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Cover photo by Dr. Ruth Sobeck.
From the President: Changing the industry's medication culture

By Jeffrey T. Berk, VMD, MRCVS

The AAEP faces many challenges communicating the many initiatives the association is pursuing at any given time. From designing more innovative ways to present continuing education to studying and influencing a multitude of equine industry and public policy issues, the association's plate often overflows with worthy endeavors. The need is greater now more than ever to communicate with you, our members, about the many opportunities and challenges the AAEP is involved with. Often a little bit of background information can be helpful to better understand a direction that the AAEP may be heading. There are a couple of issues that have recently risen to a level of increased focus: medication and ethics.

In February 2018, the AAEP Welfare & Public Policy Advisory Council, along with the association’s officers and staff, conducted a planning meeting to strategically discuss the many important equine welfare issues and narrow the Council’s focus to a short list of key issues for which the association has a chance to make an impact during the next three to four years. In this facilitated meeting, using membership surveys as a guide and incorporating comments from previous work, the group individually ranked a myriad of issues using four metrics:

- Impact to the horse
- Impact on membership (veterinarian)
- Impact to the public (real or perceived)
- Realistic ability to make a difference on this issue

Based on this discussion and rankings, the overuse and/or misuse of therapeutic medication emerged as the highest-ranked issue.

Historically, the topic of what constitutes appropriate therapeutic medication has been studied and debated extensively within the AAEP in the Performance Horse, Racing, and Professional Conduct & Ethics committee meetings, as well as in forums pertaining to horse sales. As the result of the Welfare & Public Policy Council’s meeting, medication is now ranked as the primary issue of concern regarding equine welfare. A task force has been assembled to study the issue from all angles, with the goal being to promote the appropriate use and discourage the overuse and misuse of medications.

There is an obvious overlap between medication use and the ethical considerations and ramifications of said use. Because of the chronicity of the issues surrounding medication use, the AAEP has at times been criticized for not doing enough. It has to be remembered that the AAEP is a member association and not a regulatory or governing body, and as such has no power of enforcement. The tactics used by this Medication Task Force will include the review and expansion of existing guidelines and then partnering with the various breed- and discipline-specific organizations and other industry stakeholders that have the power of enforcement. Other pieces will include education of veterinarians and mentoring of younger associate veterinarians. To frame the discussion properly, some key points are readily found in the AAEP Resource Guide:

- Regarding the medication of horses, the welfare of the horse is the primary consideration.
- It is in the best interest of horses to, when appropriate, therapeutically address any health concerns of the horse based upon a veterinary examination and any diagnostic means necessary to make an accurate diagnosis.
- Rest is an important component of addressing health concerns for horses and should always be discussed when therapeutic medication is being employed.

The culture of inappropriate use of medication is a culture which veterinarians, trainers and their employees, judges, owners, consignors and sales companies have contributed to and participated in over a long period of time, and it will require time and effort to create a healthier culture. Having received many phone calls and letters from equine veterinarians in every discipline who are frustrated by frequent pressure to overmedicate or inappropriately medicate horses and the subsequent undermining of ethical equine practice, it’s evident that the time has come for the AAEP to focus on medication and to reverse an unhealthy trend with the help of all stakeholders.
AAEP revises positions on use of vesicants and thermocautery

At its January meeting, the AAEP board of directors approved recommendations from the Racing Committee revising the AAEP’s positions on the use of vesicants and the use of thermocautery or pin firing. The AAEP, which previously supported conditional use of both therapies, no longer supports the use of either practice.

Following are the revised position statements:

**Position on the Use of Vesicants**
The AAEP does not support the use of vesicants in the management of musculoskeletal disorders and finds no scientific evidence to validate their use in the horse.

**Position on Thermocautery or Pin Firing**
When applied judiciously and in conjunction with appropriate analgesia and aftercare, thermocautery or pin firing has been considered an acceptable therapeutic modality for specific conditions in the horse. With the advent of current science-based procedures to treat specific musculoskeletal conditions in the horse, the AAEP no longer supports the use of thermocautery or pin firing.

These and all other AAEP position statements are accessible through the “Ethical and Professional Guidelines” drop-down menu at aaep.org/guidelines.

Let’s go to the replay: Access convention session recordings

If you couldn’t make it to the AAEP’s 64th Annual Convention in San Francisco or were unable to attend a session due to a schedule conflict, you can download archived recordings of all educational sessions except Table Topics at aaep.digitellinc.com/aaep.

Click the “On Demand” button and then select “AAEP Annual Convention 2018” to choose the session(s) you are interested in. There is a fee to download videos and audio; convention attendees received complimentary access to all recordings until March 7.

Additional information about this service is available by contacting the AAEP at (859) 233-0147. Tech support questions should be directed to Digitell at (877) 796-1325.
Hey Siri, where’s my membership directory?

If in years past you received the AAEP’s annual Resource Guide and Membership Directory bundled with your March issue of EVE, you probably noticed something amiss when this issue arrived in your mailbox: the AAEP has discontinued its print membership directory.

The directory has traditionally been published at a substantial expense, both financial and in terms of the staff resources and man-hours necessary to compile, edit and proof the 400-page publication. Moreover, the accuracy of the membership listings diminished as members updated their contact information throughout the year. If you relied on the directory to look up fellow members, you can visit aaep.org to access a membership search that is continually updated so that you are always looking at the most current information. Just click the orange “My Member Profile/Benefits” button at the top of the home page and then select “Membership Directory” in the navigation bar on the ensuing page. Member lookup is also available through the AAEP Publications App.

Ethical and professional guidelines, council and committee listings, and most other membership directory content can be found on the AAEP’s website.

Students and new grads: Submit case study for chance at convention trip

PowerPoint submissions due May 1

AAEP student members and recent graduates in their first year of practice or internship can win complimentary registration and a $500 travel stipend to attend the AAEP’s 2019 Annual Convention in Denver, Colo., by submitting a case presentation to be featured as an educational resource on the AAEP’s website.

Presentations must be submitted in PowerPoint. There is no limit to the number of case studies that may be submitted; however, a primary student or first-year graduate author must be identified for each submission. Submissions will be evaluated by members of the Educational Programs Committee and selected based on quality and educational merit. Participants are encouraged to work with mentors in the preparation and review of their submissions. Past case studies are available through the “Case Studies” button at aaep.org/students.

Instructions and a case study template may be requested from Carey Ross, scientific publications coordinator, at cross@aaep.org. Submissions are due May 1, and winners will be announced by Sept. 6.

Reward a difference maker with an AAEP award nomination

“If you’ll not settle for anything less than your best, you will be amazed at what you can accomplish in your lives.” —Vince Lombardi

Recognize the excellence of a colleague by nominating that individual for a 2019 AAEP award. The nomination deadline is June 1, and winners will be announced and recognized during the President’s Luncheon at the AAEP’s 65th Annual Convention in Denver, Colo., Dec. 7–11.

Nominations are being accepted in the following categories:

- AAEP Research Award
- Distinguished Educator – Academic Award
- Distinguished Educator – Mentor Award
- Distinguished Life Member Award
- Distinguished Service Award
- George Stubbs Award
- Sage Kester Beyond the Call Award
- The Lavin Cup (The Equine Welfare Award)

Visit aaep.org/about-aaep/annual-awards for nomination forms as well as additional information about the awards and selection process. You may also request a nomination form from Sue Stivers at sstivers@aaep.org or (859) 233-0147.
Immerse in ophthalmology, sports medicine at summer Focus Conference

**SUMMER FOCUS**

**Conference & Labs**

Create or expand your niche in care of the equine eye or improve your management of problematic lameness cases by taking a full-circle approach to these topics through didactic lectures and hands-on wet labs at the AAEP's Summer Focus Conference & Labs.

The conference will be held July 29–31 at Colorado State University in the C. Wayne McLwraith Translational Medicine Institute, a sophisticated research facility opened in the fall of 2018. Profiles of the two veterinary tracks follow.

**TRACK 1  Ophthalmology**

Ophthalmic diseases are common in the horse, but many of these conditions can escalate quickly and threaten a horse’s vision and utility without prompt and appropriate veterinary care. You see what you know, and the Ophthalmology track will increase your knowledge of the horse eye and its afflictions. You’ll learn how to assess and treat prevalent equine eye diseases, including corneal abrasions, corneal ulcers, immune mediated keratitis, equine recurrent uveitis, nonimmune mediated uveitis, glaucoma, cataracts, retinal lesions and ocular neoplasia. You’ll also be equipped to manage potential complications and determine when to refer a case.

**Practical takeaways:**
- Performing a thorough ophthalmic examination with basic instrumentation
- Identifying, diagnosing and treating common ophthalmic diseases
- Understanding the significance of cataracts and retinal lesions as related to vision and pre-purchase examination
- Performing basic ocular surgery
- Handling complications when cases go awry

**Two half-day, optional wet labs** will provide hands-on training in the procedures and treatments presented during lecture sessions. In small groups, wet lab participants will:
- Perform a complete ophthalmic exam, including nerve blocks, on live horses;
- Place a SPL system, flush the nasolacrimal duct, and collect cytology from the cornea on cadaver heads
- Perform surgical procedures such as eyelid wedge, conjunctival biopsy, corneal suturing, third eyelid removal and enucleation on cadaver heads
- Work up cases under the microscope using cytology and pathology slides from different ophthalmic diseases

You’ll return to practice with an improved recognition of eye diseases, a thorough understanding of when and how to intervene, and the skills to confidently expand your ophthalmology services to clients.

**Presenters:** Lectures and wet labs will be led by an international team of board-certified veterinary ophthalmologists and recognized experts from academia and private practice:

- Dr. Dennis Brooks
- Dr. Michala de Linde Henriksen
- Dr. Andrew Matthews
- Dr. Catherine Nunnery
- Dr. Caryn Plummer
- Dr. Kathryn Wotman

**CE Hours:** Lectures – 16; Lectures + Labs – 24
Whether you have clients who show English sport horses, compete in Western performance disciplines, or you simply have an interest in lameness, the Sports Medicine track will provide an all-inclusive approach to unraveling mysteries of lameness and poor performance. You’ll refine your diagnostic workup, acquire treatment therapies and explore the rapidly growing field of equine rehabilitation to expedite recovery.

Practical takeaways:
- Improving imaging and diagnosis of conditions in the distal limb, suspensory, hocks, stifle and axial skeleton
- Incorporating acupuncture and chiropractic into diagnosis and treatment
- Treating and rehabilitating conditions of the foot and suspensory
- Exploring treatment of joint disease with newer therapies such as stem cells, autologous conditioned protein, polyacrylamide gel and next-generation IRAP
- Integrating physical therapy and rehabilitation techniques into a horse’s home program

Two half-day, optional wet labs using live horses will provide hands-on training in the procedures and treatments presented during lecture sessions. For each small-group wet lab session, participants will select one of two paths:

**Session 1**
- (a) Diagnostic Imaging Lab focused on the stifle, suspensory ligament, neck and other body regions, *or*
- (b) Manual Therapies Lab focused on chiropractic, acupuncture and kinesiotaping techniques

**Session 2**
- (a) Lameness Lab focused on complete workup of a clinical lameness case, *or*
- (b) Physical Therapy/Rehabilitation Lab focused on therapeutic exercises, physical therapy modalities and proprioceptive devices.

You’ll leave the meeting with an improved skill set to efficiently manage lameness cases from discovery through recovery, diminishing the inclination or need to refer to a hospital or rehabilitation facility.

**Presenters:** Lectures and wet labs will be led by a distinguished team of practicing clinicians—including several chiropractic and rehabilitation authorities—from both private practice and from Colorado State University, which is at the forefront of equine orthopedics:

- Dr. Myra Barrett
- Dr. Sharon Classen
- Dr. Erin Contino
- Dr. David Frisbie
- Dr. Kevin Haussler
- Dr. Tim Holt
- Dr. Brad Jackman
- Dr. Sherry Johnson
- Dr. Chris Kawcak
- Dr. Melissa King
- Dr. Katie Seabaugh
- Dr. Kurt Selberg
- Dr. Melinda Story

**CE Hours:** Lectures – 15; Lectures + Labs – 23

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**Wet lab attendance is limited; register early!**

Wet lab attendance is capped at 40 for ophthalmology and 60 for sports medicine. Those who do not participate in wet labs can join with colleagues for optional group excursions in and around Fort Collins.

**Registration will open by late March at aaep.org/meetings.**
Sunshine, sports medicine served daily at Resort Symposium

With much of the United States firmly in the throes of the polar vortex in late January, 106 practitioners recharged under warm sunshine on Costa Rica’s Pacific coast at the AAEP’s 21st Annual Resort Symposium.

Three half-day educational sessions featured a new case-based format incorporating small-group breakouts and increased interaction among attendees and instructors. The engagement helped instill appropriate diagnostics and treatments for many of the afflictions causing poor performance in their clients’ athletic horses.

If the prospect of mid-winter continuing education served with a heaping side of soft sand and spectacular sunsets is something you might enjoy, make plans to join us Jan. 23–25, 2020, on the Caribbean island of Aruba for the 22nd Annual Resort Symposium. Additional information about the meeting will be announced later this year.

The AAEP thanks Boehringer Ingelheim and IDEXX for their sponsorship of the 21st Annual Resort Symposium and ongoing support of equine continuing education.

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- **The Healing Touch**
  To provide better care to your patients

- **The Personal Touch**
  To build stronger client relationships

- **Touch Points**
  To deliver the services your clients value most

[mysector-aaep-touch](touch.aaep.org)
Just a year after assisting animal relief efforts during the Santa Rosa Fires while an associate at a group practice in Sonoma County, Calif., Dr. Saralynn Specht found history repeating itself in November 2018.

Dr. Specht moved to Butte County, Calif., last May to start her own large animal mobile practice while also working part time at a small animal clinic to help fund her business. As her client roster expanded, the Camp Fire ignited in early November in what would become the most destructive wildfire in the state’s history.

When hearing that horses were being evacuated to the Butte County Fairgrounds, just four miles from her residence, Dr. Specht drove to the fairgrounds to examine its new residents. The fairgrounds soon became a major evacuation center for animals in peril and remained in that capacity until January. To the potential detriment of her growing solo practice, Dr. Specht suspended her business to shoulder a full-time volunteer role triaging and caring for evacuated animals, which numbered hundreds of horses, chickens, goats and sheep, as well llamas, alpacas, pigs and water fowl.

“It was hard,” she said. “I canceled all my appointments and pretty much let my business just tank. There was a time when I thought I made a huge mistake moving here and doing this. I had already bought all my equipment to set up my practice and I just let it go until I started back up in January when I could take appointments.”

Working around her schedule at the small animal clinic, Dr. Specht checked the evacuated animals in the mornings before returning in early afternoon and often working late into the evening treating facial and foot burns, trauma wounds, colic and dehydration. Severe cases were triaged and sent to UC Davis for treatment before returning to the fairgrounds for recovery. She even rehomed a severely burned goat for owners who lost everything in the fire.

“It was wonderful to meet the owners of these animals when we were able to reunite everybody,” she said. “Hearing these people’s stories, it really touches you. They’ve lost everything else but for them to find their animal, it means so much to them. I think it gave the community a sense that plenty of people care for them.”

Beyond providing compassionate care, Dr. Specht also worked with local home improvement stores to donate plywood, gates and other necessities; persuaded several farmers to donate their utility vehicles so volunteers could move around the fairgrounds faster; and established a GoFundMe that raised more than $2,000 for a gasoline generator. She distributed remaining funds to several families who needed money for a place to stay.

Dr. Specht is quick to acknowledge those who ran the evacuation site; her many fellow volunteers; veterinary companies that donated medication and supplies; and the Northern California Association of Equine Practitioners, which established a volunteer schedule to relieve the heavy burden on Dr. Specht and another veterinarian who had been working at the fairgrounds every day the first few weeks of the disaster.

“Many of us volunteered at various times, but Dr. Specht gave generously of her time when others, including myself, could not,” said Dr. Sarah McCarthy, who nominated Dr. Specht for the Good Works honor. “When others did not come for their shifts, she filled in. If there were emergencies when no one else was there, she was available.”

Throughout 2019, the AAEP’s Good Works for Horses Campaign will spotlight AAEP-member practitioners whose volunteer efforts are improving the health and welfare of horses. To discover the Good Works of AAEP veterinarians or nominate a Good Works candidate, visit aaep.org/horse-owners/good-works-horses. For more information on nominating a veterinarian for this program, contact Michelle Behm, AAEP communications coordinator, at mbehm@aaep.org.
Members in the News

Dr. Dan Keenan named New Jersey’s horseperson of the year

Dr. Dan Keenan, partner at Foundation Equine Wellness and Performance in Crosswicks, N.J., received the 2018 Governor’s Award for Horseperson of the Year in New Jersey during the New Jersey Breeders Awards Luncheon on Jan. 27.

Since receiving his veterinary degree from Cornell University in 1984, Dr. Keenan has practiced in New Jersey and been deeply involved in organized veterinary medicine and the horse industry, both nationally and within the state. He has served on the AAEP’s board of directors and its Educational Programs, Leadership Development, and Professional Conduct and Ethics committees; as president of the New Jersey Association of Equine Practitioners; as vice president of the New Jersey Horse Council; and on various other industry boards and committees in New Jersey.

Welcome new members, and congratulations recent graduates

New Members:
Alyson Lee Baber, DVM, Dallas, PA
Heather Leigh Cline, DVM, Hillsboro, VA
Cristina Ventura Cordeiro, DVM, Lexington, KY
Nicole Howey, DVM, Phillips, WI
Celine June Lyn Lee, DVM, Upper Castra, TAS, Australia
Sandra Martin, DVM, Allen, TX
Bryana Mitchell, DVM, Alvarado, TX
Rafal Pedziwiatr, DVM, Proszowice, Poland

Recent Graduates:
Bethany S. Austin, DVM, Groton, NY
Daphne Dodd, DVM, League City, TX
Jen Haugland, DVM, Dillon, MT
Kirstie Rissling, DVM, Ponoka, AB, Canada
Kayla Shepherd, DVM, Jordan, MN

Benefit: Save time on client education with AAEP PowerPoints

Owner education events can be a great venue to improve the daily care of client horses, strengthen client relations and introduce yourself to prospective clients. While the food and beverage menus are up to you, AAEP has shouldered much of the preparation by creating PowerPoint presentations on pertinent equine healthcare topics.

As a benefit of your membership, you can download any of the following 18 presentations. Each contains the most current information on the topic so that your clients receive fundamental knowledge that will help them maintain the health of their horses as well as recognize and respond to warning signs of different ailments and diseases.

- Colic
- Dental Care
- Disaster Preparedness
- Emergency Care
- Equine Herpesvirus (EHV)
- Foal Growth
- Foaling Mare and Newborn
- Hay Quality and Nutrition
- Immunizations
- Internal Parasites
- Lameness Exams
- Laminitis
- Neurology
- Overweight Horse
- Poisonous Plants
- The Expectant Mare
- The Older Horse
- Understanding Equine Strangles

These presentations may be downloaded from aaep.org/dashboard/clienteducation/presentations. For additional information about the owner education PowerPoints and other benefits of your AAEP membership, contact Megan Gray, member concierge, at mgray@aaep.org.
Acquire new diagnostics, effective treatments and innovative solutions to the problems you encounter in everyday practice. Join your AAEP colleagues for one or more of the following CE opportunities this year.

**360° Respiratory Tract Disorders**  
July 11-13 | College Station, Texas

*Sponsored by:*

**Summer Focus Conference & Labs**  
July 29-31 | Fort Collins, Colorado  
*Two Tracks: Ophthalmology and Sports Medicine*

**65th Annual Convention**  
December 7-11 | Denver, Colorado

For more information or to register for the summer meetings, visit [aaep.org/meetings](http://aaep.org/meetings)
Delegate Corner: AVMA to reinstate health insurance coverage

By Stuart Brown II, DVM and Rebecca Stinson, DVM

The AVMA House of Delegates (HoD) winter meeting, held January 10–12 in Chicago, Ill., featured extensive discussion on the roles and challenges of veterinary technicians as well as announcement of resumption of association-provided health insurance benefits.

The AVMA LIFE Trust and AVMA PLIT will unify under an umbrella trust in 2019, which will allow all needs to be met under one roof. Following regulatory changes in 2018, AVMA will resume offering health insurance for AVMA members, their families and employees. The rollout will be implemented on a state-by-state basis, with coverage available in at least 10 states beginning in July.

The Veterinary Information Forum focused on utilization of credentialed technicians. Discussion included recruitment, development and education as well as challenges facing these key members of the veterinary healthcare team. A motion was approved to recommend a working group to further investigate opportunities for enhancing the role of credentialed technicians and their ability to support the veterinarian. Veterinary technicians face compassion fatigue, burnout and many of the other challenges common to a career in veterinary care. This working group may provide insight into how the entire veterinary healthcare team can succeed and thrive.

Meanwhile, the HoD passed a bylaws amendment that will increase AVMA dues effective with the 2020 dues statement. Reduced dues for recent graduates and other eligible parties will be adjusted to 50% of the new full dues mount. The dues increase is needed to fund additional programming, including several well-being resources.

Elsewhere, AVMA continues to advocate in Washington, D.C., and beyond on issues such as student debt relief and the bipartisan Prevent All Soring Tactics Act recently reintroduced in Congress. Veterinary students and new practitioners are encouraged to check out the early career resources available at myveterinarylife.com.

Dr. Brown, a partner in Hagyard Equine Medical Institute in Lexington, Ky., and member of the AAEP’s Racing Committee, serves as AAEP’s delegate to the AVMA’s House of Delegates. Dr. Stinson, AAEP’s alternate delegate, is a partner in Carolina Equine Hospital in Browns Summit, N.C., and member of the AAEP’s Educational Programs Committee.

Cargill Feed & Nutrition, an Educational Partner of the AAEP since 2001, is committed to translating nutrition research into feed solutions that improve the health of horses. Cargill’s rich history of creating innovative equine nutrition solutions includes our Nutrena®, Progressive Nutrition®, Legends® and ProElite® brands of feeds and supplements.

We believe a horse’s topline plays an important role in how it performs, looks and feels. Our industry-leading topline assessment tool and a wealth of resources about topline health can be found at toplinebalance.com.

When it comes to nutrition that supports the health of your clients’ horses, Cargill’s team of equine nutrition experts is here to help you. Please visit our exclusive equine veterinarian website vetnutritioninfo.com where you will find resources to help your staff and your clients. If you have questions or a need for training and assistance, please contact us at (800) 367-4894 or visit our website.

AAEP Educational Partner Profile: Cargill

Cargill Feed & Nutrition, an Educational Partner of the AAEP since 2001, is committed to translating nutrition research into feed solutions that improve the health of horses. Cargill’s rich history of creating innovative equine nutrition solutions includes our Nutrena®, Progressive Nutrition®, Legends® and ProElite® brands of feeds and supplements.

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When it comes to nutrition that supports the health of your clients’ horses, Cargill’s team of equine nutrition experts is here to help you. Please visit our exclusive equine veterinarian website vetnutritioninfo.com where you will find resources to help your staff and your clients. If you have questions or a need for training and assistance, please contact us at (800) 367-4894 or visit our website.

A working group will examine an enhanced support role for credentialed technicians.
ALL OTHERS FALL SHORT.

Assure® Guard Gold
The Ultimate Digestive Aid

Speak to one of our Veterinary Solution Specialists to find out how Assure® Guard Gold can help you improve the health of your equine patients today.
Highlights of recent clinically relevant papers

Ketamine doses for castration
This prospective, randomised, blinded study by Hulda Harðardóttir and colleagues in the UK and Iceland compared two doses of ketamine (2.2 mg/kg and 5 mg/kg i.v.) for induction of anaesthesia in 77 Icelandic horses undergoing field castration.

Prior to induction, horses were sedated with xylazine (0.7 mg/kg), butorphanol (25 μg/kg) and acepromazine (50 μg/kg) i.v. and sedation quality was assessed 5 minutes later. Horses were randomly allocated one of the two ketamine doses and induced with i.v. ketamine and diazepam (30 μg/kg). Induction quality, surgical conditions and recovery were assessed using subjective and objective measures.

Horses that received the higher dose of ketamine became relaxed more rapidly after induction, and surgical conditions were better; however, recovery quality was subjectively worse. Five horses that received the lower dose of ketamine required additional ketamine doses during anaesthesia compared to only two that received the higher dose.

The authors concluded that a ketamine dose of 5 mg/kg i.v. may result in better surgical conditions but adversely affects recovery quality for field surgery.

Outcome of puncture wounds of the hoof
This retrospective study by Stefano Schiavo and colleagues in the UK described low-field magnetic resonance imaging (MRI) findings and long-term outcome for a group of 11 horses with solar foot penetration, deep digital flexor tendon injury and absence of concurrent sepsis in all adjacent synovial structures (distal interphalangeal joint, navicular bursa and digital flexor tendon sheath).

In three horses, the deep digital flexor tendon injury was only visible in the T2 fast spin echo sequence and contrast radiography improved diagnostic certainty. The most commonly affected area was between the distal border of the distal sesamoid bone and the facies flexoria of the distal phalanx (6/11, 55%). Six horses (60%) had an excellent outcome and returned to full athletic function (5 showjumping; 1 general purpose). Five horses (40%) were sound but had not yet resumed full work at the time of follow-up.

The findings of this study indicate that the prognosis for return to soundness can be good for horses with solar penetration, deep digital flexor injury and absence of synovial sepsis.

Equine coronavirus
In this study, Emily Schaefer and colleagues in the USA investigated the clinical, haematological, molecular and serological features of adult horses experimentally infected with equine coronavirus (ECoV).

Eight healthy adult horses were included in this study. Four horses were intragastrically infected with faecal material containing $10^9$ genome equivalents of ECoV and four horses were exposed daily to the faeces from the experimentally infected horses. Monitoring included physical examinations, as well as daily nasal swab, whole-blood and faecal collection for molecular detection of ECoV. Blood was collected every other day for haematological analysis and weekly for serological analysis.

All eight horses shed ECoV in faeces. Six of the eight horses (75%) exhibited mild, clinical disease with soft, formed manure; one horse exhibited transient pyrexia. All horses maintained total white cell counts within normal limits, but three horses developed transient lymphopenia. No statistically significant differences were observed in quantity of faecal shedding of ECoV between the two groups.

Experimental infection of adult horses with ECoV was associated with mild and self-limiting clinical signs, transient lymphopenia and faecal shedding of ECoV, which mimics natural infection. No differences between experimentally infected horses and horses exposed to ECoV-containing faeces were identified. Results of this study support a faecal-oral route of transmission.

Umbilical cord blood sampling in neonatal foals
This clinical technique article by Sunita Jeawon and colleagues in Ireland and the UK describes in detail the procedure for collecting paired blood samples from the umbilical artery and vein in newborn foals to enable stall-side blood gas analysis.

Thirty-five Thoroughbred foals >320 days' gestation from mares at one stud farm were sampled. Paired umbilical arterial and venous whole-blood samples were obtained in 30 foals, umbilical artery samples alone obtained in three foals, and umbilical vein samples alone obtained in two foals. There were no adverse events or clinical outcomes associated with the sampling protocol described. The authors found that umbilical cord blood collection for blood gas analysis was a practical clinical technique that potentially could be used as a stall-side method for assessing the in utero oxygenation and acid-base status of newborn foals.

Impact of table position in anaesthetised horses
This study by Anna Binetti and colleagues in Belgium and Switzerland describes the impact of the Trendelenburg (head down; HD) and reverse Trendelenburg (head up; HU) position on respiratory and cardiovascular function in anaesthetised horses.

Six adult horses were anaesthetised twice in dorsal recumbency. They were either placed in the Trendelenburg position (HD) followed by reverse Trendelenburg position (HU) or in reverse order. Every position was maintained for 90 minutes. The order of positions was randomly assigned at initial anaesthesia. Extensive cardiorespiratory monitoring was performed. Statistical analysis consisted of a mixed model with horses as random effect and time, position, section of anaesthesia and interaction between those as fixed effects.

When HU was applied during the first section of anaesthesia, partial pressure of arterial oxygen (PaO$_2$), oxygen saturation (SaO$_2$) and oxygen content (CaO$_2$) were significantly higher, while venous admixture, mean arterial,
right atrial and mean pulmonary arterial pressure were lower than in HD. After changing from HU to HD, PaO₂ and SaO₂ remained higher and venous admixture lower compared to the inverse order. Independent of the order, in the HD position venous admixture increased while PaO₂, SaO₂, CaO₂, venous PO₂, venous prevalence of bone marrow lesions in the distal condyles of saturation and venous oxygen content decreased over time. No significant differences were found for cardiac output, oxygen delivery, oxygen consumption and dobutamine requirement between the two positions.

The authors concluded that gas exchange is better preserved in HU compared to HD, especially if applied from the start of the anaesthesia.

**Spermatic cord stump infection**

In this retrospective study, Elaine Claffey and colleagues in the USA reported the surgical management and the short- and long-term follow-up of post-castration spermatic cord infection in 23 client-owned horses.

Medical records of horses that had been surgically treated for spermatic cord stump infection after castration were reviewed. Time from castration to presentation, diagnostic procedures, surgical complications, bacterial culture and ancillary testing, and survival to discharge were collected. Long-term follow-up was obtained by owner survey when possible. Descriptive statistics were used to report results.

Horses were aged 2–14 years (mean 4.1 years) and presented a median 33 days after castration (range 12–3561 days). Five of 23 horses required revision surgery; two because of haemorrhage and three for persistent infection. All horses survived to discharge. Long-term follow-up was available for 16 horses at a mean time of 27.4 months post-surgery (range 6–135 months). Complete resolution of clinical signs and return to previous use was documented in 14/16 horses; one horse had persistent purulent drainage and the second horse was retired because he did not return to adequate performance.

Post-castration infection of the spermatic cord had a favourable prognosis for short- and long-term survival in this population, although complications included post-operative haemorrhage and persistent infection.

**Bone marrow lesions of the distal condyles**

In this study, Cécile De Guio and colleagues in France evaluated the prevalence of bone marrow lesions in the distal condyles of the third metacarpal bone, described the anatomical distribution and correlated lesions with the presence of lameness and the level and type of activity.

All sports and pleasure horses undergoing standing low-field magnetic resonance imaging of the front fetlock region over an 8-year period were included and divided into three lameness groups according to the results of diagnostic analgesia. Bone marrow lesions were analysed and graded. Grades were compared between anatomical locations and between lameness groups. A total of 166 horses were sampled. The prevalence of bone marrow lesions was 76.5% (127/166). The most commonly affected locations were the dorsal aspects of the medial condyle (31%, 39/127) and of the sagittal ridge (28%, 36/127). There was no significant difference between both forelimbs (lame and non-lame limb) of the same horse. Lesion severity was neither significantly associated with the lameness group nor with the type or level of activity. The third metacarpal bone is high in this population and the clinical significance is not always clear. Further studies are required to elucidate the clinical significance of this finding in sports and pleasure horses.

**Dynamic testing for PPID in donkeys**

This prospective study by S. Mejia-Pereira and colleagues in Spain and the USA aimed to evaluate dynamic testing for pituitary pars intermedia dysfunction (PPID) in donkeys.

Six donkeys with clinical signs consistent with PPID and a basal adrenocorticotrope hormone [ACTH] concentration >50 pg/mL were included in the study. A dexamethasone suppression test (DST), thyrotropin-releasing hormone (TRH) stimulation test and combined DST-TRH challenge were performed in all animals during the summer months with a 1-week washout period between tests.

The TRH stimulation test identified all six donkeys as having PPID, whereas the DST and the DST-TRH identified 3/6 and 4/6 donkeys respectively. Agreement between the DST and the DST-TRH tests was poor.

The authors recommend the TRH stimulation test as a dynamic test for the diagnosis of PPID in donkeys.

S. WRIGHT

EVE Editorial Office

**References**


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Case Report

Thymic hyperplasia causing right ventricular outflow tract compression following treatment for oesophageal rupture in an Arabian colt

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Keywords: horse; oesophageal tear; cranial mediastinum; cardiac compression; thymic hyperplasia

Summary

True thymic hyperplasia has been reported sporadically in the human literature as an immunological rebound phenomenon following immunosuppressive treatment or disease. There are limited accounts in domestic species, mainly following vaccination, and thymic hyperplasia has not been a recognised condition in the horse to date. This report details a case of true thymic hyperplasia in a 10-week-old Arabian colt diagnosed by histopathology of core biopsy samples. The colt developed pulmonary stenosis caused by compression due to a space occupying lesion in the cranial mediastinum following a 3-month history of hospitalisation for treatment of traumatic oesophageal rupture with perioesophageal abscess formation. Diagnostic imaging of the cranial mediastinum was indicative of a thymic mass, and histopathology confirmed the mass was normal (hyperplastic) thymic tissue. The colt was treated with a tapering dose of corticosteroids, which led to involution of the hyperplastic tissue and resolution of pulmonary artery compression. Thymic hyperplasia may be an unrecognised sequela to chronic inflammation in horses and was only identified in this case when the size was sufficient to compress right cardiac outflow.

Introduction

Thymic hyperplasia is a rare condition reported in man, with limited reports presented in nonexperimental animals. To the authors' knowledge, this is the first report of thymic hyperplasia in the horse. The thymus in the horse forms at Day 60 of gestation, developing the thymic reticulum from endodermal tissue and the thymic capsule from mesenchymal tissue, both derived from the third pharyngeal pouch. The thymus is populated by haematopoietic stem cells originating from the aorta–gonad–mesonephros region and becomes the site of T lymphocyte maturation. In some domestic species, the thymus forms a Y shaped structure; however, in the horse the left and right cervical sections do not develop (Vejlsted 2010). The thymus begins to involute around adolescence, although, in man, it has been shown to retain partial ability to generate T lymphocytes (Naylor et al. 2005). Histopathological examination of the equine thymus shows evidence of involution by age 3 years. Involution is characterised by progressive atrophy and reorganisation of the cortex and medulla with reduction in cortical thymocytes, and increase in the extraparenchymal compartment, particularly increases in adipose tissue and extracellular matrix (Contreiras et al. 2004). There are no published studies documenting the chronology of thymic involution using ultrasound or radiography in the horse, however it has been suggested that it appears radiographically largest around age 2 months and regresses by age 1–2 years (Lester and Lester 2001).

In man, two forms of thymic hyperplasia have been recognised. True thymic hyperplasia in which the overall tissue mass is increased, with preservation of the normal histological appearance, is a rebound phenomenon observed after physiological stress. True thymic hyperplasia has been reported following chemotherapy, radiation therapy, corticosteroid treatment, thermal burns and surgery (Goldstein et al. 2015). In nodular-sclerosing Hodgkin’s disease patients treated with immunotherapy in their first peak of disease, true thymic hyperplasia is considered a favourable sign of immune recovery (Shin and Ho 1983; Scheinpflug et al. 2003). True thymic hyperplasia in calves, rabbits and birds has been reported in association with repeated immunisation; however, it has not been reported in horses (Valli 2007).

The second form, lymphoid follicular hyperplasia, is characterised by enlarged lymphoid germinal centres within the medulla and has been associated with inflammatory and autoimmune disorders including myasthenia gravis, systemic lupus erythematosus and rheumatoid arthritis (Berrih-Aknin and Le Panse 2014; Goldstein et al. 2015). Human patients with hyperthyroidism experience both true thymic hyperplasia caused by increased thyroxine, and lymphoid follicular hyperplasia attributed to the autoimmune disorder underlying the syndrome (Judd and Bueso-Ramos 1990). The case presented in this report developed true thymic hyperplasia based on the histopathology and history of chronic inflammation.

History

A 5-week-old Arabian colt presented to the University of Queensland for evaluation of dyspnoea and swelling of the ventral neck after running into a fence. On physical examination, the colt had marked stertorous breathing. There was profound swelling and crepitus of the entire ventral neck...
and a superficial flocculent mass was palpable in the midventral neck. Ultrasound and radiographic examination of the ventral neck revealed a 4 × 6 cm subcutaneous abscess and extensive gas infiltration of the subcutis and muscle extending from the head to the level of the thoracic inlet. An oesophageal tear was suspected in the mid cervical region.

Emergency tracheostomy was performed routinely. Medical management for the subcutaneous infection was initiated, comprising systemic antimicrobial therapy with benzyl penicillin (BenPen)11, 22,000 IU/kg bwt i.v. q.i.d. and gentamicin (Gentam 100)2 8.8 mg/kg bwt i.v. s.i.d., maintenance intravenous polyionic fluid therapy, meloxicam 0.6 mg/kg bwt per os s.i.d. (Metacam)3 (discontinued on Day 11), and omeprazole 4 mg/kg bwt per os s.i.d. (Omoguard)4 (discontinued on Day 13).

Endoscopy was performed the following day once the colt was stable, and confirmed a 10 cm long dorsal oesophageal tear in the mid-cervical region with a perioesophageal abscess. Under general anaesthesia, the superficial abscess was incised and the oesophagus was approached through this incision. The necrotic tissue surrounding the oesophageal tear was debrided, an oesophagostomy tube was secured in the aboral oesophagus, and a penrose drain was placed in the wound, which was left open and dressed. Antibiotic therapy was changed to trimethoprim sulfadimidine (Sulprim)2 30 mg/kg bwt via nasogastric tube b.i.d. and metronidazole (Equine Metronidazole Paste)5 10 mg/kg bwt via nasogastric tube t.i.d. from day 7 to 28 of hospitalisation.

By Day 7 of hospitalisation, the tracheotomy tube was removed. The colt was fed mare’s milk via the oesophagostomy tube. The oesophageal wound granulated sufficiently for the oesophagostomy tube to be removed on Day 34 and the colt was gradually reintroduced to oral feed.

Repeat endoscopy on Day 45 revealed the development of an oesophageal diverticulum that was separated into two compartments by a band of oesophageal mucosa. Both compartments communicated with the oesophagus (and the skin) via two oesophageal fistulae. The fistulae were debrided with a curette twice weekly via standing oesophageal endoscopy under sedation and eventually healed.

Diagnosis

Antimicrobial treatment had been discontinued for 22 days, and the colt remained clinically stable therefore discharge from hospital was being considered; however, on Day 54 of hospitalisation, a grade IV/VI left sided holosystolic murmur with the point of maximum intensity over the pulmonic valve was noted on routine physical examination. Complete blood count and serum biochemistry were unremarkable. Thoracic radiographs revealed increased radiopacity in the region of the cranial mediastinum (Fig 1). Sonographic examination of the neck and cranial mediastinum revealed a 6.8 cm diameter heterogeneous mass in the cranial mediastinum with compression of the pulmonary artery (PA; Fig 2). It was not possible to determine with ultrasound whether the content of the mass was hetroechoic fluid or soft tissue. There was turbulent flow in the PA on colour Doppler. There was mild tricuspid regurgitation and pulmonary regurgitation, but no evidence of mitral regurgitation. The systolic murmur was attributed to pulmonic stenosis as a result of compression by the cranial mediastinal mass. Contrast radiographs with iohexol administered per os showed no evidence of communication between the oesophagus and cranial mediastinum. A nuclear scintigraphy scan using technetium-99 m-labelled IgG was completed as previously described (Underwood et al. 2011). There was moderately increased focal radiopharmaceutical uptake in the region of the cranial mediastinum that corresponded to the location and approximate size of the mass identified on radiographs and ultrasound (Fig 3). The pattern of radiopharmaceutical uptake confirmed the presence of non-specific inflammation but was not consistent with the marked uptake that would be expected with an abscess (Underwood et al. 2011).

Due to the difficulty and invasiveness of performing further diagnostic evaluation in this region, the decision was made to treat the cranial mediastinal mass as a presumptive abscess seeded into the mediastinum via the oesophageal tear. The colt was treated empirically with broad spectrum antimicrobials, first with doxycycline (compounded)6 10 mg/
kg bwt per os b.i.d. for 14 days then chloramphenicol [compounded] 6 25 mg/kg bwt per os q.i.d. for 20 days. Weekly ultrasound examinations revealed that the mass increased in size from 6.8 cm on day 56 to 10.79 cm in diameter, its widest recorded point, on Day 87 (Fig 4). The PA measured 3.5 cm in diameter across its sinus in the standard right ventricular outflow tract view on Day 56, and 3.8 cm on Day 87. Colour Doppler studies of the right ventricular outflow tract on Day 87 showed that systolic flow in the PA was increasingly turbulent and the amount of tricuspid regurgitation had increased (Fig 5, Supplementary Items 1–3). Repeat examination on Day 94 showed that the mass measured approximately the same diameter (10.5 cm). Slight right ventricular enlargement was detected on M-mode through the right parasternal short axis view of the left ventricle, as the right ventricular internal diameter during diastole was 4.5 cm, approximately two-thirds the size of the left ventricular internal diameter (7 cm). There was no audible change in the murmur throughout the period of investigation.

Antibiotics were discontinued on Day 100 and ultrasound-guided aspiration of the mass with an 18 gauge 8.9 cm spinal needle was attempted under general anaesthesia on Day 101. The colt was placed in left lateral recumbency with the limbs pulled cranially, and the skin region around the third intercostal space was aseptically prepared. Ultrasound again revealed no change in the size and appearance of the mass (approximately 10.5 cm diameter). Ultrasound-guided aspiration failed to produce a fluid sample, subsequently an ultrasound-guided biopsy of the mass with a 14 gauge 22 mm automated Tru-cut biopsy (Bard Max-Core) 7 was performed using a technique previously described (De Clercq et al. 2004). A small stab incision was made in the skin and the biopsy needle was inserted along the cranial border of the fourth rib and into the mass using ultrasound guidance. Two firm tissue core samples were taken from different locations within the mass. Histopathology confirmed the biopsied tissue to be consistent with morphologically normal thymic tissue with a distinct corticomedullary junction and morphologically normal lymphoid tissue (Fig 6). Proliferation of B-cell germinal centres, which would be consistent with follicular lymphoid hyperplasia was not observed. Hyperplasia of thymic epithelial cells, which is present in some types of thymic hyperplasia and can resemble thymoma, was not seen in this case. An underlying neoplastic process was ruled out based on the normal histopathological architecture of the tissue and lack of atypical features. A diagnosis of thymic hyperplasia was reached based on the histopathology results and recent history of septic inflammation due to perioesophageal abscessation.

Interventions

Considering the histopathological diagnosis of thymic hyperplasia, lack of response to a protracted course of antimicrobials and gradual worsening of cardiac outflow tract compression and right sided cardiac enlargement, trial treatment with systemic corticosteroids was initiated in an attempt to reduce the thymic size (Steger et al. 2011). The colt was treated with dexamethasone (Dexapent) 2 at 0.05 mg/kg bwt (10 mg) i.m. s.i.d. initially for 7 days (starting on Day 105). At Day 111, the murmur had reduced to grade I-II/VI in intensity. Ultrasound of the cranial mediastinum and echocardiogram at this time revealed that the thymic parenchyma had similar sonographic appearance to previous scans but now measured
5.8 cm in diameter (reduced in size by approximately 50%) and was partially obscured by lung on the right when viewed through the triceps muscle. Tricuspid regurgitation had resolved; however, mild pulmonary regurgitation and right sided enlargement remained present. The colt was discharged after 112 days of hospitalisation for continuing therapy at home with a tapering dose of dexamethasone (Dexapent): 0.025 mg/kg bwt (5 mg) i.m. s.i.d. for 7 days, 0.0125 mg/kg bwt (2.5 mg) i.m. s.i.d. for 7 days, then 0.0125 mg/kg bwt (2.5 mg) i.m. every other day for 7 days.

Outcome

The colt returned for follow-up examination 8 months after discharge (Day 365). On presentation, the colt was bright and alert and clinically normal. The ventral neck in the region of the original oesophageal lesion was firm on palpation but not painful and the fistulae had healed with minimal scarring. No murmur was noted on cardiac auscultation. Lateral thoracic radiographs revealed a normal appearance of aerated lung in the region of the cranial mediastinum, which was not visible in previous radiographs. Ventrally there was a small soft tissue opacity cranial to the cardiac silhouette consistent with a normal thymus/thymic remnant of appropriate size for the age of the colt (Fig 7). Ultrasound from the right third intercostal space revealed a sonographically normal hyperechoic line consistent with the normal pleural surface of aerated lung (arrows) obscuring the cranial mediastinum. There was mild pulmonary regurgitation associated with a 2+ (small to medium) pulmonary regurgitation jet; the remainder of the echocardiogram was within normal limits. The PA measured 5.4 cm in diameter across its sinus in the standard right ventricular outflow tract view on Day 365. Phone follow-up was performed 2 years and 2 months after the initial presentation: the owner indicated that the (now) gelding appeared normal running in the paddock with its peers, with apparently normal growth and exercise tolerance, and that the plan was to commence endurance training as a 3-year-old per usual farm practice.

Discussion

We hypothesise that the thymic hyperplasia diagnosed in this colt was attributable to prolonged immune stimulation, as has been documented in human cases (Shin and Ho 1983; Scheinpflug et al. 2003; Goldstein et al. 2015). In this case the immune stimulation occurred as result of chronic periesophageal infection initiated by traumatic oesophageal perforation. The histopathology and clinical course are indicative of true thymic hyperplasia, which is best described as over-activation of the cell mediated immune system due to chronic inflammation. The cardiac abnormalities that developed and led to recognition and diagnosis of thymic hyperplasia were caused by the mass effect of the enlarged thymus. Compression of the lungs by massive thymic hyperplasia, an idiopathic subset of true
thymic hyperplasia, has been reported in the human literature (Lee et al. 1979; Lamesch 1983; Kobayashi et al. 1986; Linegar et al. 1993; Tan et al. 2010). The criteria for massive thymic hyperplasia are that the thymus is greater in size than the cardiac silhouette on radiographs, weighs several times the expected weight for the patient's age, and represents >2% of the patient's body mass [Linegar et al. 1993]. The current case does not meet these criteria, and does not appear to be idiopathic in nature. The majority of human massive thymic hyperplasia patients are neonates presenting for respiratory distress, and the majority of symtomatic cases of thymic enlargement are managed by surgical excision of the thymus. However, a recent report demonstrated a very high rate (44%) of unnecessary thymectomy in human patients with thymic enlargement, due to misinterpretation of thymic cysts, thymic hyperplasia and lymphoma as thymoma on computed tomography (CT) of the chest (Ackman et al. 2015). It has been suggested that corticosteroids may be effective clinically to 'shrink' a hyperplastic thymus [Steiger et al. 2011], and thymic atrophy has been documented as a side effect of corticosteroid treatment in human infants [Caffey and Di Liberti 1959; Caffey and Silbey 1960]. There are three reported cases of paediatric massive thymic hyperplasia treated with corticosteroids; however, only one had reduction in size of the thymus following treatment [Kobayashi et al. 1986]. Other case reports observed no response to corticosteroid treatment [Lee et al. 1979; Lamesch 1983; Tan et al. 2010]. In a case of true thymic hyperplasia causing laryngotracheal displacement in an infant, treatment with a 4-week course of methylprednisolone was associated with partial thymic involution and resolution of clinical signs [Wolff et al. 2011].

In the horse, cranial mediastinal masses have been identified with causes ranging from abscessation to primary neoplasms including lymphosarcoma, liposarcoma, squamous cell carcinoma, thyroid carcinoma, thymoma and also various metastatic pulmonary neoplasms [Hovda et al. 1990; Garber et al. 1994; De Clercq et al. 2004; Kondo et al. 2012]. Cranial mediastinal abscesses secondary to pneumonia have been reported to cause compression of the PA and caudal displacement of the heart [Byars et al. 1991; Griffin 2002; Sleeper et al. 2016]. Abscessation of the cranial mediastinal lymph nodes has been reported to cause compression of the trachea [Rigg et al. 1985]. Cranial mediastinal abscesses appear sonographically as fluid filled encapsulated or loculated lesions filled with echogenic debris [Byars et al. 1991; Sleeper et al. 2016]. Cranial mediastinal neoplasms have variable clinical signs based on the aetiology; pleural effusion and ventral oedema are commonly reported [De Clercq et al. 2004; Kondo et al. 2012]. Compression of the recurrent laryngeal nerve causing recurrent laryngeal neuropathy was noted in one case of cranial mediastinal lymphosarcoma [De Clercq et al. 2004]. Sonographically, cranial mediastinal lymphosarcoma appears homogenously hypoechoic except when necrosis is present within the mass [Garber et al. 1994; De Clercq et al. 2004]. Cranial mediastinal masses present a diagnostic and treatment challenge in horses due to their location as they can be difficult to image and biopsy (or drain in the case of an abscess) and surgical resection of lesions has not been documented in horses.

In the current case, the mass identified was due to hyperplasia of a normal structure and corticosteroid treatment was successful in reducing its size and abolishing the cardiac murmur and outflow obstruction. As the colt responded well to corticosteroid treatment the prognosis was good, whereas most cranial mediastinal neoplastic processes have a poor prognosis due to the difficulty of surgical access and limited practicality of chemotherapeutic therapy in the horse. The ongoing pulmonary regurgitation was considered unlikely to have an effect on the colt's future athletic performance as an endurance horse (Marr 2010). Considering the alternative treatment was thymectomy via thoracotomy or thoracoscopy, corticosteroid treatment to reduce organ size is a rational first line therapy as thymectomy has not been demonstrated in the horse. The technetium-IgG scan proved to be a helpful supportive diagnostic tool and retrospectively strengthened the diagnosis as the area of interest was immunologically active but the uptake was not as marked as would be expected with an abscess [Underwood et al. 2011]. Chest CT may have been useful to help characterise the origin and boundaries of the mass; however, biopsy and histopathology would still have been required to rule out cranial mediastinal abscess or neoplasia, as is the case in human patients [Goldstein et al. 2015]. It should be noted that the use of CT in the horse is limited by the size of the patient and available facilities, therefore would generally only be practical in young horses at referral or university hospitals.

Thymic hyperplasia should be considered a differential diagnosis in horses after chronic inflammation if clinical signs referable to cardiac outflow or tracheal compression develop and can be diagnosed readily with histopathology of core biopsy samples. Treatment with corticosteroids resulted in rapid reduction in the size of the thymus and resolution of right sided cardiac outflow obstruction in this case. It is possible that true thymic hyperplasia may be more common than previously thought in horses, as it will remain subclinical in cases without compressive sequelae.

Authors’ declaration of interests
No conflicts of interest have been declared.

Ethical animal research
Ethical review not applicable for this case report.

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Authorship
H. Smith was involved in preparation of the manuscript and final approval. C. Underwood was involved in clinical case execution, data analysis and interpretation, and final approval. A. Schaffer-White was involved in data analysis and interpretation, and final approval. A. van Eps was involved in report design, clinical case execution, preparation of the manuscript, and final approval.
Manufacturers' addresses

1 CSL Limited, Parkville, Victoria, Australia.
2 Illium, Troy Laboratories Pty. Limited, Glenndening, New South Wales, Australia.
3 Boehringer Ingelheim Pty. Limited, North Ryde, New South Wales, Australia.
4 Ceva Animal Health Pty. Limited, Glenorie, New South Wales, Australia.
5 Randlab Australia Pty. Limited, Peakhurst, New South Wales, Australia.
6 Canina Day & Night Pharmacy, Caninda, Queensland, Australia.
7 Bard Biopsy Systems, Tempe, Arizona, USA.

References


Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher’s website:

Supplementary Item 1: Right parasternal long axis view of the right ventricular outflow tract with colour flow Doppler demonstrating pulmonary regurgitation jet.

Supplementary Item 2: Standard right parasternal long axis ‘4 chamber’ view.

Supplementary Item 3: Left parasternal long axis view of the pulmonary artery and pulmonary valve with colour flow Doppler demonstrating turbulent ejection flow in the pulmonary artery (compare with low velocity flow in the adjacent aorta just deep to the pulmonary artery) and pulmonary regurgitation jet.
Case Report

First reported case of Hypoderma diana Brauer, 1985 (Diptera: Oestridae)-associated myiasis in a horse in Germany

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Keywords: horse; warble flies; equine myiasis; hypodermosis; macrocyclic lactones

Summary
A massive infestation with warble fly larvae was observed in a mare in Lower Saxony, Germany. From a herd of 20 horses, only a single mare accidentally escaped the routine treatment with macrocyclic lactone in autumn and showed the myiasis infestation next year in January. Eighteen subcutaneous nodules were found on the back ($n=2$), ribs ($n=3$), flank ($n=5$) and croup ($n=8$). Deer, the specific hosts of the warble fly Hypoderma diana, was abundant on this farm and some other risk factors for the hypodermosis are discussed herein. This is the first report of myiasis caused by H. diana in horses in Germany. This massive warble fly infestation in a horse in Germany reported here is important to alert equine health professionals concerning the prevention of this disease in the routine parasite control programme.

Introduction
Hypodermosis, an obligate parasitic furuncular myiasis caused by the host tissue invasion by Hypoderminae larvae, was one of the most important parasitic problems in cattle in Europe during the last century (Boulard 2002), affecting weight gain, welfare, bovine immune defence mechanisms (Boulard 1989) and the leather industry (Boulard et al. 2008). For this reason, coordinated control programmes in several European countries, compulsory or not, resulted in a considerable reduction of this parasitic problem in several western European countries, or even eradication, and it became a notifiable disease in France (Boulard et al. 2008). Despite the success in cattle hypodermosis control, there have been a number of recent cases of oral (Faber and Hendrikx 2006), dermal (Logar and Marinic-Fiser 2008) and ophthalmomyiasis (Kan et al. 2013; Panadero-Fontán and Otranto 2015; Bangsø et al. 2016) caused by Hypoderma tarandi, Hypoderma bovis and Hypoderma lineatum in people, which indicates the increasing risk of zoonotic transmission. Accordingly, the problems caused by the hypodermosis involve both domestic and wild animals and man, and thus its control needs to be considered under the One Health approach.

There are only few sporadic reports of hypodermosis in horses. An intracranial migration of a first-stage larva of the same aetiological agent of the cattle grub, H. bovis, was described in a horse in Montana, USA, causing an acute neurological disease (Hadlow et al. 1977). Two other H. bovis-associated myiasis cases were previously reported in horses (Anthony 1948; Rastegaev 1973). Hypoderma lineatum, another cattle warble fly, was also described causing a brain myiasis in a horse (Olander 1967). Horses are also reported as an unusual host for Hypoderma diana, the cervidae warble fly (Minár 1987; Hendrikx et al. 1989; Kudrnáčková et al. 2014).

This is the first report of a myiasis caused by H. diana in horses in Germany.

Case history
Eighteen nodules (warbles) were palpated in a 5-year-old Thoroughbred mare. Nodules were found on the back ($n=2$), ribs ($n=3$), flank ($n=5$) and croup ($n=8$) (Fig 1). These nodules contained instar larvae as confirmed by digital expulsion (Fig 2). Half of the nodules were manipulated and...
the live larvae expelled. No additional medical treatment was employed. The warbles presented themselves as approximately 1–2 cm in diameter large and only slightly elevated warbles with a typical central opening. The warbles were not painful and they disappeared within the next 6 weeks. Subsequently, the horse did not show any clinical signs and continued to become an internationally successful racing horse. No other horses on the premises were affected.

The farm is a private horse farm and there are no cattle on the farm. However, the pasture extends into an area with a lot of grassland and some patches of forest. Deer often graze on these pastures, so it is highly feasible that H. diana from deer infest horses. This particular mare accidently escaped the routine ivermectin-treatment in autumn since it was brought to a training farm in August 2014 and only returned to the stud farm in December 2014. All other horses received an anthelmintic treatment using ivermectin (oral, 200 μg/kg bwt) in November 2014. On the training farm, the horses did not graze but were always kept in stables.

A single young H. diana larva (Fig 3) was used for morphological identification on the basis of spine and peritreme features, according to Otranto et al. (2003) and in comparison to young (presumably second instar) and third-instar H. diana larvae derived from deer (Fig 4).

**Discussion**

This is the first description of Hypoderma-associated myiasis in horses in Germany. The larvae were identified as H. diana, a warble fly with low host-specificity, which usually infests hosts from the families Cervidae and Bovidae and also some nonspecific hosts such as Suidae and Equidae (Pavlásek and Minár 2014).

Hendríkx et al. (1989) described the horse as an unsuitable host for H. diana, because they observed that the second-stage larvae did not develop to the third-stage. This assumption seems reasonable, since no live third-stage larvae were found in horses up to now, only dead third-instar and live second-instar larvae (Minár 1987, 1995; Kudrnáčová et al. 2014). Herein, we also found only second-instar larvae in the horse.

While the present case represents a comparatively heavy parasitism by larvae of H. diana in horses, it may be assumed that favourable epidemiological and circumstantial conditions contributed to this strong clinical infection: (1) the presence of large numbers of deer as the natural host in the nearby forest also grazing on the same pasture as the horses; and (2) the fact that the affected horse was the only animal on this farm that was not treated with a macrocyclic lactone in the autumn before the hypodermosis was detected. The epidemiology of H. diana in horses was evaluated in a 4-year study in the Czech Republic (Kudrnáčová et al. 2014) and the peaks of infestation were observed in June and July, when the temperature was higher than 18°C and low rainfall. Kudrnáčová et al. (2014) also suggested that hosts with dark fur might be more infested, which is the case of the horse described here. The proximity to forest areas, where wild animals that are typical hosts for Hypoderma larvae, is also an important risk factor to horses (Minár 1987; Hendríkx et al.1989; Kudrnáčová et al. 2014). According to Minár (1987), the infestation of horses by the deer warble fly can occur when both the domestic and wild host are abundant at the same time and there is also a large number of parasites. At least the first of these two conditions apply in the present case while no data are available on the prevalence of H. diana in the local wild deer population.

There is no clinical study evaluating antiparasitic drugs against Hypoderma larvae in horses, but the apparent efficacy of macrocyclic lactones observed in all other horses of the herd described here is indicative that this chemical group is effective in treatment of warble fly infestations in horses. Ivermectin at very low dose (2 μg/kg bwt) is indicated as an effective and environmentally nonthreatening strategy to be employed in a wide scale hypodermosis control programme in cattle (Boulard et al. 2008). This very low dose

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is effective against first-instar Hypoderma larvae in cattle, but not recommended to treat animals infested by the third-stage larvae. Against late stages of larvae, ivermectin (Boulard 2002) and doramectin (Hendrickx et al. 1993) at the therapeutic dose (200 μg/kg bwt) and eprinomectin at 1.0 mg/bwt (Rehbein et al. 2013) were shown to be efficacious. Thus, it may be assumed that the therapeutic dosage of 200 μg ivermectin/kg bwt as used for anthelmintic treatments in horses will also be effective against at least the first and potentially also the second larval stages of H. diana in horses. The time point of treatment needs to be decided upon based on the climate/weather conditions for each geographical region and year. Female warble flies essentially do not lay eggs following the first day of frost in late autumn and the larvae need approximately 1 week to develop in the eggs, after which they may infect the host. Accordingly, treatments directed to prevent the development of warbles should be done in late autumn.

This massive warble fly infestation in a horse in Germany reported here is important to alert equine health professionals concerning the prevention of this disease in the routine parasite control programme.

Authors’ declaration of interests
No conflicts of interest have been declared.

Ethical animal research
This is a single case report. No ethical review was required. Consent from the owner to publish the case report was obtained.

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Authorship
F. Borges contributed to preparation of the manuscript. G.W. Sybrecht contributed to data interpretation and preparation of the manuscript. G. von Samson-Himmelstjerna contributed to data analysis and interpretation, preparation of the manuscript, editing of the manuscript and gave the final approval.

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Case Report

Vestibulovaginal leiomyosarcoma in a mare

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Keywords: horse; vagina; vestibule; neoplasia; leiomyosarcoma

Summary

A 14-year-old Quarter Horse mare presented for a mass within the vestibule and vagina resulting in external compression and incomplete occlusion at the external urethral opening with subsequent difficulty urinating. Examination revealed an approximately 15 × 10 cm lobulated mass within the vestibule and caudal vagina attached via a broad base dorsally. Histopathology of the mass identified a low-grade leiomyosarcoma. Complete resection was not possible, and surgical debulking of the mass was performed during standing sedation using a vessel-sealing and dividing device. The mare was discharged 3 days post-operatively without any complications. Recheck examinations performed at 1 month and 8 months’ post-surgery revealed excellent healing of the surgical site and no apparent tumour regrowth.

Introduction

Neoplasia of the reproductive tract in the mare typically involves the ovaries or external genitalia, while tumours affecting the uterus, cervix and vagina are rare. One survey found that ovarian neoplasms comprised the vast majority of reproductive tract tumours in the mare at 88.6% (McCue 1998). There are few reports in the literature of neoplasia affecting the vagina or vestibule in the mare (McCue 1998; Cooper and Valentine 2002). Leiomyomas are tumours of smooth muscle origin which are benign in nature and may interfere with reproductive function or cause luminal obstruction when located within the urogenital tract (Cooper and Valentine 2002). In contrast, leiomyosarcomas are malignant smooth muscle neoplasms which are generally considered slow to metastasise (Cooper and Valentine 2002). Both leiomyomas and leiomyosarcomas have been described in horses affecting the gastrointestinal and urogenital systems most commonly, however leiomyosarcomas are rare with only three reported cases involving the mare reproductive tract (Lofstedt et al. 1987; Hinojosa et al. 2003; Hurcombe et al. 2008).

This case report describes a leiomyosarcoma within the vestibule and vagina of a 14-year-old Quarter Horse mare that was surgically debulked under standing sedation using a vessel-sealing and dividing device (Ligasure™) without gross recurrence at 8 months’ post-surgery.

Case history

A 14-year-old Quarter Horse mare was presented to Oregon State University Veterinary Teaching Hospital for evaluation of a mass within the vestibule and vagina. The mare was evaluated by the referring veterinarian approximately 1 h prior to admission for mild signs of colic and decreased appetite. The mare reportedly did not finish her feed that morning and was displaying minor signs of abdominal discomfort by laying down more than usual. Examination by the referring veterinarian revealed that vital parameters were within normal limits; however, transrectal palpation identified a large mass within the vaginal vault and a distended bladder. Brief vaginal examination revealed the mass was filling the entire vestibule and mechanically occluding the external urethral opening which was inhibiting the mare’s ability to urinate. There was no history of dysuria or haematuria, but the mare had not been noted to urinate that morning. A urinary catheter was passed to empty the bladder prior to referral to the university.

Clinical findings

On presentation to the referral centre, the mare was bright and alert and vital parameters were within normal limits. Complete blood count and serum chemistry performed at the time of admission were within normal limits. The mare was sedated i.v. with detomidine (Dormosedan; 0.01 mg/kg), and transrectal palpation identified a large cylindrical mass, measuring approximately 15 cm in length and 10 cm in width, present within the vagina and vestibule. No abnormalities of the uterus or ovaries were palpable, but the mare did have a moderately distended bladder. Transrectal ultrasound of the mass was performed which revealed a discrete, highly loculated, heterogeneous structure without an identifiable capsule (Fig 1). A caudal epidural was performed using 2% lidocaine hydrochloride (Vedco: 0.22 mg/kg bwt) and detomidine (Dormosedan: 0.022 mg/kg bwt) to facilitate vaginal examination and hysteroscopy. Vaginal examination revealed a large, partially lobulated, mass within the vestibule that extended just beyond the vestibulovaginal junction into the most caudal aspect of the vagina. The mass was attached dorsally via a broad base with slight involvement of the right vaginal wall. Vaginoscopy was performed using a 1 m flexible videendoscope (Fujinon; 11 mm) and confirmed the presence of a mass of pink tissue filling the lumen of the vestibule and the caudal vagina (Fig 2). No abnormalities or additional masses were noted within the cervix, uterus, urethra or urinary bladder. A wedge biopsy, measuring 2 × 2 cm, was obtained by sharp dissection after evertting the mass through the vulva. The sample was placed in 10% formalin and submitted for histopathology. Due to concerns that the mare had difficulty urinating due to the mass occluding the urethral opening, a 30 French Foley catheter was placed into the urethra and the bulb was inflated to secure it in place. The mare was...
administered ceftiofur free crystalline\(^3\) (Excede; 6.6 mg/kg bwt) i.m., flunixin meglumine\(^4\) i.v. (Prevail; 1.1 mg/kg bwt), and monitored in hospital over the next several days while awaiting biopsy results. The mare was known to be difficult for administration of oral medications, and ceftiofur free crystalline\(^3\) (Excede) was used in this case to prevent ascending infection due to the presence of a urinary catheter. During hospitalisation, the mare’s vital parameters remained within normal limits, and no signs of colic or anorexia were observed.

**Diagnosis**

Histologically, the nonencapsulated mass was comprised of neoplastic spindle cells arranged both in interweaving bundles and random patterns. The cells had elongate, blunt-ended nuclei with evenly distributed chromatin and finely fibrillary cytoplasm. Seven mitotic figures were found in ten 400× fields of view. Collections of the neoplastic cells protruded into adjacent connective tissue at the margins of the mass (Fig 3). A diagnosis of low-grade leiomyosarcoma was based upon these features.

**Treatment**

The mare received a second dose of ceftiofur free crystalline\(^3\) (Excede, 6.6 mg/kg bwt) i.m. 4 days after the first dose, and 5 days after initial presentation the mare underwent standing surgical debulking of the leiomyosarcoma. She was placed in stocks and sedated with an initial bolus of detomidine\(^1\) (Dormosedan; 0.01 mg/kg), and maintained on a constant rate infusion of detomidine\(^1\) (34 mg Dormosedan added to 500 mL LRS\(^5\)). This was titrated to effect (0.4–1.3 mg/h). A caudal epidural was performed using 2% lidocaine hydrochloride\(^2\) (Vedco; 0.22 mg/kg bwt) and detomidine\(^1\) (Dormosedan; 0.022 mg/kg bwt). The rectum was evacuated and the tail was secured out of the surgical field. The perineum and vulva were prepared with Betadine solution and warm water. Doyen hand held retractors were used to retract the vulvar lips and visualise the mass. Curved Metzenbaum scissors were used to incise the epithelium surrounding the tumour, and a combination of blunt and sharp dissection was used to separate the tissue planes that attached the base of mass to the roof of the vestibule. Once an adequate tissue plane was identified, the Ligasure\(^\text{TM}\) was used to complete transection of the mass from its attachment to the roof of the vestibule and vagina. Efforts were made throughout the surgical procedure to avoid deep penetration of the perineal body and potential penetration of the adjacent rectum. After removal of the mass, it was apparent that excision was incomplete. Digital palpation of the right cranial and left mid vaginal walls revealed thickened tissue with a mild cobblestone texture that was suspicious for additional tumour tissue. No ancillary therapies were performed. The excised mass measured 15 × 9 × 2.5 cm. Post-operatively the mare was treated with flunixin meglumine\(^4\) (Prevail; 1.1 mg/kg bwt) i.v. twice daily for three doses, and then switched to oral phenylbutazone\(^2\) (Equi-Phar; 2.2 mg/kg bwt) orally once daily for 4 days. The mare did well post-surgery with minimal haemorrhage or observable discomfort. The mare was discharged 3 days post-operatively with instructions for 3 weeks of stall rest with handwalking.

**Fig 1:** Transrectal ultrasound image of the loculated heterogeneous mass within the vestibule taken on presentation.

**Fig 2:** Endoscopic image of the mass within the vagina. The endoscope has been positioned so that the camera is facing caudally viewing the most cranial portion of the mass within the vagina.

**Fig 3:** Photomicrograph (haematoxylin and eosin stained, magnification ×400) of neoplastic spindloid cells with invasion into adjacent fibrovascular tissue.
Outcome

The mare returned for a recheck evaluation at 4 weeks’ post-surgery. Her vital parameters were within normal limits, and she was reported to have been doing well at home without signs of discomfort. Vaginoscopy revealed an area of hyperaemic mucosa present on the dorsal aspect of the vestibule that extended along the right wall to the 3 o’clock position, corresponding to the previous location of the mass. She was allowed to return to her usual routine with instructions to return for a re-evaluation within the year.

The mare was re-evaluated once more at 8 months’ post-surgery. The mare had returned to regular exercise without difficulty, and the owner had no concerns regarding her health. No abnormalities were identified at her physical examination. Transrectal palpation revealed a palpably normal diestrus uterus and ovaries. Vaginoscopy identified healthy mucosa within the vestibule and vagina with a small area of scar tissue located at the 3 o’clock position. No samples were taken for biopsy and, although there was no observable evidence of tumour recurrence, the owner was advised to have annual vaginal examinations performed on the mare. The mare was sold approximately 1-year post-surgery at which time she appeared in good health, and no further follow-up was available.

Discussion

Primary neoplasms of the vestibule and vagina in the horse are rare, with benign leiomyomas being most common (McCue 1998). One retrospective analysis evaluated the occurrence of histopathologically confirmed leiomyomas and leiomyosarcomas over a 20-year period in several species, and identified 3/27 leiomyomas and 0/2 leiomyosarcomas of the vagina/cervix in mares (Cooper and Valentine 2002). As a result of infrequent occurrence of neoplasms in this location, there is little information available about clinical signs, treatment, biological behaviour, and expected outcomes. The case reported here describes the successful debulking of a low-grade leiomyosarcoma within the vestibule and vagina of a mare without macroscopic recurrence at 8 months’ post-operatively.

Leiomyosarcomas have been reported in the horse involving the oesophagus (Boy et al. 1992), stomach (Boy et al. 1992), duodenum (Mair et al. 1990), jejunum (Livesey et al. 1986), rectum (Clem et al. 1987), testes (Allison and Moeller 1999), uterus (Lofstedt et al. 1987; Hinojosa et al. 2003), vagina (Hurcombe et al. 2008) and bladder (Hurcombe et al. 2008). One case report identified a multicentric leiomyosarcoma of the mandible and frontal bone in a young horse that was suspected to originate from the vascular smooth muscle (MacGillivray et al. 2003). Typically, these tumours are locally invasive, and slow to metastasise with only one reported occurrence of metastasis in the horse (Cooper and Valentine 2002). Clinical signs are often related to luminal obstruction of the affected organ, and as such these neoplasms may go undetected for an undetermined length of time and may be incidental findings on necropsy examinations (Cooper and Valentine 2002). In the case reported here, the initial colic signs observed in this horse were thought to be the result of a distended bladder secondary to incomplete occlusion of the external urethral opening by the mass. A gastrointestinal lesion was excluded based on physical examination findings, transrectal palpation, and no recurrence of colic signs during hospitalisation after placement of a urinary catheter. Additional diagnostic tests including abdominal ultrasound, abdominocentesis with fluid analysis, and gastroscopy could have been performed to further evaluate the gastrointestinal tract. Since leiomyosarcoma has been reported to involve gastrointestinal smooth muscle, these tests could have also been used to assess for possible involvement of leiomyosarcoma in the abdomen, although no definitive exclusion of gastrointestinal involvement could have been made without exploratory celiotomy.

In the case reported here, a wedge biopsy of the mass was obtained on admission which displayed typical characteristics of a leiomyosarcoma, which included the presence of spindle-shaped cells arranged in interwoven fascicles with an oblong to bullet-shaped nucleus and the presence of mitoses (Cooper and Valentine 2002). Several stains are available to assist in diagnosis of smooth muscle tumours, including those for desmin, muscle actin and vimentin. Stains were not considered necessary in this case due to the histological appearance being characteristic of a smooth muscle neoplasm. It is important to note that a larger sample acquired through excisional biopsy or complete excision may be essential in some cases to ensure accurate diagnosis. Many of the cases reported in the available literature were diagnosed on post-mortem examination; however, biopsy collected with uterine biopsy forceps in one case of a poorly differentiated vaginal leiomyosarcoma was inconclusive requiring excisional biopsy for definitive histological diagnosis with the aid of immunohistochemical staining (Hurcombe et al. 2008).

The surgical technique used in this case was elected to enhance the opportunity for maximal tumour debulking while maintaining an intact vestibule and vaginal wall without penetration into the rectovestibular space, peritoneal cavity or rectum. A standing procedure with the aid of a caudal epidural resulted in excellent visualisation of the tissue mass, the vestibule and the vagina for surgical manipulation. The use of the Ligasure™ allowed rapid surgical debulking with minimal haemorrhage and excellent control of tissue transection depth. There is one report of an excisional biopsy of a leiomyosarcoma within the vagina although the surgical technique was not described, and the mass may have originated from the bladder (Hurcombe et al. 2008). There is a recent case description of the successful removal of an intraluminal uterine leiomyoma via an endoscopically assisted transvaginal approach that used the Ligasure™ for transection of the tumour from the uterine wall (Schneeweis et al. 2015). The Ligasure™ is a bipolar electrosurgical device that denatures collagen and elastins in vessel walls and combined with mechanical pressure results in permanent sealing of vessels up to 7 mm in diameter (Fischer Jr et al. 2012). It has been used extensively for minimally invasive procedures in the horse. It is possible that use of the Ligasure device may denature proteins within the neoplastic cells altering their activity or resulting in cell death. In addition, transection of tissue and vessels at the base of the mass with a permanent sealing device may prevent seeding of surrounding tissue with tumour cells.

Chemotherapeutic protocols may be considered for tumours with local recurrence or metastasis, although there is no evidence of efficacy for leiomyosarcoma in the horse. One reported recurrence of bladder leiomyosarcoma that occurred within 1 month after excisional biopsy was treated with a single...
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dose of doxorubicin (30 mg/m²) i.v. and dexamethasone [0.1 mg/kg] i.v. with no apparent effect on tumour growth, and the horse was ultimately subjected to euthanasia (Hurcombe et al. 2008). A retrospective study on canine intestinal leiomyosarcoma described a chemotherapeutic protocol with doxorubicin [30 mg/m² i.v. at weeks 1, 4 and 7], cyclophosphamide [100 mg/m² at weeks 1, 4 and 7] and vincristine [0.7 mg/m² at weeks 2, 3, 5 and 6], but only two dogs were treated with this protocol making it difficult to draw any conclusions regarding its effect on tumour growth (Cohen et al. 2003). Despite the lack of literature supporting the use of chemotherapy for treatment of leiomyosarcoma, it could be considered as a last resort in cases of tumour recurrence where all other options have been exhausted.

Only three cases report on the successful outcome without recurrence of leiomyosarcoma for up to 20 months’ post-surgery in the horse (Livesey et al. 1986; Clem et al. 1987; Hinojosa et al. 2003); however, long-term outcome may depend more on location of the tumour and whether this location is amenable to surgical resection and/or debulking. Reports involving tumours of the duodenum, stomach and bladder resulted in euthanasia due to an inability to resect the tumour tissue (Mair et al. 1990; Boy et al. 1992; Hurcombe et al. 2008). Growth of leiomyosarcomas is considered to be rapid in many species and this tumour characteristic was apparent in two horses with tumours affecting the uterus and vagina/bladder (Lofstedt et al. 1987; Hurcombe et al. 2008).

In humans, vaginal leiomyosarcoma is rare, but tumors recur frequently after surgical excision with metastases common and an overall poor prognosis (Ahram et al. 2004). Frequent recheck examinations are recommended to determine tumour recurrence and/or presence of metastatic disease; however, behaviour of this neoplasm in the horse remains undetermined due to its rare nature. The mare in this case report was re-examined 8 months’ post-surgery with no gross indication of tumour regrowth and only mild scar tissue present at the surgical site. Biopsy of the scar tissue was declined at that time as the mare was clinically doing well. Regrettably, the mare was subsequently sold, and no further follow-up was available.

This report suggests that surgical debulking of a primary vestibulovaginal leiomyosarcoma with the Ligasure™ device has a favourable prognosis for long-term outcome. The mare has done well up to 8 months’ post-surgery without macroscopic evidence of tumour recurrence, although recurrence remains a risk and frequent vaginal examinations to monitor for any indication of regrowth were recommended.

Authors’ declaration of interests
No conflicts of interest have been declared.

Ethical animal research
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Authorship
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References
Case Report

Aryepiglottic lymphoma in a 19-year-old Paint gelding treated with excision and adjunctive radiotherapy

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Keywords: horse; chemotherapy; lymphoma; radiotherapy; strontium

Summary

This case report describes the diagnosis and treatment of an aryepiglottic tumour in a 19-year-old Paint gelding. Diagnostic work-up included physical examination, endoscopic evaluation of the upper airway, and histopathology of the mass following removal. Treatment consisted of surgical excision of the aryepiglottic mass under endoscopic guidance followed by a 100 Gy dose of radiation delivered with strontium-90 plesiotherapy to the surgical bed at 72 h post-operatively. The radiation applicator was passed through the left nostril and the application area was confirmed via endoscopic evaluation. Histopathology, including immunohistochemistry, confirmed that the aryepiglottic tumour was T cell lymphoma. Recheck examination, including physical examination and upper airway endoscopy, was performed 1, 3 and 6 months following treatment and local recurrence was not observed. Local control with minimal morbidity can be achieved with surgical excision of equine lymphoma followed by strontium-90 plesiotherapy.

Introduction

Lymphoma is the most common haematopoietic neoplasm identified in horses and accounts for 1–3% of all equine tumours (Taintor and Schleis 2011). Clinical signs of equine lymphoma include weight loss, anorexia, depression, lethargy, ventral oedema, pyrexia, lymphadenopathy, diarrhoea and colic (Van den Hoven and Franken 1983; Sweeney and Gillette 1989; Meyer et al. 2006; Muñoz et al. 2009; Durham et al. 2012). Solitary extranodal tumours have been reported in the spleen, palate, nasopharynx, nasal passage, sinus, tongue, meninges, gingiva and pelvis (Lane 1985; Burba et al. 1991; Lester et al. 1992; Tanimoto et al. 1994; Weaver et al. 1996; Gerard et al. 1998; Rhind and Dixon 1999; Oikawa et al. 2003; Montgomery et al. 2009). Ante-mortem diagnosis of lymphoma is typically made through histopathological evaluation of biopsy specimens or cytological examination of fine needle aspirates of a suspected lesion (Mair et al. 1985; Taylor et al. 2006; Taintor and Schleis 2011). Classification systems for lymphoma in veterinary species rely on morphological features of the tumour and incorporate assignment of T- or B-cell origin or proliferative indices (Teske et al. 1994; Vernau et al. 1997; Kiupel et al. 1999).

The prognosis for horses diagnosed with lymphoma depends on the form of lymphoma and stage of disease. Current treatment options for lymphoma in the equine case include surgical excision of accessible masses, radiotherapy or administration of chemotherapeutics. Treatment has been reported to result in palliation and occasionally resolution of disease without recurrence (Taintor and Schleis 2011). The present case report describes the diagnosis, treatment and outcome of a 19-year-old gelding diagnosed with aryepiglottic lymphoma.

Case history

A 19-year-old American Paint Horse gelding presented for evaluation of coughing and dysphagia of several weeks duration. Transtracheal wash was performed 4 days prior to presentation and cellulitis of the ventral cervical region developed following the procedure. Upper airway endoscopy revealed a right-sided aryepiglottic mass. The gelding was referred for further diagnostics and treatment.

Clinical findings

Initial physical examination performed revealed a pulse rate (48 beats/min) and respiratory rate (18 beats/min) that were within normal limits. Rectal temperature (38.9°C) was increased. The gelding had feed material in both nostrils and would readily cough and snort feed material during eating. A venous blood sample was submitted for complete blood count, which revealed increased nucleated cell count 16.9 × 10⁹/L (reference range [rr] 5.5–10.5 × 10⁹/L), neutrophil count 14.5 × 10⁹/L (rr 3–7 × 10⁹/L) and fibrinogen 6 g/L (rr 1–4 g/L). Cellulitis of the ventral cervical region surrounding the transtracheal wash site was appreciated. Endoscopy of the nasopharynx revealed moderate feed contamination and an approximately 3 × 4 cm right aryepiglottic mass (Fig 1a).

Treatment

An intravenous jugular catheter was placed and the horse was administered potassium penicillin (22,000 Mu/kg bwt i.v. q. 6 h), gentamicin (6.6 mg/kg bwt i.v. q. 24 h), metronidazole (15 mg/kg bwt per os q. 8 h) and phenylbutazone (2.2 mg/kg bwt i.v. q. 12 h). The horse was sedated and restrained in the stocks. Following topical application of 35 mL of 2% lidocaine solution, the majority of the mass in the right aryepiglottic region was resected using a combination of epiglottic scissors (Embertson Esophageal Epiglottic SCS 1404-883B) and diode laser excision under endoscopic guidance. Dysphagia immediately resolved following surgical excision. Seventy-two hours following surgical excision, the gelding was again sedated and upper airway endoscopy repeated (Fig 2a). Thirty-five mL of 2% lidocaine solution was topically applied to the surgical bed. Following radiation ALARA protection...
procedures developed with institutional oversight, an Sr-90 probe with a 2 cm convex application surface was attached with medical tape to a surgical laser cutting guide (Crochet chirurgie Laser equine 60 cm) in a shielded area while wearing ring badges and two layers of surgical gloves. Medical personnel wore lead aprons during treatment while the probe was passed through the left nostril and nasopharynx to the laryngeal region. The applicator was pressed against the tumour bed over 10 min and 100 Gy was administered (Fig 2b). Endoscopy combined with application of radiation therapy took approximately 15 min to perform. After the treatment was completed, a wipe test of the probe was carried out as well as a survey of the treatment room, resulting in background radiation levels, and the source was replaced in the facility shielded cabinet. The horse was discharged from the hospital following radiotherapy.

Outcome

Histologically, the aryepiglottic mass contained a homogenous population of lymphocytic cells with a high number of CD3 + neoplastic cells, supporting a diagnosis of T cell lymphoma.

The gelding was maintained on stall rest until his first recheck appointment 1 month post-operatively. Complications related to radiotherapy were not observed in the early or late post-operative period. Local recurrence was not observed endoscopically 1 month following treatment (Fig 1b) and the gelding’s exercise was increased to small paddock turnout.

Recheck examination, including physical examination and upper airway endoscopy, was repeated 3 and 6 months after treatment and local recurrence was not observed (Fig 1c,d). At this time, the horse was back in work and in good health.

Discussion

This case report highlights the role of radiotherapy following ablative surgery in the treatment of localised equine lymphoma. Local control was maintained in this case for 6 months post-operatively with no local recurrence. Radiotherapy was utilised as an adjuvant treatment because of the conservative tissue resection technique selected in this anatomic location. No radiation-induced complications following treatment with strontium-90 were observed at the time points evaluated. This case report demonstrates that local control with minimal morbidity can be achieved with surgical excision in conjunction with radiotherapy in the treatment of solitary equine lymphoma.

Radiotherapy in the horse can be performed using either brachytherapy or teletherapy. Brachytherapy involves the use of a radioactive source (strontium-90, iridium-192 or iodine-125) through surface treatment or implantation. Common forms of brachytherapy include interstitial, where sources are placed directly into the tissue, or intracavitary, where an applicator containing sources is placed within a body cavity. Brachytherapy can also be administered using a low dose rate (LDR), with dose rates \(<2\) Gy/min, and permanent implants, while high dose rate (HDR) brachytherapy is applied with dose rates greater than \(12\) Gy/min using temporary implants. Plesiotherapy is a form of brachytherapy where the radiation is administered using a probe. Strontium 90 plesiotherapy is the direct application of radioactive strontium to a lesion. The size and shape of strontium probes can vary, but generally the strontium tip is shielded from the user by a 1 cm plexiglass pane. Strontium-90 is a pure β emitter and the prescription dose is deposited within the treatment surface at a depth of several millimetres. This treatment has been commonly used for malignant and benign corneal and conjunctival lesions in both
human and veterinary medicine (Gruning et al. 2001; Vastardis et al. 2009; Lecuona et al. 2015). Plesiotherapy has been used for a variety of small tumours in other locations in veterinary medicine (Hammond et al. 2007; Ware and Gieger 2011). Teletherapy involves deployment of radiation from an external beam, either linear accelerator or colbalt-60 machine. Teletherapy is the most commonly used radiation modality for human and small animal veterinary cases. Teletherapy requires an amply shielded treatment vault, and to treat an animal weighing over roughly 160 kg, adaptations have to be made to provide a treatment couch robust enough to support the patient (Henson and Dobson 2004). Whether radiotherapy is indicated depends upon the size and location of the tumour (Weaver et al. 1996; Vail and Young 2002; Henson and Dobson 2004; Gerard et al. 2010), and the dose is determined based upon tumour location, size and depth. Radiation therapy with three doses of megavoltage radiotherapy applied as a single beam from a 4 MV linear accelerator and given under general anaesthesia at 7 day intervals was used in one report to treat four horses diagnosed with lymphoma, three with solitary skin masses and one with a mass in the nasal passage (Henson et al. 2004), and all four horses were reported to be tumour-free for up to 8 years following treatment. An additional report of radiation therapy with two doses of 8 Gy using 6 MV photons given under general anaesthesia at 7 day intervals in a pony with extensive paranasal sinuses and nasal passage B cell lymphoma suggested that palliative treatment was successful in improving and prolonging quality of life for 2.5 years following treatment in that case (Gerard et al. 2010). Furthermore, localised equine B cell lymphoma appeared to be radiosensitive and palliative radiation therapy was a reasonable treatment option for large tumours, even in cases where the entire tumour was not accessible to be irradiated (Gerard et al. 2009). The horse in the present report had complete remission for 6 months after combined ablative surgery and radiotherapy. In a study evaluating localised lymphoma in 10 cats treated with radiation therapy, complete remission was obtained in eight cats (Elmslie et al. 1991). In the six cats that had tumour control at 6 months, the average survival was 159 weeks, with three alive at the time of follow-up (Elmslie et al. 1991).

Beta irradiation from a strontium source is a favourable treatment option for equine lymphoma for several reasons. The procedure is simple, quick and readily performed under standing sedation on an outpatient basis, although case cooperation is essential in maintaining consistent position of the strontium probe. Strontium is a pure β emitter without clinically significant photon activity, which greatly reduces the potential radiation hazards in handling the strontium source and minimises shielding costs. Radiation effects are localised to the region being treated. Acute effects, which are common and transient, include dry and moist desquamation and inflammation with reddened and possibly swollen tissues visible. Late effects can include nonhealing ulceration and necrosis (Weaver et al. 1996; Henson and Dobson 2004). Radiotherapy treatment-related complications were not noted in the horse in this case report and he did not display any signs that we would have associated with acute or late radiation effects, such as discomfort, drooling or reluctance to eat.

Prognosis in cases of equine lymphoma is a clinical challenge. Histopathology and diagnostic imaging can be used to stage and determine prognosis. The WHO has developed a clinical staging system for lymphoma in domestic animals based on anatomic site and extent of organ involvement and clinical signs (Vail and Young 2002). Clinical stage can help determine which course of treatment, including surgical excision, radiotherapy, chemotherapy or some combination thereof, is pursued in a specific clinical case. Future studies focusing on disease subtype and location in the equine patient in correlation with clinical outcome are necessary to identify prognostic features and appropriate treatment (Vail and Young 2002; Durham et al. 2012). On the basis of excellent local control rate with minimal morbidity in this case, the use of ablative surgery followed by β irradiation from a strontium source is advocated as an effective treatment for specific cases of equine lymphoma.

Authors’ declaration of interests
The authors declare that they have no conflicts of interests.

Ethical animal research
Permission was obtained from the owner of the horse described in this case study for publication of the case for educational purposes.
Source of funding

No financial support or donations of equipment or drugs were received for the development of this report or in the diagnosis and treatment of the animal about which this report was written.

Authorship

The horse described in this case was referred to the Colorado State Veterinary Teaching Hospital where the case was primarily managed by E. Hackett and L. Pezzanite. Adjunctive radiotherapy was overseen by S. LaRue and D. Leary. Contributions for preparation of the manuscript were made by L. Pezzanite, E. Hackett, D. Leary and S. LaRue. All authors gave their approval for the final version.

Manufacturers' addresses

1Sontec Instruments, Centennial, Colorado, USA.
2Vet-Aire, Inc., Ithaca, New York, USA.

References


Clinical Commentary

Strontium-90 plesiotherapy in the horse

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Summary

Strontium-90 plesiotherapy is a form of very superficial radiotherapy that is most commonly used as part of the management of ocular and periorcular squamous cell carcinomas in the horse. Although it can be an extremely effective treatment, with the ability to deliver very high doses of radiation to the tumour without affecting the surrounding tissues, the penetration is only a few millimetres, which limits its use in equine medicine to very specific situations. In addition, the availability of strontium-90 plesiotherapy is limited to specialist institutions due to the health and safety and security concerns of accessing a high activity sealed source.

Plesiotherapy is a form of radiotherapy where the radiation source is applied directly to the surface of the tumour. This involves the use of a high activity, sealed source that can be applied to a predefined area whilst observing appropriate health and safety precautions. The most commonly used plesiotherapy source in veterinary medicine is a strontium-90 probe. Strontium-90 has the advantage of a very long half-life (28.7 years); therefore, once a probe has been purchased, it continues to have a similar activity for a very long time, making it potentially quite cost effective. This is fortunate, because destruction of the source once it is no longer needed is difficult and expensive to carry out, so most institutions will keep a strontium-90 source for many years following purchase. The β radiation produced by the strontium-90 itself is too weak to be of practical use. However, strontium-90 decays to yttrium-90, which produces β radiation at 2.27 MeV as it decays. This β radiation has a very shallow depth of penetration, meaning that very high doses of radiation can be applied to the surface of the tumour without risking exposure of normal underlying tissues. The major disadvantage of this therapy is that it is therefore only suitable for extremely superficial tumours or the treatment of scars following incomplete surgical excision, as 60% of the radiation dose is absorbed in the first 1 mm of tissue. Treatment is therefore limited to very superficial lesions (usually <3 mm in depth). The radioactive source is usually around 0.8–1 cm in diameter, and is mounted on a stainless steel shaft, which incorporates a Perspex shield to protect the operator’s hand. During treatment, the source is applied directly onto the tumour surface. Depending on the location of the lesion, this may be performed under heavy standing sedation or via general anaesthesia. Many lesions require general anaesthesia for an effective treatment to ensure accurate positioning of the probe, but, depending on the horse’s temperament, lesions in some locations can be safely and effectively treated using heavy sedation alone. The duration of treatment will depend on the current activity of the probe and the size of the lesion to be treated, but is usually only a few minutes. The prescribed tumour dose is defined as the minimum dose in the target volume (which should include a 2 mm margin) and ranges from 80 to 100 Gy (Theon 1998). The surface dose will typically be in the order of 200–250 Gy, depending on the thickness of the area to be treated. Where the treatment area is larger than the size of the probe, a multiple abutting field configuration is required, with the applications over-tapping on the tumour tissue to allow effective treatment. Drawing a measured grid on the surface of the tumour using callipers and a marker pen helps to achieve accurate treatment of more extensive lesions (Fig 1). The total surface dose should not exceed 500 Gy, even if this is fractionated (Theon 1998). Fractionation is achieved by giving repeated applications of strontium-90 over a period of time. This allows an effective dose of radiation to be administered whilst minimising side-effects. Side-effects of radiation are common but are usually self-limiting. Early effects of radiation can be seen within a few weeks of the completion of a course of radiotherapy. These appear to usually be mild and self-limiting in equine cases at published dose rates using various forms of brachytherapy or plesiotherapy. Side-effects of radiation may include skin erythema, desquamation of the skin and depigmentation of the hair and/or skin (Bentzen 2006). Late effects of radiation may be seen many months or even years after treatment and can include fibrosis and cataract formation (where radiation is administered near the eye). Bone necrosis can be seen many years after radiotherapy and this can be clinically significant, although this thankfully appears to be extremely unlikely in our equine cases, with no reports of bone necrosis following radiotherapy of any form in the equine veterinary...
literature. In addition, the limited penetration of strontium-90 plesiotherapy means that the most significant complications of cataract formation (where radiation is near the eye) and bone necrosis are exceptionally unlikely to occur. However, it is imperative to get a balance between a therapeutic benefit and the inevitable associated toxicities of exposure to radiation.

Strontium-90 plesiotherapy has been most commonly used for the treatment of squamous cell carcinomas in horses, with local control rates following irradiation of ocular and periocular tumours reported as being between 83 and 100% up to 3 years after treatment (Frauenfelder et al. 1982; Walker et al. 1986; Theon 1998; Plummer et al. 2007). It has also been briefly described in the treatment of three periorbital sarcomas, where all three lesions resolved and had not recurred between 1 and 4 years following treatment (Knottenbelt and Kelly 2000). It may also be a useful adjunctive or stand-alone therapy for the treatment of other very superficial tumours in the horse. The most likely alternative use is to treat margins following incomplete surgical excision of a superficial lesion. Conservative surgery combined with radiotherapy will lead to fewer functional and cosmetic effects, with radiotherapy being used to eradicate tumour cells left behind after an incomplete excision (Theon 1998). This means that strontium-90 plesiotherapy can be used following surgical excision of a lesion to reduce the risk of recurrence in areas where a complete surgical excision is not possible. Recently, strontium-90 plesiotherapy was described as an adjunctive treatment following surgical excision of an aryepiglottic lymphoma in a gelding which gave excellent functional results (Pezzanite et al. 2019). This author has used strontium-90 plesiotherapy to treat a scar successfully following incomplete surgical excision of a small fibroblastic sarcoid located in the nostril of a young
gelding; there has been no recurrence at 18 months following the treatment despite histopathological examination of the surgical specimen confirming extension of the lesion past the surgical margins (Figs 1–5; A.R. Hollis, unpublished data).

Although the technique is simple and the results can be excellent, the availability is limited. Strontium-90 is a high activity sealed source, which has very specific security and health and safety requirements associated with its purchase, storage, use and eventual destruction. In the UK, there is no longer access to purchase new strontium applicators, so only institutions that already have the applicator can offer this therapy, at least in the UK. This means that only a few specialist institutions have access to strontium-90, which probably contributes to the minimal published data on its use in the horse. In human medicine, ruthenium-106 has taken over from strontium-90 for plesiotherapy applications, although, to the author’s knowledge, this has not yet been used in equine medicine and strontium-90 remains the only option for plesiotherapy in the horse.

Author’s declaration of interests

No competing interests have been declared.

Ethical animal research

Not applicable.

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References

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Case Report

Electroacupuncture as an additional treatment for headshaking in six horses

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Keywords: horse; electroacupuncture; trigeminal neuralgia; headshaking; neuropathic pain

Summary
Some success has been demonstrated using percutaneous electrical nerve stimulation (PENS) to treat trigeminal-mediated headshaking (TMHS) in horses. The aim of this study is to determine whether electroacupuncture (EA) can provide similar remission from the pain of this debilitating condition. EA is less invasive than PENS and can be carried out in the stable yard without the need for a hospital setting and expensive equipment. Six horses and ponies showing clinical signs of headshaking were treated with electroacupuncture of the infraorbital nerve under light sedation. The nerve was stimulated with alternating 2 and 80 Hz frequencies for a period of 25 min with the current adjusted so that there was visible twitching of the nostrils and/or lips. Follow-up treatments were given when the signs recurred or 4–7 days later if there was no initial response. The procedure was well tolerated by all the horses. Once a response was achieved, the period of remission often increased with subsequent treatments. Median remission time for the first treatment was 5.5 days (mean 7.6 days, range 0–13 days, n = 6). second treatment 8.5 days (mean 10.6 days, range 7–21 days, n = 6), third treatment 18 days (mean 28.8 days, range 6–71 days, n = 6), fourth treatment 47.5 days (mean 10 weeks, range 11 days–23 weeks, n = 6), fifth treatment 13 weeks 5 days (mean 18 weeks 5 days, range 5 weeks–6 weeks, n = 5), sixth treatment 24 days (mean 26 days, range 13–41 days, n = 3). The three horses that started treatment in 2015 received a single treatment in April or May of 2016 and were still asymptomatic at the end of the study period in October 2016. It was concluded that EA of the infraorbital nerve is an effective and well-tolerated treatment for the management of horses considered to be experiencing trigeminal-mediated headshaking.

Introduction
The syndrome termed headshaking (HS) has a characteristic and well-recognised clinical presentation that is thought to be attributable to involvement of the trigeminal nerve. It has been suggested that the condition is similar to trigeminal neuralgia in man (Cook 1980; Mair 1999; Newton et al. 2000). The human disorder is characterised by episodic, intermittent or persistent, mild or severe tingling, burning, stabbing or shooting electric shock-like pain in the facial region, which is triggered by relatively minor, often specific facial, nasal or oral stimuli. It is suggested that the equine condition is similar (Newton et al. 2000) accounting for the clinical signs observed in horses (Pickles et al. 2014). Nerve conduction studies show that affected horses have a lower stimulus threshold to trigger sensory nerve action potentials in the maxillary branch of the trigeminal nerve than healthy horses (Aleman et al. 2013; Aleman et al. 2014).

Electroacupuncture (EA) has been successfully used to treat chronic nerve/neuropathic pain in horses and man (White et al. 2001; Xie et al. 2005). Robert’s et al. (2016) described the use of PENS to treat TMHS in horses. The purpose of this study was to determine whether EA provided sufficient relief to recommend as a first line treatment for trigeminal-mediated (TM) HS. To the author’s knowledge there are no previous scientific reports of the specific use of EA for the treatment of TMHS in horses.

Electroacupuncture and percutaneous electrical nerve stimulation are similar (Cummings 2001); both modulate perception of afferent nociceptive stimuli by inhibiting afferent pain signals and by activation of descending inhibitory pathways. The low pulse rate of 2 Hz induces encephalins and acts on μ and δ receptors providing analgesia, whilst the higher pulse rates of 80–100 Hz release dynorphins and acts on κ receptors (Han 2003). This combination of frequencies is more effective than a single constant current. More detailed information on the mechanisms of EA on persistent and neuropathic pain are described by Kim et al. (2013) and Zhang et al. (2014).

Three of the horses in the current study were sensitive to sunlight so the owners were asked to use protective UV blocking face masks and/or nose nets when they were turned out or exercised. Previous studies have demonstrated that in 50–70% of affected horses there is a significant decrease in clinical signs when using these (Mills and Taylor 2003). Horses 1, 2 and 6 also wore them in the stable. It has been postulated that photic stimulation of the optic nerve by sunlight causes cross-activation of the maxillary branch of the trigeminal nerve (Madigan et al. 1995). In addition to reflecting UV light, the effect of the face mask and nose net is considered to be due to stimulation of touch and pressure receptors, the axons of which synapse with the terminals of the small unmyelinated true pain C fibres, subjecting them to presynaptic inhibition (King 1999). They also give some protection from wind, dust, pollen and thermal radiation from the sun. Full resolution of signs using just a nose net or face mask is rare (Pickles et al. 2014), and only one of the six horses in this study (Horse 4) showed an adequate response.

Materials and methods
The study was completed over a 19-month period and included four horses and two ponies (Table 1). For inclusion they were considered to be trigeminal-mediated headshakers...
<table>
<thead>
<tr>
<th>Horse</th>
<th>Age</th>
<th>Breed</th>
<th>Sex</th>
<th>Use</th>
<th>Year of purchase</th>
<th>Month and year affected</th>
<th>Seasonality</th>
<th>Grade of HS</th>
<th>Previous treatment</th>
<th>Response to previous treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>15</td>
<td>Trakehner</td>
<td>Mare</td>
<td>Dressage</td>
<td>2007</td>
<td>July 2012, May 2013, March 2014</td>
<td>July to October, May to October, March to October</td>
<td>3</td>
<td>–, Face mask, Nose net, Carbamazepine, Anaesthetic eye drops, Global Herbs PolleneX</td>
<td>Good, Good, Good, Good, Good</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>Shetland Pony</td>
<td>Mare</td>
<td>Driving as a single and as a pair</td>
<td>2005</td>
<td>June 2014, March 2015</td>
<td>June to November</td>
<td>3</td>
<td>Face mask, Carbamazepine, Acupuncture – dry needling, Homeopathic remedies</td>
<td>Good, Some improvement, No effect, No effect, Good, Good, Good, None, None, Good</td>
</tr>
<tr>
<td>3</td>
<td>8</td>
<td>KWPN</td>
<td>Gelding</td>
<td>Eventing</td>
<td>2013</td>
<td>March 2015, May 2015</td>
<td>Unknown</td>
<td>3</td>
<td>Facemask, Steroids, Nose net, Feed additives, Bedding change, Nose net</td>
<td>Good, None, None, None, None, Good</td>
</tr>
<tr>
<td>4</td>
<td>13</td>
<td>New Forest Pony</td>
<td>Gelding</td>
<td>Eventing</td>
<td>2014</td>
<td>July 2015</td>
<td>Unknown</td>
<td>3</td>
<td>Nose net, Face mask, Herbal remedy, Face mask, Corticosteroids</td>
<td>None, None, None, None, None</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>KWPN</td>
<td>Gelding</td>
<td>GP</td>
<td>2014</td>
<td>September 2015</td>
<td>Unknown</td>
<td>3</td>
<td>Nose net, Face mask, Herbal remedy, Face mask, Corticosteroids</td>
<td>None, None, None, None, None</td>
</tr>
<tr>
<td>6</td>
<td>7</td>
<td>Dutch Warmblood</td>
<td>Mare</td>
<td>All rounder</td>
<td>2016</td>
<td>May 2016</td>
<td>Unknown</td>
<td>3</td>
<td>Face mask, Herbal remedy, Face mask, Corticosteroids, Top Stock Headshaking Formula</td>
<td>Would not tolerate, Reduced nose swelling, Unknown, None, None, None</td>
</tr>
</tbody>
</table>
by the primary veterinary surgeon or referral practice and the author. Prior to inclusion each horse underwent a dental and oral examination plus nasopharyngeal endoscopy including examination of the gullet pouches in order to rule out as far as possible the presence of dental issues, tumours, infection or a foreign body. In addition, Horse 3 had dental radiography and a computed tomography scan was performed on Horse 6. All had negative findings with these diagnostic procedures and were showing clinical signs of headshaking at the time of presentation for EA. In the 19-month period no horses were excluded from the study.

All horses underwent a comprehensive clinical examination including moving in hand, on the lunge and ridden if appropriate, and a detailed medical history was obtained (Table 2). Headshaking grades at rest and at exercise were recorded for each horse and the grading system of 0–3 explained to the owners (Table 3). When possible, a video recording was made of the horse at exercise.

Assessment was made of the fit of the bridle and saddle with ridden horses. Any dental, tack or musculoskeletal issues were addressed prior to commencement of treatment in case they were contributory factors to the headshaking.

**Procedure**

Each horse was sedated with a combination of detomidine hydrochloride 10 μg/kg bwt (Domosedan)\(^1\) and butorphanol 0.025 mg/kg bwt (Torbugesic)\(^2\). This is the manufacturer’s recommendation for light sedation, but a reduced dose was often adequate. Whilst under sedation, the horse’s head was rested on a plastic covered polystyrene block or bedding bales padded with a soft blanket. Care was taken to ensure that the patient’s position was comfortable with the head in a neutral position.

The left side of the face was treated first. There was no need for the site to be clipped or scrubbed provided the horse’s skin was clean and dry. The infraorbital nerve was palpated and a sterile Chinese style acupuncture needle (0.3 × 25 mm with a coiled copper handle with guide tube)\(^3\) was inserted through the skin and slid under the nerve into the fascia between the nerve and the underlying periosteum 2–3 cm rostral to the infraorbital foramen. A variety of acupuncture needle types and sizes were tested, but early in the case series it was determined that inserting a 0.3 × 25 mm sterile Chinese acupuncture needle\(^3\) in a medial to lateral and rostral direction minimised the risk of the needle becoming displaced during the procedure. A second needle (Seirin L type needle, size no 8, 0.3 × 50 mm\(^3\)) was placed in the brachiocephalic muscle at the base of the horse’s neck on the same side.

A Cefar ACUS 4\(^4\) electrical acupuncture stimulator (this is no longer made) was used for Horses 1–4 and Horse 6; an AS SUPER 4\(^5\) digital electric needle stimulator was used to treat Horse 5 for all but the first treatment (Supplementary Item 1). Crocodile clips from the lead were attached to each needle close to the skin to prevent ‘drag’ on the needle (Fig 1). The battery-operated EA unit was switched on and the intensity of stimulation increased slowly in increments of 0.1 mA until the nostril started to twitch. This was independently controlled for the two frequency settings (2 and 80 Hz) with the CEFAJR ACUS 4. With the AS SUPER 4 the intensity of both frequencies changes at the same time. Once the twitch was observed, the intensity was increased very slowly to a level where both the twitch of the 2 Hz and the tetanic spasm of the 80 Hz were visible but not causing the horse any discomfort (Supplementary Item 2). This was maintained for a period of 25 min. If the first visible twitch caused the horse’s head to jerk rather than just a localised nostril twitch, the needle was considered to be too close to the infraorbital nerve. The current was reduced or switched off and the needle repositioned usually without the need to withdraw it completely. As the treatment progressed the intensity sometimes needed to be increased to maintain a constant level of twitch.

On a small number of occasions, the stimulus caused a local twitch around the needle that did not extend to the muzzle region or only when the intensity was increased to a level above that considered acceptable. When this occurred, the intensity was reduced and the needle slowly withdrawn a little. This usually released the tip of the needle from within a band of fascia, and the muscle(s) started to contract freely. If the lower eyelid was seen to twitch or lacrimation occurred due to inadvertent stimulation of the facial nerve (CN VII) the needle was repositioned 1–2 cm more rostrally to avoid the possibility of corneal irritation.

For the first treatment session, the whole procedure was then repeated on the other side of the face. Thereafter, if the horse was settled, treatment of the second side commenced once the first side was underway. If necessary, the sedation was topped up before treatment of the second side.

At the completion of treatment, instructions for the immediate management of the horse were dependent on the weather and the known trigger factors of the individual horse, which were avoided as far as possible. Three of the horses were known to be sensitive to sunlight and the owners were asked to keep a UV light-blocking fly mask (Cashel Crusader Fly Masks\(^6\), Premier Equine Buster Mask Xtra\(^7\), LeMieux Comfort Fly Shield Full Mask\(^8\), Equilibrium Field Relief Max Fly Mask\(^9\)) on their horse in daylight hours if tolerated and to ride or drive with an UV-blocking riding mask (LeMieux Comfort Shield Riding Mask\(^9\)) and nose net\(^6,8,9\), removing the mask only for competitions and jumping. Owners were also advised against trimming the whiskers, using a twitch or clipping the horse’s face over the infraorbital nerve. Optimum fly control was advocated with the use of fly rugs, repellents and stabiling in summer.

A daily report was requested by email including the horse’s name, the date, headshaking grades, weather conditions, exercise type and duration, plus any comments. Ridden work or driving could be undertaken the day following treatment unless the headshaking remained severe.

Horses responding to the first treatment were given a second treatment as soon as there was any sign of recurrence. Those that did not respond or showed short-lived improvement were given a second treatment 4–7 days after the first. Before each treatment, the horses were observed at exercise and graded by the author unless darkness or inclement weather prevented this. Horse 5 was examined by the author for the first treatment but was geographically too far away for follow up treatment sessions. For this case, the technique was demonstrated to two experienced equine veterinary surgeons from a referral practice who carried out treatment on the second side of the face under the author’s guidance and then performed all subsequent procedures when requested by the author who was in daily communication with the horse’s owner.

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<table>
<thead>
<tr>
<th>CASE 1</th>
<th>CASE 2</th>
<th>CASE 3</th>
<th>CASE 4</th>
<th>CASE 5</th>
<th>CASE 6</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sudden or gradual onset</strong></td>
<td>Sudden</td>
<td>Sudden</td>
<td>Unknown</td>
<td>Sudden</td>
<td>Sudden</td>
</tr>
<tr>
<td><strong>Early signs</strong></td>
<td>Reluctance to go forwards</td>
<td>None</td>
<td>Not going forward</td>
<td>Anxiety with feed bowl</td>
<td>None</td>
</tr>
<tr>
<td><strong>Main clinical signs</strong></td>
<td>Vertical head flick, Nose rubbing, Head held low in rain, snow, Sneezing, snorting, Anxiety</td>
<td>Vertical or rotatory flick, Rubbing nose on ground, Head held low, Anxiety</td>
<td>Horizontal tic precedes vertical flick, Occasional nose rubbing, Anxiety</td>
<td>Vertical tics in stable, Nose rubbing, Seeks hand on muzzle and buries face in owner's coat</td>
<td>Vertical flicks and nods, Nose rubbing on ground, Buries nose in companion's tail</td>
</tr>
<tr>
<td><strong>Dangerous behaviour</strong></td>
<td>Occasional violent striking, Lack of spatial awareness, Sunlight, rain, snow</td>
<td>Difficult to control and would push paired pony off the track, Sunlight, seeks shade</td>
<td>Can rear, bunny jump and bolt, Occasionally difficult to control when ridden</td>
<td>Challenging to handle, Can knock owner over accidentally in stable</td>
<td>Sunlight</td>
</tr>
<tr>
<td><strong>Avoidance behaviour</strong></td>
<td>Mostly at exercise, Less often in stable and field</td>
<td>At exercise only, At exercise and in the stable</td>
<td>Continuous in stable, field, at exercise</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Known triggers</strong></td>
<td>Sunlight, Pollens, especially rape, Stress</td>
<td>Sunlight, Midge, flies, Removing or changing face mask, Bright light</td>
<td>Midge, Cutting off whiskers, Stress</td>
<td>Anxiety</td>
<td>Sunlight, Stress, Applying a twitch, Removing fly mask, Putting on headcollar, Tightening noseband</td>
</tr>
</tbody>
</table>
When the horses were consistently scored at grade 0 for 3 weeks daily reporting was discontinued and owners were asked to make contact at the first sign of recurrence of clinical signs. The horses occasionally experienced a single day with mild signs before a further period of remission. They were treated when showing signs of headshaking for 2 consecutive days.

**Results**

Three mares and three geldings with an age range of 5-22 years were included in the study (Table 1). They had a clinical history of headshaking for between 3 weeks and 3 years. Horses 1 and 2 were seasonally affected during the spring and summer months; Horses 3-6 only started headshaking within the trial period, so any seasonality was unknown.

There was no resentment of the acupuncture needle placement and the procedure was well tolerated by the six horses and ponies. No serious adverse effects occurred.

An interesting variable was observed in that different muscles twitched with each horse and with the same horse on successive treatments. This is likely to be due to individual variations of the horse’s anatomy and slight differences in the positioning of the needle. Twitches were variably observed in the levator labii maxillaris (Supplementary Item 3), the levator nasolabialis (Supplementary Item 4) and orbicularis oris muscles (Supplementary Item 5). All of these receive most of their motor supply from the facial nerve and a small number of motor fibres in the infraorbital nerve. The muscle that was stimulated to contract did not appear to influence the outcome of treatment in this study but a twitch of the levator nasolabialis was the goal as affected horses selectively rub this area.

All six horses showed a reduction in the grade of headshaking and the treatment intervals for each horse are recorded in Table 4. The daily grades of the horses as reported by the owners are shown in Figs 2-7. For Horses 4, 5 and 6 the headshaking grades at rest have also been shown as they influenced the timing of treatment. Median remission time for the first treatment was 5.5 days, (mean 7.6 days, range 0–13 days, n = 6), second treatment 8.5 days (mean 10.6 days, range 7–21 days, n = 6), third treatment 18 days (mean 28.8 days, range 6–71 days, n = 6), fourth treatment 47.5 days (mean 10 weeks, range 11 days–23 weeks, n = 6), fifth treatment 13 weeks 5 days (mean 18 weeks 5 days, range 5–46 weeks, n = 5), sixth treatment 24 days (mean 26 days, range 13–41 days, n = 3).

Horse 1 was used for competitive dressage. She had been seasonally affected for 3 years prior to the start of the study and was unrideable through the spring and summer months until late October. Throughout the study, she resumed work the day after each procedure and the treatment intervals were 13 days, 3 weeks, 7 weeks, 23 weeks and 21 weeks. In the 18-month period between her third treatment in May 2015 and the end of the trial in October 2016, she scored grade 0 apart from 9 days at grade 1 and one day at grade 2. Treatment 6 was given in May 2016 and following this she had shown no further clinical signs by the end of the study in October 2016, a period of 21 weeks (Fig 2). She competed successfully in affiliated dressage competitions all year round throughout the 19-month trial period.

Horse 2, a driving pony, was first affected in 2014, between the months of June and November. The headshaking grades varied between 1 and 3 both in the stable and when driven. At the start of EA treatment in April 2015 she was graded at 2-3. (Supplementary Item 6). Between treatments 1–5, given at intervals of 5 days, one week, 3 weeks, and 6 days the headshaking lessened but was not abolished. When driven she scored grade 1 on most days (Supplementary Item 7). Treatment 5 was given on 26 June 2015 and she remained asymptomatic (grade 0) until mid-May 2016, an interval of 46 weeks. A 6th treatment was

---

**Table 3: Headshaking grades**

<table>
<thead>
<tr>
<th>Grade</th>
<th>Signs at rest in field or stable</th>
<th>Signs at exercise</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No signs at any time</td>
<td>No signs at any time</td>
</tr>
<tr>
<td>1</td>
<td>Occasional mild signs</td>
<td>Mild signs – riding still enjoyable for horse and rider</td>
</tr>
<tr>
<td>2</td>
<td>Moderate signs causing the horse some distress</td>
<td>Moderate signs and not enjoyable for horse or rider</td>
</tr>
<tr>
<td>3</td>
<td>Severe headshaking or nose rubbing at rest. Very distressed</td>
<td>Unrideable or dangerous</td>
</tr>
</tbody>
</table>

---

**Fig 1: Horse receiving electroacupuncture for headshaking.**
Horse 3 was used for eventing. He had been in his owner’s possession for 2 years when he developed sudden onset headshaking at variable grades between 1 and 3 in May 2015. This persisted until his first treatment in August 2015. Treatment intervals were 6 days, 12 days, 10 weeks and 20 weeks [Supplementary Items 8 and 9]. He occasionally showed signs on a single day between treatments but this spontaneously resolved and his eventing career continued uninterrupted. At the end of the study period he had maintained grade 0 and not received a treatment for 6 months (Fig 4).

Horse 4 developed clinical signs of headshaking in July 2015. It was well controlled with the use of a nose net but their use is prohibited in eventing under FEI rules. His signs were variable (grades 1–3) and made him unrideable at times. They were mild in the stable and exacerbated by exercise. He responded to treatment allowing him to be ridden and compete but still showed mild grade 1 signs (occasional tics) on some days in the stable and at exercise. In March 2016 he became lame and received no further follow-up (Fig 5).

Horse 5 was purchased to bring on for riding club activities in November 2014. He first showed signs of headshaking in September 2015 with variable signs ranging from grade 0 to 3 and was no longer ridden. At the first assessment in March 2016 he was not headshaking in the stable. On the lunge he constantly rubbed his nose along the ground or spontaneously burst into canter becoming distressed with violent vertical flicks of his head. This continued when brought back into the stable and sedated, making needle placement difficult. He responded to the EA with treatment intervals of 5 days, 8 days, 6 days, 7 weeks, 14 weeks and 3.5 weeks. In August 2016 the development of a pronounced firm swelling of his upper lip, thought to be due to a sting, coincided with a peak in HS grade 2 at rest (Fig 6). During the trial period his training continued. He was the only horse in the study that would not tolerate a facemask or nose net during the period of treatment.

In March 2016 he became lame and received no further follow-up (Fig 5).

Horse 6 was the most severely affected; she started headshaking 3 weeks after purchase and would not tolerate

---

**TABLE 4: Treatment intervals**

<table>
<thead>
<tr>
<th>Horse No.</th>
<th>Date of first treatment</th>
<th>Time interval to subsequent treatments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>2nd</td>
</tr>
<tr>
<td>1</td>
<td>8 April 2015</td>
<td>13 days</td>
</tr>
<tr>
<td>2</td>
<td>8 April 2015</td>
<td>5 days</td>
</tr>
<tr>
<td>3</td>
<td>21 August 2015</td>
<td>6 days</td>
</tr>
<tr>
<td>4</td>
<td>24 November 2015</td>
<td>13 days</td>
</tr>
<tr>
<td>5</td>
<td>9 March 2016</td>
<td>5 days</td>
</tr>
<tr>
<td>6</td>
<td>16 June 2016</td>
<td>4 days</td>
</tr>
</tbody>
</table>

---

*Fig 2: Horse 1. Treatment dates and headshaking grades (0–3) at exercise (black bar). T1–T6 indicate treatments 1–6 and headshaking grades <0 indicate days when the horse was not exercised.*
anything touching her nose or muzzle. At the start of treatment on 16 June 2016 she presented as grade 3 in the stable and on the lunge (Supplementary Item 10). The only short periods without any signs were momentarily when eating or when lying down in the stable. Following the first and second treatments there was an exacerbation of the clinical signs for 2–3 days. The first short period of complete remission occurred after the third treatment, scoring grade 0 for 3 consecutive days. Following the fourth EA session given 22 days after the commencement of treatment the mare was ridden for the first time. A longer period of remission occurred after the fifth treatment lasting 36 days at grade 0 (Supplementary Item 11). Treatment 6 was effective for 2 weeks and treatment 7 for just 5 days. Following an eighth treatment, the mare remained asymptomatic for the 3 weeks until the end of the study period (Fig 7) and a further 5 weeks thereafter. Since the fifth treatment the mare has been ridden regularly and lightly competed in riding club activities.

Horses 1, 2, 3, 5 and 6 continue to be monitored as part of the ongoing study.

**Discussion**

Case selection was important as this treatment is for cases with suspected trigeminal neuralgia rather than head shakers that are suffering from other underlying pathology (Lane and Mair 1987). Whilst it is difficult to be categorical as none of the horses in the study underwent posterior ethmoidal analgesia or nerve conduction studies, both the referring veterinary surgeons and the author considered TMHS the most likely diagnosis. The owners were offered a full diagnostic work-up including local anaesthesia and a computed tomography scan, but five of the six declined due to the cost.

The trigeminal nerve is the largest of the cranial nerves. It is divided into ophthalmic, maxillary and mandibular...
branches. The maxillary division supplies sensory innervation to the rostral maxillary teeth, the upper lip, the nose and part of the maxillary sinus. The infraorbital nerve is a branch of the maxillary trunk. It traverses the infraorbital canal and emerges through the infraorbital foramen where it divides into nasal and maxillary labial branches. These divide again and supply sensation to the upper lip, nostril, alveolar periosteum and gums (Sisson and Grossman 1975). Horses affected by TMHS have hypersensitive trigeminal nerves with a lower threshold for activation (Aleman et al. 2014). However, the seasonality of clinical signs and periods of remission imply a reversible functional abnormality (Pickles et al. 2014) and thus that treatment should be directed towards neuromodulation rather than destruction of the nerve. On gross pathological and histological examination of horses subjected to euthanasia for TMHS, no abnormalities of the infraorbital nerve have been found (Newton et al. 2000).

The strength of stimulation depended on two factors: the strength of the current and the proximity of the needle to the nerve. It was important to increase the intensity slowly and incrementally in order not to cause the patient discomfort by overstimulation of the nerve.

The treatment time was initially 25 min for each side of the face. It is suggested that the time is reduced to 20 min with a reduced stimulus intensity giving a smaller muscle twitch in horses that have aggravated clinical signs after the procedure in the early stages of the treatment programme (Horse 6).

The use of a face mask and nose net was considered to be an important part of the management routine when...
combined with EA. Removing the face mask was a definite HS trigger for Horses 2, 3 and 6.

A possible criticism of this study is that the horses were assessed on a daily basis by the owner and at treatment sessions by the author rather than a blinded assessment by a panel of experts. In a previous study Mair et al. (1992) suggested that owners are reliable assessors in this type of study. Owners spend the most time with the horse and observe it in its usual surroundings. Moving them to a referral centre for assessment could modify their behaviour and give a false impression of their headshaking status.

The four possible grades had distinct descriptions, making grade selection for the owners relatively straightforward (Table 3).

The use of different stimulators unavoidably occurred, as the CEFAR ACUS 4 is no longer available to purchase. The CEFAR ACUS 4 was set on 80 Hz as a high frequency and the AS SUPER 4 on 100 Hz. This is unlikely to affect the outcome as Horse 5 responded to treatment with the latter and the author also tested it for the May 2016 treatment of Horse 1 with a positive result. Further studies could be carried out to investigate the effects of using different frequencies and pulse durations.

It is possible that more than one sensory branch of the trigeminal nerve is involved (Newton et al. 2000) and neuromodulation of the mandibular or ophthalmic branches of the nerve with EA is now being performed in ongoing studies by the author. This offers the potential for treatment in cases where stimulation of the infraorbital nerve alone does not provide adequate relief.

Horse 6 was the most severely affected, with such frenzied headshaking and nose rubbing at the start of treatment that euthanasia was considered. There were a number of management changes and behavioural issues that may have contributed to her short response time of just 5 days to treatment 7. She was turned out into the sunshine immediately after this treatment and within the same week there was a change of field, bedding, bit, bridle, field companion and she was occasionally ridden without a face mask. She took an intense dislike to the new companion. This suggests that careful management of affected horses is necessary alongside any treatment of TMHS.

Summary
In this case series, EA worked effectively to reduce HS in all six of the horses. The equipment is easily portable and can be used in the stable yard, eliminating the need for these distressed horses to travel. It is a safe procedure that does not require the hospital facilities and expensive equipment that is routinely used for percutaneous electrical nerve stimulation (PENS). With some training in the technique EA can be performed within ambulatory equine practice, making it widely available to affected horses.

Author’s declaration of interests
No conflicts of interest have been declared.

Ethical animal research
Written consent was obtained from each owner prior to participation in the study which was carried out in accordance with the National Institute for Health and Care Excellence (NICE) guidelines for the management of refractory neuropathic pain in people.

Source of funding
No funding was needed for this study.

Acknowledgement
The author would like to thank Ben Taylor MESci FGS for producing the graphs.
Manufacturers' addresses

1Vetoquinol UK Ltd, Buckingham, UK.
2Zoetis UK Limited, Tadworth, Surrey, UK.
3Scarboroughs Ltd, Crewkerne, Somerset, UK.
4Cefar Medical AB, Lund, Sweden.
5Schwa-medico H O L I S T I C H E A L T H, Echinghausen, Germany
6Cashel Company, Granbury, Texas, USA.
7Premier Equine International Ltd, Goxhill, North Lincolnshire, UK.
8Horse Health Ltd, Southampton, Hampshire, UK.
9Equilibrium Products, Ashley Green, Buckinghamshire, UK.

References


Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher’s website:

Supplementary Item 1: Electroacupuncture unit treatment programs.

Supplementary Item 2: Video showing muscle twitch during treatment.

Supplementary Item 3: Video showing levator labii maxillaris twitch.

Supplementary Item 4: Video showing levator nasolabialis twitch.

Supplementary Item 5: Video showing orbicularis oris twitch.

Supplementary Item 6: Video showing Horse 2 before treatment.

Supplementary Item 7: Video showing Horse 2 after treatment 3.

Supplementary Item 8: Video showing Horse 3 before treatment 4.

Supplementary Item 9: Video showing Horse 3 after treatment 5.

Supplementary Item 10: Video showing Horse 6 before treatment.

Supplementary Item 11: Video showing Horse 6 after treatment 5 on Day 38.
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August 15-17 - Newtown, CT, USA
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September 5-7 - Heesch, The Netherlands
Sporthorse Medical Diagnostic Centre
Neck & Back

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Clinical Commentary

Electrical nerve stimulation for the management of equine trigeminal mediated headshaking

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Keywords: horse; headshaking; idiopathic; trigeminal; neurology

Previously termed idiopathic headshaking, it is now widely accepted that trigeminal-mediated headshaking (TMHS) is a more accurate term with clinical signs of TMHS considered to reflect trigeminal neuropathic pain (Pickles et al. 2014; Roberts 2014). Although involvement of the trigeminal nerve had long been suspected in the aetiology of TMHS due to the presenting clinical signs (Williams 1897, 1899), a reduced threshold of activation of the maxillary branch of the trigeminal nerve in headshaking horses compared with control horses has only been recently definitively confirmed (Aleman et al. 2013, 2014). These elegant nerve conduction studies, the seasonality of clinical signs in many headshaking horses and absence of gross or histopathological lesions in the trigeminal nerves and ganglia from headshaking horses (Newton 2001; Aleman et al. 2013; Roberts et al. 2017) are suggestive of a functional rather than structural nerve disorder, although this requires further validation. In further support of this hypothesis is the finding that the activation threshold of the trigeminal nerve in a horse with seasonal TMHS tested during a time of remission showed a threshold for activation similar to control horses (Aleman et al. 2014). Unfortunately this horse was not tested during seasonal exacerbation of headshaking signs, which would appear to be the next logical step in elucidating any seasonal malleability of the activation threshold of the trigeminal nerve.

The cause of the aberrant trigeminal nerve activity (‘hypo-sensitivity’) in equine TMHS remains frustratingly elusive. Despite its predilection for latency in the trigeminal ganglion, equine herpesvirus-1 does not appear to be involved in the pathogenesis of TMHS (Aleman et al. 2012). Some clinical similarities appear to exist between TMHS and human trigeminal neuralgia (HTN), a debilitating cause of facial pain in people, which is described by sufferers as intermittent or electric-like pain in an area innervated by the trigeminal nerve (Nurmikko and Eldridge 2001). Unfortunately this horse was not tested during seasonal exacerbation of headshaking signs, which would appear to be the next logical step in elucidating any seasonal malleability of the activation threshold of the trigeminal nerve.

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How or why some horses enter spontaneous remission of TMHS, which may last from weeks to years, is unknown. Long-term remission appears uncommon with only 5% of 109 headshaking horses reported to cease TMHS for more than one year (Madigan and Bell 2001). As headshaking horses can go into spontaneous remission (albeit rarely), some after many years of TMHS, it suggests reversibility of the trigeminal nerve hypersensitivity is possible. This offers the tantalising prospect of manipulation of the threshold activation as the Holy Grail of a true treatment, rather than just a management strategy, for TMHS. Electrical nerve stimulation is the therapeutic alteration of activity in the central, peripheral, or autonomic nervous systems by transcutaneous or implanted electrical devices. Two such therapies, percutaneous electrical nerve stimulation (PENS) and electroacupuncture, have recently been reported as successful in the management of TMHS in some horses (Roberts et al. 2016; Devereux 2019). These are a welcome addition to the armoury of TMHS treatments and appear to offer a more rational approach than prior mechanical or pharmaceutical treatments which did not address the underlying aberrant neurophysiology. Whilst these therapies do appear to show promise, cited remission times post-treatment of horses with seasonal TMHS such as those by Devereux (2019) should be interpreted with caution when they overlap with times of year when the horse would be expected to enter seasonal remission.

Therapeutic application of electricity for pain dates back thousands of years since ancient Egyptians utilised electric fish to provide pain relief (Heidland et al. 2013). Following widespread use in the 19th Century, electrotherapy fell out of favour until publication of the gate control theory of pain by Melzack and Wall (1965) led to a resurgence of interest in neurostimulation. This gate control theory is also the science that underpins the common parental response of rubbing a sore area on a child. Melzack and Wall (1965) reported that the substantia gelatinosa in the dorsal horn of the spinal cord acts as a gate control system which modulates the synaptic transmission of nerve impulses from peripheral fibres to the central nervous system. Small nociceptive A-δ and C fibres hold the ‘gate’ in an open position, while stimulation of large mechanoreceptive A-β fibres by touch, pressure or vibration close the ‘gate’ and inhibit pain transmission to the brain. Small nociceptive fibres have a higher activation threshold than larger mechanoreceptive fibres such that selective low level stimulation of mechanoreceptors can prevent or reduce pain transmission. Activation of these large A-β fibres recruits inhibitory interneurons within the substantia gelatinosa of the spinal cord which exert their inhibitory action on both large and small diameter fibres synapsing higher up the spinal cord. Additionally, activation of the descending inhibitory pathway,
which starts in the periaqueductal grey matter of the midbrain and passes through the ventral medulla into the spinal cord, occurs. Activation of this pathway results in the enhanced release of endogenous opioids and alterations of many other neuro-excitatory or inhibitory compounds including serotonin, noradrenaline, gamma aminobutyric acid (GABA), acetylcholine, substance P and adenosine (Heidland et al. 2013).

Electrotherapy of human neuromusculoskeletal pain is currently performed using transcutaneous electrical nerve stimulation (TENS), percutaneous electrical nerve stimulation (PENS) and spinal cord stimulation (SCS). In mild to moderate pain, TENS and PENS are effective, whereas SCS is useful for therapy of refractory neuropathic or ischaemic pain (Heidland et al. 2013). The electrical devices differ in regard to the amplitude [intensity], frequency, duration and pattern of the electrical currents. Percutaneous electrical nerve stimulation, which allows precise subcutaneous field stimulation targeted to specific areas of neuropathic pain, is a recognised treatment under National Institute for Health and Care Excellence (NICE) guidelines for human sufferers of neuropathic pain (Anon 2013). It has proven effective in decreasing both subjective and objective pain scores in 31 patients with chronic pain and surface hyperalgesia (Raphael et al. 2011) and has been successfully used for the treatment of neuropathic trigeminal pain syndromes (Johnson and Burchiel 2004; Slavin et al. 2006). A total of 7 out of 10 (70%) patients with post-herpetic or traumatic trigeminal neuropathic pain treated with PENS of the supra-or infraorbital nerves reported reduction in pain of at least 50% at 24 months (Johnson and Burchiel 2004). Similarly, Slavin et al. (2006) report 22 of 30 (73%) patients experienced more than a 50% reduction in pain following PENS stimulation of the trigeminal and/or occipital peripheral for craniofacial pain.

The recently developed, equine specific, neurostimulation device EquiPENS® has now been used in over 130 TMHS horses with approximately 50% successfully returning to the previous level of activity (V. Roberts, personal communication). Ultrasonographic guidance is used to direct the probe percutaneously such that it lies approximately 1 mm superficial to the infraorbital nerve prior to stimulation (Roberts et al. 2016). A detailed description of the procedure is given by Roberts et al. (2016). Response is individual and variable and a series of three initial treatments is required to determine if therapy has been successful. The median length of remission following the third treatment is reported as 15.5 weeks (range 0–24 weeks, n = 5) (Roberts et al. 2016). Further stimulation procedures can then be given as necessary at individually determined intervals as clinical signs resume, or worsen. Adverse reactions of mild swelling at the site of insertion or transient worsening of TMHS are infrequently seen following treatment and do not appear to influence response to the procedure (Roberts et al. 2016). Given the longer length of probe and closer approximation to the infraorbital nerve, greater nerve stimulation is likely to occur with EquiPENS compared with the described electroacupuncture technique (Devereux 2019).

Whilst TMHS remains an enigmatic and frustrating condition, it is encouraging to see the wealth of new information elucidated in recent years. Neuropathic pain is notoriously difficult to treat; however, the apparent functional, rather than pathological, nature of trigeminal nerve hypersensitivity in TMHS gives the real possibility that electrostimulation techniques may provide relief to horses with this distressing condition and their owners.

**Author’s declaration of interests**

No conflicts of interest have been declared.

**Ethical animal research**

Not applicable.

**Source of funding**

None.

**Manufacturer’s address**

Algotec Research and Development Ltd, Crawley, West Sussex, UK.

**References**


Case Report

Computed tomographic diagnosis of incomplete palmar cortical (fatigue) fracture of the third metacarpal bone in two young adult endurance horses

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Keywords: horse; endurance; fatigue fracture; stress fracture; third metacarpal bone

Summary

Two young adult endurance horses were referred to the Veterinary Teaching Hospital of the University of Perugia for right (Case 1) and left (Case 2) forelimb lameness during 54 km and 81 km national endurance competitions; Case 1 was a 5-year-old Arab gelding and Case 2 a 6-year-old Arab female. The day after the competition there was no swelling or deformation and the affected forelimb was maintained in protraction avoiding full weightbearing.

At walk both horses showed mild lameness with a shortening of the cranial phase of the affected forelimb. The horses demonstrated severe lameness when trotting in a straight line, and placed the limb in an abducted position.

Initial total screening radiography was performed because of the clinical signs and the suspicion of fracture, but overall radiographic findings detected were considered incidental findings. At the second examination after 7 days of box rest, both horses showed no changes in clinical signs, except for resolution of the abnormal stance; radiographic examination was repeated, but no abnormality was detected. In agreement with the owners, it was decided to proceed with diagnostic analgesia, after discussing the associated risks given the severity of the lameness; in both cases, the lameness improved significantly (Case 1) and was abolished (Case 2) within 5 min by diagnostic analgesia of the origin of the proximal suspensory ligament using 3 mL of mepivacaine. An ultrasonographic examination of the proximal suspensory area was performed using a palmar approach on the weightbearing and flexed limbs. In Case 1, there was an enlargement of the medial lobe of the suspensory ligament of the right forelimb compared with that of the left forelimb. As the diagnostic findings did not explain the severity of the lameness, a computed tomography (CT) examination was performed under general anaesthesia, with a multislice helical scanner; transverse slices were obtained from the distal row of the carpal bones to the distal third of the third metacarpal bone (McIII). Images were reformatted and displayed in bone and soft tissue windows. In both cases, the computed tomography (CT) revealed a well-defined oval/circular hypoattenuating area located at the most medial aspect of the proximal McIII; between the McIII and the axial aspect of the second metacarpal bone: this area continued distally as a hypoattenuating line in a proximomedial to distolateral direction. Thickening of the medial part of the palmar cortex was also identified, and lesions were surrounded by increased endosteal attenuation (sclerosis) of the McIII (Fig 1). In both cases the definitive diagnosis was incomplete palmar metacarpal cortical (fatigue) fracture. After the rest and rehabilitation period, re-examination performed 8 months after injury showed resolution of the lameness. In endurance horses, the principal cause of lameness is proximal metacarpal pain, with proximal suspensory desmitis, proximal palmar metacarpal stress pathology, and pathology associated with the second and fourth metacarpal bones as differential diagnoses. In these cases, the definitive diagnosis was obtained using CT examination of the proximal McIII; CT is an advanced diagnostic imaging technique that provides excellent bone detail.

Key points

- Horses had no significant radiographic findings and the final diagnosis was obtained using computed tomographic examination.
- CT findings were hypoattenuating round/oval intracortical areas located at the most medial aspect of the palmar cortex of the third metacarpal bone, close to the medial synodesmosis with the second metacarpal bone; a hypoattenuating fracture line extending distally from the irregularity in the cortical bone; and cortical thickening associated with increased endosteal density of the proximomedial aspect of the third metacarpal bone.
- Incomplete palmar metacarpal cortical (fatigue) fracture can develop in young adult endurance horses.
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**Clinical Commentary**

**Computed tomography in equine orthopaedics – the next great leap?**

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**Summary**

Computed tomography (CT) generates sectional, multiplanar images based on x-ray attenuation properties of the subject. Contrast within images is based on differences in relative tissue density. It can resolve subtle structural abnormalities within bone and soft tissue and, as such, it has potential, among other uses, to screen for pathology within bones of the appendicular skeleton in racehorses, which could predispose to catastrophic fractures. Recent technological advances have made the possibility of performing CT imaging in the standing horse a viable clinical alternative. This commentary reviews some recent developments in this field of clinical imaging in the horse.

Nuclear scintigraphy revolutionised the practice of equine orthopaedics in the 1980s. The ability to perform magnetic resonance imaging (MRI) in the standing, sedated horse was a game-changer in the early 2000s. Widespread access to computed tomography (CT) that can be undertaken without general anaesthesia may well transform our capacity to diagnose occult lesions of the appendicular skeleton in the future.

In this issue of Equine Veterinary Education, Beccati et al. (2019) illustrate two cases of incomplete fractures of the proximal, palmar cortex of the third metacarpal bone that were diagnosed through CT. The images presented illustrate relatively subtle structural pathology that would have been difficult if not impossible to identify definitively by other means. Nuclear scintigraphy would almost certainly have indicated the presence of intense bone remodelling at the locations of fracture and localised signal changes with MRI would have prompted diagnosis of injury to the bone. One might argue that these modalities would have been more appropriate in these cases. Scintigraphy would have facilitated a diagnosis without the need for diagnostic analgesia to identify the anatomical region involved and general anaesthesia (GA), both of which could have exacerbated the primary pathology. MRI could have been performed without the need for GA, although the time required for image acquisition with this modality makes precise imaging of the proximal metacarpus challenging. The option to undertake CT studies of the limbs without need for GA would have been optimal.

Conventional CT units generate images by determining the radiodensity of individual ‘pixels’ in a cross-sectional, fan-shaped scan of the subject. An x-ray generator and opposing detector(s) are mounted in a gantry, built into an annulus, through which the subject is positioned. The x-ray generator and detector are spun around the subject and multiple data sets are obtained of two-dimensional (2-D) ‘slices’ at right angles to the axis through the core of the machine. The subject is advanced progressively and precisely along this axis, thereby generating data as contiguous ‘slices’ or in a spiral pattern in the longitudinal plane. The data are processed to generate images that can be presented as sequential 2-D sections in different planes or into three-dimensional reconstructions.

While MRI and CT both produce sectional, multiplanar images, the data they provide are quite different. CT relies on x-ray attenuation properties within the subject and differences in relative tissue density for distinction of structures and lesions. MRI principally maps the presence of hydrogen atoms (largely contained in water and fat in the body) and structural information of the skeleton is inferred from this. Consequently, CT images exhibit superior definition of anatomic structures, higher resolution information about the structure of skeletal elements and detailed simultaneous bone and soft tissue imaging. In addition, CT imaging can be completed in a fraction of the time it takes to undertake MRI studies, a factor which is particularly important when imaging the standing horse.

Computed tomography has advanced significantly since it was first introduced to human medical practice in the mid 1970s. The resolution of images has increased dramatically, scan times and radiation dose rates have been cut and the cost of installing and maintaining units has fallen. This technology has been used in veterinary practice for approximately 30 years although until recently it has been necessary to conduct equine scans under GA to position the anatomical region of study through the annulus of the scanner. An ingenious bit of lateral thinking led to development of a special platform, which facilitated positioning and precise advance of a horse’s head through a conventional CT scanner (see Powell 2011). This device is now commercially available and widely used in specialist equine practice.

However, to position a horse’s limb within the annulus of the CT machine, the animal generally has to be placed in lateral recumbency and, therefore, under GA. This has several disadvantages: (1) GA is associated with a moderate risk of mortality or morbidity in horses. This risk is significantly increased if there is pathology that weakens a bone of the appendicular skeleton; (2) the cost of the whole procedure is much greater; (3) images can only be obtained with the limb nonweightbearing; (4) the process will severely disrupt a horse’s training programme, which makes it unsuitable as a routine screening tool.

Different groups have attempted to overcome the challenges of undertaking CT scans in the standing horse.
Desbrosse and colleagues have described the use of a small peripheral quantitative computerised tomography scanner (pQCT) mounted in a special jig to image the distal limb of a standing horse (Desbrosse et al. 2008). The authors reported on 47 clinical cases, of which the device had been used successfully in 30 to confirm a diagnosis of or aid surgical planning for conditions of the foot. However, the horse’s limb has to be physically lifted and placed within the core of the machine for scanning and there does not appear to be a rapid means of extricating the leg in the event that the horse panics. In addition, imaging is restricted to the distal limit of the limb.

A relatively recent development in CT has been to use larger sensors that take advantage of the cone of x-rays generated by x-ray tubes. In this way much greater volumes of tissue can be analysed in every rotation of the generator and sensor around the subject. Larger anatomical segments can be imaged per unit time than is possible with the narrow fan beam in more conventional units. So-called ‘cone-beam CT’ (CBCT) units are cheaper and easier to maintain although in people they have largely been restricted to use in dental practice. However, robotics technology has been combined with cone-beam volumetric imaging by one company in the USA to develop a system that can scan most regions of the standing horse to generate volumetric images (4DDI Equine, about the Equimagine; http://equine4ddi.com/). Up to four robots capable of operating several panels, high-speed cameras, 3D surface scanners and x-ray generators are controlled to perform co-ordinated manoeuvres around the subject. This system appears to hold great promise although it is still early days and few units have been installed to date.

Two further companies are working to develop volumetric imaging CT units specifically for use in the standing horse. One applies conventional fan-beam CT technology and a large gantry that encompasses both fore- and hindlimbs at once (Asto CT®, http://www.astoct.com/). The gantry can be positioned in the vertical or horizontal planes to image head and neck or limbs respectively. In the latter mode, the gantry can be lowered into a corresponding recess in a platform so that it is flush with the ‘ground’ surface. Once the horse has been walked into position the gantry is raised to the level required to scan the region of interest. Both limbs are imaged simultaneously. A proof of concept machine has been built and used to successfully generate images of limbs [https://www.youtube.com/watch?time_continue=5&v=pdfUHwpPPPOkW]. The Asto CT Equina™ CT machine is now commercially available.

A separate company, which has specialised in cone-beam volumetric imaging technology for imaging the lower leg in standing human patients, is also working on a design for a dedicated equine unit (CurveBeam®; http://www.curvebeam.com/). Cone-beam machines do not necessarily rely on a continuous ring that extends around the patient, but can be arranged as separate arms either side of the subject, one of which carries the x-ray generator and the other, the detector. The two arms swing in perfect alignment around the subject. Consequently, the subject can walk between the arms to stand on a central platform, which remains stationary while the arms rotate around it during data acquisition. The emphasis of this design is a small footprint, low cost and practicality of deployment at widespread veterinary clinics and mobile vans. It appears that an equine unit is still at the relatively early stages of design although the prospect of a practical solution seems promising.

One further group has briefly reported development of a CBCT unit to image structures of the distal limb in the standing horse (Koch et al. 2017). Cross-sectional imaging was attempted in 22 cases and successfully achieved in 21 of these. Intrasynovial contrast was used in eight cases to facilitate imaging of soft tissue structures.

The option to perform CT examinations on the limbs of standing horses safely, quickly and affordably will be a leap forward for diagnosis of lameness. Perhaps even more valuable, it potentially will offer a tool to use to screen horses at risk for repetitive stress bone injuries (Muir 2014). A tome of convincing evidence has been accumulated to demonstrate that the majority of fractures that affect racehorses (and, probably, endurance horses) are the catastrophic culmination of repetitive stress injuries. Foci of intense remodelling, coalescing microcracks and short, unicortical fractures in the cortices and subchondral regions of bones act as stress-risers from which catastrophic fractures originate. Images obtained using standing MRI can indicate the presence (or likely presence) of such injuries although the anatomical resolution of the images and the practical constraints of performing MRI (principally the prolonged scan times) limit the efficacy of this modality for screening purposes. Over 70% of fractures that result in euthanasia of racehorses originate in the fetlock. While our ability to detect subtle lesions in critical anatomical locations in this joint has improved through application of dedicated radiographic projections the sensitivity and specificity of radiography alone is inadequate (Davis et al. 2017).

Routine CT scans of populations of horses will no doubt reveal a spectrum of different defects in bones which have potential to cause problems. Currently, while the evidence is convincing, the conclusion that catastrophic fractures originate from lesions associated with repetitive stress injury remains hypothetical. Also, there is evidence that the incidence of defects in subchondral bone at the location from where fractures develop is far higher than that of fracture. Why do some of these lesions progress and others not? Are there critical features that can be quantified to make assessment of findings sufficiently specific to gain the confidence of the racing industry to ensure at risk horses are prevented from racing (Dubois et al. 2014)? Before standing CT could be used as an effective screening tool, we will require answers to these questions. However, I believe that answers will be found and, just as scintigraphy has saved the lives of thousands of racehorses since its introduction in the 1980s, I predict standing CT will have a positive impact on the safety of racing in the future.

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References
Pasture-associated stringhalt: Contemporary appraisal of an enigmatic syndrome

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Summary

Although described clinically for several centuries, stringhalt remains an intriguing and enigmatic condition. In pasture-associated stringhalt (PSH), the clinical sign of exaggerated, prolonged hindlimb flexion is associated with a peripheral neuropathy affecting the larger myelinated axons that is thought to be the result of exposure to a plant-derived neurotoxin. It is likely that multiple host and environmental risk factors interact to produce PSH and the precise aetiology has not yet been elucidated. Drought-affected, poor-quality pasture and the presence of *Hypochoeris radicata* (commonly referred to as Catsear, Flatweed and False Dandelion) are recognised risk factors. Affected horses are typically mature and taller animals are considered more susceptible. Most horses with PSH recover spontaneously if removed from the presumptive source of toxin; however, recovery can be prolonged, taking several years for some horses, and might be incomplete in occasional cases. A wide range of therapies have been attempted in horses with PSH including phenytoin, thiamine, taurine, infiltration of digital extensors with botulinum toxin and lateral digital extensor myotenectomy procedure. The efficacy of these treatments is uncertain since controlled trials have not been performed and the spontaneous recovery of most horses makes any response to treatment difficult to interpret.

Introduction

Stringhalt is a condition of horses characterised by excessive and prolonged flexion of one or both hindlimbs during forward or backward movement. The condition has been recognised for centuries and was referred to as “springhalt” in Shakespeare’s play King Henry VIII, first performed in the early 1600s. Other terms for stringhalt include Hahnenritt (German for rooster kick), and more recently, equine reflex hypertonia (Mayhew 2009; Hahn 2015). Classical (or unipedal) stringhalt, predominantly affecting only one hindlimb, most often follows injury to one dorsal tarsal/metatarsal region [Supplementary Item 4]. However, the condition is considered to be idiopathic (Crabill et al. 1994; Sullivan 2002). Pasteure-associated stringhalt (PSH) appears to be the result of exposure to a plant-derived neurotoxin or neurotoxins and subsequent peripheral neuropathy. Often referred to as Australian stringhalt, PSH has also been termed “outbreak” or “epidemic” stringhalt, as the condition commonly affects multiple animals in the same paddock and time period (Kendall 1887; Cahill et al. 1986; Gay et al. 1993; Araya et al. 1998; Takahashi et al. 2002; Torre 2005; Domange et al. 2010; De Pennington et al. 2011). PSH is most often reported in horses grazing poor quality, drought-affected pastures and, although occasionally asymmetrical, the condition is invariably bilateral. Initially described in Australia and New Zealand, PSH has been reported in Europe, North and South America, and Asia (Cahill et al. 1986; Takahashi et al. 2002; Araujo et al. 2008; Mayhew 2009; Domange et al. 2010; De Pennington et al. 2011).

Clinical presentation and diagnosis

Horses with PSH have characteristic, though very variable, hyperflexion of both hindlimbs when attempting to move (Fig 1, Supplementary Item 1 and 2). A grading system has been proposed (I–VI) based upon prior reports in the literature (Huntington et al. 1989; Domange et al. 2010). In mild cases (grades I and II, Table 1) the gait abnormality might only be apparent when the horse is excited or nervous, when it is turned sharply, or when it is forced to walk backward. Clinical signs can often be exacerbated while walking the horse down a slope, after a sudden stop or following hard exercise. Horses with more severe PSH exhibit a hopping action in which hyperflexion becomes progressively more exaggerated and of increased duration. In some horses, flexion is so extreme that the dorsum of the fetlock contacts the ventral abdomen and the duration of hyperflexion becomes so prolonged that both hind feet leave the ground, almost at the same time, even while walking (grades IV and V, Table 1 and Supplementary Item 2). In extreme cases, horses are unable to rise without assistance (grade VI) (Pemberton and Caple 1980; Cahill et al. 1985; Huntington et al. 1989; Domange et al. 2010; Draper et al. 2014). Although both hindlimbs are invariably involved in cases of PSH, clinical signs can show some asymmetry (Huntington et al. 1989; Mayhew 2009). The gait abnormality is often worse in cold weather and appears to be worse in horses that appear agitated. The severity of hyperflexion might decrease after the initial few steps but the gait typically remains abnormal. Muscle atrophy occurs in most affected horses, with the long and lateral digital extensor muscles the most severely affected. Distal limb muscle atrophy is often obvious in the early stages of PSH. Many horses, particularly those with prominent signs of long duration, have atrophy of the thighs and adductor muscles.
In such cases muscle wastage may extend to the entire hindquarters (Huntington et al. 1989; Domange et al. 2010).

A range of other gait abnormalities has been described in some cases of PSH including variation in the degree of hindlimb fetlock flexion, abduction of the limb during hyperflexion and caudal thrust of the hindlimb at the onset of protraction (Mayhew 2009). These variations in clinical signs might reflect the complexity and range of neuromuscular structures affected by the presumptive toxin. Very occasionally, the forelimbs are also affected in horses diagnosed with PSH. In these cases, knuckling, hypermetria and atrophy of the forelimb and knuckling of the hindlimb have been described in addition to hindlimb hyperflexion (Huntington et al. 1989). A high incidence (up to 20% in some reports) of laryngeal hemiplegia has been reported amongst affected horses in several outbreaks of PSH and the abnormal vocalisation noted in some cases of PSH probably reflects laryngeal dysfunction (Cahill et al. 1985; Huntington et al. 1989; Araujo et al. 2008; Domange et al. 2010). The majority of horses with PSH have a normal demeanour and appetite; however, changes in behaviour have been reported. In a small number of severely affected horses, such findings have included increased aggression and obtundeness (Huntington et al. 1989; Domange et al. 2010).

Diagnosis of stringhalt has to be based on the clinical signs and absence of other neurologic and orthopaedic abnormalities. The distinction between bilateral PSH and classical unipedal stringhalt is usually apparent and can be supported by some evidence of trauma to the hock region and to presence or absence of epidemiological features discussed below. Results of routine haematological analyses are typically noncontributory. Low plasma vitamin E concentrations and mild increases in muscle enzymes (creatine kinase and aspartate aminotransferase) and liver enzyme activity have been noted in occasional cases of PSH but abnormalities are inconsistent, usually mild and unlikely to be of clinical significance (Pemberton and Caple 1980; Araya et al. 1998; Gardner et al. 2005; Domange 2009; Domange et al. 2010). Electromyographic (EMG) studies of hindlimb muscles in horses with PSH have shown increased insertional activity, fibrillation potentials and positive sharp waves, consistent with denervation (Huntington et al. 1989, 1991; Takahashi et al. 2002; Gardner et al. 2005; Armengou et al. 2010). Furthermore, mean conduction velocity of the peroneal nerve in four horses with PSH was approximately one-third that of a control horse (Huntington et al. 1989). Abnormalities in EMG recordings gradually returned toward normal paralleling the clinical recovery in three horses with PSH when monitored over a period of 8 months (Huntington et al. 1989).

The gait abnormality in PSH can vary considerably between individual horses and, as mentioned, some horses can display changes in their gait that are not typical of PSH. As a consequence, PSH might be difficult to distinguish from a number of other neuromuscular or musculoskeletal conditions, particularly when the case is mildly affected. Differential diagnoses for PSH might include shivers, Scandinavian knuckling disease (acquired equine polynuropathy), lathyrism, fibrotic myopathy and upward fixation of the patella, in addition to conditions affecting upper motor neuron innervation of the hindlimbs. It appears that horses with pain, or even irritating stimuli (such as application of a leg wrap) relating to the distal limb or hoof may produce a stringhalt-like gait (Supplementary Item 3). In most cases, careful examination of the gait and assessment of the history should allow differentiation between these conditions and PSH.

Shivers is a relatively rare movement disorder that has recently been shown to be associated with degeneration of Purkinje cell axons within the deep cerebellar nuclei (Valberg et al. 2015). Horses with shivers show protracted hyperflexion of the hindlimb when the limb is manually lifted or when the horse is backed. Some affected horses will hyperextend (rather than hyperflex) their hindlimbs during backing. Forward movement is performed normally in most horses with shivers. However, a recent study described a subset of affected animals that also had intermittent hindlimb hyperflexion during forward movement (Draper et al. 2014). Muscle atrophy, which is expected in stringhalt as a consequence of the neuropathy, is also reported in horses with shivers. Interestingly, shivers also appears to occur more

### TABLE 1: Grading scheme for categorisation of stringhalt affected horses adapted from Huntington et al. (1989) and Domange et al. (2010)

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Only noticeable when horse was backed, turned or stressed.</td>
</tr>
<tr>
<td>II</td>
<td>Slight limb jerkiness when horse moves off at a walk or trot.</td>
</tr>
<tr>
<td>III</td>
<td>Moderate hyperflexion noted when walking or trotting especially when initiating or stopping movement.</td>
</tr>
<tr>
<td>IV</td>
<td>Severe hyperflexion with hindlimbs hitting abdomen when backing and turning. Horse is unable to trot.</td>
</tr>
<tr>
<td>V</td>
<td>Hindlimb held hyperflexed for prolonged periods when initiating movement which is characterised by plunging, leaping, hopping motion.</td>
</tr>
<tr>
<td>VI</td>
<td>Prolonged recumbency following grade IV-V stringhalt gait.</td>
</tr>
</tbody>
</table>

![Fig 1: Horse with clinical signs of pasture-associated stringhalt displaying exaggerated hyperflexion of the hindlimb.](Image)
frequently in taller horses. Features of shivers that do not seem to be present or occur infrequently in stringhalt include abduction of the hindlimb during hyperflexion, elevation of the tailhead and facial twitching. In addition, shivers tends to be a progressive disease rather than resolving spontaneously (Baird et al. 2006; Draper et al. 2014). Clearly there appears to be an overlap in the clinical signs of stringhalt and shivers and this is hampered by a lack of definitive diagnostic testing in many cases. As a consequence, the two conditions might be difficult to confidently separate clinically. Distinction might be aided by epidemiological features, particularly where there is exposure to Hypochaeris radicata and the presence of multiple affected animals.

Acquired equine polyneuropathy (AEP; commonly referred to as Scandinavian knuckling syndrome) is a condition that shares some epidemiological and pathological features with PSH. However, rather than hindlimb hyperflexion, affected horses usually have symmetrical digital extensor dysfunction with knuckling of the metatarsophalangeal joint and stumbling (Hahn et al. 2008; Grondahl et al. 2012). Severely affected horses can become rapidly recumbent and many are subsequently subjected to euthanasia but, as noted in PSH, mildly affected animals often make a full recovery over several months (Grondahl et al. 2012). Like PSH, the condition occurs in outbreaks but most cases of AEP occur between mid-winter and spring. AEP has been anecdotally linked to feeding practices (affected horses have often been fed wrapped forage) but epidemiological studies have not yet found differences in management (including feeding practices) between affected and unaffected horses (Wolff et al. 2014). Limited studies have shown that, as with stringhalt, AEP is associated with injury to the peripheral nerves but it is the Schwann cells that appear to be the primary target with subsequent demyelination (Hahn et al. 2008; Grondahl et al. 2012). Both conditions may represent a spectrum of a peripheral neuropathy induced by a plant-associated toxin manifesting in different clinical presentations.

Pathological findings
To date, pathologic lesions identified in horses with PSH have been restricted to the peripheral nervous system (PNS) and to the distal muscles supplied by affected nerves. Although signs including behavioural changes may be indicative of CNS dysfunction, histopathological lesions have not yet been described in the brain of affected horses (Cahill et al. 1986; Huntington et al. 1989; Slocombe et al. 1992; Mayhew 2009). Additionally, histological evaluation of the spinal cord in affected animals has so far been unrewarding (Cahill et al. 1986; Slocombe et al. 1992; Domange et al. 2010).

At a histological level, PSH is characterised by a Wallerian-type distal axonopathy with decreased numbers of large myelinated nerve fibres within peripheral nerve trunks, and perineurial fibrosis (Cahill et al. 1985; Slocombe et al. 1992; Domange et al. 2010). Generalised demyelination is not present. Rather, the larger, longer myelinated nerves such as the tibial, deep and superficial peroneal and recurrent laryngeal are generally most affected (Slocombe et al. 1992). Other common findings include Schwann cell proliferation and “onion bulb” formations indicative of demyelination and re-myelination of affected neurons (Cahill et al. 1986; Slocombe et al. 1992; Domange et al. 2010). Some of the early hallmark signs of distal axonopathies such as myelin digestion chambers, macrophages infiltration, myelin debris and axon fragments occur but may not be obvious in post-mortem samples from more chronic cases, but might be apparent in ante mortem samples or samples collected from more acute cases (Slocombe et al. 1992; Armengou et al. 2010). Given their role in regulation of limb motion, lesions within muscle spindles might be expected, although a systematic study of these structures has not been reported to date.

Changes consistent with neurogenic atrophy have been described in the dorsal cricoarytenoid, cranial tibial, lateral digital extensor, long digital extensor, gracilis and deep digital flexor muscles (Cahill et al. 1986; Slocombe et al. 1992; Domange et al. 2010). When examined, the most severe changes have been found in the dorsal cricoarytenoid muscles (Cahill et al. 1986; Slocombe et al. 1992; Domange et al. 2010). Histologically, muscle fibres appear shrunken, angular and pale and in some instances muscle fibres might be completely absent leaving only compacted epimysium. In some horses, affected muscle groups are simply severely atrophic while in others there is extensive replacement with fibrous connective tissue and fat. Whether this reflects some selectivity in the mechanism of neuromuscular injury or is a result of further injury to already atrophic muscles is unknown.

Compensatory hypertrophy of scattered muscle fibres in the margins between atrophic and normal areas of muscle is a common finding (Fig 2). Histochemical staining shows that, of the remaining muscle fibres, the relative proportion of type I (oxidative type) fibres is increased indicating a loss of type II fibres in horses with PSH. This loss of type II fibres, hence change in ratio of fibre types, has been noted in other neuromuscular disorders (Andrews et al. 1986; Van den Haven et al. 1988; Slocombe et al. 1992).

Fig 2: Masson’s trichrome stained digital extensor muscle ×100 from the hindlimb of a horse with longstanding grade III-IV pasture-associated stringhalt. Normal muscle bundles are on the left with muscle bundles that have undergone extensive atrophy on the right. The two regions of this muscle are separated by a dense band of connective tissue. Affected muscle appears hypercellular, and individual muscle cells are small, angular and irregular in outline, and show marked fibre size variation. Bar indicates 100 µm.
Epidemiology

Pasture-associated stringhalt most often occurs in horses grazing poor quality pasture on unimproved soils (Cahill et al. 1985; Huntington et al. 1989; Araya et al. 1998; Domange et al. 2010). The presence of H. radicata (Catsear, Flatweed, False Dandelion; Fig 3) in pastures grazed by horses that develop PSH has been consistently reported (Pemberton and Caple 1980; Cahill et al. 1985; Huntington et al. 1989; Mayhew 2009; Domange et al. 2010). H. radicata is a perennial, edible herb native to Europe but an invasive weed that has been introduced to Australia, New Zealand, the Americas and parts of Asia. An Australian study reported that 50 of 52 horses diagnosed with PSH had grazed on pastures containing a large amount of H. radicata and a more recent report from France identified exposure to H. radicata in 69 of 70 affected horses (Pemberton and Caple 1980; Cahill et al. 1985; Huntington et al. 1989; Mayhew 2009; Domange et al. 2010).

Other weeds, including Taraxacum officinale (Common Dandelion) and Malva parviflora (Marshmallow, Mallow Weed), have very occasionally been associated with PSH cases (Pemberton and Caple 1980; Huntington et al. 1989; Takahashi et al. 2002; Armengou et al. 2010). Cases typically occur in late summer or early autumn after several weeks of grazing the incriminated pastures and reports of PSH typically increase during drought conditions (Kannegießer 1989; Domange et al. 2010). H. radicata has a long tap root (Fig 3) affording the plant some resistance to drought conditions. This plant, might therefore, provide green herbage in paddocks with otherwise sparse dry forage. However, some horses have also been observed to selectively graze H. radicata (Pemberton and Caple 1980; Huntington et al. 1989).

The onset of clinical signs can be delayed and disease might not become evident until one to 3 weeks after removal from affected paddocks (Huntington et al. 1989; Gardner et al. 2005). Multiple horses in the same paddock are usually affected and, occasionally, all exposed animals will develop clinical signs. However, more commonly, only a proportion of horses develop signs, suggesting that exposure alone is insufficient to cause disease (Cahill et al. 1985; Huntington et al. 1989; Araya et al. 1998; Takahashi et al. 2002; Domange et al. 2010). Most cases of PSH occur in mature full-sized horses, with taller animals appearing to be at greater risk, although the condition has been described occasionally in ponies, younger horses and donkeys (Huntington et al. 1989; Araya et al. 1998; Araujo et al. 2008; Domange et al. 2010). It has been speculated that young or smaller animals might be protected from PSH by virtue of the shorter length of their neurons.

Cattle and sheep grazing pastures incriminated in PSH are not affected. This presumably is because toxins are broken down by rumen microflora. Other monogastric grazing species also do not appear to be affected.

Pathogenesis and possible aetiologies

The gait abnormalities of PSH are often exacerbated when affected horses appear agitated or disturbed. Conversely, sedation ameliorates clinical signs in some animals (Huntington et al. 1989; Takahashi et al. 2002; Domange et al. 2010). This, and the observation that some horses with PSH exhibit changes in behaviour, has been interpreted to support CNS involvement in the pathogenesis of PSH (Dixon and Stewart 1969; Huntington et al. 1989, 1991; Domange et al. 2010). Despite these observations, the neurologic lesions in horses with PSH have been entirely restricted to the peripheral nerves to date. The recent report of cerebellar lesions described in horses with the allied syndrome shivers suggests that further investigation of the CNS in horses with PSH might be warranted (Valberg et al. 2015).

Disease affecting the peripheral nerves is expected to produce hyporeflexia and hypotonia rather than the hyperreflexia and hypertonia observed in PSH. There is no ready explanation for this discrepancy but a well-accepted hypothesis suggests that the neuropathy preferentially involves the larger type 1a- and 1b- afferent fibres and/or γ motor efferent nerve fibres supplying muscle spindles and Golgi tendon organs (Fig 4) (Mayhew 2009). These axons form part of the myotatic reflexes synapsing with inhibitory interneurons within the spinal cord that modulate motor tone and the onset of volunteer and reflex alpha motor neuron firing. Dysfunction of these circuits would be expected to lead to disinhibition with resultant hypertonicity and hyperreflexia (Mayhew 2009). Involvement of the entire hindlimb is a result of the passive mechanical structures that comprise the reciprocal

Fig 3: Hypochoeris radicata (left) present in a paddock with horses displaying signs of Pasture-associated stringhalt. Note poor quality pasture. On the right is an uprooted specimen highlighting the length and nature of the tap roots. Note branched stems and rough haired leaves differentiating the plant from the common dandelion (Taraxacum officinale). Image courtesy of Dr Xenia Newland.
apparatus of horses’ hindlimbs (Mayhew 2009; Hahn 2015). This hypothesis is supported by the observation that myotenectomy of the lateral digital extensor reduces gait abnormalities in many affected horses (Torre 2003; Mayhew 2009; Domange et al. 2010; Dyson and Ross 2011).

Although there is a consistent epidemiological association between the presence of *H. radicata* and the development of PSH, attempts to experimentally induce stringhalt have been limited and largely unsuccessful (Seddon and Belschner 1926; Araujo et al. 2008). Injection of a “concentrated extract of *H. radicata* into laboratory animals” did not induce clinical signs consistent with PSH (cited by Pemberton and Caple 1980). A stringhalt-like gait was induced in a 6-month-old colt fed large amounts of *H. radicata* (9.8 kg dry matter/day) over a 50-day period, collected from paddocks that had contained horses with clinical PSH. Interestingly, the colt’s gait improved when the *H. radicata* was collected from a paddock in which there were no affected horses and worsened again when changed back to the original source (Araujo et al. 2008). While these findings are interesting and support the role of *H. radicata* in PSH, the rapid change, and particularly the rapid improvement, in clinical signs is not consistent with natural disease. Furthermore, young (and smaller) animals are rarely affected with PSH and further work is required in this area of investigation.

A number of studies have attempted to identify a neurotoxin or toxins produced by *H. radicata* that could explain the clinical signs of PSH. Ingestion of *Lathyrus* spp. (sweet pea) plants causes disinhibition of neural impulses and produces a hypermetric, stringhalt-like gait (Mayhew 2009). Although several toxic agents have been identified in these plants, the neurotoxicity is thought to be due to neurotransmitter agonists (Spencer et al. 1986; Holbrook et al. 2015). Mycotoxins are well recognised causes of neurological diseases in grazing animals and have frequently been suggested as a cause of PSH (Pemberton and Caple 1980; Cahill et al. 1985). However, pathological lesions consistent with known mycotoxincoses have not been detected in cases of PSH. Although examination of soil samples collected from paddocks that had contained horses with PSH revealed high levels of fungal microflora, the clinical significance of this observation is unclear (Huntington et al. 1989). No evidence of fungal elements was found in samples of *H. radicata* or pasture litter from pastures grazed by affected horses (Barry 1956; Huntington et al. 1989; El-Hage 2011). Screening of leaf, flower and stem samples from *H. radicata* collected from paddocks in which horses had developed PSH using gas chromatography–mass spectrometry (GC-MS) did not reveal any evidence of fungal alkaloids including those known to be associated with neurotoxicities (El-Hage 2011).

In contrast to the many negative or inconclusive results, dose-dependent increases in urine, liver and brain concentrations of scyllo-inositol were measured in mice fed a freeze dried extract of *H. radicata* flowers, although they did not develop gait abnormalities (Domange et al. 2008). Scyllo-inositol is a biomarker found in increased concentrations in several neurodegenerative diseases and supports the presence of a neurotoxic entity produced by *H. radicata*.

![Fig 4: Diagrammatic representation of the myotatic reflex arc involving the neuromuscular spindle.](image-url)

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Three guaianolides have been identified in the roots and aerial parts of *H. radicata* (Bohmann and Bohmann 1980). The guaianolides belong to the sesquiterpene lactone class of chemical compounds with well-known cytotoxic properties, but their role, if any, in PSH is unknown. In a recent pilot study using GC-MS, numerous differences in the metabolic profiles were identified between *H. radicata* samples collected from pastures that had contained horses with PSH and samples collected from pastures with no known cases of PSH. The significance of those differences remains to be determined (El-Hage 2011).

There is now evidence to suggest that *H. radicata* produces toxic metabolites only following chemical or climate induced stress (Bohmann and Bohmann 1980; Maruta et al. 1995; El-Hage 2011; MacKay et al. 2013). Metabolic profiles, again determined by GC-MS, differed between plants deprived of water (to simulate drought conditions) and those receiving adequate water, but it is not yet known whether these differences are related to disease in grazing horses (El-Hage 2011). Leaves of *H. radicata* exposed to the stressor copper chloride secreted fungitoxic sesquiterpenes and alkenals (Maruta et al. 1995). Recently, dose-dependent neurotoxicity of an extract from aerial parts of *H. radicata* plants subjected to chemical (copper chloride) stress was documented in cultured murine nerve cells (MacKay et al. 2013). The observed degenerative changes resembled those following exposure to repin, a sesquiterpene lactone, that is believed to be the toxic agent of yellow star thistle (*Centaurea solstitialis*) and the cause of nigropallidal encephalomalacia in horses (Roy et al. 1995; MacKay et al. 2013).

**Treatment and management strategies for horses with PSH**

Numerous therapies have been suggested for the treatment of PSH, and, while some of these have been described in the peer-reviewed literature, none have been assessed in large-scale blinded or controlled studies (Dixon and Stewart 1969; Huntington et al. 1991; Kannegieter and Malik 1992; Wijnberg et al. 2009; Domange et al. 2010; El-Hage 2011). The reported success of any treatment for PSH must, of course, be considered in the context that the vast majority of affected horses recover spontaneously following removal from the putative source of toxin. Most horses recover over a period of 6–18 months, but mildly affected horses (grades I–II) can recover more quickly. It should be noted that recovery can be extremely prolonged requiring over 2 years for complete resolution in some severe cases. Severely affected horses might be subjected to euthanasia if they become recumbent for prolonged periods. A very small number of horses never appear to recover completely, perhaps as a result of severe muscle wastage or fibrosis (Cahill et al. 1985; Huntington et al. 1989; Domange et al. 2010).

**Myotectomy of the lateral digital extensor**

Surgery for stringhalt has been reported for over 300 years (Markham 1644); whilst myotectomy has been advocated for classical stringhalt, efficacy of the procedure in the management of PSH has been a point of some contention (Cahill et al. 1985; Huntington et al. 1989; Crabill et al. 1994; Sullins 2002; Domange et al. 2010; Dyson and Ross 2011). Some horses with PSH have been reported to improve by several grades immediately following lateral digital extensor myotectomy, although others only recovered after a prolonged convalescence (Cahill et al. 1985; Huntington et al. 1989; Domange et al. 2010). This has created some doubt regarding the value of the procedure in light of the spontaneous recovery of most horses (Cahill et al. 1985; Huntington et al. 1989); however, one report has suggested that the technique can be successful in many (11/13) horses with PSH (Torre 2005).

**Botulinum toxin infiltration**

Botulinum toxin type A (Botox A) is a potent neurotoxin that has been used to manage a number of hypertonic or spastic muscular conditions in man (Pathak et al. 2006). Horses are considered exquisitely sensitive to the effects of Botox A and a single report of its use in two horses presenting with classical stringhalt provided some encouraging results. Following infiltration of 100 IU four times over 21 days into either the lateral or long digital extensor muscles and 300 IU into the vastus lateralis at Day 28, improvements in electromyographic and clinical parameters were observed over 2–3 months (Wijnberg et al. 2009). Anecdotal reports of prolonged clinical improvement following Botox A administration provide some basis for further investigation of its use in horses affected with stringhalt.

**Muscle relaxants**

Mephenesin, a centrally acting muscle relaxant, produced rapid reduction of the hypertonia in a single horse with PSH following systemic (intravenous or intramuscular) administration of mephenesin but this effect was transient (Dixon and Stewart 1969). The authors proposed that mephenesin might modulate the response of CNS centres and neural tracts that might be responsible for the hypertonicity in PSH. Because of its short duration of action and potentially serious side effects in human patients, mephenesin now has limited availability and has been largely replaced by methocarbamol. Although anecdotally used to treat PSH, the efficacy of methocarbamol in PSH has not been reported.

Baclofen, an analogue of the inhibitory neurotransmitter γ-aminobutyric acid, is used as a skeletal muscle relaxant primarily to treat spastic muscular conditions in man (Standaert and Roberson 2010). Baclofen has been trialled in horses with PSH on the basis that it might downregulate hyperactive stretch reflexes (Pedersen et al. 1974). Administration of baclofen (1 mg/kg bwt orally q. 8 h) to 10 horses that had had signs of PSH for between 4 months and 4 years resulted in improvement in clinical signs in eight of the 10 horses. However, clinical signs regressed slightly or returned to pretreatment levels in seven of those eight cases once treatment was withdrawn (Kannegieter and Malik 1992). A later report indicated no changes in a horse with PSH following a 9-day course of baclofen starting at 7.1 mg/kg bwt orally q. 12 h and increasing to 10 mg/kg bwt orally q. 8 h for the last 7 days of treatment (Takahashi et al. 2002).

Phenytoin has perhaps been the drug most often administered to horses with PSH and, at least anecdotally, appears to be the most consistently effective. Phenytoin is a sodium channel blocker that has been suggested to modulate tetanic muscle contractions and aberrant nerve activity (Woodbury 1982). Oral administration of phenytoin at dosages of 15 mg/kg bwt q. 12–24 h to horses with PSH...
generally result in a degree of clinical improvement while
the drug is administered. Additionally, EMG recordings from
the long digital extensor muscle indicate a reduction in
abnormal spontaneous electrical activity in horses
receiving phenytoin (Huntington et al. 1991; Takahashi
et al. 2002). It has been suggested that the mild
tranquilisation that often accompanies phenytoin
administration might be responsible for amelioration of
clinical signs and, for most horses, clinical deterioration
occurs after cessation of treatment (Takahashi et al. 2002;
Gardner et al. 2005; Domange et al. 2010). Variations in
pharmacokinetics have been reported following both oral
and i.v. administration and might explain the lack of
efficacy in some horses (Soma et al. 2001). Given this
variability, monitoring plasma concentrations is
recommended particularly for long-term administration
(Beech et al. 1988; Huntington et al. 1991; Soma et al.
2001). However, aside from mild sedation few if any
adverse effects have been noted in horses administered
phenytoin for extended periods (Takahashi et al. 2002;
Domange et al. 2010). It is of course important to
recognise that the administration of phenytoin (and other
drugs) might be regulated in competitive animals.

Miscellaneous treatments
Thiamine (vitamin B1) is an essential cofactor in neuronal cell
metabolism, neurotransmitter production and myelin synthesis
(Puri 2014). It has been commonly used in the treatment of
human peripheral neuropathies (Ang et al. 2008). Although
there is little evidence to support any benefits of
administration in man, thiamine has been used with
anecdotal reports of success in the treatment of PSH
(Huntington et al. 1989; Domange et al. 2010). Taurine is a
sulfur-containing compound with metabolic activity in many
tissues including the mammalian nervous system, where it
appears to modulate neuronal excitability (Birdsall 1998). In
a small number of horses, taurine (10 g orally q. 24 h) appeared
to have a quite dramatic and repeatable calming effect in
horses with behavioural changes thought to be related to
PSH (Domange et al. 2010). Antioxidants including tocopherol
(vitamin E), ascorbic acid (vitamin C) and dimethyl sulfoxide
have been administered to horses with PSH presumably to
reduce oxidative injury to distal axons of the long nerves
(Armengou et al. 2010). Other supplements recommended
for the treatment of PSH include L-tryptophan, magnesium
and potassium bromide for purported neuromodulatory
effects. Mycotoxin binders have been promoted for both the
prevention and treatment of PSH. There is little theoretical
basis for many of these supplements and no scientific
evidence to support the use of any of them.

Conclusions and future directions
Despite continuing advances in diagnostic and analytical
technologies, there are still many gaps in our understanding
of PSH. The techniques used in some of the earlier landmark studies
may have been insufficient to detect the pathological lesions
that would explain the clinical manifestation of PSH. The recent
finding of cerebellar changes in horses with shivers suggests that
the application of newer diagnostic techniques might also bear
fruit in horses with PSH. The use of noninvasive technologies such
as magnetic motor-evoked potentials to assess the function of
descending motor tracts may provide further insight into horses
with PSH. Similarly, magnetic resonance imaging techniques
may identify peripheral nervous system dysfunction. This
modality is a well reported PNS imaging modality in human.
These potentially valuable techniques have not been commonly
used in cases of PSH to date and may aid both
diagnosis and assessment of disease severity.

Targeted scrutiny of the neuromuscular relays (including
muscle spindles) suggested to be involved in the
pathogenesis of the gait abnormality of PSH might also be
rewarding. Definitive identification of a causative toxin and
an understanding of the exposure required to cause disease
would be a major advance in the management of grazing
horses in high-risk pastures. The in vitro and laboratory animal
studies evaluating extracts from (stressed) H. radicata appear
promising and might provide sensible targets for a
preventative strategy. However, until a definitive lesion and/or
toxic agent are identified, recommendations for the
prevention and management of PSH must remain empirical.
PSH is well known to occur in certain geographical regions
and might even be restricted to specific paddocks. Reducing
known risk factors by improving poorer pastures with fertilisers
and/or introduced grasses such that H. radicata and other
weeds are out-competed would seem logical. Supplementary feeding to reduce reliance on grazing might
be a useful strategy if horses cannot be moved to another
paddock. Once the clinical signs of PSH develop, the
affected horse almost certainly has a distal axonopathy of
the longer nerves. A prolonged recovery period is required,
although nearly all affected horses will eventually recover
once removed from the offending pasture.

Authors’ declaration of interests
No conflicts of interest have been declared.

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Authorship
Each author contributed substantially to the preparation of
this review manuscript.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher’s website:

Supplementary Item 1: Video: Horse with Grade II–III Pasture-associated stringhalt (courtesy Dr Soodi Ilkhani).

Supplementary Item 2: Video: Horse with Grade V Pasture-associated stringhalt (courtesy Dr Jemma Bergfeld).

Supplementary Item 3: Video: Stringhalt-like gait induced by application of travel wraps to hindlimbs limbs (courtesy Miss Amy Waldron).

Supplementary Item 4: Video: Horse with Classical (unilateral) stringhalt following a proximal metatarsal injury (courtesy Dr Kayo Kawaguchi).
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Critically Appraised Topic

In horses with liver disease, does histological evaluation of biopsies provide better prognostic information than results of blood tests?

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Keywords: horse; liver; biopsy; prognosis; bile acids

Summary

Equine hepatic disease is commonly encountered in first opinion and referral practice (Dunkel et al. 2015). Determining prognosis is key to managing client expectations as long-term treatment is often required. Biopsy results are traditionally thought to provide the best prognostic information, but the procedure is invasive and more expensive than blood tests (Durham et al. 2003b). The PICO question was designed to help determine whether biopsy is still recommended as the best prognostic test, based on the available evidence.

PICO question

In horses with liver disease, does histological evaluation of biopsies provide better prognostic information than results of blood tests?

P: Patient
Horses with liver disease.

I: Intervention/indicator
Histology of biopsies.

C: Comparison intervention/control
Blood tests.

O: Outcome
Accuracy in providing prognosis.

Search method

A PubMed search was performed using the terms: (equine or horse) AND (liver or hepatic) AND (prognosis OR outcome). The results were screened to identify studies which were relevant to the PICO question.

Exclusions

Papers older than 25 years, papers that did not relate to the PICO question (e.g., diagnosis of liver disease without investigation of prognosis); secondary sources of information (book chapters/review articles).

Studies included

One retrospective cohort study (Dunkel et al. 2015) compared serum bile acid (SBA) concentrations and a modified histopathological biopsy score for prediction of prognosis; one retrospective study (Durham et al. 2003a) assessed the utility of serum biochemical and haematological data in determining prognosis; one retrospective study (Durham et al. 2003b) developed a histopathological biopsy score and applied it retrospectively to horses with suspected liver disease to assess prognosis. Two retrospective case series (West 1996 and McGorum et al. 1999) compared concentrations of serum biochemical and haematological results between survivors and non-survivors.

Summary of evidence

Dunkel et al. 2015

A retrospective study compared serum bile acid (SBA) concentrations with histological score for prediction of short-term (survival to discharge) and long-term (survival greater than 6 months) prognosis in 81 horses with biopsy confirmed hepatic disease. In addition to the biopsy score developed by Durham et al. (2003b; see below), this study attempted to determine whether specific histological changes that contribute to the biopsy score were related to prognosis. Overall, 90% of horses survived short term and 83% survived longer than 6 months. In comparison to horses that survived, those that did not survive had significantly higher SBA, globulin, fibrinogen and total bilirubin concentrations and lower lactate dehydrogenase and albumin concentrations. Sensitivity and specificity of SBA and biopsy scores are reported in Table 1. As well as overall biopsy score, the presence of several pathological changes relating to both reversible (for example inflammation) and irreversible pathology (such as portal and bridging fibrosis) were associated with a poorer prognosis.

Relevance to PICO question

This is the only study that has directly compared blood values with histological evaluation of biopsy specimens. The authors concluded that histological score had a better specificity compared with SBA concentration.

Durham et al. 2003a

A retrospective study compared various serum biochemical and haematological data between survivors and non-survivors in 116 horses with liver disease. Serum biochemical and haematological results were categorised for statistical evaluation. Table 2 summarises the key differences between survivors and non-survivors.

Although biopsy score was not specifically compared with clinicopathological findings, a multivariable model including biopsy score identified a significantly increased risk of non-survival in horses with higher scores, in particular those with scores greater than 7/14.
Relevance to PICO question
This study provides evidence that there is a significant difference between survivors and non-survivors for some haematological and biochemical parameters.

Durham et al. 2003b
A biopsy grading system was devised which included the presence or absence, as well as the severity of fibrosis, reversible and irreversible cytopathology, inflammation, haemosiderosis and bile duct proliferation. The grading system was retrospectively applied to 73 horses with a suspected hepatopathy and 12 normal horses, and a weighted score (0–14) was then developed based on survival at 6 months. Comparison with other possible predictors of survival was not performed. Horses with total biopsy scores between 2 and 6 were 12 times less likely to survive to 6 months than horses with biopsy scores of 0 (hazard ratio 12.04; 95% CI 1.34–107.81; P=0.026), and those with biopsy scores between 7 and 14 were 46 times less likely to survive (HR 46.01; 95% CI 5.92–357.45; P<0.001).

Relevance to PICO question
This study provides evidence that by quantifying the severity of histological changes, a biopsy score can be utilised for prognostic purposes. The study population is likely to be relevant to modern equine practice in the UK, and the survival rate (in contrast to the two studies below) would also be consistent with cases currently seen in referral practice. Although blood results for this population were reported in the previous study, direct comparison of the utility of biopsy score vs. blood results is not possible with the information provided.

McGorum et al. 1999
A retrospective case series reported clinicopathological findings in 50 horses with hepatic disease, comparing values between survivors and non-survivors. A biopsy was obtained from 17/50 but histological findings were not reported nor was outcome in these cases. In contrast with the previously reported studies, a higher mortality rate of 72% (36/50) was reported, with half the cases diagnosed with pyrrolizidine alkaloid toxicity. Significant differences between survivors and non-survivors were identified for: GGT, GLDH and SBA (Table 3).

Clinical implications
Although the level of evidence is not high, and all studies had obvious weaknesses, the populations studies in the more recent publications are likely to be relevant to both first opinion and referral equine practice in the UK. Based on the available evidence, histological evaluation of hepatic biopsies provides better prognostic information than does the results of blood tests. Of the routinely performed blood tests, SBA concentration provides the best prognostic information.

## TABLE 1: Sensitivity and specificity of serum bile acid (SBA) and biopsy score for long-term survival (Dunkel et al. 2015)

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBA ≥16 μmol/L</td>
<td>78.6</td>
<td>65.7</td>
</tr>
<tr>
<td>SBA ≥20 μmol/L</td>
<td>57.1</td>
<td>80.6</td>
</tr>
<tr>
<td>Histological score &gt;2</td>
<td>64.3</td>
<td>95.5</td>
</tr>
<tr>
<td>Histological score &gt;3</td>
<td>50</td>
<td>100</td>
</tr>
</tbody>
</table>

## TABLE 2: Hazard ratios for non-survival in horses with hepatic disease (Durham et al. 2003a)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Hazard ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkaline phosphatase (AP) activity (IU/L)</td>
<td>&gt;900 vs. &lt; 301</td>
<td>10.66 (1.36–83.47)</td>
<td>0.024</td>
</tr>
<tr>
<td>Gamma glutamyl transferase (GGT) activity (IU/L)</td>
<td>&gt;399 vs. 100</td>
<td>4.54 (1.00–20.49)</td>
<td>0.049</td>
</tr>
<tr>
<td>Total bile acid concentration (mmol/L)</td>
<td>&gt;20 vs. &lt; 11</td>
<td>9.69 (2.09–44.97)</td>
<td>0.004</td>
</tr>
<tr>
<td>Globulin concentration (g/L)</td>
<td>&gt;45 vs. &lt; 31</td>
<td>13.24 (2.95–59.47)</td>
<td>0.001</td>
</tr>
<tr>
<td>Red blood cell count (1/L)</td>
<td>&gt;10 × 10^12 vs. 0–7</td>
<td>6.63 (1.92–22.85)</td>
<td>0.003</td>
</tr>
<tr>
<td>White blood cell count (1/L)</td>
<td>&gt;10 × 10^9 vs. 0–6</td>
<td>5.01 (1.06–23.65)</td>
<td>0.042</td>
</tr>
</tbody>
</table>

## TABLE 3: Comparison of serum biochemical abnormalities in survivors vs. non-survivors (McGorum et al. 1999)

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Number abnormal</th>
<th>Non-survivors (median)</th>
<th>Survivors (median)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GGT (IU/L)</td>
<td>50/50</td>
<td>560</td>
<td>205</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GLDH (IU/L)</td>
<td>31/35</td>
<td>46</td>
<td>14</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>SBA (μmol/L)</td>
<td>31/37</td>
<td>52</td>
<td>12</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Conclusions

Hepatic biopsy is recommended to provide a more accurate prognosis for horses with hepatic disease.

Author’s declaration of interests

No conflicts of interest have been declared.

Ethical animal research

This is a literature review and thus no ethical considerations for this manuscript are relevant.

Source of funding

None.

References


Correspondence

Response to the Clinical Commentary on electrical nerve stimulation for the management of equine trigeminal mediated headshaking by Dr K. J. Pickles

Dear Editor

First, I would like to acknowledge the valuable contribution of Dr Kirstie Pickles to our current understanding of trigeminal-mediated headshaking (TMHS) in horses. In response to the clinical commentary (Pickles 2019), there are a couple of points that are worthy of further discussion.

When comparing the efficacy of electroacupuncture (EA) and EquiPENS, the commentary states that ‘given the longer length of the probe and closer approximation to the infraorbital nerve, greater nerve stimulation is likely to occur with EquiPENS compared with the described electroacupuncture technique’.

The current understanding is that the electric field strength is highly concentrated at the needle or probe tip and decays rapidly with increasing distance from the tip (Boezaart 2006; Mayor 2007; Silva et al. 2012). It also depends whether the needle/probe is electrically insulated or uninsulated, as the electrical fields generated are quite different. With an insulated needle or probe, the current is only present in a sphere around the needle tip, thus the high current density means that a low threshold current is sufficient to stimulate the nerve. Uninsulated needles transmit the current throughout their entire length – maximum current density at the tip with a lesser zone extending up the shaft. Provided the tip of the needle is close to the nerve and the current intensity and pulse duration (pulse width) exceed the threshold intensity for the target nerve, the length of the needle or probe is unlikely to have any significant influence.

The closer the stimulating electrode is to the nerve the lower the current intensity required for its excitation; stimulation of the nerve (as monitored by the muscle twitch due to the connections of the infraorbital nerve with the buccal branch of the facial nerve, Li et al. 2009) at a low current intensity confirms close positioning of the acupuncture needle tip to the nerve. This is possible without ultrasound guidance due to the superficial site of the readily palpable infraorbital nerve. Where ultrasound guidance would be helpful is to avoid the occasional occurrence when the needle touches or penetrates the nerve causing overstimulation, which is uncomfortable for the patient and requires a minor adjustment to the positioning of the needle tip.

In human patients, the position of the needle tip near a sensory nerve is confirmed when the patient reports a radiating paraesthesia with each pulse in the distribution area of the nerve (Boezaart 2006), but this is not possible in a sedated horse. This author has performed further trials in equine patients using a more focused needling technique (Mayor 2007) with two needles positioned 2–3 cm apart under a single infraorbital nerve rather than using the brachiocephalic muscle. These unpublished results suggest that this is no more effective than treatment with a single needle in horses that show a good response to treatment or those that do not respond. Similarly, placing one needle under the infraorbital nerve and the second needle close to a mandibular branch of the trigeminal nerve rather than in the brachiocephalic muscle appears to give no further benefit.

The second point to mention is that while I accept that some of the remission times quoted include the time when the horse would be expected to enter seasonal remission, only two of the six horses were known to be seasonal headshakers. This was made clear within the context of the paper and the accompanying graphs and table (Devereux 2019). One year on from the end of the study it can now be reported that the two horses (horses 2 and 3) that only required a single treatment in the spring of 2016 have not needed any treatment in 2017 and thus have entered longer-term remission following the EA treatment.

It would appear that both EA and PENS are effective for the treatment of trigeminal-mediated headshaking in an encouraging proportion of cases and both have their place in different situations. The advantage of EA is that it can be performed in the field without the use of ultrasound if this is not available, thus making the treatment accessible to a greater number of horses. The needle tip can be positioned in an optimum site to achieve maximum stimulation of the infraorbital nerve with little or no distress to the horse. Local anaesthetic needs to be used with care if used for insertion of the EquiPENS probe as local anaesthesia of the tissue being stimulated blocks acupuncture analgesia (Lindley and Cummings 2006). Hopefully, this correspondence will generate further interest and discussion to improve the treatment for this painful and distressing condition.

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References


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I would like to thank Ms Devereux for the interesting points she raises in her correspondence regarding electrical nerve stimulation. What remains to be described for both electroacupuncture and EquiPENS therapies are large, multicentre studies of efficacy and safety. It is anticipated that this will be published for EquiPENS in the near future.

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References


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