reported combining an increased dietary fat/oil supplement with a reduction in the simple sugars fed 43% (13/30; all Shivers horses) reported an improvement of at least 50% in clinical signs (Figure 6).

Management: An increase in activity was instituted in 41% of Shivers horses (Table 5; Figure 6). Of these horses 67% showed some improvement. Of these 67%, the most common percentage improvement was 25-50%. Less than 10% in all three groups reported a worsening of signs when working under saddle or harness. Permanent removal of hind shoes or sedation for shoeing were the practices that made farrier work easier in 39% (62/157) of horses across all of the Shivers groups.

Treatments: Many treatments were given to all three affected groups. These included alpha-2 agonists (n=19), NSAIDs (n=46), muscle relaxants (n=12), phenytoin (n=1),
carbamazepine (n=1), gabapentin (n=1), and fluphenazine (n=1). Eight horses also received herbs, 27 acupuncture and 57 chiropractic attentions across groups. There was no consistent improvement reported for any treatment with the exception of the alpha-2 agonists that appeared to provide temporary cessation of the signs to facilitate farrier work on the hind limbs.

**Confirmed Shivers versus Controls**

*Signalment:* The mean age was 13.1 years for the Confirmed S and 10.5 years for the Control group. The Confirmed S group contained significantly more Draft and TB/WB breeds and fewer Other breeds compared to the Controls (p=0.002) (Table 6). The proportion of males: females was significantly higher (p=0.04) in Confirmed S (5.8:1 male: female) than in the Control group (1.6:1) (Table 6). There were 2 stallions and 25 geldings within the Confirmed S group. The mean height of the Confirmed S was significantly taller (p<0.0001) (173.1 ± 6.2 cm; ~17.0 hands) than the Control group (161.0 ± 10.3 cm; ~16.0 hands). Body condition was most commonly reported to be ideal for both Confirmed S and Controls. When breed, height and gender were considered together within a multiple logistic regression model height was the single significant predictor variable (p=0.006).

*Management:* Use (pleasure, competition or Draft work) was not different between Confirmed S and Controls. Dressage (8/27) was the most common use for Confirmed S and pleasure/trail riding (19/50) was the most common use for Controls. There was a
similar bimodal distribution for stall time in both the Confirmed S and Control horses of <1hr/day or 12-16hr/day.

Precipitating Factors: Precipitating factors preceding Shivers signs in the Confirmed S were compared to the Control group and no significant differences in the reported frequencies were noted (p=0.25). Long distance road transportation was the most commonly reported factor [Confirmed S 33% (9/27) and Control 32% (16/50)]. There was no significant difference between the illnesses reported by Confirmed S and Controls.

Diet: At the time of the survey, the most commonly reported forages received by both groups were mixed pasture [Confirmed S 59% (16/27) and Control 80% (40/50)] and grass hay [Confirmed S 70% (19/27) and Control 60% (30/50)]. There was no significant difference between the proportion of Confirmed S horses and Control horses receiving commercial grain or the amount of grain fed per day to these groups. Forty one percent (11/27) of Confirmed S horses received a commercial grain ration as did 58% (29/50) of Controls. Most commonly between 1-2.2kg was fed per day to Confirmed S (9/27) and Control (29/50) horses. Fat supplementation was provided to 5 out of 27 Confirmed S and 4 out of 50 Control horses. The Confirmed S group received vitamin E (10/27), selenium (6/27), a mineral or salt block (23/27) and a joint supplement (7/27) most commonly. The Control group most frequently received a joint supplement (12/50), mineral or salt (40/50) block. Only 2 out of the 50 Control horses received vitamin E and 4 out of the 50 Control horses received selenium suppletions. The Confirmed S horses received significantly more vitamin E supplementation than the Control horses
This was the only significant dietary difference between Confirmed S and Controls.

**Discussion**

Thirty one percent (94/305) of the cases of movement disorders submitted for the present study fitted our initial clinical definition of Shivers in which a movement disorder occurred with backwards walking. An expanded definition of Shivers-FHF that included the additional signs of occasional hypertonic flexion of pelvic limbs with forwards walking increased the number of horses with Shivers to 51% of submitted surveys. The definition was expanded because, in the authors’ experience, intermittent pelvic limb hypertonic flexion when turning sharply or initiating forwards walking has developed in Shivers horses we have followed over time. Thus, although such a movement bears comparison with another postural and movement disorder, Stringhalt, we believe the horses in the present study represented a group of horses with a more advanced stage of Shivers, involving hypertonic flexion of a pelvic limb when forwards walking. Although hypertonic flexion occurs with Stringhalt it is reported to occur consistently with each stride [10]. It is possible that some of the remaining 49% of submissions that only showed hyperflexion when lifting the hind limb had early signs of Shivers, however, these were omitted because other painful musculoskeletal conditions could not be ruled out. Nevertheless, many of the remaining submissions had a variety of other abnormal movements suggesting that many different movement disorders exist in horses that previously have been loosely interpreted as Shivers.
The results of the present study clearly indicate that Shivers is a chronic movement disorder with a predilection for horses over 16.3 hands tall. Within our logistic model, height was the only significant predictor of Shivers. It is possible that the greater height of Shivers horses was influenced by the fact that the affected breeds in the present study are taller than unaffected breeds. The strong influence of height on the development of Shivers also could be due to the fact that males are generally taller than females[11, 12], and predominated in the Shivers groups. In fact, four times more males than females were afflicted with Shivers, which surpassed the more balanced gender ratio in our control group. Such a gender bias has previously been reported for movement disorders such as hereditary spastic paraplegia (HSP) in humans where the male to female ratio is 1.7:1[13]. In HSP, the gender bias is believed to reflect a neuroprotective effect of oestrogen[14] that has been reported to augment retrograde neuronal transport[15]. If Shivers is an autosomal genetic trait and oestrogen is protective, the male bias could reflect the fact that the disease is more penetrant in males. A genetic basis for Shivers has been suggested previously and is supported by the strong breed predilection with largely Draft, Warmblood and Thoroughbred breeds being affected. The young age of onset of Shivers could support a genetic basis for Shivers. Over 40% of horses with Confirmed and FHF Shivers developing signs between 2 and 4 years of age and the majority of Suspected cases had an onset of 5-7 years. The later onset in Suspected S cases could be a result of the less stringent requirement for veterinary diagnosis in this group leading to inclusion of other movement or musculoskeletal disorders. At present, however, there is no firm data to support or disprove a genetic basis for Shivers. The present study would seem to
rule out infectious disease and trauma as causes of Shivers as they were not consistently a part of the history of Shivers horses.

Interestingly, there is another neurological disorder in horses that affects the same breeds, tall horses and is more prevalent in males. Recurrent laryngeal neuropathy (RLN) is a peripheral mononeuropathy commonly affecting proportionately more male Draft, Warmblood and Thoroughbred horses [16-20]. It results in a failure of abduction of the left arytenoid. Tall horses are believed to be particularly predisposed because of the extremely long length of the recurrent laryngeal nerve in these horses[21]. Thus, the high incidence of RLN in males and tall breeds is speculated to be due to the longer length of their peripheral nerves and the associated additional metabolic demands for maintaining longer axonal transport mechanisms. Others have suggested, however, that a genetic basis exists for RLN [22]. While a peripheral neuropathy affecting long peripheral nerves is also possible for Shivers cases, muscle biopsy findings and limited neuropathologic studies of Shivers cases have not identified neurogenic myofibre atrophy [23] or a peripheral neuropathy to support such a hypothesis [7, 8]. The only study of the central and peripheral nervous system of two Shivers horses did not identify neurologic lesions upon a thorough histopathologic examination with haematoxylin and eosin stains [7].

An equivalent frequency of potential precipitating factors such as long-distance travel, illness, abuse, minimal turnout and excessive or no exercise occurred in both the Shivers and Control groups. However, owners commented that such factors temporarily precipitated more severe Shivers signs in susceptible horses, which eventually were
followed by stabilization after removal of the precipitating factor. The finding that 6-16% of Shivers cases showed clinical improvement, across the 3 affected groups, was largely accounted for in owner comments as an improvement following abeyance of such factors. No owner reported a permanent improvement in signs over time, nor did anyone indicate that signs of Shivers ever disappeared. The finding that precipitating events cause a temporary worsening of Shivers signs is consistent with the authors’ personal observation of 6 of the horses in the present study that were donated to the University of Minnesota. Upon arrival after more than 4 hours of transport, these horses showed severe signs of Shivers, which improved within several days but did not disappear.

Owners of Shivers horses tried numerous treatment regimens to attempt to improve signs of Shivers. The most common dietary change was an increase in dietary fibre and fat, with close to half (48%) the owners who implemented this change, reporting some improvement in the disease. Originally, the reason why fat was added to the diet of Shivers horses was because of the misconception that Shivers was caused by PSSM [7]. Since many of the breeds affected with Shivers also have a high prevalence of PSSM, the addition of oil may relieve some of the myopathic signs caused by PSSM but probably have no effect on a probable neuropathic origin of Shivers signs [5, 23]. Another common dietary change was the addition of a Vitamin E supplement along with selenium. Vitamin E was likely provided in the hopes that it would have a neuroprotective effect [24]. Supplementation would, in general, be recommended if serum vitamin E deficiency is found.
Increased daily activity including increased turnout as well as riding/driving, were other strategies employed to attempt to stabilize signs of Shivers. Forty one percent of Shivers horses that underwent an increased exercise regimen were reported to show some degree of improvement in clinical signs. Increased activity could maintain muscle strength and could also reinforce essential neuronal connections through continued use, thereby potentially delaying progression of the disease. In spite of the best therapeutic attempts that owners could provide, overall, 60% of cases progressively worsened over time in the owners’ possession. In the Confirmed and Shivers-FHF groups, 64 and 74% of horses, respectively, showed progression of signs. Progression was less in the Suspected group at 43% possibly because of less stringent documentation of Shivers allowing for other disorders to be included. Bias might also exist in Shivers-FHF and Confirmed S groups in that these owners might have had veterinary examinations because their horses had progressive disease whereas owners in the Suspected S group could have been less concerned and may not have had a veterinary examination because their horse’s signs were not as severe or as progressive. In the few published reports of Shivers available, clinical signs are reported to commonly remain static for a period of time but ultimately progress to involve severe hind limb atrophy, reduced strength and hypertonic flexion [1]. In the present study, progressive signs of Shivers appeared to include intermittent hypertonia of the pelvic limbs for a few steps when walking forwards and in about one third of cases, a perceived reduction in strength and muscle atrophy. Of note were the 19% of Shivers horses, which showed signs of facial twitching while backwards walking. Such signs may indicate much more complex involvement of neural pathways than a peripheral neuropathy.
The results of the present study provide a refined clinical case definition of Shivers. Further, results show that Shivers is a gradually progressive chronic movement disorder that has a predilection for male horses of Warmblood, Thoroughbred and Draft breeds 17 hands tall and over. The case definition arising from the present study is that Shivers is an equine postural and movement disorder characterized by hypertonic flexion or extension of the pelvic limbs induced by backwards walking and manual lifting of the pelvic limbs and may include intermittent hypertonic flexion when turning sharply or walking forward. To diagnose Shivers, therefore, it is essential that backwards walking be included in the neurologic and lameness examination of horses. Further, backwards walking after a period of stall rest would be an important aspect of prepurchase examinations of Draft, Thoroughbred and Warmblood horses. The results of this study suggest that over time on average 60% of horses will show progressive clinical signs and the only significant means owners reported to modulate clinical signs was regular exercise and a low starch high forage diet supplemented with vitamin E. Shivers continues to be an economically important clinical syndrome in tall mature horses.
Table 4: Comparison of age, height, gender ratios, breed distribution and reported clinical signs within the three Shivers-affected groups [Mean ± SD reported].

<table>
<thead>
<tr>
<th>Clinical Parameter</th>
<th>All Shivers</th>
<th>Shivers FHF</th>
<th>Confirmed Shivers</th>
<th>Suspected Shivers</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>157</td>
<td>63</td>
<td>27</td>
<td>67</td>
</tr>
<tr>
<td>Age: Mean(yrs)</td>
<td>13.5 ± 5.3</td>
<td>13.6 ± 5.2</td>
<td>10.5 ± 4.6</td>
<td>14.3 ± 5.4</td>
</tr>
<tr>
<td>Median(yrs)</td>
<td>13.0</td>
<td>13.0</td>
<td>10.5</td>
<td>14.0</td>
</tr>
<tr>
<td>Height: Mean(cm)</td>
<td>170.5±9.1</td>
<td>169.6±10.5</td>
<td>173.1±6.2</td>
<td>169.6±8.4</td>
</tr>
<tr>
<td>Median(cm)</td>
<td>172.72</td>
<td>172.7</td>
<td>173.7</td>
<td>172.7</td>
</tr>
<tr>
<td>Male: Female ratio</td>
<td>127:30</td>
<td>53:10</td>
<td>23:4</td>
<td>51:16</td>
</tr>
<tr>
<td>(or 4.2:1)</td>
<td>(or 5.3:1)</td>
<td>(or 5.8:1)</td>
<td>(or 3.2:1)</td>
<td></td>
</tr>
<tr>
<td>Draft:WB+TB:Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>93%</td>
<td>92%</td>
<td>96%</td>
<td>91%</td>
<td></td>
</tr>
<tr>
<td>86%</td>
<td>88%</td>
<td>85%</td>
<td>85%</td>
<td></td>
</tr>
<tr>
<td>Elevated tail head</td>
<td>92/157:</td>
<td>32/63:</td>
<td>20/27:</td>
<td>40/67:</td>
</tr>
<tr>
<td>59%</td>
<td>51%</td>
<td>74%</td>
<td>60%</td>
<td></td>
</tr>
<tr>
<td>39%</td>
<td>38%</td>
<td>44%</td>
<td>34%</td>
<td></td>
</tr>
<tr>
<td>Weakness</td>
<td>52/157:</td>
<td>27/63:</td>
<td>9/27:</td>
<td>16/67:</td>
</tr>
<tr>
<td>33%</td>
<td>43%</td>
<td>33%</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Exercise intolerance</td>
<td>32/157:</td>
<td>15/63:</td>
<td>9/27:</td>
<td>8/67:</td>
</tr>
<tr>
<td>20%</td>
<td>24%</td>
<td>33%</td>
<td>12%</td>
<td></td>
</tr>
<tr>
<td>19%</td>
<td>22%</td>
<td>19%</td>
<td>16%</td>
<td></td>
</tr>
<tr>
<td>Progressed</td>
<td>49/157:</td>
<td>40/63:</td>
<td>20/27:</td>
<td>29/67:</td>
</tr>
<tr>
<td>60%</td>
<td>64%</td>
<td>74%</td>
<td>43%</td>
<td></td>
</tr>
</tbody>
</table>

*Significantly (p<0.05) fewer Draft horses and more WB +TB were in the Shivers-FHF vs. Confirmed or Suspected S groups
Table 5: Comparison of management changes implemented to attempt improvement in the signs of Shivers, and any associated improvements noted by the owners

<table>
<thead>
<tr>
<th>Management change</th>
<th>All Shivers</th>
<th>Shivers FHF</th>
<th>Confirmed Shivers</th>
<th>Suspected Shivers</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>157</td>
<td>63</td>
<td>27</td>
<td>67</td>
</tr>
<tr>
<td>Increased forage</td>
<td>18%</td>
<td>13/63: 21%</td>
<td>1/27: 4%</td>
<td>13/67: 19%</td>
</tr>
<tr>
<td>Improvement*</td>
<td>48%</td>
<td>10/13: 77%</td>
<td>0/1: 0%</td>
<td>3/13: 23%</td>
</tr>
<tr>
<td>Increased Fat</td>
<td>50%</td>
<td>33/63: 53%</td>
<td>10/27: 37%</td>
<td>36/67: 54%</td>
</tr>
<tr>
<td>Improvement</td>
<td>48%</td>
<td>21/33: 67%</td>
<td>4/10: 40%</td>
<td>13/36: 36%</td>
</tr>
<tr>
<td>Increased vitamin E</td>
<td>41%</td>
<td>29/63: 46%</td>
<td>9/27: 33%</td>
<td>27/67: 40%</td>
</tr>
<tr>
<td>Improvement</td>
<td>42%</td>
<td>12/29: 41%</td>
<td>3/9: 33%</td>
<td>12/27: 44%</td>
</tr>
<tr>
<td>Increased selenium</td>
<td>27%</td>
<td>15/63: 46%</td>
<td>4/27: 15%</td>
<td>24/67: 36%</td>
</tr>
<tr>
<td>Improvement</td>
<td>42%</td>
<td>10/15: 67%</td>
<td>0/4: 0%</td>
<td>8/24: 33%</td>
</tr>
<tr>
<td>Increased activity</td>
<td>41%</td>
<td>31/63: 49%</td>
<td>9/22: 41%</td>
<td>24/50: 48%</td>
</tr>
<tr>
<td>Improvement</td>
<td>69%</td>
<td>18/31: 58%</td>
<td>7/9: 78%</td>
<td>17/24: 71%</td>
</tr>
</tbody>
</table>

*Improvement: any level of improvement from 10 to 75% was included in these proportions
Table 6: Comparison of age, height, gender ratios and breed distribution between Confirmed Shivers cases and the Control group.

*** Significant difference across rows at P< 0.001

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Confirmed Shivers</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>27</td>
<td>50</td>
</tr>
<tr>
<td>Age: Mean (yrs)</td>
<td>10.5 ± 4.6</td>
<td>13.1 ± 6.5</td>
</tr>
<tr>
<td>Median (yrs)</td>
<td>10.5</td>
<td>12.5</td>
</tr>
<tr>
<td>Height: Mean (cm)</td>
<td>173.1 ± 6.2***</td>
<td>161.0 ± 10.3</td>
</tr>
<tr>
<td>Median</td>
<td>173.7</td>
<td>163.6</td>
</tr>
<tr>
<td>Gender ratio (M:F)</td>
<td>23:4 (or 5.8:1)</td>
<td>28:17 (or 1.7:1)</td>
</tr>
<tr>
<td>TB+WB (n/total n: %)</td>
<td>14/27: 52% **</td>
<td>22/50: 44%</td>
</tr>
<tr>
<td>Draft (n/total n: %)</td>
<td>11/27: 40% **</td>
<td>9/50: 18 %</td>
</tr>
<tr>
<td>Other (n/total n: %)</td>
<td>2/27: 8% **</td>
<td>19/50: 38%</td>
</tr>
</tbody>
</table>

** Significant difference across rows at P< 0.01

TB + WB = Thoroughbreds and Warmbloods
Other = all breeds not classified as Warmbloods, Thoroughbreds, Drafts or their crosses
**Figure 6:** The percentage of horses per Shivers group that reportedly showed an improvement of at least 50% in their clinical signs of Shivers with the associated management or dietary change. Figures above columns represent the number of owners reporting >50% improvement out of the total number reported to have tried the management or dietary changes. Horses with increased activity and increased vitamin E and selenium could have had concurrent dietary changes. Horses with increased forage did not have any other dietary modifications.
Conclusions

Historically there has been inconsistency in the definition of Shivers [1]. The majority of descriptions of Shivers indicate that signs are induced by walking backwards and when hind limbs are manually lifted [1-12]. Some authors, however, describe additional signs of Shivers as hyperflexion of one or both hind limbs [4, 5, 11-13], whereas others only describe elevation of the croup, tail elevation with quivering and muscle fasciculations over the hind quarters [3, 7, 14-16]. Confusion also arises in distinguishing Shivers and Stringhalt [17], fibrotic myopathy and upward fixation of the patella [1, 18]. The present research used video analysis of a large number of Shivers cases identified by owners or referring veterinarians and an epidemiological study to provide a better clinical definition of Shivers and to identify risk factors for Shivers.

The results of the present study clearly indicate that there are several movement disorders that are often classified as Shivers. One movement disorder that was distinguished from Shivers was termed a Hitch. Unlike Shivers, horses with a Hitch walk backwards normally but intermittently show mild hyperflexion of one or both hind limbs during forwards walking, when the horse is calm. Signs disappear when the horse is animated and when the limb is manually lifted.

A second group of horses had the sole sign of showing standing hyperflexion when the limb was manually lifted. This was termed standing-HF. Such horses walk forwards and backwards normally, however on manual lifting of one or both hind limbs there is
marked hyperflexion and in some instances abduction of that limb. These signs are shared with numerous painful conditions of the hind limb and thus were not considered pathognomonic for Shivers.

The definition of Shivers resulting from the present study necessarily included difficulty manually holding up the hind limbs and difficulty walking backwards. Two major groups were recognized. Shivers-HF is characterized by hyperflexion and abduction of the hind limbs. Shivers-HE is characterized by hyperextension and rigidity of the hind limbs when walking backwards to a point where the hind limbs can be ‘camped out’ behind and the horse cannot back-up. The vertical displacement of the hind limb is significantly higher for horses with Shivers-HF compared to Shivers-HE when walking backwards but both Shivers-HF and -HE horses walk forwards in a manner comparable to controls. Furthermore, both Shivers-HF and -HE can show croup and tail head elevation with quivering and muscle fasciculations and facial chorea during backwards walking. Signs Shivers-HF and HE can rarely affect the forelimbs [1].

Signs of Shivers can progress in Shivers-HF horses to involve hyperflexion and abduction of the hind limbs whilst walking forwards. Shivers-Forward Hyperflexion (Shivers-FHF) was used to describe this state. Shivers-FHF was characterized by severe hyperflexion and abduction of the hind limbs on almost every stride when walking backwards and during the first few strides or when quick directional changes occurred with walking forwards. Both forwards and backwards walking in Shivers-FHF is characterized by greater hyperflexion of the hind limbs than occurs with either Shivers-
HF or the movement disorder Stringhalt. Shivers-FHF cases also tend to have a significantly longer stride time, when first moving forwards, compared to Stringhalt and other Shivers-HF or –HE cases.

Rule outs for Shivers include Stringhalt, which upon walking backwards look very similar to Shivers-HF cases. Stringhalt, however, produces consistent hyperflexion of the hind limbs during forwards walking unlike Shivers-HF and FHF. Furthermore, when walking backwards, Stringhalt cases tend to have a longer stride time compared to normal, Shiver-HF, -HE, and -FHF horses.

The results of our epidemiological study indicated that there are certain factors that are common to Shivers horses. Signs of Shivers most commonly manifest themselves by the time a horse is 7 years old. Compared to control horses, Shivers-HF and –HE cases are more frequently male, tall (> 16.3hh) and of Thoroughbred, Warmblood or Draft breed types, although height was the only significant predictor variable within our logistic regression model. In at least half of Shivers horses clinical signs appear to progressively worsen over time. Diet, management factors and history of trauma or illness significantly associated with Shivers were not identified. Owners did not consistently report any therapeutic, dietary or management changes that resolve clinical signs completely, however providing regular exercise and turnout, and increasing forage, fat and supplementing vitamin E and selenium were reported by owners to reduce the severity of signs in some horses.
Limitations

In total there were over 300 hundred responses to questionnaires received, however only 70 videos were received in which owners completed a full dynamic display of their horses such that the authors could fully evaluate the horse for movement disorders. This led to relativity small numbers of Confirmed Shivers cases, however, it did allow for specific and consistent diagnosis of Shivers amongst these cases thus making the epidemiological data more reliable. A Suspected Shivers group was established to include those cases where owners described signs of Shivers compatible with either a diagnosis of Shiver-HF or Shivers-HE but a video was unavailable for review by the authors. Unfortunately, this may have impacted the accuracy of reported signs. Interestingly, however, this group did not have significantly different signalment, clinical signs or progression of signs from the Confirmed Shivers groups. Thus, signs of Shivers may be so distinctive during backwards walking that Shivers can easily be recognized by owners. The data for suspected cases was included as a separate group from Confirmed Shivers in our analysis and increased the overall number of Shivers cases.

Where there is no definitive diagnostic test available to identify a particular disease with 100% certainty there will always be the possibility of false positive and negative diagnosis. This is the inherent limitation with the diagnosis of Shivers as no ante or post mortem test is currently available to definitively identify truly affected cases. This means that the diagnosis relies entirely on veterinarians recognizing characteristic signs attributable to Shivers. This has been difficult to perform as there were no in-depth
studies available describing the entire extent of Shivers’ clinical signs. After a very thorough review of the literature available throughout the last 100 years, and after evaluating submitted videos of Shivers cases, two different Shivers phenotypes (Shivers-HF and –HE) were identified. Further it was recognized that additional signs are present when Shivers-HF progresses to Shivers-FHF. The results of the present studies should improve the reliability of Shivers diagnosis amongst practitioners, whilst awaiting a definitive antemortem diagnostic test.

A detailed kinematics study involving horses displaying Shivers and Stringhalt signs would have been superior to the basic video analysis performed. Errors were likely introduced by not being able to standardize the walking surface, walking speed, distance and angle from the camera. Unfortunately, it was not possible to have a large number of horses with movement disorders in one location where more sophisticated kinematics could be performed. To overcome this, video selection was stringent, and was based upon the best quality videos in which the horses were on an even surface and deemed parallel to the camera. Our basic analysis describing the vertical displacement of a hind limb over one stride highlighted significant differences among hind limb movement of Shivers phenotypes, Stringhalt and other lameness. The one-dimensional analysis (vertical displacement) used to describe the hind limb displacement in the present study was not able to describe another dimension that would have captured abduction of the limb. Abduction is an important aspect of the hind limb hyperflexion of Shivers-HF horses but likely not other movement disorders. Thus, a more complex kinematic analysis might have further distinguished Shivers, stringhalt and other lameness cases. To overcome this
limitation, gait abnormalities were subjectively described in addition to the objective analysis.

The definitions used to select horses for video analysis horses were based on an extensive literature review. Thus, in each case horses demonstrated very clear, classical signs of Shivers, Stringhalt, fibrotic myopathy and upward fixation of the patella. While this allowed for clear differences to be seen between the different movement disorders, it might not capture distinguishing features in mild cases or subtle cases of these movement disorders.

Although the Shivers-HF and –HE are both termed Shivers in the present study, it is possible that they represent two different disease processes that simply share certain clinical signs. The term Shivers will remain a clinical descriptor of difficulty walking backwards until the underlying etio-pathology(s) is identified. The authors suggest that these two presentations of ‘Shivers’ continue to be grouped under this heading for these reasons; 1) historically they have been recognized as variations of the same disease, 2) both phenotypes are induced by backing up and manually lifting of the limbs and 3) they share many similar signs such as tail head elevation, muscle fasciculations and facial chorea. The progression of signs were also similar between the two phenotypes.

Within the questionnaire responses received low numbers of owners reported having tried the same management changes decreasing the power of the study to detect actual differences. This limited the conclusions that could be drawn from these replies. The
percentage improvement in clinical signs of Shivers noted where a management or dietary change or a drug therapy had been trialed was also reported by the owners of the horse, and so the results will not be as reliable as if a clinical research project was conducted. The concerns regarding owner-reported information applies however to all questionnaires of this type and so are an inherent limitation of this study design.

**Further Work**

This epidemiological study, and consensus on definitions for hind limb movement disorders in horses is an excellent foundation for further research. This research needs to center upon finding the underlying etiology of Shivers, and other movement disorders such as Stringhalt (although more information is available regarding this [17, 19-21]). Possible directions that could be taken to further investigate the underlying etiology of Shivers include genetic studies to try and identify an underlying mutation producing the Shivers phenotype, histopathological studies to identify a lesion and location common to Shivers patients and thus providing a gold-standard diagnostic test. Once a gold standard test is available, possible ante-mortem tests could, hopefully, be developed to allow for differentiation of Shivers cases from other hind limb movement disorders; ideally even very early or mild cases.

As Shivers has been reported to affect families of related Draft breeds [1, 4, 15] pedigree analysis of these families may provide insight in to the pattern of inheritance of Shivers. This may also provide further epidemiological data regarding Shivers-HF and Shivers-
HE. The mode of inheritance is unlikely to be a simple Mendelian inheritance given that there is no published data showing affected stallions produce affected progeny. If related individuals are identified that have Shivers, collection of DNA from these individuals could then be used for more advanced genetic analysis to see if a mutation (s), causing Shivers could be identified.

Finding the lesion associated with Shivers will require very detailed, multi-organ system pathology studies involving necropsies of many horses that display very clear phenotypes that can only be attributable to Shivers-HF and Shivers-HE. It will be interesting to compare the lesions of Shivers-HF, and –HE to one another and then also see if they are comparable to other movement disorders affecting the hind limbs. Narrowing down a specific body system to be evaluated is difficult but fairly extensive work has been carried out to investigate if a myopathy underlies the signs and at present it does not appear to [4, 15, 22]. A neurological basis appears most likely given the induction of signs when the horse walks backwards, involvement of involuntary muscle fasciculations, tail quivering and facial chorea and spastic or hyperflexive nature of the gait abnormalities. Recently an underlying problem affecting the central pattern generators within the lumbosacral enlargement was postulated to be an area of interest for a possible lesion of Shivers [23]. Central pattern generators (CPGs) produce the rhythmic movement of the hind limbs, coordinating flexor and extensor contraction and relaxation, to produce a walking pattern [24-26]. There are thought to be CPGs for forwards and backwards walking in the pelvic and thoracic limbs that not only coordinate movement between thoracic limbs, say, but also between the thoracic and pelvic limbs (in
quadrupeds) [27, 28]. Thus, it seems plausible that if there is a lesion in the hind limb backwards walking CPGs potentially the characteristic signs of hyperflexion or hyperextension of the hind limbs, induced by backwards walking, may be seen if flexor and extensor coordination is disrupted.

If a lesion could be identified within the CPGs it would be very interesting to investigate the Shivers-FHF individuals to see if lesions within the forward CPGs could be identified, which could possibly explain the clinical signs. A prospective investigation in to the progression of the pathology would be interesting as well.

Although this study provided a solid foundation for differentiating many equine hind limb movement disorders from each other, controlled kinematics studies are needed to definitively and accurately identify the underlying differences between the many gaits displayed. Kinematic analysis that allows for gaits to be described in three dimensions would be preferable to make sure the abduction of the limbs etc., can be formerly described.

From the epidemiological data collected here it is very clear that there is a great need for therapeutic and management strategies that may help to at worst alleviate symptoms, or at best cure signs. Expanding this survey to institute consistent dietary trials in Shivers horses would make therapeutic recommendations more reliable. If controlled treatment trials of Shivers patients can be conducted, with a range of different medications (choosing those that could modulate neurological disease potentially), it may be possible
to make advancements in this area. Potential medications that could be trialed include phenytoin, gabapentin and carbamazepine, as these have all been historically used, with differing success levels in Stringhalt and other neurological problems in horse. If a drug was found that consistently improved Shivers signs this could also aid in identifying the underlying pathophysiology.
References


Appendix 1

Shivers Questionnaire
1. SHIVERS SURVEY

1. BASIC INFORMATION

Enter date: MM / DD / YYYY

2. Please enter the following horse owner information:

Name: 
Address: 
Address 2: 
City/Town: 
State: 
ZIP/Postal Code: 
Country: 
Email Address: 
Phone Number: 
Veterinarian's Name: 
Veterinarian's Phone Number: 

3. Veterinarian Information:

4. Horse Information:

Horse's Registered Name: 
Horse's Nickname: 
Horse's Year of Birth: 
Horse's Height: 

5. Horses' Gender:

- Female, Intact
- Female, Spayed
- Male, Intact
- Male, Castrated

6. Basic Information

What is Horse's Breed: 
Horse's Current Body Condition: 
What is Horse mainly used for: 
How much time does horse spend in stall, per day: 

For Horse: 
If Other breed, please enter here: 

[ ]
7. Was horse imported from another country?
   - Yes
   - No

If yes, from which country?

8. Is Horse Alive?
   - Yes
   - No

9. If NO, how did horse die?
   - [ ] Other, please describe here

10. Which of the following symptoms does the horse exhibit?

- [ ] Muscle Twitching
- [ ] Muscle Wasting/Atrophy
- [ ] Weakness
- [ ] Exercise Intolerance
- [ ] Unexplained Lameness

11. Symptoms
   - At what age did you first observe symptoms?
   - How frequently does horse exhibit symptoms?
   - What do the symptoms seem to be associated with?
   - How have the horse's symptoms progressed over time?

   For Horse's Symptoms:

   For Other, please enter additional information here

12. If FRONT LIMBS are affected, which leg is worse?

13. If HIND LIMBS are affected, which leg is worse?

14. Do horse's symptoms change when under saddle or harness?
### Shivers Research

**15. Additional Symptoms:**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>YES/NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does the TAIL elevate and tremble when horse is asked to back up?</td>
<td></td>
</tr>
<tr>
<td>Are the horse's FACE/LIPS/EYES affected?</td>
<td></td>
</tr>
<tr>
<td>Does the horse show any symptoms when asked to BACK UP?</td>
<td></td>
</tr>
<tr>
<td>Does the horse shown any symptoms when asked to move FORWARD?</td>
<td></td>
</tr>
<tr>
<td>Does the horse have trouble STANDING for the FARRIER?</td>
<td></td>
</tr>
</tbody>
</table>

**16. Which limb(s) does the horse have trouble standing on?**

- [ ] Right forelimb
- [ ] Left forelimb
- [ ] Right hindlimb
- [ ] Left hindlimb

If other, please describe here:

---

#### 3. HISTORY

**17. What STRESS did horse experience within ONE YEAR prior to onset of Shivers symptoms? (Choose all that apply)**

- [ ] Major Surgery
- [ ] Illness requiring Hospitalization
- [ ] Long distance transport (over 6 hours)
- [ ] Trailer accident
- [ ] Airplane Transport
- [ ] Illness requiring stall rest

If other, please describe here:

---

**18. What STRESS has horse experienced SINCE onset of Shivers symptoms? (choose all that apply)**

- [ ] Major surgery
- [ ] Trailer accident
- [ ] Long distance transport (over 6 hours)
- [ ] Illness requiring hospitalization
- [ ] Abuse/Neglect
- [ ] Airplane travel

If other, please describe here:

---

**19. Did symptoms change after the stress listed above?**

- [ ] Yes
- [ ] No
20. Did horse have NEUROLOGIC disease within ONE YEAR prior to onset of symptoms?
   - Yes
   - No

21. If yes, what specifically did the horse have?
   - [Input Field]

If other, please describe here:
   - [Input Field]

22. Did horse have GASTROINTESTINAL disease within ONE YEAR prior to onset of symptoms?
   - Yes
   - No

23. If yes, what specifically did the horse have?
   - [Input Field]

If other, please describe here:
   - [Input Field]

24. Did horse have ENDOCRINE/HORMONAL disease within ONE YEAR prior to onset of symptoms?
   - Yes
   - No

25. If yes, what specifically did the horse have?
   - [Input Field]

If other, please describe here:
   - [Input Field]

26. Did horse have LAMENESS within ONE YEAR prior to onset of symptoms?
   - Yes
   - No

27. If yes, what specifically did the horse have?
   - [Input Field]

If other, please describe here:
   - [Input Field]

4. CURRENT DIET
Shivers Research

### 28. What FORAGE(S) does horse currently receive? (choose all that apply)

- Mixed pasture
- Timothy
- Bermuda Grass
- Alfalfa

If other, please describe:

### 29. What CONCENTRATE(S) does horse currently receive? (choose all that apply)

- No concentrates
- Commercial ration
- Re-Leve
- Oats
- Corn
- Sweetfeed
- Fat/oil

If other, please describe:

### 30. Approximately how much concentrate does horse receive per day? (in pounds)


### 31. What SUPPLEMENT(S) does the horse currently receive? (choose all that apply)

- No supplements
- Selenium
- Vitamin E
- Joint Supplement
- Mineral block
- Salt block
- Electrolytes

If other, please describe:

### 5. TREATMENTS

### 32. Have you tried any DIET CHANGES to alleviate symptoms of Shivers?

- Increased forages
- Increased oats
- Increased sweetfeed
- Increased corn
- Increased commercial ration

- Increased Re-Leve
- Increased fat/oil
- Decreased forages
- Decreased oats
- Decreased sweetfeed

- Decreased corn
- Decreased commercial ration
- Decreased Re-Leve
- Decreased fat/oil

If other, please describe:

---

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Shivers Research

33. How effective were the diet changes at alleviating symptoms of Shivers?

34. Did you try any SUPPLEMENT CHANGES in order to alleviate symptoms of Shivers?
   - Increased Vitamin E
   - Increased selenium
   - Increased mineral block
   - Increased salt block
   - Increased electrolytes
   - Increased joint supplement
   - Decreased Vitamin E
   - Decreased selenium
   - Decreased electrolytes
   - Decreased mineral block
   - Decreased salt block
   - Decreased joint supplement

   If other, please describe here:

35. How effective were the supplement changes at alleviating symptoms of Shivers?

36. Did you try any ACTIVITY CHANGES to alleviate symptoms of Shivers?
   - Increased riding/training
   - Increased labor/pulling
   - Increased turnout
   - Decreased riding/training
   - Decreased labor/pulling

   If other, please describe here:

37. How effective were the activity changes at alleviating symptoms of Shivers?

38. Please describe any SURGERY you tried to alleviate symptoms of Shivers:

39. How effective was the surgery at alleviating symptoms of Shivers?

40. Have you tried any MEDICATIONS in order to alleviate symptoms of Shivers?
   - Xylazine
   - Banamine
   - Muscle relaxer (ie Robaxin)
   - Bute
   - Phenytoin
   - Tranquilizer
   - Herbs
   - Other

   If herbs or other, please describe here:
41. How effective were the medications at alleviating symptoms of Shivers?

42. Please describe any SHOEING CHANGES you tried to alleviate symptoms of Shivers:

43. How effective were the shoeing changes at alleviating symptoms of Shivers?

44. Please describe any CHIROPRACTIC you tried to alleviate symptoms of Shivers:

45. How effective was chiropractic at alleviating symptoms of Shivers?

46. Please describe any ACUPUNCTURE you tried to alleviate symptoms of Shivers:

47. How effective was acupuncture at alleviating symptoms of Shivers?

6. FURTHER INFORMATION

48. FURTHER INFORMATION

- Do you know of any related horses with similar symptoms? [ ] Yes [ ] No
- May we contact you for further information? [ ] Yes [ ] No
- Would you be interested in participating in future studies? [ ] Yes [ ] No

If you have any further details about your horse or comments on the survey, please let us know here:
Appendix 2

Shivers Control Questionnaire

<table>
<thead>
<tr>
<th>Shivers Control Survey</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Shivers Study; Owner’s Details</strong></td>
</tr>
<tr>
<td>1. Please enter the following information:</td>
</tr>
<tr>
<td>Name:</td>
</tr>
<tr>
<td>Email Address:</td>
</tr>
<tr>
<td>Phone Number:</td>
</tr>
</tbody>
</table>

| **Shivers Study; Shivers Control Horse 1; Basic Information** |
| Please fill in the following basic information about ONE NORMAL horse, that is FOUR YEARS OLD OR MORE AND LIVES WITHIN 1-2 MILES OF YOUR HORSE WITH SHIVERS. |
| Please DO NOT fill this questionnaire in regard to your horse with SHIVERS. |
| 2. Please fill in the following information for Shivers Control Horse 1. |
| Name: |
| Registered Name: |
| Year of Birth: |
| Height (in hh): |

<p>| <strong>3. Please fill in the following information.</strong> |</p>
<table>
<thead>
<tr>
<th>Breed</th>
<th>Body Condition</th>
<th>What is the horse’s main use?</th>
</tr>
</thead>
<tbody>
<tr>
<td>For Horse 1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>4. Was the horse imported?</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Yes</td>
</tr>
<tr>
<td>☐ No</td>
</tr>
</tbody>
</table>

If yes where from? |

<p>| <strong>Shivers Study: Shivers Control Horse 1; Management and Diet</strong> |
| Please answer the following questions in relation to the management and diet of this horse. |</p>
<table>
<thead>
<tr>
<th>5. On average how many hours per day is the horse in a stall or stable?</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Less than 1 hour</td>
</tr>
<tr>
<td>☐ 1-4 hours</td>
</tr>
<tr>
<td>☐ 5-8 hours</td>
</tr>
<tr>
<td>☐ 9-12 hours</td>
</tr>
<tr>
<td>☐ 13-16 hours</td>
</tr>
<tr>
<td>☐ 17-20 hours</td>
</tr>
<tr>
<td>☐ More than 21 hours</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6. When not stalled or stabled, what does the horse have access to? (Check all that apply)</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Pasture</td>
</tr>
<tr>
<td>☐ Dry Lot</td>
</tr>
<tr>
<td>☐ Arena - Indoor or Outdoor</td>
</tr>
<tr>
<td>☐ Other</td>
</tr>
<tr>
<td>☐ Other (please specify)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>7. What forage does the horse receive? (Check all that apply)</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ Mixed pasture/grass</td>
</tr>
<tr>
<td>☐ Timothy Hay</td>
</tr>
<tr>
<td>☐ Bermuda Grass</td>
</tr>
<tr>
<td>☐ Alfalfa Hay</td>
</tr>
<tr>
<td>☐ Hay Cubes</td>
</tr>
<tr>
<td>☐ Oat Grass</td>
</tr>
<tr>
<td>☐ Mixed grass hay</td>
</tr>
<tr>
<td>☐ Other</td>
</tr>
<tr>
<td>☐ Other (please specify)</td>
</tr>
</tbody>
</table>
### Shivers Control Survey

8. **What concentrates does the horse receive? (Check all that apply)**

- [ ] Oats
- [ ] Re-Leve (For PSSM/EPSM/Tying Up)
- [ ] Corn
- [ ] Sweetfeed
- [ ] Fat/Oil
- [ ] Commercial Ration

Commercial Ration Name

9. **How much total concentrate ration does the horse receive per day (in lbs)?**

10. **Which supplements does the horse receive? (Check all that apply)**

- [ ] None
- [ ] Selenium
- [ ] Vitamin E
- [ ] Joint Supplement
- [ ] Mineral Block
- [ ] Salt Block
- [ ] Electrolytes
- [ ] Devil’s Claw (No-Bute)
- [ ] Ration Balancer
- [ ] Other

Other (please specify)

### Shivers Study: Shivers Control Horse 1: Medical History

Please fill in the following questions relating to the horse's medical history.
### Shivers Control Survey

#### 11. Has your horse ever had or experience any of the following: (Check all that apply)
- [ ] Major Surgery
- [ ] Illness requiring hospitalization
- [ ] Illness requiring stall rest
- [ ] Trailer Accident
- [ ] Long Distance Travel (over 6 hours)
- [ ] Airplane Transport
- [ ] Abuse/Neglect
- [ ] Other: 
  - Other (please specify)

#### 12. Has the horse ever had any of the following neurological problems? (Check all that apply)
- [ ] Wobbler's Syndrome/Cervical Vertebral Malformation
- [ ] Trauma leading to Neurological Signs
- [ ] Equine Herpes Myeloencephalitis
- [ ] Anaplasmosis (Equine Granulocytic Disease)
- [ ] Viral Encephalitis (EEE/WEE/VEE)
- [ ] Equine Protozoal Myelencephalitis (EPM)
- [ ] Spinal Abscess
- [ ] West Nile Virus (WNV)
- [ ] Bacterial Meningitis
- [ ] Roaring (Recurrent Laryngeal Neuropathy)
- [ ] Other
  - Other (please specify)
Shivers Control Survey

13. Has the horse ever had any of the following lameness problems and if so which group of limbs did it affect? (Check all that apply)

<table>
<thead>
<tr>
<th>Problem</th>
<th>Forelimb</th>
<th>Hindlimb</th>
<th>Never Experienced</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laminitis/Founder</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Limb Fracture</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tendon/Ligament Injury</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tendonitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stifle Injury</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pelvic Trauma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stringhalt</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spavin - Bone or Bog</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteochondrosis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (please specify)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

14. If your horse had a significant lameness issue, please provide details about the treatment and whether the lameness resolved.

[Blank space for details]

15. Has the horse ever been diagnosed with any of the following endocrine or hormonal problems?

- [ ] Equine Cushings’ Disease (Pituitary Pars Intermedia Dysfunction)
- [ ] Equine Metabolic Syndrome/Insulin Resistance
- [ ] Hypothyroidism
- [ ] Other

Other (please specify)
16. Has the horse ever been diagnosed with any of the following muscle diseases or disorders? (Check all that apply)

- Polysaccharide Storage Myopathy (PSSM/EPSPM)
- Recurrent Exertional Rhabdomyolysis (RER)/Tying Up
- Hyperkalemic Periodic Paralysis (HYPP)
- White Muscle Disease (Low Selenium/Vitamin E)
- Vitamin E Responsive Muscle Atrophy and Weakness
- Pasture or Atypical Myopathy
- Other

Other (please specify)

17. Has the horse ever suffered from any of the following gastrointestinal disorders? (Check all that apply)

- Diarrhea/Colitis
- Gastric Ulceration
- Parasitism
- Liver Disease
- Right Dorsal Colitis
- Colic
- Other

Other (please specify)

18. Has the horse been diagnosed with any other medical condition?
Shivers Control Survey

19. Does the horse receive any medications on a routine basis? (Check all that apply)

☐ Phenylbutazone (Bute)
☐ Flunixin meglumine (Banamine)
☐ Firocoxib (Equioxx or Previcox)
☐ Muscle Relaxant (eg Robaxin)
☐ Phenytoin
☐ Pergolide (Cushing’s Therapy)
☐ PSGAGs/Hyaluronan (Adequan or Legend)
☐ Omeprazole (Gastrogard or Ulcergard)
☐ Other

Other (please specify)

Shivers Study; Shivers Control Horse 1; General Questions

Please answer the following questions about the horse.

20. Does the horse have any problems with farriery work of the forelimbs/front limbs (ie does the farrier struggle to either trim or shoe the forelimbs/front limbs)?

☐ Yes
☐ No

If yes please describe below
Shivers Control Survey

21. Does the horse have any problems with farriery work to the hindlimbs/back feet (ie does the farrier have any problems trimming or shoeing the hindlimbs/back feet)?

- Yes
- No

If yes please describe the issues below

22. Does the horse back-up normally?

- Yes
- No

If no please describe the abnormalities seen below

23. Does the horse exhibit any of the following signs? (Check all that apply)

- Muscle Twitching
- Muscle Atrophy or Wasting
- Unexplained lameness
- Weakness
- Exercise Intolerance

Thank you for filling out these questions for Control Horse Number 1, now you will be asked the same questions but for Control Horse Number 2.

This questionnaire was repeated for the second Control horse.