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EQUINE VETERINARY EDUCATION/AMERICAN EDITION

VOLUME 35 NUMBER 10

OCTOBER 2023



EQUINE VETERINARY EDUCATION

American Edition | October 2023



The official journal of the American Association of Equine Practitioners, produced in partnership with BEVA.

IN THIS ISSUE:

Eating the young is not always a long-term survival strategy

Clinical application of the wooden shoe to complement surgical management of laminitis and other foot-related diseases in the horse: A report of three cases

A synopsis of wearable commercially available biometric-monitoring devices and their potential applications during gallop racing

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Eating the young is not always a long-term survival strategy

By Peter Morresey, BVSc, MVM, MACVSc, DACT, DACVIM, CVA



Dr. Peter Morresey

I watched this great nature documentary a few years ago where a particular tree flowered and fruited every 17 years. The local rat population boomed in response. When the fruit was gone, the rats invaded the local town and ate what they could before the locals rose up and drove them back out to the surrounding countryside. Then, faced with a lack of resources, the female rats dutifully ate their offspring in the nest restoring balance to the ecosystem.

This is prompted by a recent posting on Facebook regarding the effects of itinerant specialists entering a region, performing the high-dollar work (lameness evaluations), then leaving emergency coverage and less lucrative tasks to veterinarians early in their career trying to establish themselves but instead becoming discouraged by the actions of others. There are two sides to this, and we've all been on at least one by action or circumstance. You can't dictate how someone makes their living, but you can feel for those affected and look at a bigger picture.

A classic situation occurred at my second locum position in New Zealand. I had arrived at the mixed practice to cover for a clinician before he left town on vacation. He had graduated one year before me and aspired to a career as an equine veterinarian. He was focused on his goal and is now deservedly the CEO of a large equine practice. On Friday night, just as he was preparing to leave town, a regular equine client called on emergency distressed over a post-castration complication. The kicker was the castration was not performed by the practice. Rather, Dr. S (to maintain anonymity), the traveling equine "specialist," had on his northern circuit around the mountain castrated the horse on Tuesday before completing the "tour de castration" and was now back home on Friday night three hours away, no doubt with his feet up resting.

Not wanting to leave the new graduate (me) in a bad spot, the clinician changed his plans and we drove together to the client's farm. There we were presented with a large seroma at the castration site on each side. This can happen to anybody. If you haven't had a complication, you haven't done enough. I am sure Dr. S would have agreed. Turns out this was a horse my colleague was scheduled to service; however, the client stated, "Well, I heard Dr. S was coming to town so I got him to do it."

To my colleague's credit, he was meticulous and professional in his approach to the horse, rendering the care

needed with skill and compassion. The conversation with the client, however, was very direct and his dismay was clearly stated as follows: "We are not Dr. S's (expletive) after-hours service." Can't say I could see any fault with that sentiment. You have to own your own stuff.

Here is the lesson: If you are to provide a service, you need to back up that service, or create an environment where back up can and will be professionally and graciously provided. That starts with you establishing relationships that are mutually beneficial prior to the need for them.

I remember too well being personally on the wrong side of this issue. A chronically managed case doing well (severe heel bulb laceration) was without notice suddenly in the care of another practitioner, with my management opportunistically called into question by this more senior clinician. It is no accident my refusal to illegally prescribe an anabolic to a competing horse (detailed in the ethics feature in the September 2021 issue of *EVE*) allowed an opportunity for another veterinarian to fulfill a need, and this opportunity was taken along with the longstanding client.

While I never met him, Dr. B was the "joint guru" around one place I worked. He would come to the barn and the adulation began. He could look at a joint and know it needed to be injected, and he was quick to say "get this joint X-rayed" because he didn't have a radiography machine. So my resident had to follow behind taking radiographs and making diagnoses. By swooping in and eschewing a rational diagnostic approach, Dr. B was passively devaluing the input of the resident, taking a systematic approach and reducing them to a minor supporting role.

Maybe we could look at the equine veterinary profession in its current state as rhyming with the ecosystem in the opening paragraph. There's plenty of fruit at the moment. Why eat the young now? Also, it is not as if we have a surplus of young to consume to ensure the survival of the more established members of the community. It is clear fewer graduates are entering equine practice, and many are not staying very long. So why act in a way that may cause them to become discouraged?

So what are YOU going to do to create a more sustainable equine veterinary ecosystem? Perhaps we should all take a little time to look past our billing sheet into a wider world where we have a duty to pay forward the opportunities we were given to those coming behind us who model their behavior on what we do. Perhaps if corporate gets weary, you may be needing that young veterinarian to buy your practice. Karma has a long memory.



5 things to know about AAEP this month

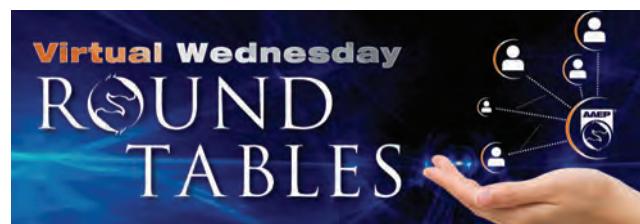
1. Save \$100 by registering for the in-person AAEP Annual Convention in advance of the event at convention.aaep.org. A virtual option is also available.
2. Leave the convention with new knowledge and a new job by participating in the virtual Career Fair. Log into your Career Center account at jobs.aaep.org and indicate you'll be attending the Career Fair.
3. Facilitate a positive workplace environment by downloading new handbooks on communication and physical/mental safety from the Practice Culture Subcommittee at <https://tinyurl.com/2v6e9z23>.
4. The Foundation for the Horse recently received the largest single gift in its 29-year history—\$1 million from a horse-owning couple in Pennsylvania.
5. Save on your next work truck and avoid uncomfortable dealer negotiations using The Veterinary Club's new contract with MKT Fleet. See page X for details.

Virtual Round Tables conclude October 25; to return in 2024

The third season of Virtual Wednesday Round Tables wraps up Oct. 25 with the session “50 Ways to Lose Your License.”

As a reminder, Round Tables are recorded and archived for viewing on-demand. Visit aaepanywhere.org, the free-to-members online learning platform, to view the list of available sessions with links to external resources.

Virtual Wednesday Round Tables will resume in spring 2024. If you are interested in serving as a Round Table panelist next year, simply check the appropriate box when completing or updating your Volunteer Interest Form accessible through the My Member Profile/Benefits button



at the top of aaep.org. Round Table moderators are compensated for their work.

The AAEP thanks its Virtual Wednesday Round Table sponsors:



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In 2022, over 77,000 copies of *Equine Veterinary Education* totaling nearly 7 million pages were printed and mailed to AAEP members. If you like receiving a print copy of the journal in your mailbox every month, there is no need for you to do anything. We'll keep mailing it to you.

If your readership habits trend toward digital instead of print, or if you simply want to minimize

your carbon footprint, you can opt out of receiving a print copy of *EVE* and instead access each month's issue online or through the AAEP On-the-Go app. Switching to digital would reduce your paper consumption by more than 1,000 pages per year.

The digital edition of *EVE* is generally available on the AAEP website and On-the-Go app prior to its print counterpart dropping in the mail. Before making the switch,

you are encouraged to check out a recent digital issue at aaep.org/equine-veterinary-education or on the app. To download the app, search “AAEP On-the-Go” at your app store.

If you like the digital edition and want to make the switch, simply update your preferences:

1. Go to aaep.org/dashboard
2. Select “Update Your Contact Information” (you may be asked to log in)
3. Scroll down and check the box beside “Do not send me a printed version of *Equine Veterinary Education*”

If you should ever change your mind and want to resume receiving a print issue, simply follow the steps above and uncheck the box. A similar checkbox appears for *Convention Proceedings* if you would prefer to access the compilation of papers presented at the annual convention through the AAEP website or On-the-Go app in lieu of receiving a print copy.

If you have questions about the digital AAEP publications, contact John Cooney, publications coordinator, at jcooney@aaep.org or (859) 233-0147.

New resources published to enhance practice culture

A healthy team-based practice culture can reduce employee turnover, enhance the workplace environment and improve profitability. Two important contributors to a positive workplace culture are communication and physical and mental safety.

The Practice Culture Subcommittee of the AAEP's Commission on Equine Veterinary Sustainability has published a pair of handbooks that will help practices strengthen these two (of seven) pillars that contribute to a positive workplace culture in which employees feel respected and valued.

The first is *Communication Boundaries for the Equine Practice*. For both practice owners and associates, this resource discusses how to set effective boundaries in practice through conversation. Situational examples include both client and practice team communication.

The second is *The Key to Successful Teams for the Equine Practice Owner*, which offers a roadmap for practice leaders to establish a culture of psychological safety in which team members feel more engaged, innovative and productive through a shared expectation that teammates will not be embarrassed, rejected or punished for sharing ideas, taking risks or soliciting feedback.



Both handbooks are available as PDF resources through the Practice Culture button accessible within the Commission on Equine Veterinary Sustainability section of the website at <https://tinyurl.com/2v6e9z23>.



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Cassandra Worthy

Start big

Educational sessions begin with a bang this year as both the keynote presentation and Milne Lecture will be held on Thursday, Nov. 30. During her morning keynote address, sponsored by Merck Animal Health, Change Enthusiasm® Global Founder and CEO Cassandra Worthy will invigorate and inspire by sharing strategies for transforming workplace culture from surviving change to growing through change.



Dr. Patrick McCue

At the afternoon's Milne Lecture, sponsored by Platinum Performance, renowned theriogenologist Dr. Patrick McCue will trace significant advancements in equine reproduction and analyze the current state of practice in the field, helping advance your diagnosis, treatment and management of stallions, mares and neonates.

Navigate your career lattice

If your idea of catching the wave of opportunity includes catching a fresh start, you're in luck. Dozens of practices looking to hire will be participating in the virtual Career Fair. To participate:

1. Create or log into your AAEP Career Center account at jobs.aaep.org.
2. Upload your resume if you haven't done so already.
3. Indicate on your account page that you'll be attending the Career Fair. This will flag your résumé for participating employers to review and contact you (confidentially if you wish).

You may also view a list of participating practices. Contact Megan Gray, member concierge, at mgray@aaep.org with any questions.

Acquire a license to thrive

Learn how colleagues are amending their practice protocols, philosophies and ideals to increase career sustainability at the Member Roundtables on Wednesday, Nov. 29. These facilitated discussions will be led by members of the respective subcommittees on Practice Culture and Compensation from 1:00–2:30 p.m. and on Emergency Coverage and Internships from 3:00–4:30 p.m.

Be in the know

Keep up with all the goings-on in San Diego. Like the AAEP Annual Convention on Facebook at facebook.com/AAEPConvention; and follow @AAEPhorseDocs and use the hashtag #AAEPSanDiego to view posts on X (formerly known as Twitter) and see photos on Instagram.

In addition, check your inbox each evening for news, recaps and more in the Convention Daily, sponsored by Arenus Animal Health.

Finally, download the AAEP Convention app, sponsored by CareCredit, to develop your itinerary, browse sessions and speakers, access *Proceedings* papers and more. Search "AAEP Education" at your app store to download.



Quell your hunger

Satisfy your mid-morning or afternoon craving with a free snack at any of four new Grab 'n Go stations located throughout the trade show. Grab 'n Go snacks are sponsored by Asto CT, Boehringer Ingelheim Animal Health and LubrisynHA Family of Products.

Join the discussion

Meet others who share your professional or personal interests by finding a seat at one of the Lunchtime Chats tables in the seating area of Hall C each day of the trade show. Tables will be organized by subject and will include a mix of clinical and general interest topics that change each day. This is a great way to meet new colleagues who may share similar professional or personal interests.



Laugh out loud

If one thing has become clear from storyteller events at previous conventions, it is that some of your colleagues could have lucrative side hustles as standup comedians! Enjoy an evening of engaging and lighthearted fun at Vet Story Night, Thursday, Nov. 30 from 8:00–10:00 p.m. at the Marriott Marquis.

Reserve your seat for \$65 (or \$35 for students, residents, interns and techs). Purchase price includes theater seating and a complimentary beverage. Table sponsorships are available and include a one-hour pre-event reception. Learn more at convention.aaep.org/vet-story-night.

Vet Story Night is sponsored by Merck Animal Health, Boehringer Ingelheim Animal Health and Zoetis. All proceeds benefit The Foundation for the Horse.



Dance the night away

Create some final memories of good times with friends and colleagues in San Diego at The After Party on Saturday, Dec. 2 from 8:00–10:30 p.m. at the Marriott Marquis. Enjoy a night of music, dancing and fun courtesy of event sponsor Zoetis. The After Party is free for all registered convention attendees.

Break a sweat

An all-abilities 5K fun run through downtown San Diego will be held Friday, Dec. 1 at 6:30 a.m. The following morning from 7:00–7:45, Sunrise Yoga will be held on the lawn between the convention center and Hilton Bayfront hotel and a Harborwalk Boot Camp will include stops along the route for bodyweight and aerobics exercises. Advance registration is required for each at convention. aaep.org. There is a \$35 fee for the fun run. These fitness events are sponsored by Boehringer Ingelheim Animal Health.

Register early and save

Register online at the reduced rate of \$725 through Nov. 26; after this date, the rate increases by \$100. On-site registration at the San Diego Convention Center begins Nov. 28 at 3:00 p.m. The last day to reserve a room at the AAEP-member rate at the contracted hotels is Nov. 8.

If unable to join your colleagues in San Diego, you may register for the Virtual Convention and receive on-demand access to recordings of all educational sessions as well as live access to a dozen Table Topics being re-offered via Zoom the week of Dec. 11. CE hours from on-demand recordings can be earned through Dec. 31, 2024. In-person attendees receive complimentary access to the virtual offerings.

Register in advance for best rate: **convention.aaep.org**

Invest in patient and self-care at the 25th Annual Resort Symposium

Pack your flip-flops and sunscreen for unforgettable CE in Costa Rica



Acquire 15 hours of engaging, evidence-based CE and unlimited hours of relaxation and rejuvenation for the year ahead at the AAEP's 25th Annual Resort Symposium in Costa Rica, Jan. 22–24, 2024.

The silver anniversary edition of this destination event will be held at the J.W. Marriott Guanacaste Resort, a hacienda-style oceanfront retreat just steps from the soft, white sand beaches and warm waters of the Pacific Ocean.

During half-day educational sessions, strengthen your diagnostics and treatment of equine gastric ulcer syndrome as well as your ability to image and treat horses with neck and back pain as well as stifle and tendon sheath injuries. All sessions will be led by board-certified specialists.

After sessions, focus on yourself by relaxing on the beach, at the pool or enjoying optional group excursions with your colleagues. Excursions include a sunset catamaran sail, surfing lessons, kayak and snorkeling tour, standup paddle-boarding tour and horseback riding tour. View the educational program, book your hotel room, and register for the meeting and optional group excursions at aaep.org/meetings/resort-symposium.



Thanks to Zoetis for its sponsorship of the 25th Annual Resort Symposium.

FOUNDATION

Pennsylvania horse owners make record gift to The Foundation

Gift to fund new grant opportunities starting in 2024

The Foundation for the Horse has received a \$1 million gift from Pennsylvania horse owners and equine enthusiasts Robert "Bob" and Toni Mallet. This is the largest single gift in The Foundation's 29-year history.



The Mallets' generosity will allow The Foundation to expand its direct care of domestic horses in need and

establish new grant opportunities for many years to come.

"Unfortunately, some horses need to be rescued, and my wife and I feel strongly about the abuse and neglect of these magnificent animals," said Bob Mallet. "Therapeutic riding gives older horses a second career, and they seem to enjoy their work. These horses need veterinary care which, in some cases, the centers cannot afford. Our hope is this



Bob and Toni Mallet with Saddlebred mare "Untouched" aka Gayle.

fund will inspire others to support horse-related or animal charities of their choice."

The Mallets' connected with The Foundation through their longtime veterinarian and AAEP member Dr. Jim Zeliff. Their remarkable contribution will serve as the cornerstone for an array of transformative grants and pioneering initiatives, empowering programs that provide essential care for horses in need within the U.S.

Starting in late spring of 2024, a series of four annual grant opportunities through The Foundation will come to fruition, each focused on a specific facet of equine support.

- The Equine Support Grant, aimed at nonprofit facilities, will offer solace and attention to these magnificent animals.
- The Equine Rescue Response Grant will extend a helping hand to equines caught in the midst of abuse, neglect, abandonment or seizure incidents.
- The Equine Vet Care Grant will ensure that life-saving medical attention is within reach for equines housed in nonprofit facilities.
- The Equine Intake Care Grant will increase the chances of successful adoption for equines entering nonprofit facilities by supporting advanced veterinary care to overcome non-life-threatening health challenges.

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NATIONAL VET TECH WEEK
OCTOBER 15-21, 2023

Dr. Dean Peterson, longtime Wisconsin practice owner, dies at 82



Dr. Dean Peterson

AAEP Honor Roll member Dr. Dean Peterson, founder of Janesville Animal Medical Center in Milton, Wisc., passed away July 24. He was 82.

After receiving his veterinary degree in 1971 from Michigan State University, Dr. Peterson worked for seven years in Kentucky and West Virginia before returning to his native Wisconsin to establish his mixed animal practice. Over the next four decades, he specialized in horses but also took care of cattle, hogs, sheep, goats, dogs and cats.

Dr. Peterson supported organized veterinary medicine at the local, state and national levels. His AAEP service included terms on the Biological and Therapeutic Agents, Political Liaison and Practice Management committees in the 1990s and the Student Relations Committee from 2006–2008.

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Members in the News



Dr. Stowe Burke joins TRF board of directors

Dr. Stowe Burke, owner of Burke Equine Therapy in Saratoga Springs, N.Y., has been appointed to the Thoroughbred Retirement Foundation board of directors. The TRF provides sanctuary to retired Thoroughbreds throughout their entire lifetime.

Dr. Burke practiced on the racetrack for 20 years before establishing his current practice, which specializes in providing advanced veterinary care and therapeutic services to equine athletes. Dr. Burke received his veterinary degree from the Cummings School of Veterinary Medicine at Tufts University.

Dr. Stowe Burke

Two members elected to AVMA committee posts

Drs. Barb Crabbe and Steven Dow have been elected to committee service within the American Veterinary Medical Association (AVMA).

Dr. Crabbe has been elected to the Council on Veterinary Service, representing private practice, predominantly equine. A veterinary graduate of the University of California, Davis, Dr. Crabbe owned a general equine practice near Portland, Ore., for over 30 years and is now involved with curriculum development in veterinary ethics. She serves on the AAEP's Professional Conduct and Ethics Committee.



Dr. Barb Crabbe



Dr. Steven Dow

Dr. Dow has been elected to the Council on Biologic and Therapeutic Agents, representing private clinical practice, predominantly equine. A longtime practitioner with Prescott Animal Hospital in Prescott, Ariz., Dr. Dow served on the AAEP's Scholarship and Racetrack Regulatory committees. He received his veterinary degree from Colorado State University.

AHC appoints four members

The American Horse Council has re-elected Dr. Rick Mitchell as chair of its board of trustees and appointed Dr. Katie Flynn as chair of the Health and Regulatory Committee. Separately, Dr. Tom Lenz and the late Dr. Glenn Blodgett (posthumously) have been named AHC emeritus trustees.



Dr. Rick Mitchell



Dr. Katie Flynn



Dr. Tom Lenz



Dr. Glenn Blodgett

Dr. Mitchell, who has served on the AHC board since 2012, is co-founder and partner-owner of Fairfield Equine Associates in Newtown, Conn. A veterinary graduate of Oklahoma State University, Dr. Mitchell is an AAEP Distinguished Life Member who served on the AAEP board of directors from 2000–2002 and as member or chair of 10 different councils and committees.

Dr. Flynn is senior staff veterinarian for the United States Equestrian Federation and recipient of the 2019 AAEP President's Award. She received her veterinary degree from the University of Glasgow, Scotland, and she previously chaired the AAEP's Infectious Disease Committee and served on the Welfare and Public Policy Advisory Council.

Dr. Lenz served as the AAEP representative on the AHC board of trustees from 2009–2022, and he served as chair of the AHC's Welfare Committee and the United Horse Coalition. An AAEP Distinguished Life Member, Dr. Lenz received his veterinary degree from the University of Missouri and served as AAEP president in 2003.

Dr. Blodgett joined the AHC board of trustees in 2015 as the AQHA representative. He served on the AHC's Health and Regulatory, Equine Welfare and Racing committees until his death on Nov. 20, 2022. An AAEP Distinguished Life Member and veterinary graduate of Texas A&M University, Dr. Blodgett was the longtime resident veterinarian and manager of the horse division of the famed Four Sixes Ranch in Guthrie, Texas.

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Highlights of recent clinically relevant papers

RECUMBENCY IN MARES WITH DYSTOCIA

This study by Heather Roe and co-workers in the United States evaluated recumbency at hospital admission as a risk factor for survival of mares and foals following dystocia management, and subsequent mare fertility.

Data collected from medical records at Rood and Riddle Equine Hospital of mares with dystocia included mare signalment, ambulation status, survival data and foaling records. Mare survival and fertility were analysed using chi-squared tests. Foal survival was analysed using Fisher's exact test. Odds ratios were calculated using multivariable logistic regression.

The analysis included 1038 ambulatory mares and 41 recumbent mares. Survival rates after dystocia resolution were 90.5% (977/1079) in mares and 37.3% (402/1079) in foals. Ambulatory mares had higher odds of survival (OR 6.93, 95% CI 3.25–14.78) than recumbent mares. Foals delivered from ambulatory mares had higher odds of survival (OR 22.7, 95% CI 3.11–165.44) than foals delivered from recumbent mares. Fertility was not statistically different for surviving Thoroughbred mares within 3 years of dystocia resolution between ambulatory and recumbent mares.

Mare and foal survival was significantly decreased when mares with dystocia were recumbent at hospital admission, but subsequent mare fertility was not affected by ambulatory status.

CARDIORESPIRATORY ULTRASOUND PROTOCOL

In this study Kari Bevevino and co-workers in the United States appraised a point-of-care ultrasound (POCUS) protocol for evaluating the cardiac and respiratory systems in horses.

The objectives were to (a) Describe the windows of a POCUS protocol for cardiorespiratory assessment of horses (CRASH); (b) Estimate the number of acoustic windows that can be acquired by a sonographer-in-training; (c) Estimate the time required to complete the protocol for specific groups of horses; (d) Describe the sonographic abnormalities detected in horses presented with cardiovascular, respiratory, or systemic disease.

The study population consisted of 27 healthy horses, 14 horses competing in athletic events, and 120 horses with clinical disease. A pocket-sized ultrasound device was used to acquire 7 sonographic cardiorespiratory windows in various clinical scenarios. The duration of the examination was timed, and images were evaluated for

diagnostic quality. Abnormalities in horses with clinical disease were determined by an expert sonographer.

The CRASH protocol could be performed in healthy and diseased horses in hospital, barn, and competition settings between 5.5 ± 0.9 (athletic horses) and 6.9 ± 1.9 min (horses with clinical disease). Thoracic windows were obtained most consistently, followed by right parasternal long-axis echocardiographic windows. Frequently detected abnormalities were pleural fluid, lung consolidation, B-lines, and moderate-to-severe left-sided heart disease.

The CRASH protocol was feasible using a pocket-sized ultrasound device in various groups of horses, could be completed rapidly in a variety of settings, and frequently identified sonographic abnormalities when evaluated by an expert sonographer. The diagnostic accuracy, observer agreement, and utility of the CRASH protocol merit further evaluation.

HYPERTRIGLYCERIDAEMIA TREATED WITH SGLT2 INHIBITORS

This study by US-based Eleanor Kellon and Kathleen Gustafson reported on hypertriglyceridaemia in equines with refractory hyperinsulinaemia treated with sodium-glucose cotransporter-2 (SGLT2) inhibitors.

A cohort of 20 equines (15 horses, 4 ponies, and 1 miniature mule) treated with SGLT2 inhibitors due to refractory hyperinsulinaemia, owned by members of the Equine Cushing's and Insulin Resistance Group, were followed. The index case was a 23-year-old gelding with a 2-year history of recurring laminitis that began canagliflozin therapy to control hyperinsulinaemia which was no longer responsive to metformin. Significant weight loss was noticed 6–10 weeks following the start of therapy. Two days later he was hospitalised with signs of colic and hyperlipaemia but was bright, alert, and eating well throughout. Canagliflozin was discontinued and triglycerides returned to normal reference values within 10 days. A subsequent study of 19 other horses on SGLT2 inhibitors revealed varying degrees of hypertriglyceridaemia, all asymptomatic.

The authors concluded that while this class of drugs holds great promise for cases of refractory hyperinsulinaemia and laminitis that do not respond to diet or metformin therapy, hypertriglyceridaemia is a potential side effect. The animals in this study remained asymptomatic and eating well. Further study of hypertriglyceridaemia in horses on SGLT2 inhibitors and the possible mitigating effect of diet is indicated.

MUSCULOSKELETAL PAIN

This study by UK-based Sue Dyson and Danica Pollard documented observations made during the ridden exercise of 150 horses with a history of poor performance, comparing Ridden Horse Pain Ethogram (RHPE) scores before and after nerve blocks ± change of saddle. An RHPE score of $\geq 8/24$ reflects the likely presence of musculoskeletal pain.

The most frequent lameness grade when ridden was 2/8 (range: 0–4); 35% of the horses had no overt lameness but lacked hindlimb impulsion. The most frequent RHPE score was 9/24 (range: 2–15/24), which declined to 2/24 (range: 0–12) after the interventions and was associated with improved gait quality and rideability. Despite recent professional saddle fit, an ill-fitting saddle contributed to poor performance in 37% of the horses. This study highlights the importance of ridden exercise in the investigation of poor performance/low-grade lameness and the value of the RHPE to verify the presence of musculoskeletal pain. Nerve blocks are vital to determine the source(s) of pain that compromise performance.

FEMOROPATELLAR OCD

This study by Pearce Sloan and co-workers in the United States described femoropatellar osteochondrosis dissecans (OCD) in juvenile Thoroughbreds and compared the racing performance of affected horses to siblings and unaffected horses from the same sale.

Radiographic reports from 27 Thoroughbred auctions of weanling (aged 5–11 months) and yearling (aged 12–22 months) horses were reviewed to identify femoropatellar OCD. Racing performance was compared between affected animals and two unaffected controls for each affected animal (a maternal sibling and an age- and sex-matched animal from the same sale).

Femoropatellar OCD was identified in 429 horses with North American race records. OCD was present on 519 lateral trochlear ridges and 54 medial trochlear ridges. There were more males in the affected group (70%) than in the sibling-unaffected group (47%). Case racing performance was compared to 1042 siblings and 757 sale matched controls. There were significant but small decreases in racing metrics of affected animals and increases in males for years raced, total starts, starts for 2–5 years of age, total placings, and placings at 2–4 years of age. Analysis of specific lesion metrics revealed weak correlations for performance outcomes (positive and negative) resulting in an inability to draw firm conclusions.

CONCENTRATED FAECAL MICROBIOTA TRANSPLANT

This study by Rebecca Di Pietro and co-workers in Canada evaluated the effects of concentrated faecal microbiota transplant on the equine faecal microbiota after antibiotic-induced dysbiosis.

One healthy 11-year-old horse was selected as a faecal donor and 9 horses were given trimethoprim sulfadiazine (TMS) for 5 days

to induce dysbiosis. Horses received either a concentrated FMT (cFMT, $n=3$), fresh unconcentrated FMT (fFMT, $n=3$), or 10% glycerol solution (vehicle, VEH, $n=3$) by nasogastric tube for 3 days. Faecal samples were collected on Days 0, 4, 9, 11, and 21 for microbiota analysis (Illumina sequencing).

The TMS significantly changed the bacterial composition of horses' faeces (Day 0 vs. Day 4). The composition of the cFMT and fFMT recipient horses was significantly different after transplantation compared to after antibiotic-induced dysbiosis (Day 4 vs. Day 11), whereas the microbiota of the vehicle recipients was not, indicating that both protocols induced transient changes. However, the preparation of FMT solutions markedly changed the original composition present in the donor's faeces, with significant enrichment of *Escherichia* genus in the cFMT. Individual susceptibility to restoration of the microbiota was observed in horses, similar to what is known for other species. These results suggest that concentrating bacteria should not be recommended in preparation of FMT solutions and that further research is required to improve current methods recommended to perform FMT in horses.

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Metastatic undifferentiated sarcoma in a horse

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SUMMARY

A 6-year-old Thoroughbred gelding was presented for a multi-lobular, 20 × 9 × 10 cm, cranioventral cervical mass extending from the level of the hyoid apparatus to the proximal cervical region (Figure 1). The mass developed over 9 months but began enlarging rapidly 4 months prior to hospital presentation. Previous biopsies were inconclusive. The gelding was in good body condition, clinically healthy and the mass was firm and nonpainful on digital palpation. Ultrasonographic examination of the mass revealed a heterogenous structure with indistinct margins separate from the thyroid gland and extending caudally from the level of the hyoid apparatus. A second incisional biopsy of the mass was not performed because of its recent behaviour (rapid enlargement) and an excisional biopsy was elected. Surgical resection of the

mass was performed under general anaesthesia. The firm mass was sharply and bluntly dissected outside of the presumed pseudo-capsule and removed. Histopathology and immunohistochemistry staining revealed an undifferentiated sarcoma with incomplete margins. Diagnostic staging tests, re-excision and adjuvant chemotherapy were recommended, but the horse died suddenly before further treatment could be pursued. Post-mortem examination revealed a recurrent cranioventral cervical mass in addition to haemothorax and widespread intra-thoracic and intra-abdominal multiorgan metastasis. To the authors' knowledge, this report documents the first undifferentiated sarcoma with systemic metastatic disease resulting in the sudden death of a young horse.

KEY WORDS

horse, sarcoma, systemic metastatic disease



FIGURE 1 Photograph of the cranial neck of a 6-year-old Thoroughbred gelding. A large mass is evident at the cranial, ventral neck.

Key points

- In horses with atypical equine soft tissue masses of the neck, gross and histologic pathologic examination should be performed.
- A preoperative metastatic screening including thoracic radiographs, rectal palpation, and percutaneous abdominal ultrasound should be considered in equine cases where a soft tissue sarcoma is suspected.
- Whenever possible, a wide-margin en-bloc resection should be performed in cases of undifferentiated sarcomas.

Undifferentiated sarcomas in humans and veterinary species

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Summary

Undifferentiated sarcomas, more correctly known as undifferentiated pleomorphic sarcomas (UPS), are a form of soft tissue sarcoma. They appear to be uncommonly diagnosed in veterinary species but represent the second most common form of soft tissue sarcoma in human adults. There is an evolving nomenclature around these tumours, with older reports referring to 'malignant fibrous histiocytoma', but these have been reclassified into several different tumour types, including the UPS. This makes review of the literature challenging, as many tumours previously referred to as malignant fibrous histiocytomas have been reclassified and are not the same as the UPS. *En bloc* surgical excision is the mainstay of treatment in all species, although adjunctive radiotherapy and perioperative chemotherapy improve the prognosis in humans, and should be considered in horses diagnosed with this tumour type. Metastasis is uncommon in all species but can be devastating when it occurs.

Undifferentiated sarcomas are a form of soft tissue sarcoma, which may be more correctly referred to as undifferentiated pleomorphic sarcomas to match the definitions used in human oncology. Broadly, soft tissue sarcomas can be classified into two genetic types – those with simple genomics associated with simple alterations, and those with complex genomics with complex karyotypes (Widemann & Italiano, 2018). Undifferentiated sarcomas have complex genomics. These pleomorphic tumours were originally classified as malignant fibrous histiocytoma, which was first described in 1964 (O'Brien & Stout, 1964), but subsequent work has reclassified these into various subtypes, namely myxofibrosarcomas, pleomorphic liposarcomas/rhabdomyosarcomas and undifferentiated pleiomorphic sarcomas (Widemann & Italiano, 2018). In human medicine, undifferentiated pleiomorphic sarcomas (UPS) are one of the more common soft tissue sarcomas seen in adults, representing 10% of soft tissue sarcomas, usually occurring between 50 and 70 years of age, and are rarely found in children (Henderson & Hollmig, 2012). The aetiology of these lesions remains unclear, and their clinical features are non-specific. They are typically deep-seated lesions on the limbs or trunk that enlarge rapidly and painlessly (Widemann & Italiano, 2018).

In one retrospective study, 55% of lesions involved the extremities, followed by the trunk (35%), retroperitoneum (9%) and left atrium (1%) (Chen et al., 2019). UPS are a histological diagnosis of exclusion, based on the absence of a specific line of differentiation following careful histological evaluation and ancillary techniques. The major differential diagnoses are poorly differentiated carcinoma, melanoma, dedifferentiated liposarcoma, pleomorphic liposarcoma, pleiomorphic lipomyosarcoma, myxofibrosarcoma, pleiomorphic rhabdomyosarcoma and malignant peripheral nerve sheath tumours (Widemann & Italiano, 2018).

Management of UPS is challenging in any species. In humans, surgery with wide margins is the cornerstone of the treatment of non-metastatic lesions, and this is frequently combined with perioperative chemotherapy and radiotherapy. Adjuvant radiotherapy is used to improve locoregional outcomes (Widemann & Italiano, 2018). A large phase 3 clinical trial demonstrated that perioperative chemotherapy showed a clear benefit in terms of overall survival (Gronchi et al., 2017), and doxorubicin is likely to be the first choice for single-agent chemotherapy. Sadly, patients with advanced UPS have the worst outcome of all soft tissue sarcoma

subtypes (Savina et al., 2017). Metastasis is especially likely to occur in lesions >5 cm in size, with one study finding post-treatment metastatic disease in 37.6% of patients with larger lesions (Vodanovich et al., 2019). Overall, 5-year and 10-year survival rates of patients with UPS were 60% and 48%, respectively (Vodanovich et al., 2019).

In veterinary medicine, UPS have been reported in dogs, cats, cattle, pigs and horses, in a wide variety of locations, and with no clear age predisposition across the species (Brown et al., 2007; Carmalt & Linn, 2013; Choi et al., 2011; De Zani et al., 2011; Ghibaudo et al., 2008; Gleiser et al., 1979; Hendrick et al., 1992; Huyghe et al., 2014; Kim et al., 2018; Morris et al., 2002; Renlund & Pritzker, 1984; Sanders et al., 1996; Sartin et al., 1996; Seiler & Wilkinson, 1980; Tanimoto et al., 1988; Van Biervliet et al., 2004; Waters et al., 1994). A review of the veterinary literature can be challenging, because many older reports use the old nomenclature of malignant fibrous histiocytoma, and the subsequent reclassification of these means that the veterinary cases should ideally also be reclassified to more accurately inform the reader as to the exact tumour type. It is likely that, for example, the case series of 14 Flat-Coated Retrievers (Morris et al., 2002) would now be considered to have histiocytic sarcoma, and therefore should not be considered to be representative of dogs with UPS. With those caveats in mind, the literature has only relatively limited information about this condition in veterinary species, with only occasional, small case reports and case series present. However, the prognosis is universally poor if the metastatic disease has developed. Metastatic disease has been reported in dogs, although it is not common, and UPS is considered to be more likely to be locally invasive than metastatic in dogs (Kim et al., 2021). There are only limited reports of this tumour type in the horse. To the authors' knowledge, there is only one report of metastatic undifferentiated sarcoma in the equine veterinary literature, and metastasis was only discovered when the horse died unexpectedly 6.5 weeks after surgical excision of the lesion (Zetterstrom et al., 2023). Frustratingly, an initial biopsy of the lesion did not yield a diagnosis, and the tumour type was only discovered following incomplete surgical excision (Zetterstrom et al., 2023). In humans, a core needle technique is preferred over open incisional biopsy and fine-needle aspiration is not recommended due to insufficient sampling (Robles-Tenorio & Solis-Ledesma, 2023). Furthermore, an image-guided core biopsy is recommended if an initial biopsy is unfruitful (Robles-Tenorio & Solis-Ledesma, 2023). An accurate diagnosis ahead of treatment allows for more complete assessment and treatment planning, and would also be useful in equine cases as staging would ideally be performed prior to surgical intervention, especially with large lesions. However, realistically, histological diagnoses can be challenging, and it may not be practical to continue to pursue a definitive histological diagnosis ahead of surgical excision. Given the paucity of equine data, this tumour type also appears to be extremely rare and is unlikely to be high on the differential diagnosis list prior to a definitive diagnosis via histology. Regardless, the standard of care for human head, neck, trunk and extremity UPS is *en bloc* surgical excision with microscopically negative margins (Robles-Tenorio & Solis-Ledesma, 2023), and this would be expected to be the same

in veterinary species. The addition of adjunctive radiotherapy and/or chemotherapy may improve the prognosis and should be considered in equine cases, where this is practicable. Overall, however, the prognosis appears to be fair to guarded, even in the absence of metastasis, and owners should be counselled accordingly.

AUTHOR CONTRIBUTIONS

Anna R. Hollis is the sole author of this work.

CONFLICT OF INTEREST STATEMENT

No conflict of interest has been declared.

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EVERY DAY COUNTS.

CONTINUED TREATMENT IS CRUCIAL TO MAINTAINING A HEALTHY HORSE AND CONTROLLING THE SIGNS OF PPID.



CONTROLLED SIGNS:

Clinical signs improved within 3 months and continued through 6 months.¹



PROVEN SUCCESS:

3 out of 4 horses evaluated were considered treatment successes.¹



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IMPORTANT SAFETY INFORMATION: PRASCEND has not been evaluated in breeding, pregnant or lactating horses. Treatment with PRASCEND may cause loss of appetite. Most cases are mild. If severe, a temporary dose reduction may be necessary. PRASCEND tablets should not be crushed due to the potential for increased human exposure. PRASCEND is contraindicated in horses with hypersensitivity to pergolide mesylate or other ergot derivatives. Keep PRASCEND in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose. Dogs have eaten PRASCEND tablets that were placed in food intended for horses or dropped during administration of the tablets to the horses. Adverse reactions may occur if animals other than horses ingest PRASCEND tablets. Refer to the package insert for complete product information.

¹Prascend® (pergolide tablets) [Freedom of Information Summary], St. Joseph, MO; Boehringer Ingelheim Inc.; 2011.

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Prascend®

(pergolide tablets)

1 mg

Brief Summary: This information is not comprehensive. Before using Prascend® (pergolide tablets), please consult the product insert for full prescribing information. The product insert may be obtained from your veterinarian or by visiting www.prascend.com.

Dopamine receptor agonist for oral use in horses only

Caution: Federal law restricts this drug to use by or on the order of a licensed veterinarian.

Description: PRASCEND Tablets are rectangular light red colored, half-scored tablets containing 1 mg pergolide, as pergolide mesylate. Pergolide mesylate is a synthetic ergot derivative and is a potent dopamine receptor agonist.

Indication: The control of clinical signs associated with Pituitary Pars Intermedia Dysfunction (PPID) in horses.

Dosage and Administration: Administer orally at a starting dose of 2 mcg/kg once daily. Dosage may be adjusted to effect, not to exceed 4 mcg/kg daily. It has been reported that pergolide tablets may cause eye irritation, an irritating smell, or headache when PRASCEND Tablets are split or crushed. PRASCEND Tablets should not be crushed due to the potential for increased human exposure and care should be taken to minimize exposure when splitting tablets.

The tablets are scored and the calculated dosage should be provided to the nearest one-half tablet increment (see Table 1).

Table 1 Dosing Table		
Body Weight	Dosage	
	2 mcg/kg	4 mcg/kg
136 - 340 kg (300 - 749 lb)	0.5 tablet	1 tablet
341 - 567 kg (750 - 1,249 lb)	1 tablet	2 tablets
568 - 795 kg (1,250 - 1,749 lb)	1.5 tablets	3 tablets
796 - 1,022 kg (1,750 - 2,249 lb)	2 tablets	4 tablets

Dosage should be titrated according to individual response to therapy to achieve a low-cost effective dose. Dose titration is based on improvement in clinical signs associated with Pituitary Pars Intermedia Dysfunction (PPID) and/or improvement or normalization of endocrine tests.

In some cases, adverse events were reported after a dose increase (see Post-Approval Experience). If signs of dose intolerance develop, the dose should be decreased by half for 3 to 5 days and then titrated back up in 2 mcg/kg increments every 2 weeks until the desired effect is achieved.

Contraindications: PRASCEND is contraindicated in horses with hypersensitivity to pergolide mesylate or other ergot derivatives.

Warnings: Do not use in horses intended for human consumption. Keep PRASCEND in a secure location out of reach of dogs, cats, and other animals to prevent accidental ingestion or overdose.

Precautions: PRASCEND tablets that were placed in food intended for horses or dropped during administration of the tablets to the horses. Adverse reactions may occur if animals other than horses ingest PRASCEND tablets (see Post-Approval Experience).

Human Warnings: Not for use in humans. Do not ingest the product. Keep this and all medications out of the reach of children. PRASCEND should not be administered by persons who have had adverse reactions to ergotamine or other ergot derivatives. Pergolide, like other ergot derivatives, may cause emesis, dizziness, lethargy or low blood pressure.

Pregnant or lactating women should wear gloves when administering this product. It has been reported that pergolide tablets may cause eye irritation, an irritating smell, or headache when PRASCEND Tablets are split or crushed. PRASCEND

Tablets should not be crushed due to the potential for increased human exposure and care should be taken to minimize exposure when splitting tablets. Store this product separately away from human medicinal products and handle this product with care to avoid accidental ingestion.

In case of accidental ingestion seek medical advice immediately and show the package leaflet or the label to the physician.

Precautions: Treatment with PRASCEND may cause inappetence. The use of PRASCEND in breeding, pregnant, or lactating horses has not been evaluated. The effects of pergolide mesylate in breeding, pregnant, or lactating horses are not known. Administration of pergolide mesylate to pregnant horses suggests that it may interfere with reproductive functions such as lactation. PRASCEND is approximately 90% associated with plasma proteins. Use caution if administering PRASCEND with other drugs that affect protein binding. Dopamine antagonists, such as neuroleptics (phenothiazines, domperidone) or metoclopramide, ordinarily should not be administered concurrently with PRASCEND (a dopamine agonist) since these agents may diminish the effectiveness of PRASCEND.

Adverse Reactions:

Pre-Approval Experience: A total of 122 horses treated with PRASCEND Tablets for six months were included in a field study safety analysis.

Table 2 Summary of the most common adverse reactions (N=122)

Clinical sign	# Cases	Cases (%)
Decreased appetite	40	32.8
Lameness	22	18.0
Diarrhea/Loose stool	12	9.8
Colic	12	9.8
Lethargy	12	9.8
Abnormal Weight Loss	11	9.0
Laminitis*	10	8.2
Heart murmur	10	8.2
Death	8	6.6
Tooth disorder	8	6.6
Skin abscess	7	5.7
Musculoskeletal pain	6	4.9
Behavioral change	6	4.9

*Three new cases and 7 pre-existing, recurring cases

Inappetence or decreased appetite occurred at one or more meals in 40 of 122 horses treated with PRASCEND. At the baseline evaluation 1.6% of owners reported a history of inappetence or decreased appetite as compared to the 32.8% of horses that experienced inappetence or decreased appetite during the study. Most cases of inappetence were transient and occurred during the first month of treatment; however, some horses experienced sporadic inappetence throughout the study.

Weight loss required a temporary reduction in dose due to inappetence during the first month of the study. Both horses returned to their original doses within 30 days. Weight loss occurred in more than half of the horses in this study; however, weight loss that was considered abnormal was only reported in 11 horses. Lethargy was reported in 9.8% of horses during the study. Behavioral changes were noted in 6 horses including aggression, kicking, agitation, nervous behavior and increased activity. One horse required a temporary reduction in dose due to energetic behavior during the first month of the study. Eight horses died or were euthanized during the study due to worsening of pre-existing conditions (laminitis, dental abscess, colic, rectal prolapse, rectal strangulating lipomas, large colon volvulus). One mare was inadvertently enrolled in the study while pregnant and experienced dystocia resulting in the death of the foal.

Post-Approval Experience (2019): The following adverse events are based on post approval adverse drug experience reporting for PRASCEND. Not all adverse events are reported. It is not always possible to reliably estimate the adverse event frequency or establish a causal relationship to product exposure using these data.

The following adverse events in horses are categorized in order of decreasing reporting frequency by body system and in decreasing order of reporting frequency within each body system:

General: anorexia, lethargy, weight loss Gastrointestinal: diarrhea, abdominal pain/cramps

Dermatological: alopecia, hyperhidrosis, dermatitis

Musculoskeletal: laminitis, muscle stiffness/tension

Neurological: ataxia, seizure, muscle tremors

Behavioral: aggression (to other horses and humans), hyperactivity (anxiety, agitation), other behavioral changes (stupor-like behavior, spooky, unpredictable, confused)

Clinical pathology: anemia, elevated liver enzymes, thrombocytopenia

The above adverse events were reported in some horses at starting dose levels, while in the others following a dose increase.

Death (including euthanasia) has been reported. Adverse events have been reported in dogs following ingestion of tablets prepared for administration to horses.

To report suspected adverse reactions, to obtain a Safety Data Sheet (SDS), or for technical assistance, contact Boehringer Ingelheim Animal Health USA Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact the FDA at 1-888-FDA-VETS or 1-800-FDA-4-VETS.

Effectiveness: A field study evaluated the effectiveness of PRASCEND for the control of clinical signs of PPID. A total of 122 horses with PPID were enrolled in the study, 112 of which were included in effectiveness evaluations. The success of each horse was based on results of endocrinology testing (dexamethasone suppression test or endogenous ACTH test) and/or improvement in clinical signs related to PPID (hirsutism, hyperhidrosis, polyuria/polydipsia, abnormal fat distribution, and/or muscle-wasting) on the Day 180 evaluation. Based on endocrine testing and investigators' clinical assessment scores, 86 (76.1%) of the 113 evaluable cases were treatment successes.

Animal Safety: In a six-month target animal safety study healthy adult horses received PRASCEND administered orally, once daily, at doses of either 0 mcg/kg, 4 mcg/kg, 6 mcg/kg, or 8 mcg/kg (0X, 1X, 1.5X, or 2X the maximum recommended dose). There were eight healthy horses (four males and four females) in each treatment group.

PRASCEND treated groups had lower mean heart rates and higher mean temperatures than the control group. Horses in all treatment groups had minimum heart rates within the normal range and maximum temperatures below 101.5°F. One 1.5X horse experienced a mild episode of spasmodic colic on Day 3 that resolved after treatment with flunixin meglumine.

Mean red blood cell counts and hemoglobin values were lower in PRASCEND treated groups as compared to the control group. Other hematologic parameters including hematocrit, white blood cells, absolute neutrophils, and absolute lymphocytes exhibited mild, transient decreases as compared to the control group. The hematologic parameters generally decreased over the first 30 to 60 days after treatment initiation and then returned to values similar to pre-treatment levels. No treatment related alterations were identified on histopathology evaluation of bone marrow.

Storage: Store at or below 25°C (77°F).

How Supplied: PRASCEND tablets are available in 1 mg strength – packaged 10 tablets per blister and 60 or 160 tablets per carton.

NDCC04-4489-01 - 60 tablets

NDCC04-4489-02 - 160 tablets

Approved by FDA under NADA # 141-331

References:

¹Orth, D.N., Holscher, M.A., Wilson, M.G., et al. (1982) Equine Cushing's Disease: Plasma Immunoreactive Propriolopiomelanocortin Peptide and Cortisol Levels Basally and in Response to Diagnostic Tests. *Endocrinology*, 104(4):1430-41

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Large fibrosarcoma of the equine distal limb treated by surgical excision using a harmonic scalpel

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SUMMARY

An 18-year-old Warmblood gelding was presented for investigation of a large mass over the medial and plantar aspect of the left distal metatarsal and fetlock region. The mass was first identified 4 months prior to referral, following a traumatic incident, and had over time gradually increased in size. On presentation at the referral centre, a large (widest circumference: 47 cm), firm, immobile mass was present over the medial and plantar aspects of the distal metatarsal and metatarsophalangeal region of the left hindlimb which was firmly adhered to the underlying structures. Radiographs of the left hind distal limb revealed a prominent soft tissue swelling which was not associated with any overt osseous abnormalities. On ultrasonographic examination, the mass was mainly confined to subcutaneous tissues and exhibited heterogeneous echogenicity.

The mass was initially excised incompletely as it was not possible to safely establish a plane of dissection between the mass and surrounding soft tissues. Residual portions of mass were subsequently excised in layers as extensively as possible with only limited surgical margins being obtained. After

excision, the surgical site was lavaged and closed in three layers.

The excised mass (185 mm × 118 mm × 72 mm) had a multilobular and disorganized fibrous tissue appearance with poorly defined margins. Based on the location, clinical, histological and immunohistochemical features, the mass was determined to represent a fibrosarcoma.

The gelding was discharged from hospital 6 weeks after surgery and gradually resumed full-time turnout. Twelve months after surgical resection, no signs of recurrence were evident.

This case report documents the novel use of a harmonic scalpel in the treatment of distal limb equine neoplasia, highlighting that this instrument may represent a useful alternative for surgical management of fibrosarcoma in horses.

KEY WORDS

horse, distal limb swelling, fibrosarcoma, harmonic scalpel, surgical excision



FIGURE 1 Intra-operative photograph showing surgical excision of the distal limb mass using a harmonic scalpel.

Key points

- Fibrosarcoma should be considered a potential differential diagnosis in horses presented with a persistent and/or slow growing focal distal limb swelling.
- Fibrosarcoma in the distal limb of horses can be treated successfully by surgical excision using a harmonic scalpel.
- The use of a harmonic scalpel should be considered as an alternative to sharp excision when treating infiltrative tumours and may be particularly useful in regions where the extent of excision is limited or where minimisation of collateral tissue damage is essential.

Treatment challenges in equine fibrosarcomas: Can the harmonic scalpel help in the treatment success?

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Summary

Fibrosarcoma is relatively uncommon aggressive neoplasm, representing less than 3% of all neoplasms recorded in horses. Successful treatment of fibrosarcoma can be challenging in equine and recurrence is a common late complication. The accompanying paper by Bellitto et al. (2023, *Equine Veterinary Education*, 10.1111/eve.13808) illustrates the successful surgical treatment of a large fibrosarcoma over the medial and plantar aspect of the left distal limb in an 18-year-old Warmblood gelding. The authors report on the success of treatment after surgical excision of the tumour under general anaesthesia using a harmonic scalpel. The gelding recovered well after 1 year of surgery with no recurrence at that time. Further clinical studies are recommended to compare the harmonic scalpel with other modalities like surgical lasers and conventional sharp excision for treatment of fibrosarcoma in horses as well as to understand the potential benefits of using the harmonic scalpel when treating infiltrative tumours such as fibrosarcoma. The publication of this case report in *Equine Veterinary Education* is of clinical importance to equine practitioners when treating equine infiltrative neoplasms such as fibrosarcomas.

In this case report, Bellitto et al. (2023) have described an innovative and helpful procedure for the surgical excision of a large fibrosarcoma over the distal limb in an 18-year-old gelding using a harmonic scalpel.

Fibrosarcoma is a malignant connective tissue neoplasm, representing 1.9% of all cutaneous and musculocutaneous neoplasms in horses (Valentine, 2006) and less than 3% of all neoplasms (Roels et al., 1998). There has been no extensive study of equine fibrosarcomas, and most records of fibrosarcomas are sporadic cases. In the published case reports, fibrosarcomas were recorded in the premaxilla, prepuce, mammary gland, kidneys, periosteum, omentum, oropharynx, nasomaxillary sinuses, rostral mandible, paranasal sinuses, tarsal groove, humerus, epaxial musculature, abdominal cavity and wall, thoracic vertebrae, and uterus (Bass et al., 2017; Carmalt & Linn, 2013; Govaere et al., 2011; Harvey et al., 1987; Jorgensen et al., 1997; Mostafa et al., 2007; Riggot & Quarmby, 1980; Roels et al., 1998; van den Top et al., 2008; Voros et al., 1993).

Fibrosarcoma is most commonly observed in mature animals (Bass et al., 2017; Bellitto et al., 2023; Govaere et al., 2011; Kannegieter et al., 2010; Lechartier et al., 2015). Nevertheless, young animals are also at risk (Horbal & Dixon, 2016; Hyde, 2016; Roels et al., 1998). There is no sex or breed predilection for equine fibrosarcomas (Hyde, 2016). The aetiology and pathophysiology of fibrosarcoma are still unknown. Nevertheless, fibrosarcoma has been recorded following an equine influenza vaccine (Kannegieter et al., 2010), a burn injury (Schumacher et al., 1986) and a traumatic incident (Bellitto et al., 2023).

The prognosis for fibrosarcoma is guarded due to its invasiveness, metastasis in 25% of the cases and recurrence (Gerard, 2009; Riggot & Quarmby, 1980; Villalobos, 2022). Although fibrosarcoma is a malignant mesenchymal neoplasm with fibroblasts as the predominant cell type, it is more likely to be locally invasive than to metastasise. The deeply located, large and rapidly growing tumours are more likely to be malignant (Villalobos, 2022). In view of the

unfavourable prognosis, the animal may be euthanased (Govaere et al., 2011; Harvey et al., 1987; Jorgensen et al., 1997; Koester et al., 2012).

Fibrosarcomas have a high rate of recurrence due to inadequate surgical margins or seeding of the neoplastic cells (Lechartier et al., 2015; Riggot & Quarmby, 1980). Since recurrence is common after surgical excision of fibrosarcomas, regular examinations are recommended to ensure the absence of new growths, as Bellitto et al. (2023) did in the described gelding after 5, 9 and 12 months after surgical excision.

Metastasis of fibrosarcomas is rarely recorded in horses (Koester et al., 2012). The most common sites for metastasis of fibrosarcoma include the lung, liver, heart, mediastinum, humerus, kidney, intestines, skeletal muscle, lymph nodes and spleen (Govaere et al., 2011; Jorgensen et al., 1997; Reinerston, 1974).

Fibrosarcomas vary markedly in their shape and size; therefore, diagnosis of equine fibrosarcoma should be confirmed by biopsy with histopathology and immunohistochemical staining (Bellitto et al., 2023; Harvey et al., 1987; Kannegieter et al., 2010). With advancement of diagnostic imaging techniques such as radiography, ultrasonography (US), computed tomography (CT) and magnetic resonance imaging (MRI), detection of tumour invasion into deeper tissues is significantly improved increasing the likelihood of success of complete surgical excision and decreasing the risks of recurrence (Bass et al., 2017; Harvey et al., 1987; Villalobos, 2022). As shown in the recent case report, US played a crucial role in the diagnosis of fibrosarcoma because it revealed that the mass was mainly confined to subcutaneous tissues and showed heterogenous echogenicity as well as normal digital flexor tendons; therefore, no significant lameness at walk was noticed. Also US was applied at 9-month reassessment and revealed moderate thickening of soft tissues at the surgical site but without recurrence of the tumour. In addition, radiography was important in the described gelding to exclude any boney abnormalities.

Histologically, fibrosarcoma consists mainly of fibroblasts with various amounts of collagen. Fibroblasts appear as spindle-shaped cells arranged in interwoven or herringbone patterns typically with scant cytoplasm and elongate to oval nuclei with inconspicuous nucleoli (Folpe, 2014; Govaere et al., 2011). Fibrosarcoma is characterised by staining positive for vimentin and negative for desmin, actin, and factor VIII (Ramaekers et al., 1988; Villalobos, 2022). In the gelding described in the accompanying report, the diagnosis was confirmed by histopathology and immunohistochemistry as low-grade fibrosarcoma. In addition, metastasis was excluded in the recorded case due to absence of systemic clinical signs such as weight loss, respiratory difficulty or enlargement of regional lymph nodes.

Complete blood count (CBC), serum chemistry and urinalysis are also beneficial as a general screen before considering surgery (Hyde, 2016). On the other hand, cytology has a limited value in diagnosis of fibrosarcomas because fibrosarcoma sheds low number of neoplastic cells and the neoplastic cells are similar in appearance to those of benign neoplasms and reactive tissues (Story et al., 2005).

Knowing the size, location, stage and histologic grade of fibrosarcomas will help guide treatment planning (Villalobos, 2022). The grade of fibrosarcomas (low, intermediate and high) depends on the degree of differentiation, the number of mitotic figures per 10 high-power fields, percent necrosis and Ki-67 (a proliferation marker) level. Therefore, there are several treatment options of fibrosarcoma such as surgical excision, radiotherapy, local chemotherapy, systemic chemotherapy either alone or together with surgical excision. Nevertheless, there are several treatment challenges in equine fibrosarcomas such as the anatomic location, size, grade, slow growth rate, infiltrative nature and freezing resistance of the neoplasm, experience of the surgeon and cost.

Regarding surgical excision of fibrosarcoma with clean margins or amputation, it is considered the best treatment option (Carmalt & Linn, 2013; Hyde, 2016; Kannegieter et al., 2010; Story et al., 2005). The invasive nature of fibrosarcomas is a big challenge; therefore, conventional sharp surgical excision with wide surgical margins (3cm) is usually recommended. Sometimes, fibrosarcomas are developed in regions of the body not allowing wide excision like distal limbs as mentioned in the accompanying case. Failure of complete surgical excision usually results in recurrence of fibrosarcoma after surgery. The best chance for complete excision of fibrosarcoma is during the first surgery. In addition, recurrent fibrosarcoma has a greater potential for metastasis, and the time to recurrence often shortens with each subsequent attempt at excision (Villalobos, 2022).

Also, laser or conventional debulking followed by adjunctive treatment with chemotherapy and/or radiotherapy may be beneficial for enhancing local control and decreasing the recurrence rate (Hewes & Sullins, 2006; Horbal & Dixon, 2016; Riggot & Quarmby, 1980; Spugnini et al., 2016, 2021; Villalobos, 2022). Radiotherapy is less effective for fibrosarcoma than other tumours (Hyde, 2016); however, treatment success has been reported in some cases (Gerard, 2009; Roels et al., 1998). Fibrosarcoma in bones is less responsive to local chemotherapy and radiation due to limited local tissue penetration and slow growth rate of the neoplasm (Bass et al., 2017).

Regarding cryosurgery, it is usually not applied for fibrosarcomas in equine because the tumours are resistant to freezing. Moreover, fibrosarcomas generally do not respond well to conventional doses of radiation. Nevertheless, higher doses and stereotactic radiation have controlled ~50% of fibrosarcomas for 1 year (Villalobos, 2022).

As regards chemotherapy, local chemotherapy with 5-fluorouracil as a topical application, intralesional injection of cisplatin or implantation of cisplatin containing biodegradable beads resulted in successful treatment of equine fibrosarcomas (Hewes & Sullins, 2006; Horbal & Dixon, 2016; Roels et al., 1998; Strubbe, 2001). Chemotherapy may be useful as the main therapy or adjunct therapy with surgical excision (Roels et al., 1998). Systemic chemotherapy with surgery may be an option as well. Tyrosine kinase (T-K) inhibitors may improve treatment efficacy. Doxorubicin combined with other agents like carboplatin, cyclophosphamide, vincristine, dacarbazine and methotrexate is usually applied for the treatment of fibrosarcomas. Although chemotherapy may induce

temporary adverse effects, it can improve the length and overall quality of life; it is seldom curative (Villalobos, 2022).

In the accompanying case report, the authors used the harmonic scalpel for the first time to excise a large fibrosarcoma in the gelding. Use of the harmonic scalpel in the described gelding led to minimal bleeding during surgery and absence of recurrence.

The harmonic scalpel has been introduced to the markets by Ethicon in 1998 (HARMONIC® Scalpel Shears) for simultaneous cutting and cauterisation of the tissues (Dutta, 2016). Ultrasonic energy is commonly applied in the harmonic scalpel where this energy is converted to mechanical energy at the active blade (Seehofer et al., 2012). The active blade transmits high-grade frictional force, while the inactive upper arm holds tissue in apposition.

The harmonic scalpel depends on ultrasonic technology, and it is used to cut and coagulate tissue at temperatures lower (3–4 times) than those produced by traditional electrocautery technique and lasers. Therefore, its application during surgery decreases thermal damage and leads to minimal postoperative pain (Dutta, 2016).

The rationale for using the harmonic scalpel is the relatively low temperatures (80°C) at which it divides tissue compared with other modalities, which should reduce lateral thermal injury. The division of tissues results from high-frequency ultrasound energy (55,000Hz), which disrupts protein hydrogen bonds within the tissue. Blood vessels are sealed by denaturation of the protein coagulum that occurs due to tamponade and coaptation (Cheng et al., 2018; Dutta, 2016).

The harmonic scalpel has three compatible probes that are the shear, blade and hook. The shear can seal blood vessels up to 7mm diameter, whereas the hook and blade can seal blood vessels up to 2mm in diameter. The active blade of the harmonic scalpel vibrates longitudinally against an inactive blade over an excursion of 50–100µm (Dutta, 2016). Variation in pressure applied by the surgeon determines the cutting speed and degree of coagulation (Dubiel et al., 2010).

The main advantages of the harmonic scalpel include reduction of intraoperative blood loss, tissue damage (minimal lateral thermal spread), the operation time, smoke production, postoperative drainage and seroma development, precise dissection, reliable haemostasis for stronger large blood vessel, and absence of charring (Dutta, 2016; Lenihan et al., 2004; Litta et al., 2010). On the other hand, the cost of the harmonic scalpel may be prohibitive for some owners (Dutta, 2016).

In human medicine, the harmonic scalpel is commonly used in otolaryngology and other surgeries (Cheng et al., 2018; Lenihan et al., 2004; Litta et al., 2010). In equine practice, the harmonic scalpel has been applied for laparoscopic ovarioectomy, ovariohysterectomy, excision of fibrosarcoma and thyroidectomy with successful results (al Naem et al., 2022; Bellitto et al., 2023; Delling et al., 2004; Düsterdieck et al., 2003).

The accompanying paper by Bellitto et al. (2023) documents the use of a harmonic scalpel in the treatment of distal limb fibrosarcoma and describes the beneficial role of this instrument for surgical management of fibrosarcoma in horses. I completely agree with the authors that the 12-month follow-up period does not demonstrate recurrence of this neoplasm; however, it is possible that recurrence

of the neoplasm may take longer than 12 months and further follow-up would be required to document longer-term outcome.

Use of the harmonic scalpel for excision of large invasive tumours, particularly those located at areas with limited surgical margins or where minimisation of collateral tissue damage is essential, may be a promising procedure in veterinary practice in the future. The success of treatment in the described gelding should encourage further clinical trials in cases of infiltrative neoplasms in horses to document the role of the harmonic scalpel in the treatment success of neoplasms such as fibrosarcomas in equine.

AUTHOR CONTRIBUTIONS

This is a sole author contribution.

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Strategies to relieve intraluminal obstructions in inaccessible segments of the ascending, transverse and descending colon

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INTRODUCTION

Enteroliths, faecaliths, ingested foreign bodies and bezoars are examples of focal intraluminal obstructions that can lodge in inaccessible parts of the gastrointestinal tract (Hanson & Schumacher, 2021; Hassel, 2002; Klohnen, 2013; Oreff et al., 2020; Pierce et al., 2010). Gastrointestinal segments that are particularly difficult to surgically access and manage include stomach, duodenum, distal ileum, base and dorsal body of caecum, aboral right dorsal colon, transverse colon and the most oral and aboral limits of the descending (small) colon (Marshall & Blikslager, 2019). The accompanying article published in the September 2023 issue by Machado Amaral Rosa et al. (2023) describes the use of pneumatic lithotripsy to aid in resolution of enterolith obstructions in the oral and aboral descending colon and to prevent need for a second enterotomy in removal of an enterolith from the left dorsal colon.

APPLICATION OF LITHOTRIPSY

Lithotripsy has been used to fragment uroliths in the horse (De Bernardis et al., 2019; Katzman et al., 2016; Nolazco Sassot et al., 2020), as well as other mineralised concretions. This article describes application of the pneumatic lithotripsy to enteroliths. The efficacy and efficiency of lithotripsy in fragmenting mineralised concretions appears to be dependent on the size of the concretion and on its composition. Uroliths as large as 10–12 cm have been fragmented within the bladder of female horses (Nolazco Sassot et al., 2020), whereas <10 cm urolith size have been described for male horses (De Bernardis et al., 2019; Katzman et al., 2016). This size difference is attributed to the ease of removing urolith fragments from the bladder in the relatively large and expandile mare

urethra compared to the narrower and more limited access via a perineal urethrotomy in male horses.

The composition and surface characteristics of the mineralised concretion are also important when considering the efficiency of lithotripsy. The article by Machado Amaral Rosa et al. (2023) noted that smooth-surfaced enteroliths were more difficult to fragment than irregular-surfaced enteroliths, as were enteroliths with rigid cores and less porosity. Similarly, type 1 calcium carbonate uroliths in horses have been described as easier to fragment than the harder and smoother type 2 calcium carbonate uroliths (De Bernardis et al., 2019). Although ingesta and foreign bodies, such as hay nets, twine, plastic or rope, can serve as a nidus for mineralised concretions, most enteroliths have small, solid niduses, such as metal fragments, rocks or grains of sand (Hassel, 2002; Pierce, 2009). Clinical experience, supported by available geochemical analysis of typical equine enteroliths, would suggest that the majority of enteroliths are not hollow-centred formations (Blue & Witkopp, 1981; Hassel et al., 2001; Rouff et al., 2018; Dechant, personal observation).

Machado Amaral Rosa et al. (2023) stated that advantages of their pneumatic lithotripsy technique for the management of enteroliths include ability to use smaller enterotomies through sites that are remote to the site of obstruction and reduced surgical time. Comparisons for surgery time were made to an isolated case report describing a particularly difficult presentation of obstructive enterolithiasis (Barrett & Munsterman, 2013). In another report of surgical management of enterolithiasis, mean surgery time was 128 ± 31 min (range 70–200 min) with 13% requiring 1 enterotomy, 83% of surgeries requiring 2 enterotomies and 4% requiring 3 enterotomies (Torrent Crosa et al., 2020). In this case series, mean surgery time was 135 min (range 120–145 min) with 4 cases requiring 1 enterotomy and 1 case requiring 2 enterotomies (Machado Amaral Rosa et al., 2023). This suggests that while the time advantage of

pneumatic lithotripsy for enterolithiasis proposed by Machado Amaral Rosa et al. (2023) may not be as profound as described.

In studies evaluating survival following surgical management of ascending colon or descending colon enterolithiasis, short-term survival was 95%–96% with no difference in incidence of complications between enterotomies of the pelvic flexure or descending colon (Hassel et al., 1999; Pierce et al., 2010). Pneumatic lithotripsy as described in this case series does require an enterotomy to introduce the instrument. Although the enterotomy may be smaller than those needed to directly remove an enterolith, the proximity of the enterotomy and the nonsterile lithotripter to the abdominal incision and the time needed to fragment the enterolith, which prolongs the time the intestinal lumen is open, should be balanced against the benefits of a smaller enterotomy.

Pierce et al. (2010) documented that 87% of horses with descending colon enterolithiasis had some degree of mural damage. Although Machado Amaral Rosa et al. (2023) did not experience full-thickness intestinal perforation with their technique, one case did develop partial thickness penetration of the intestinal wall despite the lithotripsy procedure being directed at an enterolith that was well exteriorised from the abdomen and readily accessible in a location 30cm from the pelvic flexure. In lithotripsy disruption of ureteroliths in people, ureteral perforation or extra-ureteral migration of ureteral calculi occurred in approximately 0.85% of cases, with surgeon inexperience and longer operative times being associated with increased complication rates (Georgescu et al., 2014). An ex vivo study comparing lithotripsy damage on urinary tract tissue found that tissue damage and risk of perforation was affected by the type of lithotripter, tissue type, probe force and duration of contact between probe and tissue (Sarkissian et al., 2015). While it is not known how this information extrapolates to equine intestine, equine surgeon experience is likely to be limited with this technique and it is important to be as careful when using pneumatic lithotripsy as the authors of this case series emphasise (Machado Amaral Rosa et al., 2023).

Pneumatic lithotripsy as described in this case series (Machado Amaral Rosa et al., 2023) is a useful tool for the surgeon to have in their toolbox when presented with obstructive enterolithiasis. Pneumatic lithotripsy is limited to mineralised concretions, and other types of intraluminal obstructions can occur, such as foreign body or faecalith obstructions. It is important for the surgeon to be knowledgeable about other techniques for mobilising intraluminal obstructions because other techniques may be more appropriate or preferred by the surgeon.

RIGHT DORSAL COLON OR DESCENDING COLON ENTEROTOMY TECHNIQUE

For all of these procedures, at least one enterotomy will be necessary. Whenever an antimesenteric taenia is present, the enterotomy incision should be located within the centre of the taenia (right dorsal colon or descending colon) (Archer et al., 1988; Beard et al., 1989).

Unless the enterotomy will be in a segment that can be exteriorised away from the abdomen, such as the pelvic flexure, the affected segment of intestine should be isolated from the rest of the abdomen with moistened laparotomy sponges and sterile plastic barrier drapes. If the targeted intestine is being elevated under tension, the segment can be supported and elevated by a sterile hand within the abdomen. Stay sutures (or Babcock forceps) should be used within the taenia prior to the enterotomy incision to stabilise and elevate the site to reduce contamination. Suction should be used throughout the procedure to aspirate blood and ingesta to minimise leakage of intestinal contents and contamination of the surgical field. Closure of the enterotomy should be done in two layers using 2-0 absorbable suture: a full-thickness apposition continuous pattern for the first layer and oversewn by an inverting seromuscular continuous pattern (Hassel, 2002). While the inclusion of mucosa within descending colon enterotomies has not been determined to be essential (Beard et al., 1989), it does appear to be advantageous to compress submucosal vessels for the large colon (Doyle et al., 2003). Since intramural or submucosal haematomas can occur spontaneously in the descending colon (Hanson & Schumacher, 2021; Schumacher & Mair, 2002), full-thickness closure of descending colon enterotomies appears prudent as well. While lumen diameter is not limiting for closure of right dorsal colon enterotomies, it is important to be precise with conservative suture bite sizes and minimal inversion when closing descending colon enterotomies. The enterotomy site should be carefully lavaged and cleaned of any contamination before the intestinal segment is returned to the abdomen.

RESOLUTION OF INTRALUMINAL OBSTRUCTIONS THROUGH VENTRAL MIDLINE CELIOTOMY

For intraluminal obstructions that are known preoperatively to be located in the right dorsal colon, transverse colon and oral descending colon, the celiotomy incision should be positioned relatively more cranial on ventral midline, starting at least 5–10 cm cranial to the umbilicus (Hassel, 2002). If the location of the obstruction is not known preoperatively (faecalith, foreign body, false negative radiographs for enteroliths), extending the incision more cranially may aid exteriorisation of these intestinal segments.

The basic strategy for mobilising right dorsal colon and oral to mid-transverse colon obstructions is hydropulsion. This entails using intraluminal lavage through a pelvic flexure enterotomy to evacuate all ingesta oral to the obstruction (right dorsal colon, including ampulla coli, and oral transverse colon, as applicable). Once the colon is emptied of ingesta, water distension of the colon combined with gentle ballottement of the obstruction can free it from the mucosa and allow it to move orally into the ampulla coli where it then can be manipulated within the dorsal colon and exteriorised from the abdomen (Hanson & Schumacher, 2021; Hassel, 2002; Oreff et al., 2020; Pierce, 2009). This author has observed on some occasions that the transverse colon appears to spasm orally to obstructions in the

transverse colon, and this spasming does not consistently relax with fluid distension. One strategy that may ease intestinal spasming is topical application of 2% lidocaine (Hassel & Yarbrough, 1998). Conservative doses (~0.1 mg/kg IV) of butylscopolammonium bromide appears to be helpful in relaxing these intestinal spasms, allowing oral movement of the obstruction and resolving the obstruction, although the author is mindful of the cardiovascular effects of this drug in the anaesthetised horse (Loomes, 2020). Typically, intraluminal obstructions within the right dorsal colon or transverse colon are too large to be removed via the pelvic flexure enterotomy, so a second enterotomy must be performed or if appropriate, a lithotripsy technique used such as described by Machado Amaral Rosa et al. (2023).

For obstructions that are not resolved by hydropulsion, particularly obstructions in the mid to distal transverse colon and very oral descending colon or the very aboral descending colon, retro-pulsion or retrograde flushing may be a useful technique (Hanson & Schumacher, 2021; Klohnen, 2013; Oreff et al., 2020; Pierce, 2009; Pierce et al., 2010; Schumacher & Mair, 2002; Taylor et al., 1979). Retropulsion was used in 13% of descending colon enterolith obstructions in one case series (Pierce et al., 2010). Retropulsion is the use of water distension and hydropressure of the intestine aboral to the obstruction via a high enema. The success of this technique requires the emptying of ingesta from oral to the obstruction and relaxation of the oral segment to allow movement of the obstruction. Retropulsion should only be used for obstructions that cannot be accessed otherwise because the intestine adjacent and oral to an obstruction is often compromised by some degree of mural damage and may be prone to rupture (Pierce et al., 2010).

To facilitate the elevation of oral segments of the descending colon to the level of the abdominal incision, the use of nondepolarising neuromuscular blocking agents, such as atracurium, pancuronium, etc., by the anaesthetist may allow relaxation of the body wall so that the abdominal incision can be manually pushed downward to allow exteriorisation of most oral descending colon (Hassel, 2002). Another suggested technique is to temporarily remove the horse from positive pressure ventilation to decrease the abdominal movements with each breath and facilitate exteriorisation of the very oral descending colon (Klohnen, 2013). It is important to emphasise that neuromuscular blocking agents and removal of positive pressure ventilation cannot be performed together because neuromuscular blocking agents also paralyse the respiratory muscles and positive pressure ventilation is an essential requirement during neuromuscular blockade. The applicability of either of these techniques will depend on the experience, comfort and pharmaceutical repertoire of the anaesthesia staff.

Another technique to facilitate aboral movement of an intraluminal obstruction within the descending colon is partial thickness taeniotomy (Hassel, 2002; Hassel & Yarbrough, 1998; Klohnen, 2013; Pierce, 2009; Schumacher & Mair, 2002). This technique can be used to advance an obstruction a few centimetres (4–15 cm) aborally to allow the enterotomy to be made in a more exteriorised segment of descending colon or in a segment of descending colon that has not been compromised by the pressure of the obstruction (Hassel & Yarbrough, 1998). A partial thickness taeniotomy is performed by

creating a seromuscular incision in the middle of the antimesenteric taenia approximately 8–15 cm aboral to the obstruction (Hassel, 2002; Hassel & Yarbrough, 1998). The partial thickness seromuscular incision is extended orally to the level of the obstruction using Metzenbaum scissors or a scalpel blade. This incision allows maximum stretching of the mucosa within the taeniotomy, effectively increasing the intraluminal diameter. Gentle pressure is applied to the obstruction to advance it aborally, being careful to monitor when the stretched mucosa begins to rupture or the desired location for the enterotomy is achieved (Hassel, 2002; Hassel & Yarbrough, 1998). At that time, manipulations should be stopped and the enterotomy is extended through the mucosa in a controlled manner to allow the removal of the enterolith. Closure of the enterotomy is routine, as described earlier.

SECONDARY ABDOMINAL APPROACHES

Alternative surgical approaches to access the most oral limits of the descending colon include left paramedian (De Oliveira Dearo et al., 2009) or left flank laparotomy (Turek et al., 2019). In both instances, an initial ventral midline celiotomy was used for exploration, diagnosis and localisation of the obstruction and determination that it was not accessible through a ventral midline approach. In the De Oliveira Dearo et al. (2009) report, sufficient exposure of the affected descending colon for enterotomy through the secondary paramedian approach was facilitated by elevating the obstructed segment of the oral descending colon by a surgeon with their arm through the ventral midline incision. The details of the location and surgical technique left flank laparotomy approach in Turek et al. (2019) were not sufficiently described to determine if it was a paramedian approach while the horse was in dorsal recumbency or if the horse was repositioned into right lateral recumbency (after closing the original celiotomy incision). Other reports describing flank laparotomy for descending colon lesions were based on financial or patient constraints and flank laparotomy was not performed to improve access to the oral or aboral limits of the descending colon (Herbert et al., 2021). A right flank laparotomy was used to access an obstruction within the descending duodenum when a ventral midline approach was not successful (Durham, 1998).

For very aboral descending colon obstructions, either a paramedian approach or a parainguinal approach (Barrett & Munsterman, 2013; Turek et al., 2019) can be used to improve access for exteriorisation. Similar to the secondary paramedian approach described by De Oliveira Dearo et al. (2009), elevation of the descending colon to a parainguinal or parainguinal incision can be facilitated by a surgeon with their arm through the ventral midline incision. Barrett and Munsterman (2013) utilised a right parainguinal approach for their surgery; however, they comment that a left parainguinal approach may be more advantageous based on the descending colon anatomy (Barrett & Munsterman, 2013; Klohnen, 2013). The sidedness for the parainguinal incision could be determined in surgery via a ventral midline celiotomy or through manipulation of a palpable obstruction via rectal palpation based on which side allows

easier elevation, as well as the preferences of the surgeon (which depends on their handedness and where they stand relative to the horse (caudal or craniolateral)).

CONCLUSIONS

Many intraluminal obstructions of the ascending, transverse and descending colons can be manipulated, exteriorised, accessed and removed through routine enterotomy approaches. The case series by Machado Amaral Rosa et al. (2023) highlights the successful use of pneumatic lithotripsy to facilitate the resolution of obstructive enterolithiasis through small enterotomies remote to the site of obstruction. This provides the surgeon with another tool to consider when challenged by similar types of obstructions. It is important to recognise that pneumatic lithotripsy may not be safe or effective for all intraluminal obstructions. Awareness of other strategies or secondary abdominal approaches to address these challenging presentations can help improve the surgeon's ability to problem solve in these situations and achieve successful resolution of the obstruction.

CONFLICT OF INTEREST STATEMENT

No conflicts of interest have been declared.

ETHICS STATEMENT

Not required for this clinical commentary.

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Clinical application of the wooden shoe to complement surgical management of laminitis and other foot-related diseases in the horse: A report of three cases

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SUMMARY

Three horses with severe foot pathology were managed with surgery and application of a wooden shoe. Case 1, a 12-year-old Warmblood sport mare presented for treatment of iatrogenic septic arthritis which developed supporting limb laminitis in the contralateral hindlimb. Serial radiographs confirmed progressive deterioration of the laminitis (Figure 1). The mare was eventually managed with deep digital flexor tenotomy and required multiple wooden shoe resets. Creating a recess in the dorsal solar surface of the shoe reduced pressure points caused by the penetration of the distal phalanx through the sole and improved her comfort.

Case 2, a 15-year-old Quarter Horse mare presented with severe, chronic bilateral front limb laminitis, along with severe swelling and ulceration on the left front coronary band caused by hoof wall impingement. Forefoot radiographs revealed signs of severe laminitis with dorsal rotation and lateral sinking on both feet. The mare underwent partial hoof wall resection to alleviate pressure and impingement of the detached hoof wall. Additionally, a modified foot cast, which included a wooden shoe, was applied.

Case 3, a 1-year-old Trakehner colt presented with subsolar abscessation and distal phalanx sequestration in the left front limb. Mild chronic

laminitis was observed on radiographic examination. The condition required extensive surgical debridement of infected and devitalised tissues, leaving little healthy hoof tissues for weight support. The delicate condition was managed with a wooden shoe, which allowed redistribution of weight to the limited viable palmar foot structures that remained.

Although all three horses would have fulfilled the grounds for humane euthanasia, they were successfully managed and had a favourable outcome. This article advocates for the wooden shoe as an effective tool for redistributing weight on the foot, alleviate pain, enhance biomechanics and serve as a valuable tool in the post-surgical management of laminitis and other foot-related injuries in horses.

KEY WORDS

horse, hoof, laminitis, therapeutic farriery, sequestrum



Key points

- The wooden shoe is a valuable complementary tool for veterinarians and farriers to use after surgery for foot-related issues.
- The wooden shoe enhances biomechanics, allows even weight distribution on the solar surface of the foot, and can be easily manipulated to avoid focal pressure from the distal phalanx.
- The wooden shoe may be a useful treatment option for many severe foot conditions, providing veterinarians with a potential alternative to humane euthanasia of the patient.



FIGURE 1 Case 1: Lateromedial radiographic projection showing distal displacement of the distal phalanx.

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Computed tomography of the equine elbow: A subchondral bone lesion in a novel location

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SUMMARY

A yearling Oldenburg filly presented for acute severe right forelimb lameness, localised to the elbow joint by intra-articular anaesthesia. Radiographs initially revealed no abnormalities; however, the mare failed to respond to intra-articular medication of the right elbow joint with corticosteroid. Repeat radiographs 2 months later identified an ill-defined heterogeneous opacity within the medial humeral epicondyle. Computed tomographic (CT) examination of the elbow under general

anaesthesia revealed a region of osseous resorption, measuring 23 mm proximodistally and 1 cm mediolaterally, surrounded by a sclerotic rim within the medial epicondyle of the right humerus that extended from the physis to its distal margin. The mare underwent arthroscopy during which the CT findings were largely confirmed, and additional cartilage defects were seen. The lesion was surgically debrided, and the elbow joint was treated with intra-articular stem cell therapy 3 weeks post-operatively. The filly was sound 6 months after the final treatment. This case report is the first to describe resorptive pathology within the medial humeral epicondyle in the equine elbow; CT descriptions of cyst-like resorptive lesions within the elbow are currently limited to the proximomedial radius and medial humeral trochlea, similar to radiographic reports. The horse's young age, sudden onset of lameness, unusual location and radiologic progression of the lesion suggest a developmental or traumatic aetiology. It was not possible to conclusively define the aetiology of the lesion. Radiography underestimated the extent of the lesion compared to computed tomography, which was valuable for surgical planning and contributed to the successful outcome of the case.



FIGURE 1 Sagittal computed tomographic reconstruction (bone window) of the right elbow; the black and white arrowheads, respectively, indicate osseous resorption and sclerosis within the medial humeral epicondyle.

KEY WORDS

horse, computed tomography, cubital joint



Key points

- Resorptive pathology has not previously been described in the medial humeral epicondyle.
- Computed tomography provided valuable information regarding the extent of the lesion compared to radiography and assisted surgical management of the case.

Alternative approach for fracture fixation following implant infection in a Salter-Harris type-II fracture of the proximal phalanx in a Warmblood foal

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SUMMARY

A 2-day-old female Warmblood foal (70kg) presented with a closed, displaced Salter-Harris type-II fracture of the proximal physis of the left hind first phalanx. The fracture was repaired with four 4.5mm cortical screws and wire in a figure-of-8 pattern applied on the lateral and medial aspect of the phalanx, respectively. A 4.5mm cortical screw was additionally inserted in lag-fashion to engage the lateral metaphyseal spike.

Three days postoperatively, medial and proximal displacement of the distal fracture fragment and implant infection were apparent and revision surgery was performed. Previous implants were removed. The fracture was reduced using pointed reduction forceps. Temporary fracture stabilisation was achieved by inserting a Steinmann pin through a stab incision into P1 across the fracture plane in a dorsoproximal-plantarodistal direction. A 4.5mm cortical screw was inserted via a stab incision in a proximolateral-distomedial direction in lag-fashion across the proximal P1 physis. Following the removal of the Steinmann pin, a second 4.5mm cortical screw was inserted transphyseal in a dorsoproximal-plantarodistal direction (Figure 1).



FIGURE 1 Dorsoplantar radiograph of left hind Salter-Harris fracture type-II following implant infection and revision surgery.

Postoperatively, the foal was bearing full weight on the left hindlimb. The distal-limb cast was removed 4 weeks after surgery and replaced with a Robert-Jones bandage. Six weeks after revision surgery, radiographic examination confirmed fracture healing, and the implants were removed. Nineteen months following implant removal, the horse did not show any sign of lameness, despite a shortening of the proximal phalanx compared to the contralateral limb.

In cases of postoperative implant instability and infection, implant removal often becomes necessary. However, placing new implants in the previous location with local infection is not considered safe. To avoid this problem, this report describes an alternative approach for screw positioning in case of previous implant infection in a Salter-Harris type-II fracture of the proximal physis of the first phalanx.

KEY WORDS

horse, first phalanx, implant infection, foal, Salter-Harris fracture type-II



Key points

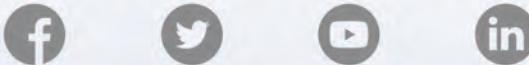
- Infected Salter-Harris type II fracture can be stabilised successfully with two 4.5 mm cortical screws and external coaptation in a foal.
- Transphyseal screw placement during the growth phase is compensated by adjacent growth plates.
- The case report describes an alternative approach to be considered in case of complications with standard methods of repair.



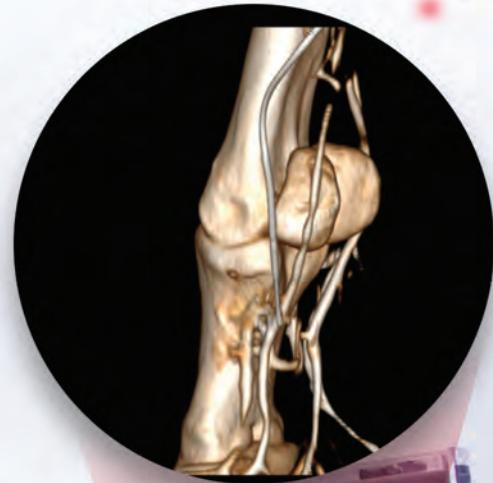
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Femoral B-cell neurolymphomatosis in a horse with multicentric lymphoma

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SUMMARY

An 18-year-old Freiberger gelding was presented with a history of intermittent left hindlimb lameness after an acute onset two weeks prior to referral. The lameness had not responded to anti-inflammatory therapy prescribed by the referring veterinarian. Physical, orthopaedic and neurological examinations revealed signs compatible with ipsilateral femoral nerve dysfunction. Transrectal sonographic examination showed a marked increase in the diameter of the left femoral nerve (Figure 1). The results of electromyography of the left hind quadriceps muscle were compatible with denervation attributable to neuropathy. Evaluation of the cerebral spinal fluid (CSF) revealed pleocytosis consisting of medium-sized lymphocytes, 5%–10% of which were positive for CD3 and CD79a. Neoplasia was suspected and steroid therapy was started. However, exacerbation of the clinical signs occurred and the horse was euthanised. Histopathological evaluation showed

neurolymphomatosis of the left femoral nerve as the cause of the lameness. Infiltration of tumour cells was also seen to a lesser extent in the right femoral nerve, spinal cord, various parts of the cardiovascular system, renal capsules, an abdominal lymph node and the subcutis of the left stifle and upper lip. Histochemical evaluation revealed 60%–70% of the neoplastic lymphocytes were positive for CD20 and CD79a and up to 40% were positive for CD3. Based on all the findings, B-cell lymphoma was tentatively diagnosed. This unique case report emphasises that, although lymphomatous infiltration of nerves is rare, it should be part of a differential diagnosis for neuropathy in horses.

KEY WORDS

horse, electromyography, femoral nerve, lymphoma, ultrasonography



Key points

- Transrectal ultrasonography can be used to image the femoral nerve, from the lumbosacral plexus, where the fibres meet from the third through sixth lumbar spinal nerves.
- Electromyography (EMG) can be done under sedation; moderately prolonged insertional activity and moderately abnormal spontaneous activity (fibrillation potentials and positive sharp waves) suggest denervation secondary to neuropathy.
- This is the first described case of femoral mononeuropathy as the primary clinical finding in horses with neurolymphomatosis. The term neurolymphomatosis describes lymphocytic infiltration of a B-cell lymphoma of neural structures and is rare in horses.

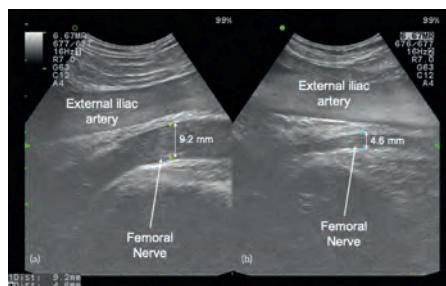


FIGURE 1 Sonograms obtained via transrectal ultrasonography of the left (a) and right (b) femoral nerves located adjacent to the external iliac artery.

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Equine retinal detachment in the United Kingdom: 23 cases (2010–2020)

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Summary

Background: Few reports describe the aetiology, presentation and diagnosis of retinal detachment in horses. Equine recurrent uveitis (ERU) and trauma are the most common causes of equine retinal detachment in the United States, but no studies have characterised the disease within the United Kingdom.

Objectives: To describe clinical presentation, aetiology and diagnostic examination findings of horses with retinal detachment within a UK-based population.

Study design: Retrospective case series.

Methods: Medical records of horses presented to a single UK referral centre between 2010 and 2020 were reviewed. Horses were diagnosed with retinal detachment by clinical examination and/or ultrasonography, and details of clinical presentation, aetiology and examination findings were recorded.

Results: A total of 23 horses were included. There were 13 geldings and 10 mares with a median age of 9 at presentation (range 4 days to 17 years). Warmbloods were the most common breed ($n=8$). Unilateral cases ($n=21$) were more common than bilateral ($n=2$). ERU was the most common aetiology ($n=10$) followed by trauma ($n=8$). Three cases presented post-intraocular surgery, one congenital and one secondary to primary glaucoma. Ultrasound confirmed diagnosis in 23 (100%) cases, but only nine could be visualised by direct ophthalmoscopy. Cataracts, posterior synechiae and vitreal debris were found commonly in both the ipsilateral and contralateral eye affected.

Main limitations: Small sample size. Single-centre retrospective study which may not be representative of the entire UK population. Histological confirmation of cases was not obtained.

Conclusions: Causes of retinal detachment in the studied population are like those previously reported in the USA and most cases presented with complete detachment. Ocular ultrasound is useful in the diagnosis of retinal detachment when the fundus cannot be directly assessed. The presence of retinal detachment should be considered in non-visual eyes presenting with cataracts, vitreal debris and posterior synechiae.

KEY WORDS

horse, eye, United Kingdom, ultrasound, uveitis

INTRODUCTION

Retinal detachment is defined as the separation from the inner neurosensory cell layer from the outer retinal pigmented epithelium (Gilger, 2022). This manifests clinically as partial or complete vision loss in the affected eye, which can compromise the likelihood of return to the horse's previous performance level (Utter et al., 2010) or potentially result in euthanasia if the condition is bilateral.

Reports documenting retinal detachment in horses in the literature are sparse, but previous cited causes include equine recurrent uveitis (ERU), complications of intra-ocular inflammation, secondary to trauma, congenital ocular anomalies, optic neuritis and post-phacoemulsification (Edelmann et al., 2014; Mätz-Rensing et al., 1996; Strobel et al., 2007).

A single previous publication describes clinical presentation, diagnosis, treatment and outcome in a USA hospital population (Strobel et al., 2007). Other ophthalmic conditions have been shown to differ in their clinical presentation and disease progression with respect to different geographical regions (Matthews & Gilger, 2009). The aforementioned study cites equine recurrent uveitis (ERU) as the most common cause of retinal detachment in the USA, but the prevalence of this disease in the United Kingdom has consistently been reported to be much lower, with recent data suggesting *Leptospira* as an uncommon aetiology compared to Europe and the USA (Malalana et al., 2017). The aetiological and clinical findings in a UK equine patient population with retinal detachment are currently unreported.

The purpose of this retrospective study is to describe the aetiology, clinical presentation and diagnostic examination findings in horses with retinal detachment within a UK-based hospital population.

MATERIALS AND METHODS

Medical records of horses presented to the Philip Leverhulme Equine Hospital, University of Liverpool between January 2010 and December 2020 were searched for a diagnosis of retinal detachment. Ophthalmic examination was performed in each case, including indirect and direct ophthalmoscopy and assessment of vision, including pupillary light reflex, menace response and dazzle reflexes. Indirect ophthalmoscopy was performed using a standard 20 dioptre handheld lens with a light source (Finoff transilluminator; Heine Optotechnik GmbH & Co. KG), and direct ophthalmoscopy was performed with an ophthalmoscope (Beta 200; Heine Optotechnik GmbH & Co. KG). Ultrasonography of the globe was performed in all cases, using a transpalpebral technique with a linear probe of 9–12 MHz (11L, Logiq S8; GE Healthcare). Images were acquired in both the sagittal and transverse planes. Sedation using detomidine hydrochloride, or romifidine hydrochloride alone or in combination with butorphanol was used to facilitate the examination if deemed necessary. A palpebral nerve block using 1–2 mL of mepivacaine hydrochloride was also performed if required.

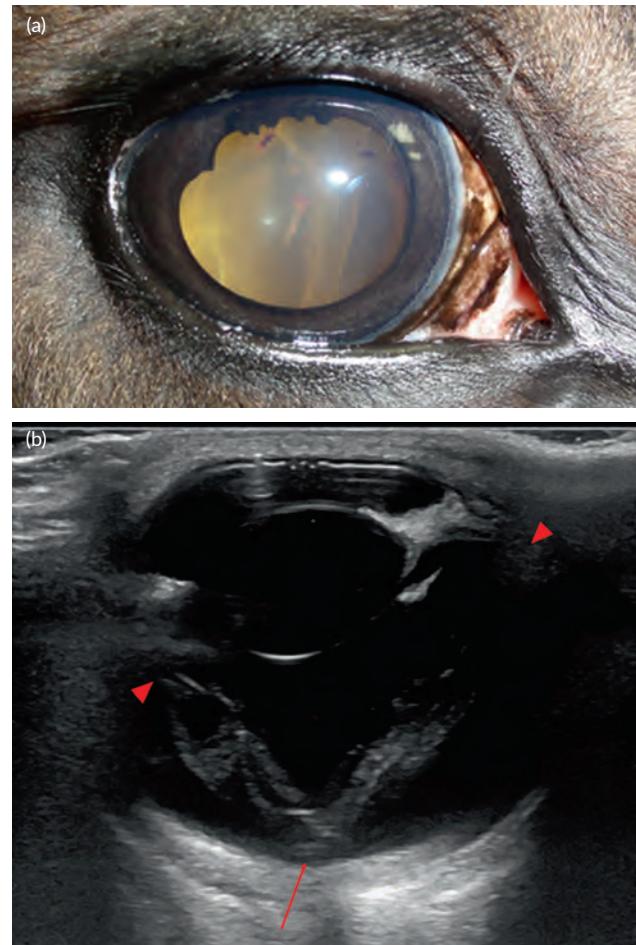


FIGURE 1 (a) Multiple grey tissue folds are evident floating within the vitreous indicating retinal detachment in this case. This horse presented post-vitrectomy. Irregularity of the pupillary margin is present, consistent with previous episodes of uveitis. (b) Ultrasonographic appearance of retinal detachment in the same horse. The retina is visible as multiple hyperechoic linear opacities within the vitreous and has the characteristic 'seagull wing' appearance, with attachments remaining at the points of insertion at the optic nerve head (arrow) and ora ciliaris (arrowhead).

Horses were eligible for inclusion in the study if a diagnosis of retinal detachment was reached. Horses were diagnosed with retinal detachment based on clinical and ultrasonographic appearance. Retinal detachment is visualised ultrasonographically as two hyperechoic lines extending from the optic nerve to the ora ciliaris on either side, within the posterior segment. This creates the characteristic 'seagull wing' appearance. Retinal detachments were diagnosed as either partial or complete. Partial detachments appeared as focal hazy areas of retina with subretinal accumulation of fluid. Complete detachments generally presented as grey sheets of tissue emanating from the optic nerve. Clinical and ultrasonographic findings were considered together to give a diagnosis of retinal detachment (Gilger, 2022) (Figure 1a,b).

Case details were recorded, including age, breed, sex, presenting signs and aetiology. Aetiology was determined either from the clinical history (e.g. history of recent trauma, previous recurrent

episodes of uveitis, recent intra-ocular surgery) or concurrent abnormalities within the eye (e.g. the presence of posterior synechiae and dyscoria in uveitic eyes indicating chronic recurrent episodes). Information regarding the eye affected, concurrent ipsilateral and contralateral ocular pathology, whether the detachment was partial or complete, and whether the condition was uni- or bilateral was also extracted.

RESULTS

A total of 23 horses were included in the study. There were 13 geldings and 10 mares, including one 4-day-old filly. The median age of presentation was 9 years (range 4 days to 17 years). Warmbloods ($n=8$), Cobs ($n=4$), Welsh breeds ($n=3$), Andalusians ($n=1$), Lusitanos ($n=1$), Haflingers ($n=1$), Shetlands ($n=1$), Polo Ponies ($n=1$), Thoroughbred crosses ($n=2$) and unknown breeds ($n=1$) formed the patient population.

The right eye presented with the condition in 11/23 (47.8%) cases. The left eye presented in 10/23 (43.5%) cases, and in 2/23 (8.7%) cases, the condition was bilateral. The most common reasons for initial presentation to the clinic were assessment of previously diagnosed uveitis ($n=6$), or cataracts ($n=5$), with ($n=3$) presenting with a history of known trauma, and ($n=3$) presenting at post-intra-ocular surgery assessment. Two cases presented due to abnormal ocular appearance, and apparent blindness or loss of vision was the primary reason for presentation in two cases. One case was also presented for suspected glaucoma, and another as part of a pre-purchase examination. Case details and presenting complaints are summarised in Table 1.

Menace response, pupillary light reflexes (PLR) and dazzle reflexes were absent in 14/22 (63.7%) cases. A weak PLR was present in 8/22 (36.4%) cases, and a menace response and/or dazzle reflex also remained in three of those eight cases. In one case, the responses to vision tests were not recorded. All cases which retained menace responses or dazzle reflexes were deemed to have partial detachment, and three cases with a weak PLR had complete detachment. In one case with a PLR, the nature of retinal detachment was not recorded.

All cases underwent complete ophthalmic and ultrasonographic examination. Retinal detachment was diagnosed on ophthalmic examination of the retina in conjunction with ultrasound in 9/23 (39.2%) cases, and 14/23 (60.8%) cases were diagnosed on ultrasound alone, due to an inability to visualise the fundus. Ultrasound was confirmatory of retinal detachment in 23 (100%) cases. Cataracts obscured the fundus in 9/14 (64.0%) cases, hyphaema in 3/14 (21.4%), anterior chamber fibrin in one case and corneal oedema in another case.

The most common aetiology recorded was ERU, which occurred in 10/23 (43.5%) cases, followed by trauma in 8/23 (35.0%) of cases. All cases defined as ERU had either a clinical history of recurrent episodes or intra-ocular changes associated with recurrent uveitis. Trauma was diagnosed from clinical history. Other recorded

aetiologies were as post-surgical complications in three cases, one congenital case in a 4-day-old foal and one due to primary glaucoma (Figure 2). This case was diagnosed as such because it presented with increased intra-ocular pressure (IOP) (as measured by rebound tonometer; Tonovet, iCARE, Icare Finland Oy), buphthalmos and retinal detachment in the absence of signs of chronic uveitis or active inflammation or signs of any other causative pathology, for example, neoplasia.

In 17/22 (77.3%) cases, the detachment was considered complete at the time of presentation, 5/22 (22.7%) had partial detachment, and in one case, the information was not recorded (Table 2).

Of the horses included, 23/25 affected eyes displayed concurrent ipsilateral pathology in addition to retinal detachment, and for two cases, this information was not recorded. Of the 21 cases of unilateral retinal detachment, 10 cases (47.6%) also demonstrated abnormalities in the contralateral eye, 11 cases (52.4%) had no ocular abnormalities in the contralateral eye.

Of the 21 unilaterally affected cases, the most common ipsilateral pathology recorded was the presence of a cataract ($n=11$, 52.4%), followed by posterior synechiae ($n=8$, 38.1%) and vitreal debris ($n=4$, 19.0%). Periorbital soft tissue pathology and hyphaema were reported in three cases, along with aqueous flare in two cases, lens subluxation in two cases, changes in IOP in two cases, corneal oedema in two cases and corneal opacity in two cases. The presence of iris rests, corneal ulceration and Haab's striae were each reported in single cases. In unilaterally affected cases, cataracts were also the most frequently identified abnormality in the contralateral eye ($n=6$, 28.6%), followed by vitreal debris ($n=5$, 24.0%). Iris rests, changes in IOP, corneal oedema, leuocochoria, buphthalmos, chorioretinitis, band keratopathy and iris cyst were each reported in single cases (see Table 3).

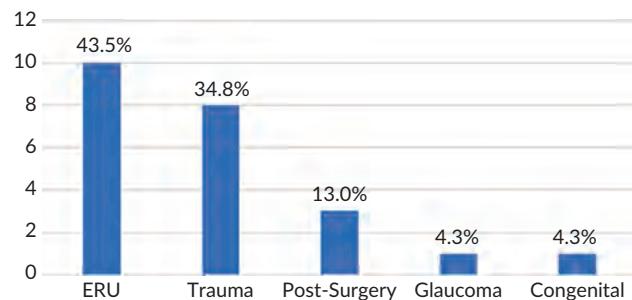
In the two bilateral cases, cataracts, corneal oedema, aqueous flare, anterior chamber collapse and vitreal debris were identified in both eyes in one case, and corneal ulcers were identified in both eyes in the other (see Table 4).

DISCUSSION

Retinal detachment in horses is a serious condition which invariably results in partial or complete vision loss in the affected eye. It occurs when there is a cleavage in the plane between the inner neurosensory retina and the outer retinal pigmented epithelium. Multiple types of retinal detachment are well described in other species, though scientific reports distinguishing different types in horses are lacking. Different types include bullous detachment (due to accumulation of fluid between the neurosensory retina and retinal pigmented epithelium), rhegmatogenous detachments (due to tears in the retina), tractional detachments (from fibrinous strands which form following the resolution of inflammation or haemorrhage) or following blunt force trauma (Gilger, 2022). ERU was the most common cause of retinal detachment both in this study and in

TABLE 1 Age, gender, breed, eye affected and presenting complaint for all horses.

Case	Age (years)	Gender	Breed	Eye affected	Presenting complaint
1	10	Gelding	Pony	R	Bilateral cataracts
2	5	Gelding	Andalusian	R	Cataract
3	4 days	Filly	Warmblood	Bilateral	Blindness
4	7	Gelding	Warmblood	Bilateral	Blindness
5	17	Gelding	Welsh C	L	Trauma
6	8	Mare	Warmblood	L	Acute onset cataract
7	5	Gelding	Lusitano	R	Re-exam post-vitrectomy
8	9	Gelding	Welsh x	R	Uveitis
9	15	Mare	Warmblood	L	Abnormal ocular appearance
10	10	Mare	Warmblood	R	Trauma
11	15	Gelding	Haflinger	R	Re-exam post-phacoemulsification
12	7	Gelding	Cob	L	Uveitis
13	10	Mare	Welsh Section A	L	Re-exam post-phacoemulsification
14	16	Mare	Warmblood	R	Bilateral cataracts
15	11	Mare	Cob	L	Abnormal ocular appearance
16	6	Mare	Cob	L	Uveitis
17	9	Gelding	TB x	R	Trauma
18	6	Gelding	Shetland	L	Uveitis
19	10	Gelding	Warmblood	R	Uveitis
20	8	Gelding	TB x	L	Cataract
21	11	Mare	Cob	L	Uveitis
22	13	Mare	Polo	R	Glaucoma
23	6	Gelding	Warmblood	R	Pre-purchase exam

**FIGURE 2** Aetiology of equine retinal detachment in a UK hospital population.

the previous report (Strobel et al., 2007) and ERU is the most common cause of accumulation of fluid between retinal layers, but also commonly results in fibrinous traction bands following the resolution of inflammation (Gilger, 2022). It follows that either bullous or tractional detachments are likely to be the most common types in horses; however, this information is not yet reported.

This is the first report to describe the clinical presentation, aetiology, diagnostic and examination findings in a UK horse population with retinal detachment. The most frequently reported aetiology was ERU (43.5%), followed by trauma (34.8%), which are findings

consistent with a previous study examining a USA hospital population. This cited ERU as a cause in 67.5% of cases, followed by trauma (25%) (Strobel et al., 2007). The proportion of cases due to trauma was relatively higher in this study, potentially reflecting the lower prevalence of ERU in the UK horse population (Malalana et al., 2017).

Detachment manifests clinically as reduced or absent responses to cranial nerve function tests, including menace responses, dazzle reflexes and PLR. Of the reported cases, 8/22 (36.4%) retained a weak PLR, and three of these eight cases retained a dazzle reflex and/or menace response. These three cases were all partial detachments, and hence retained some vision processing ability which explains the residual function. However, 3/22 (13.6%) cases continued to display a weak PLR despite complete retinal detachment. This is possible due to intrinsically photosensitive retinal ganglion cells (ip-RGCs) which have the ability to slowly depolarise in response to light stimulus even when detached from the retinal pigmented epithelium and underlying choroid and contribute to pupillary constriction (Markwell et al., 2010). Therefore, the possibility of complete retinal detachment should not be excluded in the presence of a positive PLR, and it should be noted that in partial detachment, positive responses to vision tests can still occur.

Ultrasonography was confirmatory of retinal detachment in 23/23 (100%) of cases in this series, and in 14/23 (60%) was the sole method of diagnosis. This is consistent with previous literature,

TABLE 2 Aetiology, diagnostic method, eye with retinal detachment and whether complete or partial retinal detachment were present on examination.

Aetiology	Diagnosis—Ultrasound (US) or clinical exam (CE)	Eye affected—Left (L), right (R) or both (B)	Complete (C) or partial (P)
ERU (<i>n</i> =10) (43.5%)	US (<i>n</i> =6)	R (<i>n</i> =4)	C (<i>n</i> =8)
	CE/US (<i>n</i> =4)	L (<i>n</i> =5)	P (<i>n</i> =1)
		B (<i>n</i> =1)	Unknown (<i>n</i> =1)
Trauma (<i>n</i> =8) (34.8%)	US (<i>n</i> =6)	R (<i>n</i> =4)	C (<i>n</i> =6)
	CE/US (<i>n</i> =2)	L (<i>n</i> =4)	P (<i>n</i> =2)
Post-surgery (<i>n</i> =3) (13.0%)	US (<i>n</i> =1)	R (<i>n</i> =2)	C (<i>n</i> =2)
	CE/US (<i>n</i> =2)	L (<i>n</i> =1)	P (<i>n</i> =1)
Glaucoma (<i>n</i> =1) (4.3%)	US	R	P
Congenital (<i>n</i> =1) (4.3%)	CE/US	B	C

which found ultrasound essential in diagnosis in 26/46 (56%) of eyes (Strobel et al., 2007). Furthermore, a survey documenting ultrasound abnormalities within equine eyes also found ultrasound to have greater sensitivity at detecting retinal detachment than direct evaluation (Gialletti et al., 2018). However, ultrasound also has the potential to misdiagnose diseases in eyes with poor image contrast, showing only moderate to acceptable agreement with histology for the diagnosis of retinal detachment in one study (Gallhoefer et al., 2013). Consideration of imaging findings in conjunction with direct ophthalmoscopy and the overall clinical picture is warranted before a diagnosis is made.

The common aetiologies of retinal detachment reported in this study are conditions with a high incidence of cataracts and anterior chamber pathology (Gilger, 2010), or in the case of trauma, are likely to present with periorbital swelling and haemorrhage, meaning that visualisation of the posterior segment is challenging in most cases. Ultrasonography should therefore be considered in evaluation of severe uveitis and ocular trauma patients where a direct view of the fundus is obscured. This will increase the likelihood of diagnosing retinal detachment and therefore more accurately inform prognosis for vision.

Vitreal debris was a common concurrent finding in this report and can appear similar to retinal detachment on ultrasound examination. Careful differentiation from retinal detachment is required to prevent misdiagnosis, and referral for a second opinion should be considered by the inexperienced practitioner, or if there is any doubt in the interpretation of imaging findings. Vitreal changes can take the form of linear hyperechoic opacities floating within the vitreous, or degeneration which results in point-like echogenicities (Gialletti et al., 2018). The former can be differentiated from retinal detachment by identifying points of insertion of the retina at the optic nerve head and bilaterally at the ora ciliaris, which gives rise to the 'seagull wing' appearance (Figure 1b). In contrast, vitreal membranes tend to be thinner and not follow any specific pattern of insertion, which is a key difference from retinal detachment, since almost all complete detachments maintain a fixed point within the fundus (Valentini et al., 2010). Retinal detachments also tend to have increased echogenicity and be less mobile than vitreal membranes

(Scotty, 2005). Techniques such as contrast-enhanced ultrasonography has shown to be superior to B-mode ultrasonography in humans and small animals in distinguishing retinal detachment from vitreal membranes (Han et al., 2001; Labruyere et al., 2011). However, preliminary work in horses has shown marked inter-individual variation and poor reproducibility (Blohm et al., 2020). More work is needed to demonstrate the clinical utility of this technique in horses.

Cataracts, posterior synechiae and vitreal debris were the most common abnormalities found in the ipsilateral eye in unilateral cases of retinal detachment. These are common features of ERU (Gilger, 2022; Malalana et al., 2020) and their frequency in the presence of retinal detachment in this study emphasises the need for thorough evaluation of the fundus in chronic uveitis cases, especially when the eye appears non-visual. In this study, 47.6% of cases of retinal detachment also displayed abnormalities in the contralateral eye, where cataracts and vitreal debris were the most frequently identified findings. This reflects ERU as the most common aetiology for retinal detachment, which is often a bilateral condition (Malalana et al., 2020) but indicates that detailed examination of both eyes in suspect retinal detachment cases is warranted. Retinal detachment occurring without concurrent pathology or an apparent inciting cause is infrequent, occurring in only 3/140 cases in one histologic study of equine ocular disease (Flores et al., 2020).

This report is limited by its retrospective nature and small number of cases. The study population consists of patients presented to a single referral hospital over a 10-year period, which may not be reflective of the wider UK horse population. However, the main findings are consistent with a previous report published from a population presented to two USA referral hospitals over a 7-year period, which provides preliminary evidence that the causes and clinical presentation of retinal detachment do not have the same spatial or temporal variation among the global horse population as with other ocular conditions (Matthews & Gilger, 2009). In addition, though the cases recorded had a clinical diagnosis of retinal detachment, histopathological examination in any eyes which were subsequently enucleated would have provided further confirmation. Furthermore, due to the retrospective nature of this study, it was not possible to distinguish between different types of retinal detachment and

TABLE 3 Aetiology, ipsi- and contralateral ocular abnormalities recorded in unilateral cases of retinal detachment.

Case	Aetiology	Diagnosis—ultrasound (US) or clinical exam (CE)	Eye affected—right (R), left (L) or both (B)	Right eye abnormalities	Left eye abnormalities
1	ERU	US	R	Cataract, posterior synechiae	Cataract, vitreal debris
2	ERU	US	R	Cataract, posterior synechiae, iris rests	None
5	Trauma	CE/US	L	Cataract	Not recorded
6	Trauma	US	L	None	Cataract
7	Post-vitrectomy	CE/US	R	Dyscoria	None
8	Trauma	US	R	Posterior synechiae, eyelid laceration, hyphaema, aqueous flare, lens subluxation, vitreal debris	None
9	Trauma	US	L	None	Cataract, posterior synechiae
10	Trauma	US	R	Periorbital swelling, hyphaema, chemosis, aqueous flare, vitreal debris	None
11	Post-phacoemulsification	US	R	Anterior chamber fibrin	None
12	ERU	CE/US	L	Lens subluxation	Not recorded
13	Post-phacoemulsification	CE/US	L	Vitreal debris	Corneal opacity, vitreal debris
14	ERU	US	R	Cataract, decreased IOP	Cataract
15	ERU	US	L	Cataract, leuchochoria, vitreal debris	Cataract, posterior synechiae, collapse of anterior chamber, lens subluxation
16	ERU	CE/US	L	None	Cataract, posterior synechiae, dyscoria, vitreal debris
17	Trauma	US	R	Eyelid lacerations, hyphaema, corneal ulcer, increased IOP	None
18	ERU	CE/US	L	Cataract, vitreal debris	Corneal opacity
19	ERU	US	R	Cataract, posterior synechiae, collapse of anterior chamber, corneal oedema	Horizontal band keratopathy, iris cyst, cataract
20	Trauma	US	L	None	Cataract
21	ERU	US	L	Corneal oedema, buphthalmos, increased IOP, iris rest, vitreal debris	Cataract, posterior synechiae, Haab's striae, dyscoria
22	Glaucoma	US	R	Corneal oedema, vitreal debris	None
23	Trauma	CE/US	R	Cataract	Focal chorioretinitis

TABLE 4 Aetiology and ocular abnormalities in bilateral cases of retinal detachment.

Case	Aetiology	Diagnosis—ultrasound (US) or clinical exam (CE)	Eye affected	Right eye abnormalities	Left eye abnormalities
3	Congenital	CE/US	Bilateral	Corneal ulcer	Corneal ulcer
4	ERU	CE/US	Bilateral	Cataract, corneal oedema, aqueous flare, collapse anterior chamber, vitreal debris	Cataract, corneal oedema, aqueous flare, collapse anterior chamber, vitreal debris

accurately describe them. This would have added detail to the descriptive findings of this disease and originality to the report.

In conclusion, this study provides original descriptive data pertaining to the clinical presentation, aetiology, examination

findings and diagnosis of retinal detachment among horses in a UK population. The small sample size precludes firm conclusions, but it appears that common aetiologies and clinical findings are like those previously reported in the USA. Ultrasonography was

highly useful for the diagnosis of this condition in this report, and therefore should be considered as part of a thorough ophthalmic examination where direct visualisation of the fundus is not possible. Cataracts, vitreal debris and posterior synechiae were common concurrent findings, and so the possibility of retinal detachment should be explored and excluded when these are present in an apparently non-visual eye. The distinction between inflammatory vitreal membranes and retinal detachment should be carefully made because the presence or absence of the latter determines prognosis for vision, and therefore is crucial to accurately determine.

AUTHOR CONTRIBUTIONS

E. Halliwell was involved in manuscript preparation and data interpretation. F. Malalana was involved in data collation, execution and preparation of the manuscript. Both authors gave their final approval of the manuscript.

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CONFLICT OF INTEREST STATEMENT

No conflicts of interest have been declared.

ETHICS STATEMENT

This research was approved by the University of Liverpool Veterinary Research Ethics Committee. Approval number: VREC1178.

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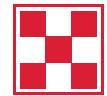
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Questionnaire study of nuclear scintigraphy protocols in equine clinical practice: Preliminary data

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Summary

Background: Nuclear scintigraphy is commonly used as a diagnostic tool in equine medicine, particularly in the orthopaedic field. However, the scintigraphy protocol varies in the literature.

Objectives: To gather data on scanning protocols and radiation safety measures commonly employed in equine practice.

Study design: Prospective, descriptive, and questionnaire-based study.

Methods: An electronic survey was distributed by Medical Imaging Electronic to clinics using an equine scanner scintigraphy unit ($n=150$). The survey was designed to document staff experience therewith, operating procedures, and radiation safety practices.

Results: The response rate was 30% (45/150). Scintigraphy was used as a diagnostic tool in 6.8%–22.2% of the horses that presented for lameness examination. The most commonly used bone tracer was hydroxyethylene diphosphonate (51.1%; 23/45). The vascular and pool phases were rarely (<10% of horses) performed. The whole-body scintigraphy was performed in 61–90% of the horses in 53.3% (24/45) of the participating clinics. The acquisition time of 90s per image was commonly used (46.7%, 21/45). Fifty-five percent of the operators underestimated or did not know the personnel's radiation exposure during the acquisition of bone scintigraphy and 34% of the personnel did not wear radiation protective clothes. Non-musculoskeletal scintigraphy was never or rarely used in 88.9% of the clinics.

Main limitations: The relatively low response rate may indicate that the reported findings are not fully representative of all equine practices.

Conclusions: This survey provides preliminary data, which may be used to establish a guideline for equine nuclear scintigraphy in the future.

KEY WORDS

horse, bone scan, lameness, MiE, nuclear medicine, radiation safety

INTRODUCTION

The first documented use of nuclear scintigraphy in horses dates back to the 1970s, in which scintigraphy of the musculoskeletal apparatus was performed (Ueltschi, 1977). The scintigraphy images represent the spatial distribution of the radiopharmaceutical in horses, which depends on blood perfusion and osteogenic activity (Quiney et al., 2018). As functional changes often precede

structural ones, musculoskeletal scintigraphy can detect pathological processes in bone before they become radiographically apparent. Scintigraphy can also be used to locate the potential areas of abnormal osseous turnover in horses with chronic and/or vague lameness (Archer et al., 2007). To improve the scintigraphy image quality, acquiring images with higher counts (gamma rays) is recommended to reduce the noise (Lo et al., 2009). This can be accomplished by increasing the administered radioactivity dose (Sporn,

Berner, Brehm, et al., 2014) or prolonging the acquisition time (Ross & Stacy, 2010). A typical activity administered to a human patient is around 600 MBq, which produces an effective dose equivalent to the patient body of 5 mSv (Whitelock, 2015). In horses, the recommended radioisotope dose for musculoskeletal scintigraphy is 14.8–18.5 MBq/kg bwt (Ross & Stacy, 2010). Therefore, the personal exposure dose while a horse is being scanned is likely to be significant because the staff need to stand close to the horse for a relatively long period (Gatherer et al., 2007). The exposure radiation dose of the horse holder for whole-body scintigraphy is estimated to be 22 µSv/h (Sommerfeld, 2016). Therefore, it is recommended to wear radiation protective clothing (Steyn & Uhrig, 2005).

By selecting the radiopharmaceutical and imaging sequence, scintigraphy can be used to demonstrate pathological processes in virtually any organ system (Cock et al., 2006; Davies et al., 2010; Votion & Lekeux, 1999). In horses, nuclear medicine is rarely used to study structures other than the musculoskeletal system. Recently, new nuclear medicine modalities have been adapted and applied in the equine orthopaedic field, such as single photon emission computed tomography (Harding et al., 2021) and positron emission tomography (Spreit et al., 2019).

The current study aimed to provide preliminary data about equine nuclear scintigraphy with focus on the scanning protocol and radiation exposure regarding the usage of nuclear scintigraphy in horses. These data may be used to establish a guideline for equine nuclear scintigraphy in the future.

MATERIALS AND METHODS

Survey design

The study was a prospective, descriptive survey. The survey comprised 29 questions: four open-ended and 25 close-ended multiple-choice questions with the opportunity to include additional comments at the end. The survey was designed by two veterinarians,

German board specialists of veterinary diagnostic imaging and equine sport medicine. Questions in the questionnaire were formulated based on expert veterinary advice together with, and following thorough review of the relevant literature. Several questions were included to reflect the geographic distribution of the respondents ($n=3$), the percentage of horses undergoing bone scintigraphy and their signalment, including age and discipline ($n=3$), indication for bone scintigraphy as diagnostic modality ($n=2$), radioisotope preparation ($n=6$), acquisition protocol ($n=9$), radiation safety practices ($n=3$) and other questions related to non-musculoskeletal scintigraphy ($n=3$).

Distribution of the survey

The survey was adapted for use on personal computers, tablets, and smartphones, using the web platform Google Forms. An email was sent by Medical Imaging Electronics (MiE) GmbH, Seth, Germany to equine clinics ($n=150$) that owned a gamma camera and performed scintigraphy with an invitation to participate in the survey, together with a link to the survey. Data collection started on 23 April 2020 and was concluded on 30 August 2021. The questionnaire could only be answered once per link and could not be edited after submission. Reminders were sent to non-respondents three times (every 4 months).

Statistical analysis

Data from the online responses were exported into an Excel spreadsheet before analysis was undertaken. The descriptive statistical analysis included the average, frequencies, and percentages. The results were rounded up to the nearest integer.

The percentage of the horses undergoing bone scintigraphy per month was calculated from the estimated lameness caseload and bone scintigraphy (questions 4 and 8, respectively). The minimum

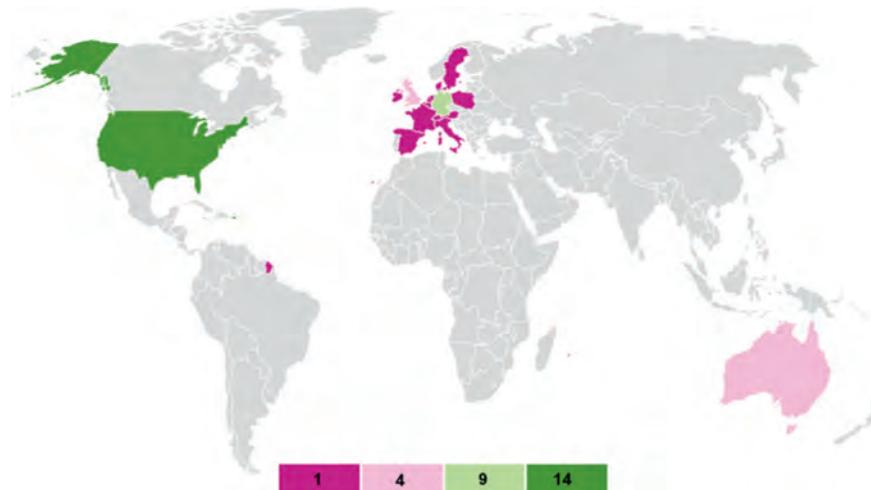


FIGURE 1 The geographic distribution of the respondent clinics. Clinics from Hong Kong and Singapore were not labelled.

duration of the (bone phase) scintigraphy examination of the entire musculoskeletal system was calculated based on the number of acquired images and the acquisition time per image (questions 22 and 23, respectively).

RESULTS

Forty-five clinics responded and returned a completed questionnaire. This represented a 30% return rate. The geographic distribution of the responding clinics is summarised in Figure 1. Thirty-five clinics (78%) owned an equine scanner unit manufactured by MiE GmbH.

Usage of scintigraphy as a diagnostic tool

The average number of lameness examinations of the respondent clinics was 146 cases per month (range 15–500). The percentage of the horses undergoing bone scintigraphy as part of the lameness examination ranged between 6.8% and 22.2%.

Signalment and indication of bone scintigraphy

The indication for scintigraphy varied among the clinics. Multiple limb lameness and lameness that was difficult to be localised by diagnostic anaesthesia were the common indications for bone scintigraphy (21%–40% of the horses). Fifty-seven percent of the horses undergoing bone scintigraphy were aged between 6 and 10 years and 25% were between 11 and 15 years. The disciplines of the horses were diverse, showing a tendency for dressage and showjumping (Figure 2).

Radioisotope preparation

^{99m}Technetium (^{99m}Tc) was the only radioisotope used for bone scintigraphy. One-third of the respondent clinics (35.5%; 16/45) had their own laboratory to elute ^{99m}Tc from the molybdenum generator on-site, whereas the remaining clinics (64.4%; 29/45) ordered the labelled radioisotope ready for administration from an external nuclear facility.

The used radioisotope dose was 10MBq/kg bwt in 24 clinics (53%), <10MBq/kg bwt in nine clinics (20%) and >10MBq/kg bwt in 12 clinics (27%) (Figure 3a). The clinics that prepared the radioisotope on-site ordered a molybdenum generator at a different range of activity depending on their caseload per week. Eight of the 16 clinics ordered a molybdenum generator with an activity of 5–10 GBq, four clinics ordered one >10 GBq, and four clinics ordered a <5 GBq generator.

If multiple horses were scheduled to be scanned per day, 25% of the respondents administered the radioisotope on all the horses simultaneously (within 30 min). The most commonly used bone-seeking agent was hydroxyethylene diphosphonate (HDP; 57%), followed by methylene diphosphonate (MDP; 32.2%) and dicarboxypropane-diphosphonate (DPD; 10.8%) (Figure 3b).

Acquisition protocol

The majority of the respondents (80%; 36/45) started the image acquisition between 2 and 4 h post radioisotope administration and only seven clinics started earlier (<2 h). For the whole-body scan, 46.7% (21/45) of the clinics acquired 31–40 images, 31.1% (14/45) and 22.2% (10/45) acquired >40 and <30 images, respectively (Figure 3c). The acquisition time per image amounted to 90 s in 48.9% (22/45) of the clinics and 60 s in 33.3% (15/45) of the clinics, with four clinics using one lasting <60 s and four clinics, one lasting 120 s (Figure 3d). Based on that, the minimum scan duration for the whole body ranged between 34.8 and 51.2 min.

The scintigraphic examination of the entire body was performed in 61%–90% of the cases admitted for lameness examination in 60% (27/45) of the clinics. The other clinics performed regional scintigraphy in the majority of the cases. One clinic never performed whole body bone scintigraphy. In contrast, another clinic performed whole body scintigraphy for all cases. The vascular phase was never performed in 37.8% (16/45) of the clinics, and rarely (<10% of scintigraphy examinations) in 55.6% (25/45). The pool phase was never performed in eight clinics, rarely (1%–10% of the cases) in 25 clinics, usually (>50 of the cases) in seven clinics, sometimes (11%–50% of the cases) in three clinics, and two clinics performed the pool phase for each horse undergoing scintigraphy.

Diuretics were used by 64.4% (29/45) of the clinics. Diuretics were used only if the bladder was full and interfered with anatomical

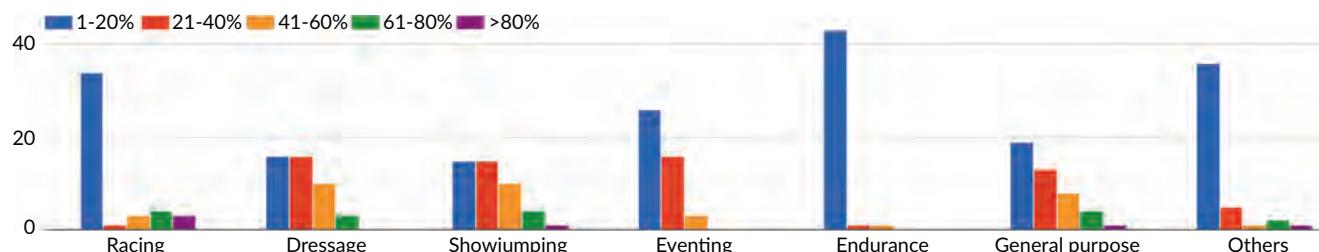


FIGURE 2 The distribution of the horse disciplines that underwent musculoskeletal scintigraphy in 45 clinics as part of lameness examination.

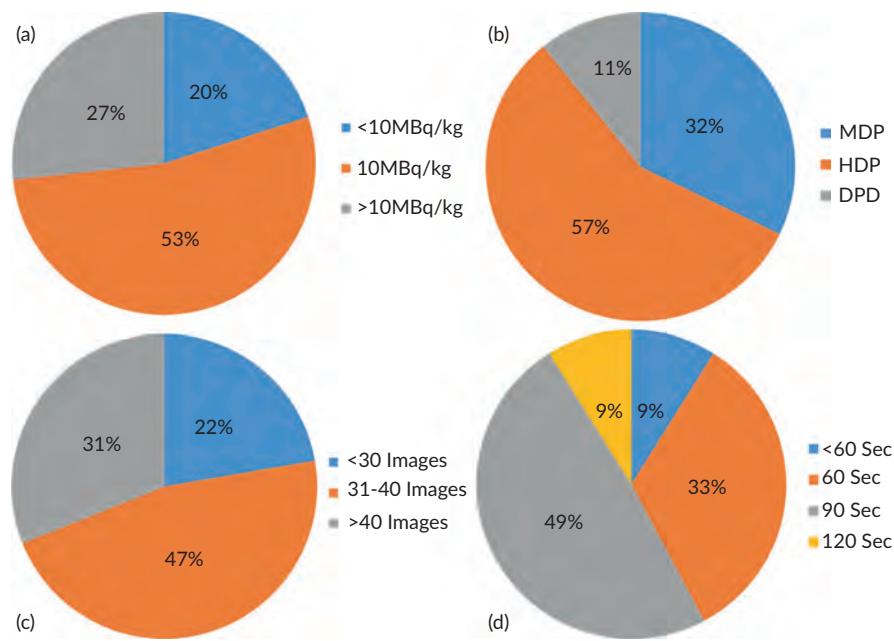


FIGURE 3 Diagrams show a part of the scintigraphy protocol of 45 clinics including radioisotope dose (a), the bone-seeking agents (b), the total number of images to scan the whole body (c), and the acquisition time per image (d).

regions of interest (during the examination) in 14/29 (48.3%) of the clinics; 11/29 (37.9%) of the clinics administered diuretics 1 h post radioisotope administration and four clinics administered diuretics together with the radioisotope.

Personnel radiation exposure

The number of personnel involved during the bone scintigraphy examination was three or less in 88.9% (40/45) of the clinics and four or more in five clinics. The personnel always wore lead radiation protective clothing during the image acquisition in 53.3% (24/45) of the clinics. The staff in 15/45 (33.3%) of the clinics never wore protective clothing and only the personnel holding the horse wore protective clothing in six clinics. The personnel in 25/45 (55.6%) of the clinics estimated the radiation exposure dose received by the horse holder during scintigraphy for 2 h to be <15 μ Sv, and the personnel in 14/45 clinics did not know the radiation exposure dose. The personnel in four clinics estimated the dose to be between 15 and 30 μ Sv and 31 and 50 μ Sv ($n=2$), respectively. The average isolation period of the horses post bone scintigraphy was 41.9 h and ranged between 24 and 72 h.

Non-musculoskeletal scintigraphy

Lung scintigraphy was never performed in any surveyed clinics except in one educational institute, which used it for research purposes. Thyroid scintigraphy was performed by 3/45 clinics. The caseload of thyroid scintigraphy was performed once every 2 years in one clinic and less than five cases per year in two clinics. Similar

to thyroid scintigraphy, lymphoscintigraphy was rarely used, only in 6/45 clinics with a caseload of one case every 2 years.

DISCUSSION

The current study aimed to provide preliminary data regarding the usage of nuclear scintigraphy in horses. Such data are essential to establish a standardised protocol for equine bone scintigraphy. The scintigraphy protocol should compromise image quality, workflow economics, and personnel safety (Sporn, Berner, Brehm, et al., 2014; Vija et al., 2005). Scintigraphy was used as a diagnostic tool in 6.8–22.2% of the horses admitted for lameness. Most horses undergoing bone scintigraphy were aged between 6 and 10 years, which is in agreement with a previous study (Quiney et al., 2018). This age group reflects the majority of the horses that are active in sports and training and thus more predisposed to injuries. The most common disciplines of the horses were dressage and showjumping. These disciplines are highly predisposed to a suspensory ligament injury in the hindlimbs (Murray et al., 2006) in association with sacroiliac joint region pain (Dyson, 2007). This injury combination is often diagnosed using scintigraphy in these horses (Gorgas et al., 2009), which may explain why these disciplines underwent scintigraphy more than the others. For the same reason, the primary indication of scintigraphy was multiple limb lameness and lameness that is difficult to be localised by diagnostic anaesthesia.

The recommended dose of 99m Tc is 14.8 to 18.5 MBq/kg bwt (Ross & Stacy, 2010). In the present study, the radioisotope dose varied between the clinics, with the majority using a dose of 10 MBq/kg bwt or higher (53.3% and 26.7%, respectively). The dose rate can be

adjusted according to age, that is, it increased by about 10% in older horses, and decreased by 10% in juveniles because of the difference in metabolic activity of the bone tissue (Selberg & Ross, 2012). However, low doses may result in inadequate image quality if insufficient counts are obtained. On the other hand, high doses of ^{99m}Tc may affect the biodistribution of bisphosphonate (Cronhjort et al., 1998). For instance, blood clearance rates of HDP prepared with high levels of ^{99m}Tc are significantly slower than those prepared with less total technetium (Hung et al., 1996). The biodistribution primarily depends on the clearance of the radiopharmaceuticals from the blood into organs, tissues, or lesions. Alteration of the radioisotope biodistribution can have a significant clinical impact on safety and diagnostic imaging accuracy.

The most frequently used diphosphonate as a bone-seeking agent was HDP, followed by MDP, and DPD, respectively. The bone uptake of ^{99m}Tc -diphosphonates is strictly related to chemical structure (Cronhjort et al., 1998). The adsorption of the diphosphonates to bone tissue is due to the -P-C-P- chain, while other pharmacological features are determined by the structure of the side chains (Cronhjort et al., 1998). It has been claimed in humans that DPD and HDP have higher rates of uptake by the bone, enabling higher bone uptake and a shorter time between administering and imaging compared to MDP (Pauwels et al., 1983). The effect of the above mentioned bone-seeking agents on the image quality of bone scintigraphy in horses has been investigated, and the results showed that the different ^{99m}Tc -diphosphonates affected the image quality quantitatively (Mageed et al., 2022). However, the difference in the image quality was not detected clinically.

One-third of the clinics prepared the radioisotope on-site and therefore ordered molybdenum generators. Half of them ordered a generator with an activity of 5-10GBq, which enabled bone scintigraphy of 8-18 horses/week weighing 500kg at a dose of 10MBq/kg bwt. One has to bear in mind that the molybdenum eluate contains 87.5% ^{99m}Tc and 12.5% stable (non-radioactive) Tc. The percentage of stable Tc increased with time post elution. Therefore, it is assumed that the ordered prepared radioisotope from an external nuclear facility may contain a higher percentage of stable Tc. The stable Tc is chemically identical to ^{99m}Tc , and thus, it can compete with ^{99m}Tc for binding sites of fixed concentrations of stannous ion and chelating reagents, which can negatively influence the image quality (Hung et al., 1996). Similarly, the use of "aged" ^{99m}Tc eluates has been reported to decrease labelling efficiency (Hung et al., 1996). Based on that, administering the radioisotope to the horse immediately after preparation is recommended. This is crucial if more horses are scheduled to be scanned on the same day. The survey revealed that only 25% of the clinics administered the radioisotope of those horses intended to be scanned at the same period of time. Further research is warranted to address the image quality and "old" Tc.

The average time interval between administering the radioisotope and imaging varied among the clinics. The majority of the respondents (80%) started the image acquisition of the bone phase between 2 and 4h post radioisotope administration, and only four clinics started earlier (<2h). Recently, it has been reported that the

optimal time frame after injection of ^{99m}Tc -HDP to achieve scintigraphic images with the best possible contrast and adequate count rates is 4-6h, particularly in the anatomical area with thicker soft tissues such as the thoracolumbar region (Sporn, Berner, Brehm, et al., 2014; Sporn, Berner, Winter, et al., 2014). An alternative method would be to increase the acquisition time for these anatomical regions to overcome the gamma attenuation. To the best of our knowledge, the usefulness of this methodology has not been reported. The shorter interval between administering the radioisotope and image acquisition decreases the bone/soft tissue uptake ratio and thus may reduce the image quality. From a radiation point of view, the radiation dose rate decreased by 56% at 3h post radioisotope injection (Mageed et al., 2020). Therefore, it is recommended to commence bone scintigraphy 3h post radioisotope injection.

The results show that the vascular and pool phases were rarely performed. One of the main indications of the vascular phase is aortoiliacofemoral thrombosis. The pool phase has been reported to be insensitive to soft tissue injuries, and negative results do not preclude the presence of significant injuries (Dyson & Weekes, 2003). Ultrasonographic imaging can also be used to diagnose this condition and, as it does not involve ionising radiation, may offer a safer alternative to pool phase studies (Rijkenhuizen & Pokar, 2019).

In the current study, the most commonly used acquisition time per image ranged between 90s in 48.9% of the clinics and 60s in 33.3%. It is recommended to acquire images with higher counts (i.e. signal) to reduce the noise and thus increase the image quality (Lo et al., 2009; Mageed et al., 2022). This can be accomplished by increasing the acquisition time (Murray et al., 2006; Vija et al., 2005). The impact of the acquisition time (60 vs. 90 vs. 120s) on image quality has been recently studied, and the results show that increasing the acquisition time does not necessarily improve image quality (Mageed et al., 2022). Therefore, it is recommended to decrease the acquisition time and to use an "on the fly motion correction" software to minimise the number of images and thus radiation exposure of the personnel. The minimum duration of scintigraphy examination of the entire musculoskeletal system ranged between 34.8 and 51.2min. The reported scintigraphy duration did not include the time of the horse and the gamma camera positioning.

The exposure radiation dose of the staff member holding the horse is estimated to be $22\text{ }\mu\text{Sv/h}$ (Sommerfeld, 2016). Interestingly, only 13.3% of the personnel correctly estimated the radiation exposure dose of the horse holder, and 55.6% and 31.1% underestimated or did not know, respectively. Therefore, it is unsurprising that in one-third of the clinics, the personnel involved in the scintigraphy acquisition never wore lead apron protective clothing. It has been reported that protective clothing reduces the radiation dose by factors of 3.6-5.7 times (Steyn & Uhrig, 2005). The scintigraphic imaging room is considered a "controlled" room in which personnel should wear lead personal-protective equipment. The recommended lead apron is 5mm in thickness that would absorb up to 94.5% of the gamma radiation at the level of 150kV (Sommerfeld, 2016).

Another factor that may reduce the personnel radiation dose is keeping a distance of 30cm from the horse (Mageed et al., 2020).

The primary radiation hazard of personnel exposure in equine scintigraphy is radioactive urine. It is common practice in equine bone scintigraphy to administer furosemide 1 h before the examination to reduce the risk of urination during the image acquisition and misinterpretation due to the superimposition of radioactive urine in the pelvis. Furthermore, diuretics may wash out the unbound radioisotope in soft tissue and thus improve image quality and reduce the radiation dose (Mageed et al., 2020). However, it has been found that administering furosemide neither enhances the image quality nor does it reduce the radiation dose rate (Mageed et al., 2020). Therefore, it is recommended to use a diuretic only if the radioactivity in the bladder interferes with the acquisition of images.

Non-musculoskeletal scintigraphy such as pulmonary (Votion & Lekeux, 1999), thyroid (Davies et al., 2010) and lymphoscintigraphy (Cock et al., 2006) is documented in horses and infrequently used in routine clinical practice. None of the respondent clinics performed pulmonary scintigraphy for clinical/diagnostic purposes. Thyroid and lymphoscintigraphy were rarely performed in 13.3% of the surveyed clinics.

Based on the results of the current study and the published equine literature, the use of ^{99m}Tc -HDP at the dose of 10 MBq/kg bwt for musculoskeletal scintigraphy is recommended. The radioisotope should be administered as soon as it is eluted. The examination should start 2–3 h post radioisotope administration and use an acquisition time of 60–90 s. The images of anatomical regions with thicker soft tissues should be acquired 4 h post radioisotope administration. The number of personnel involved during the image acquisition should be three or less and all of them should wear lead radiation-protective clothing, including coveralls and disposable hand gloves. The distance between the horse and the holder should be at least 30 cm.

The current study has limitations. The relatively low response rate may indicate that the reported findings are not fully representative of all equine practices. Furthermore, the relatively low response rate impeded in-depth statistical analysis. Reported response rates for electronic questionnaires vary widely and no consensus on what constitutes a normal response rate seems to exist, with suggested values including 50%, 60% and 75% (Christley, 2016). To increase the response rate, a reminder was sent to the non-respondents. This increased the response rate in the current study by 27%.

It could be argued that the survey underrepresents the clinics not using the equine scanner from MiE. The objective of the present study was to provide preliminary data to establish guidelines for equine scintigraphy. Therefore, it was necessary to collect the data from the clinics using the same equipment and setup. To the best of our knowledge, the equine scanner unit provided by MiE has the highest market share. Furthermore, direct distribution of the survey by MiE would ensure that many clinics using nuclear scintigraphy worldwide participate in the survey. Another limitation of the study was that some data were estimated rather than retrospectively collected, which may influence the accuracy of the generated results. We believe that retrospectively collecting the data would discourage the respondent from participating or return a fully completed survey.

In summary, bone scintigraphy was used as a diagnostic tool in 6.8%–22.2% of the lameness cases in clinics that responded to the questionnaire. One-third of the clinics prepared ^{99m}Tc on-site. The most commonly used diphosphonate was HDP, which was administered to the horses at a dose of ≥ 10 MBq/kg bwt. The vascular and pool phases were rarely performed. However, whole-body scintigraphy was performed in 61%–90% of the cases in 60% of the participating clinics. The most commonly used acquisition time per image was 90 s, making the minimum duration of the whole body scan between 34.8 and 51.2 min. Non-musculoskeletal scintigraphy was rarely used. Fifty-five percent of the clinics underestimated or did not know the radiation hazard of bone scintigraphy.

AUTHOR CONTRIBUTIONS

All authors contributed equally in this work.

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CONFLICT OF INTEREST STATEMENT

Mario Lindner is an employee of Medical Imaging Electronics GmbH; however, the company played no role in determining the content of this study.

ETHICS STATEMENT

The current study was a questionnaire and did not involve any animal materials. Therefore, no ethical clearance is needed.

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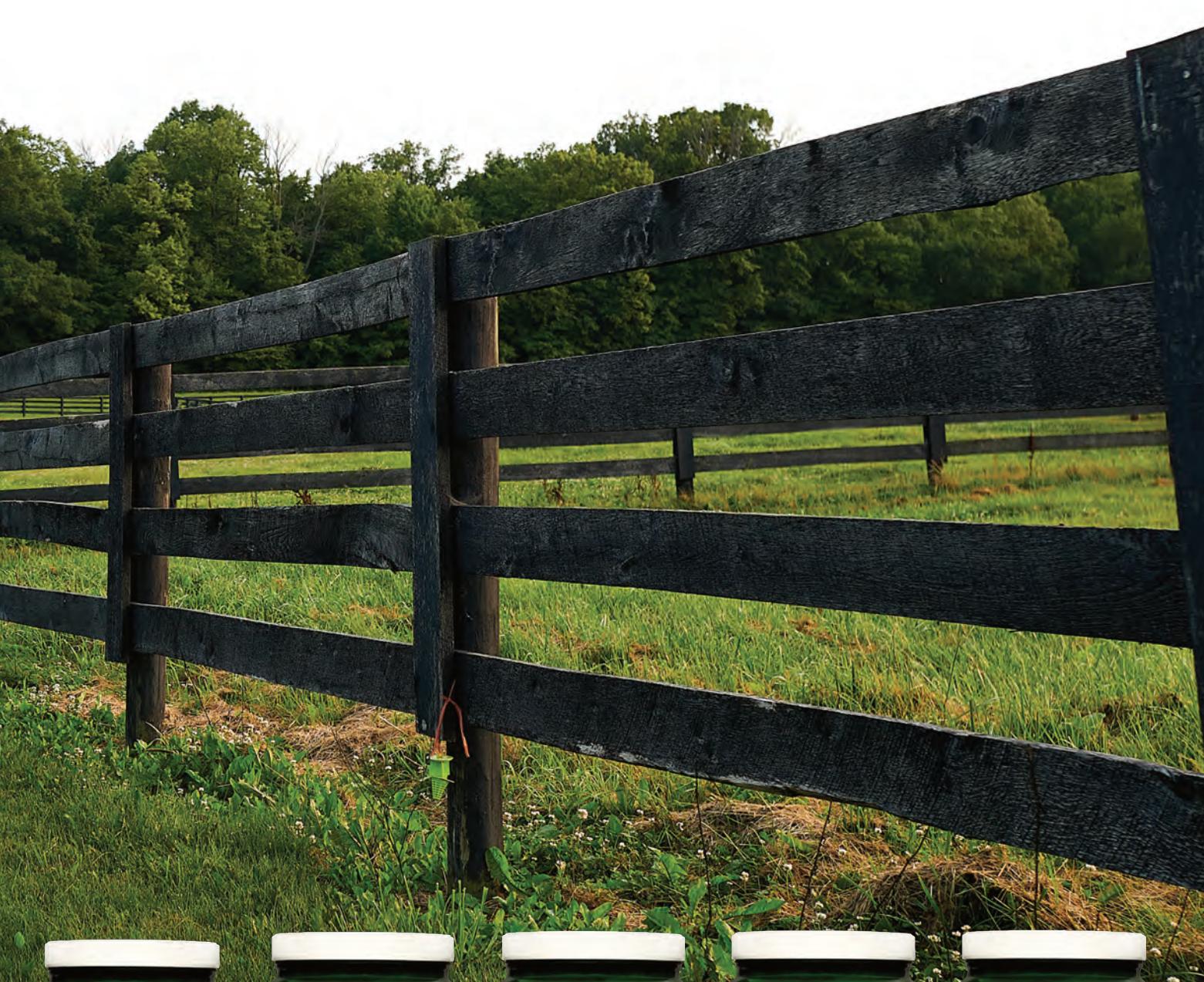
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The hygienic aspects in the management of strangles

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Summary

Streptococcus equi subsp. *equi* (*S. equi*) is a frequently encountered pathogen in equine practice. *S. equi* causes infection of the upper airways of horses, a condition known as *strangles*. *Strangles* is a highly contagious disease and may be economically devastating as well. Difficulties in the eradication of the disease using vaccines and medical treatments make hygienic measures crucial in order to limit transmission of the pathogen during outbreaks. This review aims to elucidate the challenges in handling an outbreak of *strangles* as well as develop a basic plan on how such an outbreak is handled in a hygienically optimal fashion. The results of this review suggest a longer environmental survival time of *S. equi* than previously assumed and support the importance of modification of surfaces for proper disinfection with appropriate disinfectants. Furthermore, the efficiency of using a colour-coding system in dividing healthy, exposed and clinically affected horses is discussed. Individual temperature monitoring twice daily is recommended for the identification of diseased horses before they pose a contagious risk. Additionally, changing clothes between visiting different stable units is likewise recommended, to minimise transmission of disease. In conclusion, veterinarians, personnel and horse owners at equestrian centres need to be aware of the importance of isolation, monitoring and dividing the site into zones according to the risk of infection. Finally, it can be concluded that regardless of size, practical biosecurity measures can be implemented within all equine facilities.

KEY WORDS

horse, biosecurity, epidemiology, hygiene, hygienic measures, outbreak management, prevention, *Strangles*, *Streptococcus equi* subsp. *equi*

INTRODUCTION

Streptococcus equi subsp. *equi* (*S. equi*) is a common pathogen within equine practice. The bacteria cause disease in the upper respiratory system, a condition known as *strangles*. The infamous name of the disease is derived from the clinical signs of airway obstruction displayed in horses that suffocate from the enlarged and abscessed lymph nodes in the throatlatch (Cordoni et al., 2015; Waller, 2014). Most commonly, the submandibular and retropharyngeal lymph nodes are affected. Even though *strangles* holds a relatively low mortality rate, the morbidity rate is high. The disease is a major challenge

worldwide due to its contagious nature, the risk of quarantine and the associated substantial economic impact on the equine industry (Boyle et al., 2018; Duran & Goehring, 2021; Sweeney et al., 1989).

THE BACTERIUM

The *Streptococcus* family constitutes Gram-positive, non-motile cocci that form chains in different lengths. The genus is catalase negative and facultative anaerobic. The conventional way of differentiating between species is laboratory differentiation using either

haemolysis, biochemical testing or Lancefield grouping. *S. equi* is a Lancefield group C streptococcus and is characterised by its ability to ferment maltose but not trehalose, sorbitol or lactose and to display β -haemolysis on blood agar (Timoney et al., 1995). Most species within *Streptococcus* live as commensals on the mucosae of the upper respiratory tract or the lower urogenital tract and result in opportunistic infections. In contrast, *S. equi* is not considered a commensal, but a host-restricted pathogen that causes infection of the respiratory system (Quinn et al., 2011; Waller, 2013).

EPIDEMIOLOGY AND PATHOGENESIS

Horses of all ages are susceptible to infections with *S. equi*, but more severe clinical signs are commonly seen in younger, naive horses (Pusterla et al., 2011; Sweeney et al., 2005). Older horses are often less severely affected and recover more rapidly (Boyle et al., 2018; Pusterla et al., 2011).

Transmission of the pathogen occurs, when the organism is either inhaled or ingested after direct contact with mucopurulent exudate from an infected horse or indirectly by contact with contaminated equipment (Boyle, 2017). After entry, it attaches to cells in the crypts of the naso- and oropharyngeal tonsils using the surface binding proteins, from where it penetrates the epithelium and enters the lymphoid tissue. Within 3 h after infection, the bacteria reaches the lymph nodes of the head and neck (Timoney & Kumar, 2008).

A few hours later the organism translocates to the submandibular and retropharyngeal lymph nodes that drain the pharyngeal and tonsillar region (Duran & Goehring, 2021; Timoney & Kumar, 2008) where it replicates and triggers an inflammatory response. This results in an influx of a large number of neutrophils. Simultaneously, the peptidoglycans in the cell wall of the organism stimulate the complement system and the generation of chemotactic factors. However, the organism has a number of virulence factors protecting it from the host's immune system, such as a hyaluronic acid capsule, superantigens and M-like proteins (SeM) (Tartor et al., 2020). SeM is one of the most important virulence factors, as it prevents the activation of the alternative and classical complement pathways (Boyle et al., 2009; Quinn et al., 2011). In combination, the virulence factors provide improved resistance to phagocytosis, explaining the fact that neutrophils to some extent are unable to phagocytise the organism. This requires, however, the presence of both the hyaluronic acid capsule and SeM surface proteins, as the antiphagocytic quality of SeM is reduced in the absence of the hyaluronic acid capsule (Boyle, 2017; Timoney et al., 2014; Waller, 2014).

CLINICAL SIGNS

In the acute phase of strangles, clinical signs include fever and neutrophilia, which occur shortly after infection (Waller, 2014). Other characteristic clinical signs include mucopurulent nasal discharge, which originates from the rupture of retropharyngeal lymph node

abscesses into the guttural pouches. These lymph nodes are generally swollen and painful (lymphadenopathy) (Boyle, 2017; Quinn et al., 2011; Sweeney et al., 2005). The immunocompetence of the infected horse has a great impact on the severity of the disease. Older horses often exhibit a less severe form of the disease characterised by acute onset of fever ($<42^\circ\text{C}$), nasal discharge and small abscesses, whereas younger horses tend to have a more severe outcome of the disease characterised by lymph node abscessation that subsequently opens and drains (Boyle, 2017; Boyle et al., 2018; Dwyer, 1995). Moreover, pharyngitis resulting in dysphagia can be observed among horses of all ages, with the risk of some affected horses becoming either anorexic or reluctant to eat. Attempts to swallow food and water may be followed by reflux through the nares.

Two to 3 weeks after infection, mucosal and systemic immune responses are stimulated, coinciding with mucosal clearance of *S. equi* (Boyle et al., 2009; Galan & Timoney, 1985). Most horses recover from strangles over a period of weeks (~98%), although sequelae from *S. equi* infection including depression, listlessness and guttural pouch empyema as well as chondroid development in the guttural pouches are not uncommon (Pusterla et al., 2011; Sweeney et al., 2005). Long-term immunity to strangles occurs in most horses after infection (approx. 75%), if not treated with antibiotics (Boyle et al., 2018; Galan & Timoney, 1985; Tiwari et al., 2007). Just after the convalescent phase, horses are resistant to re-infection (Boyle et al., 2018; Galan & Timoney, 1985). It is still not evident how long the convalescent phase persists (Delph et al., 2019; Nally et al., 2000; Sheoran et al., 1997; Waller, 2014).

Subclinical, persistent carriers

Despite the development of an antibody response, some horses fail to clear all abscess material from their guttural pouches or sinuses (approx. 10%) and the residual purulent material may form chondroids that can remain in the horse for several years or even a lifetime (Duran & Goehring, 2021; Newton, Wood, & Chanter, 1997; Newton, Wood, Dunn, et al., 1997; Verheyen et al., 2000).

The presence of such subclinical, persistently *S. equi*-infected carriers likely contributes to the maintenance of increased levels of immunity and extended strangles-free status within isolated herds of previously infected horses (Duran & Goehring, 2021). Older horses, with waning immunity and vaccinated animals have limited susceptibility to *S. equi* and can develop a mild form of strangles ('atypical or catarrhal strangles') (Whitlock et al., 2019). Nevertheless, these animals still shed virulent *S. equi* organisms, that can result in severe disease in more susceptible horses (Duran & Goehring, 2021; Sheoran et al., 1997).

The persistent carriers of *S. equi* represent a special challenge in clinical practice as they represent a hidden reservoir of *S. equi*, while showing no clinical signs of strangles. Persistent carriers may transmit the organism to susceptible horses and thereby complicate eradication of disease outbreaks. Consequently, identification of these carriers is of utmost importance with regards to

both eradicating and minimising the disease, as a previous study has shown that a single carrier has the ability to shed millions of bacteria into the water of a water trough in the pasture, after a single sip of water (Waller, 2014).

The persistent infection is usually a result of incomplete drainage of the guttural pouches (Pringle et al., 2019), leaving live *S. equi* able to persist for years in what seems like clinically recovered horses (Robinson et al., 2013). Additionally, silent carriers can shed large amounts of bacteria for several months after an outbreak underlining the importance of detecting and treating these carriers. Identification of subclinical carriers is not an easy task. In theory, all horses that have recovered from strangles, should be considered potential subclinical carriers. Confirmation of a strangles-recovered horse as a 'subclinical carrier' can be verified by (repeated) nasal swabs, nasopharyngeal swabs, nasopharyngeal lavage or guttural pouch lavage. Nasal swabs and nasopharyngeal swabs have, however, been shown to be low yield for carriers (Boyle et al., 2017), while others have reported that nasal pharyngeal washes have been shown to be superior to nasopharyngeal swabs (Lindahl et al., 2013). In a study by Boyle et al. (2017) endoscopically guided guttural pouche lavage was found to be 50 times more likely to find carriers than nasopharyngeal samples, however, Pringle et al. (2019) were able to find horses with nasopharyngeal samples, and not in guttural pouch lavages. Preferably, more than one of these diagnostic tools is therefore recommended to be used. Yet, the most common diagnostic procedures are nasal- and nasopharyngeal samples, which are prepared and analysed by culture and quantitative polymerase chain reaction (qPCR), followed by interpretation of the results. A positive result from qPCR can be obtained from horses that carry live bacteria and constitute a risk for transmission of the disease but a positive result can also be obtained in the presence of non-viable bacteria without the risk of transmission of the disease. Therefore, the qPCR result should be combined with sample culturing to determine if the bacteria are viable. If both the qPCR and culture show positive results, it is safe to presume that the horse is a carrier and hereby constitutes a risk for disease transmission (Newton et al., 2020). However, a qPCR-positive horse should always be considered as positive (and risk for transmission) even if the sample is culture negative, as samples may die en route to the laboratory facilities (Pusterla et al., 2021). In the case of a qPCR-positive/culture-negative sample, the horse should be re-sampled and qPCR/culture analysed, as studies have shown that horses can be qPCR-positive/culture-negative and then become positive on culture again (Pringle et al., 2019).

TREATMENT

In animals with lymph node abscessation, hot packing and topical softening agents can help in the development and maturation of the masses, speeding up the resolution (Sweeney et al., 2005).

In clinically severe cases, treatment may include the use of antibiotics, as it provides a temporary clinical improvement, particularly if the horse shows dyspnoea due to partial upper airway obstruction

(Boyle, 2017; Waller, 2014). Penicillin is the antimicrobial of choice for treating acute strangles, although *S. equi* is considered sensitive to most antibiotics, except aminoglycosides (Pringle et al., 2020). A short course (3–5 days) of penicillin administration has proven effective during the acute phase to prevent abscessation and reduce fever, lethargy and upper airway obstruction (Mallicote, 2015). The use of antibiotics in the treatment of *S. equi*-infected horses is still considered controversial, as horses treated with antibiotics are less likely to develop immunity to *S. equi* infections and are more susceptible to re-infection as soon as the antibiotic treatment is discontinued (Boyle, 2017; Waller, 2014). In addition, antibiotics are not recommended for horses that have already formed external abscesses, as this will prolong the resolution. Non-steroidal anti-inflammatory drugs (NSAID) are recommended to decrease swelling and fever and hereby promote well-being and eating (Gutiérrez & Patricia, 2013). Hot compresses or topical treatment can be beneficial as a means to accelerate the maturation of abscesses, whereas fully matured external abscesses successfully can be lanced to allow drainage (Boyle et al., 2018). In addition, daily lavage of open abscesses using 3%–5% povidone iodine solution is useful to accelerate resolution along with alleviation of the compression upon the surrounding structures such as the pharynx (Boyle, 2017). The treatment of choice in case of persistent infection with guttural pouch empyema is repeated lavage via either an endoscope, an indwelling catheter or a chambers catheter.

It has proven effective to add 20% acetylcysteine in buffered saline solution to the lavages (Boyle, 2017; Newton, Wood, & Chanter, 1997; Newton, Wood, Dunn, et al., 1997; Waller, 2014). If chondroids are present, removal can be performed by either non-invasive methods (endoscopically guided grasping forceps, basket snare, diathermic snare, a wire loop and retrieval basket) or by surgery (Freeman, 2015; Waller, 2014).

VACCINE PROPHYLAXIS

Both cell-free and live vaccines are available worldwide. Due to the lack of data concerning the protection they provide, vaccination against strangles has previously only been rarely used in Europe (Reinhold & Venner, 2010). The Equilis StrepE vaccine, which is based on a different live strain of *S. equi* injected into the upper lip of the horse, has until recently been the only available vaccine in Europe. The drawbacks of Equilis StrepE® (MSD, UK) vaccine include a short-lasting effect of up to 6 months (Rendle et al., 2021), and that Equilis StrepE® does not allow for differentiating infected from vaccinated animals (DIVA principle) capability, which has been demonstrated in serological monitoring of an outbreak after use of this vaccine (J.R. Newton, unpublished data) (Boyle et al., 2018).

However, recent research has provided great progress towards the launch of a new vaccine, Strangvac® (Intervacc, Sweden). Strangvac® was authorised for the European market in 2021, and to what degree the vaccine will limit the challenges with *S. equi* in clinical practice only time will tell, but the initial observations are promising (Robinson et al., 2018).

In addition, a modified-live bacterial vaccine, Pinnacle® (Zoetis, US) is available in the US. The vaccine offers some advantages as intra-nasal administration avoids local injection-site reactions that can occur with parenteral *S. equi* vaccines (Boyle et al., 2018), but other adverse side effects such as the risk of vaccine-induced infections have been reported.

S. EQUI SURVIVAL TIME

Laboratory conditions versus real-world conditions

Several studies have highlighted the ability of *S. equi* survival on surfaces in different environments (Cursons et al., 2015; Durham et al., 2018; Weese et al., 2009). Some of these studies were conducted under controlled and moderately constant conditions different from what is usually seen in equine facilities (Lindahl et al., 2013), whereas other studies demonstrate the survival capacity of *S. equi* in environments more similar to real-life conditions (Durham et al., 2018; Weese et al., 2009). According to Jorm (1992), it is important to keep in mind that laboratory studies are unable to mirror real-world conditions, as the results of each study only apply when the conditions in the particular facility are similar to those under which the study was conducted.

Survival capacity on different surfaces

Results of a laboratory study, examining the survival time of *S. equi* on two different types of surfaces, showed that the survival time on glass was shorter compared to that on wood, indicating that survival is enhanced when the surface is rough, thus harder to clean and easier for bacteria to survive on (Jorm, 1992). This is in accordance with the observations by Durham et al. (2018), who also found a major difference in survival time on various different surfaces. In contrast, Weese et al. (2009) found no effect of surface type when investigating the survival of *S. equi* on different dry surfaces (bare wood, painted wood, metal and rubber) but showed that the bacteria persisted longer in mucus, which provides both protection, moisture and nutrition (Weese et al., 2009). The lack of effect of surface type for the survival of *S. equi* is likely to be explained by inadequate statistical power (low sample size) rather than actually demonstrating true biological differences (or in this case, lack of biological differences). Additionally, the same study examined the effects of weather conditions such as sunlight, cloudiness, rainfall and temperature. They concluded that sunlight had a significant effect on the persistence of *S. equi*, showing that none of the inoculated samples survived for more than 24 h when exposed to sunlight (Table 1). This is in agreement with the findings of Durham et al. (2018), who demonstrated a poor survival of *S. equi* on an outdoor fence post, during both winter and summer (Durham et al., 2018). While ideally any fence should be washed and disinfected after an outbreak (Dwyer, 1995), this suggests that

an outdoor wooden fenced paddock can be left unused for a couple of days before being taken into use and considered infection-free, especially when exposed to direct sunlight.

In the study by Durham et al. (2018), the beneficial impact of temperature and humidity for the survival of *S. equi*, respectively, could not be separated. Nevertheless, the dry sites showed a high survival time and growth rate of *S. equi* in the winter due to lower temperatures and higher humidity, whereas wet sites had a high growth rate solely attributed to temperature since the humidity did not change (Durham et al., 2018). Conclusively, the winter weather, characterised by low temperatures and high humidity, promotes the survival time of *S. equi*, particularly shown by the presence of *S. equi* on shoe soles, stomach tubes, buckets and wood posts (Table 2 and 3). Hence, humid conditions favour the growth and survival of *S. equi* in the environment, which is critical to remember as decisions in regard to isolation and disinfection measures are made.

The results by Durham et al. (2018) suggest a much longer survival time than previously reported. The study holds a median survival time between 2 and 9 days depending on the season. However, survival for up to 34 days was observed at wet sites during winter (Table 1). This emphasises the need for an isolation plan, in particular, for facilities with high in-out activity of horses. Though, it is important to keep in mind that even though growth and survival of *S. equi* are found, more than 10^4 colony-forming units (CFU) of *S. equi* are required to manifest strangles infection in immunocompetent adult horses, at least under experimental settings (Rendle et al., 2021).

Only a single study has addressed the potential transmission of the bacteria via visitors' clothes. This study demonstrates the ability of different *S. equi* strains to survive on different types of clothing material. Independent of strains, *S. equi* survived for at least 24 h on both T-shirt and jacket material, suggesting that transmission via clothes constitutes a notable risk (Frost et al., 2018). Hence, ideally, a fresh set of protective clothing should be worn when entering another area on the premises to minimise the spread of the bacteria (Dwyer, 1995). All the evaluated *S. equi* isolates seemed to survive longer on the T-shirt material than on the surface of the jacket material, which might be related to structural differences between the two fabrics. However, material type alone is not the only factor influencing bacterial retention, as shown by difficulties in the removal of bacteria when washing polyester halters (Frost et al., 2018).

BIOSECURITY MEASURES AS A METHOD OF OUTBREAK CONTROL

The proper surface for the most suitable chemical disinfectant

As most stables consist of a combination of rubber mats, raw wood, metal, concrete, asphalt as well as sand and dirt on these

TABLE 1 Survival of *Streptococcus equi* subsp. *equi* on different surfaces.

Study	Contamination sites	Materials and methods	Sampling	Culturing	Results
Survival of <i>Streptococcus equi</i> on surfaces in an outdoor environment (Weese et al., 2009)	Four sites included in the study were placed in an enclosed, gravel-based courtyard exposed to direct sunlight for most of the day, and wildlife contact was prevented with a steel frame structure 1. Unpainted wood, spruce 2. Painted wood, spruce with two coats of latex fence paint 3. Rubber feed bin 4. Metal feed bin	All four sites were contaminated with 1mL <i>S. equi</i> inoculum at eight different areas of 15×5 cm pr. site The study was conducted between 5 July and 21 September 2007 Meteorological data were recorded daily: Effect of sunlight (sunny/partly cloudy/cloudy) Temperature (high/low) Rain (yes/no)	A cotton swab was moistened with PBS and wiped thoroughly over the area to be sampled. Sampling was performed immediately after inoculation (day 0) and on days 1, 3, 5, 7, 10, 14, 21, 28, 35 and 42 or until two negative samples were obtained from a specific surface type.	-	Survival was short all over, ranging from <1 to 3 days No effect of rain or surface type on the persistence of <i>S. equi</i> was observed. There was, however, an effect of sunlight, with the survival of 24-h or less on 24/24 samples tested during a sunny period, versus 9/16 (56%) samples tested during partly cloudy and 20/24 (83%) samples tested during cloudy periods. No effect of daily high or low temperature was observed. There was no difference in the persistence of <i>S. equi</i> in saline versus mucus inocula (however, when the analysis was repeated categorising outcome as <1 day and ≥1 day, there was a significant difference, demonstrating <i>S. equi</i> persisting longer in mucus)
A study of the environmental survival of <i>Streptococcus equi</i> subspecies <i>equi</i> (Durham et al., 2018)	Seven sites were included in the study. Site 1 is placed outdoors Sites 2–7 are placed indoors in a wooden shed 1. Top of fence post, in shadow 2. Plain untreated pine wood 3. Rubber sole of a shoe placed sole-down on the plain plastic surface 4. Cotton overalls 5. Inside the end of translucent plastic nasogastric tube (wet environment) 6. Between removable float blade and holder of steel dental rasp 7. Bottom of a plastic bucket containing a few millimetres of plain rainwater (during summer a small amount was added daily to maintain a wet environment) None of the seven sites had been in contact with any chemical disinfectants	All seven sites were contaminated with 10mL <i>S. equi</i> inoculum The study was conducted during summer (7–15 August 2013) and winter (7 November–17 December 2013) Minimum and maximum temperature (summer: 9–32°C, mean = 18, 8°C. Winter: -2.9 to 14.5°C, mean = 5.2°C) Relative humidity (summer: 63–82%, mean = 70%. Winter: 79–94%, mean = 87%) All sites were visibly clean but were not prewashed for the study.	Sampling intervals From inoculation to day 5: 24 h Day 6–23: 48 h Day 24-end: bi-weekly At every sampling, six samples were collected from every site with cotton swabs. Dry sites: The swab was moistened in sterile isotonic saline before swabbing an area at the site not previously sampled by rubbing vigorously for 15 s Wet sites: The swab was immersed in the liquid	Samples were cultured and after incubation, growth was scored from 0 to 4 according to where growth happened on the four streaked sections 0 = no growth 1 = growth in the first section 2 = growth in the first and second section 3 = growth in first, second and third section 4 = growth in all four sections The 3-day-growth score was calculated as the sum of growth over the first 3 days at every site	Survival of <i>S. equi</i> occurred at all sites from 24-h postinoculation (except the outdoor fence post). The longest period over which <i>S. equi</i> was successfully cultured in the summer were obtained from the stomach tube at 7 days, with failure to culture subsequently at 9 days. The longest period over which <i>S. equi</i> was successfully cultured in the winter was obtained from the bucket at 30 days, with failure to culture subsequently at 34 days. Stronger survival was seen in the winter at all sites and as demonstrated by the 3-day-growth score, the survival was significantly higher in wet sites. The most vigorous growth in both summer and winter was in the stomach tube, whereas the poorest was on the outdoor fence post.

TABLE 2 Efficacy of different disinfectants on *Streptococcus equi* subsp. *equi*.

Study	Equine pathogens	Contamination sites	Disinfectants evaluated	Results
Disinfecting equine facilities Dwyer (1995)	This paper includes an evaluation on cleaning and disinfecting equine facilities based on specific pathogens. Rotavirus is observably the most difficult to kill.	Most equine facilities (barn, temporary stalls, horse vans and so on) are made of a combination of the following materials: wood, concrete blocks, asphalt, metal, rubber mats or commercial flooring material. Floors can also be composed of sand, dirt-compacted clay or other organic materials.	Commercially available disinfectants generally fall into one of the following groups: Phenolic disinfectants: will kill rotavirus and are effective in the presence of organic matter. These are the disinfectants of choice for use in horse facilities. Iodophors (10%): will kill rotavirus in the presence of organic matter. Are routinely used as skin antiseptics (handwash). QACs: do not kill rotavirus and are inactivated in the presence of organic matter Formaldehyde: highly toxic. Formaldehyde fumigation is not recommended for use in horse facilities. Or hypochlorites (bleach) and chlorhexidine	Farm managers need to consider unknown factors present in the environment, and the presence of organic matter such as manure, urine, blood, discharge and dirt can render some disinfectants useless. Raw wood is the material most commonly used in construction stall walls. Wood as well as concrete blocks are porous and have a rough surface which can trap organic matter and pathogens. Wood makes disinfection practically impossible. Asphalt is used as flooring and can be washed and disinfected easily. Sand, dirt or compacted clay floors cannot be adequately cleaned.

surfaces, it is difficult to completely disinfect the stables in case of an outbreak. The most suitable disinfectant depends on the particular surface (Dwyer, 1995; Weese et al., 2009). In the process of choosing the most effective disinfectant, many factors are to be considered, such as the bactericidal capacity of the chemical to be applied on a particular surface and yet remain active against the pathogen, economic cost and efficiency in the presence of organic matter (Dwyer, 1995). The importance of efficiency in the presence of organic matter cannot be emphasised enough due to *S. equi* being shed in organic matter (nasal discharge). It is, however, crucial to keep in mind that any disinfectant may pose a potential risk to both horses and humans as well as any other animals entering the facilities, such as damage to the respiratory epithelia if inhaled in high concentrations (Dwyer, 1995). Additionally, not only the facilities themselves cause a risk of transmission. As stated above, any equipment used in the facilities must be considered a risk factor as well and should also be incorporated into the cleaning and disinfection plan.

Streptococcus equi has a high survival capacity on different sorts of raw wood (Jorm, 1992), stalls built with wooden material may need to be modified by creating a smoother and waterproof surface and thereby enabling easier cleaning and disinfection (Dwyer, 1995).

When choosing among chemical disinfectants, the purpose of the product is highly important. For the disinfection of hands and equipment, iodophors (10%) are the disinfectant of choice (Dwyer, 1995). Although it would be preferable to use iodophors to disinfect an entire barn due to their high efficacy in the presence of organic matter, it is too expensive for large-scale use (Jorm, 1992). The high efficacy of iodophors, such as 10% w/v povidone iodine undiluted (Betadine Antiseptic Liquid), has been demonstrated in a laboratory study from 1995 (Table 2), where the disinfectant eliminated *S. equi* on a surface of the glass and untreated wood (Jorm, 1992). Furthermore, it states that chlorhexidine gluconates and glutaraldehydes are very suitable for large-scale disinfection of a barn (Jorm, 1992), while quaternary ammonium compounds (QACs) and chlorine-containing compounds are less suitable due to their inactivation in the presence of organic matter (Dwyer, 1995; Jorm, 1992). As Dwyer (1995) found that phenolic disinfectants are highly effective in the presence of organic matter and is the disinfectant of choice when disinfecting entire horse facilities. Though it should be accentuated that the chemical is caustic to skin and mucous membranes and can lead to burns and eye injuries. Thus, it is important to wear eye goggles and protective clothes while using disinfectant. Furthermore, it can cause harm and potentially be lethal to animals and humans if inhaled in very high concentrations, and therefore it is important to leave the stable empty and allow it to dry completely before reintroducing the horses (Dwyer, 1995).

No horse facilities are completely alike. The frequency of disinfecting the stalls depends on the disease history, the type and use of the horses as well as the movement of horses to and from the facility. Dwyer (1995) states that a thorough cleaning and disinfection twice

a year (autumn and spring) is sufficient to control equine pathogens for riding academies, shows and racing stables.

Due to the differences within equine facilities, it is debatable which measures are most suitable.

Figure 1 suggests a stepwise disinfection plan that can be applied in most facilities (Dwyer, 1995).

TABLE 3 Transmission of *Streptococcus equi* subsp. *equi* via clothes.

Study	Materials and methods	Results
Investigation of the potential transmission of bacteria, including <i>Streptococcus equi</i> spp., <i>equi</i> between stables via the visitors' clothes (Frosth et al., 2018)	Two different common textile materials were used; a softshell material with an inside of fleece commonly used in jackets, and a cotton material commonly used in t-shirts. Both materials were washed several times before the study, and then cut into pieces of 8 x 11 cm and individually placed in large petri dishes. In total, 264 pieces of fabric were contaminated with three different types of <i>S. equi</i> strains. Sterile cotton tubular retention bandages were worn externally on the sleeves by visitors to 21 stables, aiming to illustrate the bacterial contamination of clothing during horse handling.	Difference in the survival of the three <i>S. equi</i> strains on the two different clothing materials was observed. Survival was notably longer on T-shirt material than on jacket material but varied between the strains. All strains survived at least 24 h on both fabrics. No isolates of <i>S. equi</i> were found on retention bandages worn on sleeves, since there had not been any recent experiences with strangles in any of the stables. Of the 27 samples, 13 were, however, positive for <i>S. zooepidemicus</i> , which is closely related to <i>S. equi</i> and therefore used as a surrogate marker that likely reflects the ease of transfer of this bacteria when handling horses.

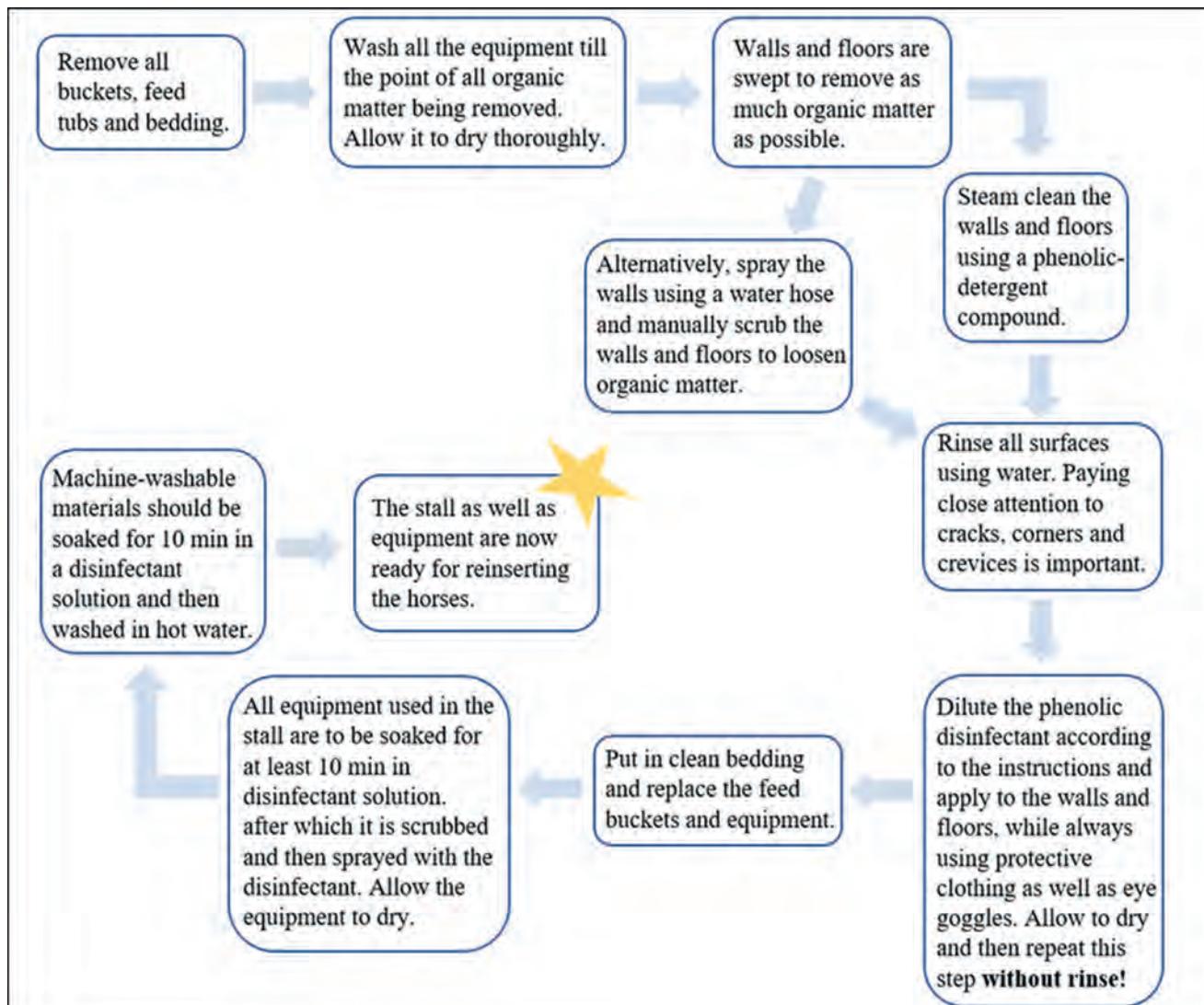


FIGURE 1 Flow chart for disinfection of equine facilities in case of an outbreak of strangles. Modified according to Dwyer (1995).

ISOLATION AND MONITORING USING A COLOUR-CODING SYSTEM

Shedding of *S. equi* commences 2 days after the onset of fever (Boyle, 2017), providing an opportunity to isolate infected horses before they constitute a risk of disease transmission. This requires that

the staff is aware of the presence of the disease within the facilities and monitors the temperature several times daily. Richmond (2015) as well as others (Quinn et al., 2011; Waller, 2013) suggest an approach of dividing the premises into different areas in case of an outbreak, in order to limit the transmission. For that purpose, colour-coding horses, areas and equipment is a useful method (Figure 2).

The premises are divided into three areas; red, amber and green (Richmond, 2015; Waller, 2013). As an increase in temperature is evident prior to shedding, temperature-monitoring is key. If any signs of fever are found in the amber or green zone, the particular horse

should be moved to the red zone. In order to avoid disease transmission within the three zones, ideally different staff members should handle the horses in each zone. If this is not possible the staff members should begin the colour-guided separation process at the lowest risk zone and move towards the highest risk zone (from green to amber to red) (Waller, 2013, 2014). Not all facilities have enough stables for this kind of colour-coded division. Instead, exposed horses can be isolated from other horses by placing them in a stall at one end of the barn leaving a couple of empty stalls in between the exposed and healthy horses, as demonstrated in Figure 3.

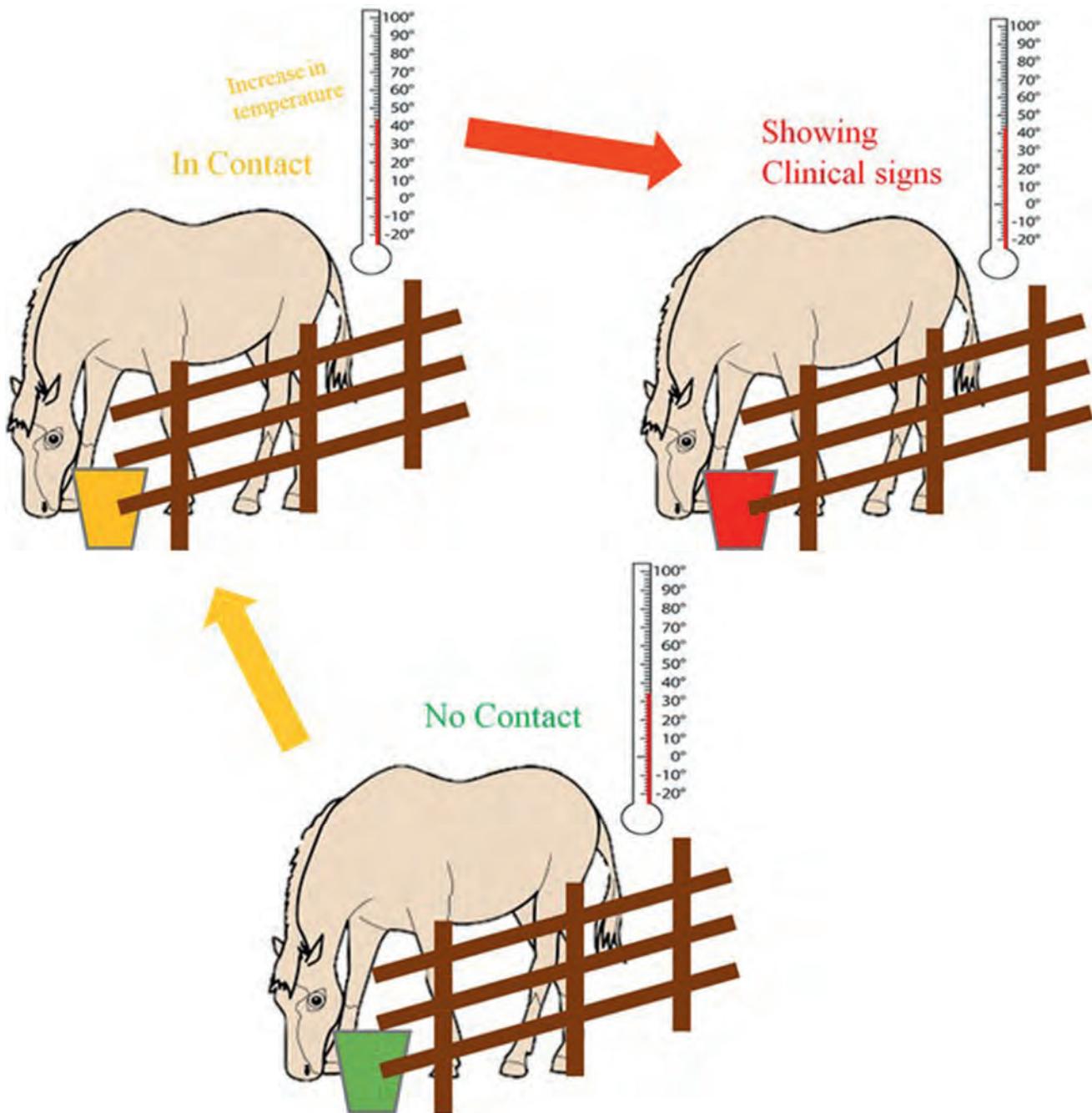


FIGURE 2 Recommended isolation and management strategy for minimising the impact of a strangles outbreak, showing how to colour code the premises and equipment as well as how to monitor and move horses from different areas. For example, the horse in the amber zone is demonstrating an increase in temperature and is therefore moved to the red zone. Modified after Waller (2013).

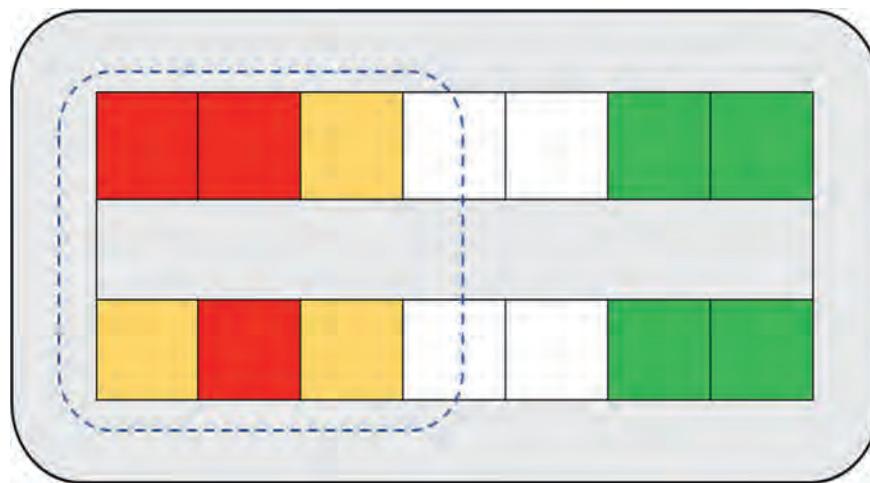


FIGURE 3 Schematic drawing of a 14-stall barn. The red stalls contain diseased horses, whereas the amber stalls contain potentially exposed horses, and the green stalls contain healthy horses. The white stalls are empty in order to create distance between the exposed and healthy horses.

If no barn is available to isolate *S. equi* potentially infected horses, they can alternatively be divided into smaller groups with clinically affected horses together and horses without clinical signs together, using different paddocks to separate the groups from each other. Although strangles, like other respiratory diseases, can be transmitted by aerosols, the risk of disease transmission can be limited by leaving at least 5.25m of space between the fence line of paddocks. Ideally, the fences should have a smooth surface and be cleaned prior to using the paddocks for isolation. For general control of equine contagious diseases (including strangles), newly introduced horses to the premises should always be accompanied by vaccination history, health certificate and information on their place of origin. Ideally, all newly introduced horses should be kept in 21 days of quarantine to reveal if the horse has been infected prior to arrival. As described above persistent carriers of *S. equi* often lack clinical signs, emphasising the importance of the isolation period as well as a testing procedure. The subclinical carriers will continue shedding bacteria if not identified and treated and thus pose a risk of disease transmission to the existing herd. Carriers seem to have a highly intermittent shedding pattern of *S. equi* (George et al., 1983), for which reason it is suggested to obtain at least three culture-negative samples with 7 days in between sampling, prior to a horse being declared a non-persistent carrier of *S. equi* (Sweeney et al., 1989). Nevertheless, as mentioned above, state-of-the-art is to combine culture with qPCR, as there is a risk of false-negative interpretations based solely on culture samples (Morris et al., 2020). Theoretically, all horses being present at a barn on which an outbreak of strangles has occurred should be considered potential carriers, and nasopharyngeal washes should optimally be performed on all horses in the barn. Subsequently, if a horse is tested culture-positive for *S. equi*, further investigations should be performed, and the guttural pouches visually examined by endoscopy to determine if empyema or chondroids are present. If chondroids are present, they should be removed (George et al., 1983; Verheyen et al., 2000; Waller, 2013). A combined antigen A+ and antigen C iELISA is available in Europe for serological screening to determine whether a horse has been exposed to *S. equi*.

It has a high level of sensitivity and specificity to identify horses that should be tested for persistent carriage of *S. equi* (Robinson et al., 2013).

Evidently, the number of available stables at the premises and the farm management play an important role in making decisions on whether and how to isolate the various groups of horses based on clinical status as described above. The economic cost of isolation should be compared to the potential cost of an outbreak. Riding academies as well as stables holding show horses and stallions should always have a routine isolation policy, as the economic cost of an outbreak could be overwhelming, whereas a farm holding only two horses for recreational use may not have the need for systematic isolation, as this might be uneconomical (Dwyer, 1995). Generally, protracted outbreaks of strangles can lead to great economic consequences for the infected stables, leaving small riding academies on the edge of financial ruin due to large veterinary bills combined with low income (Moloney et al., 2013).

To sum up, the implementation of an isolation and disinfection plan will greatly improve the chances of minimising or avoiding an outbreak of strangles. It is crucial that this plan is made before an actual outbreak occurs, ensuring that every aspect is covered, and everyone knows exactly how and what to do (Richmond, 2015). However, if a plan has not been prepared prior to an outbreak, the head of management is urged to outline an isolation strategy in collaboration with a veterinarian, to avoid prolonged resolution as well as decreasing the risk of (re)-contamination on surfaces and equipment with *S. equi*. Lack of a feasible management plan may hence result in prolonged resolution and might even leave some subclinical carriers undetected or surfaces and equipment *S. equi*-contaminated, posing a risk of re-infection to the herd.

CONCLUSION

In conclusion, in case of a strangles outbreak, the most important aspects related to biosecurity and hygienic measures involve

knowledge on the survival of *S. equi* in the environment, division of premises into different risk groups with isolation of infected horses, monitoring and sampling of exposed horses to detect persistent carriers as well as thorough cleaning and proper disinfection of all facilities and equipment. Thorough cleaning of all equipment and different surfaces, and possible modification of difficult surfaces may be required, followed by disinfection with a suitable disinfectant. Colour-coding the premises and thereby dividing healthy, exposed and sick horses is crucial in order to limit transmission and thereby eradicate the disease. Ideally, every colour group ought to have their own assigned staff members and associated equipment; alternatively, staff members are to move from the lowest risk area to the highest risk area. Furthermore, possible transmission via clothes should lead to choosing a clothing fabric not prone to adhesion, and ideally, visitors are recommended to change clothes between visiting different stables or applying single-use plastic ware. Identification of tentative newly infected horses by surveillance of temperature and culture samples *S. equi*, followed by treatment or isolation if a rise in temperature occurs or if *S. equi* is detected in the sample material, is crucial to limit transmission of the bacteria. At least three negative nasopharyngeal washes must be obtained before a horse can be declared *S. equi* negative. If a horse is found to be a persistent carrier, guttural pouch lavage must be performed, and any chondroids present should be removed.

Basic biosecurity measures should become a top priority in the future. All equine facilities need to have an updated practical plan in case of a strangles outbreak to limit the disease. Prevention and efficient elimination of *S. equi* is becoming far more feasible due to proper implementation of serological tests, biosecurity measures as well as greater awareness on identifying subclinical carriers.

FUTURE PERSPECTIVE

Ideally, every equine facility must set up instructions on how to handle an outbreak. In the long term, hopefully, the gathered knowledge on strangles and the hygienic measures in the event of an outbreak presented in this review will add to the establishment of barn-specific evidence-based plans of action and thereby reduce the number of strangle outbreaks worldwide.

AUTHOR CONTRIBUTIONS

A. Kristensen drafted the manuscript. D. Adler, M. Green and R. Olsen contributed to all sections. A. Kristensen produced the figures.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest to declare.

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A synopsis of wearable commercially available biometric-monitoring devices and their potential applications during gallop racing

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Summary

Amidst discourse surrounding the racing industry's social licence to operate, the welfare of racehorses and jockeys is often at the forefront of discussions. Specifically, catastrophic events and the sudden death of horses on race days tend to capture media attention and often place the racing industry under public scrutiny. While such occurrences are not frequent, they have negative ramifications on the welfare of both racehorses and jockeys. The development and application of advanced monitoring technology could provide greater insight into the physiological precursors that immediately precede sudden death on race days and enable retrospective analyses of catastrophic events that take place. Most importantly, the application of such technology could ultimately aid racetrack personnel in identifying and intervening with horses at increased risk of catastrophic events, right up until the start of a race. This would inevitably improve the safety and welfare of horses and jockeys. Thus, the current review details key cardiovascular, respiratory and thermometry biometrics for racehorses and examines the currently available commercial devices with potential applications during racing. This review also highlights the importance of gathering biometric data for retrospective analyses of catastrophic events and their implications on the welfare of racehorses and jockeys.

KEY WORDS

horse, cardiovascular, respiratory, thermoregulatory, welfare

INTRODUCTION

On top of being a lucrative sport with deep cultural roots, Thoroughbred racing plays an integral role in many global economies (Hitchens et al., 2015; Parker & Beedell, 2010; Suggett, 1999). Similar to human track and field athletes, equine athletes have a high physiological demand placed on them, reaching top speeds exceeding 70 km/h while racing (Mercier & Aftalion, 2020). In a bid to achieve such speeds, substantial demands are placed on each horse's cardiovascular, respiratory, musculoskeletal and thermoregulatory

systems. Unfortunately, these physiological demands may trigger cardiac arrhythmias, respiratory disorders, musculoskeletal injuries, or heat stress, resulting in tragic, often lethal consequences for both horses and jockeys. Although relatively uncommon, occurring sporadically in an estimated 0.44 in 1000 race starts (Boden et al., 2006), race day fatalities have negative implications on the welfare of racehorses and jeopardise the social licence of the industry to operate.

Catastrophic events are typically the result of musculoskeletal injuries and cardiorespiratory-related disorders, many of which are

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believed to preface sudden death (SD). SD refers to the acute collapse or fatality of an apparently healthy horse possessing no clinical signs of injury or poor health, occurring during or soon after a race (Boden et al., 2005; Lucke, 1987; Physick-Sheard & Slack, 2020). While musculoskeletal injuries reportedly account for 63%–74% of all SDs (Bimson et al., 2022; Boden et al., 2005, 2006; Clegg, 2011; Hitchens et al., 2019), cardiorespiratory disorders have also been reported to account for 56%–81% of SDs on race days (Boden et al., 2005; Lyle et al., 2011; Navas de Solis et al., 2018). Given the practical and social implications on racehorse and jockey safety, the racing industry continues to make efforts to minimise and prevent the occurrence of SDs. Such efforts include modifications to the rules of racing and the development of better monitoring tools. Nevertheless, a considerable number of these commercially available devices are performance-focused, with little, if any, currently suited for health monitoring during races (Nath et al., 2022; Ter Woort et al., 2022; Vitale et al., 2021; Williams et al., 2019). Moreover, the few that are used during racing typically monitor stride characteristics for the assessment of risks and/or occurrences of musculoskeletal injury (Wong et al., 2022). In the interest of further reducing preventable race day fatalities, it is important to recognise that cardiorespiratory disorders and heat stress are also critical contributors to SD on race days. Therefore, this review details the vital biometrics in monitoring a racehorse's cardiovascular, respiratory and thermoregulatory health and further discusses the currently accessible, wearable commercial devices capable of measuring cardiorespiratory biometrics and temperature, with particular focus towards their potential application on race days.

CARDIOVASCULAR, RESPIRATORY AND THERMOMETRY BIOMETRICS

Cardiovascular biometrics

Heart rate

Racehorse trainers commonly utilise heart rate (HR) data to monitor a horse's fitness, response to physical exertion, training recovery and performance potential (Evans & Rose, 1988; Williams et al., 2019). A horse's HR can also give an indication of the presence of underlying cardiovascular disorders. For example, an elevated HR for the level of exertion is known as disproportionate tachycardia and can be attributed to atrial fibrillation (AF) (Decloedt et al., 2015; Verheyen et al., 2013). As cardiovascular disorders are reflected in HR deviations from baseline, HR is a vital biomarker for monitoring the health of racehorses.

Whilst there are multiple devices capable of measuring HR, an electrocardiogram (ECG) with a minimum sampling frequency of 500Hz is the most reliable means of visualising premature depolarisations (Stucke et al., 2015). An ECG measures the electrical activity of the heart, which is charted in the form of a QRS complex

consisting Q, R and S waves (Martis et al., 2014). As the ECG is the gold standard for diagnosing and distinguishing between physiological and pathological cardiac arrhythmias (Decloedt et al., 2021; Reef et al., 2014; Vitale et al., 2021), there is a considerable amount of literature detailing its applications (Ellis et al., 2022; McGurin, 2015; Mitchell, 2019; Ter Woort et al., 2022). Of the various available ECG monitors, the Televet100 (<https://www.televet.de/products/televet-100/>) is routinely used by equine veterinarians to obtain ECGs of diagnostic quality and is often employed in scientific studies as the gold standard ECG that other devices are validated against (Nath et al., 2022; Verheyen et al., 2013; Welch-Huston et al., 2020).

While an ECG is a highly regarded veterinary investigative tool, there are drawbacks to its use. The ECG is not typically an element of routine veterinary checks unless an arrhythmia warrants further investigation (Reef, 1985; Reef et al., 2014). Moreover, AF, for instance, can be complex to predict using an ECG due to the intermittency and often brevity of the disorder (Alexeenko et al., 2021). Obtaining a good quality ECG trace is highly dependent on electrode position, skin contact and calls for a trained practitioner's interpretation of the signal (Frippiat et al., 2021; Keen & O'Connor, 2021). Further, the quality of an ECG progressively declines from walk, trot, to canter, limiting its viability for measuring cardiovascular biometrics during top-range efforts, such as in racing, where cardiovascular disorders most commonly surface (Frick et al., 2019).

Heart rate variability

Heart rate variability (HRV) refers to the variance in the time intervals between consecutive heartbeats and is a reflection of the dynamic but nonadditive interactions between the parasympathetic and sympathetic nervous systems (Stucke et al., 2015). It is typically measured by variations in interbeat intervals (IBI) or R-R intervals, which refer to the time between two successive R-waves in a QRS signal (Mitchell & Schwarzwald, 2021). While oscillations in the frequency of IBI are healthy and normal, both increases and decreases in IBI variability from normal sinus rhythm can be indicative of cardiovascular disorders (Mitchell & Schwarzwald, 2021). A decreased HRV can signify stress, the anticipation of exercise, or heart failure (Mitchell & Schwarzwald, 2021), while a higher HRV has commonly been found in horses with respiratory disorders, AF and other cardiac arrhythmias (Broux et al., 2018; Mitchell & Schwarzwald, 2021). Some studies have demonstrated the use of HRV as a cardiovascular measure of pain, anxiety and stress responses of the autonomic nervous system (Gehlen, Faust, et al., 2020; Gehlen, Loschelder, et al., 2020; Mejía-Mejía et al., 2020; Reid et al., 2017; Stucke et al., 2015; von Borell et al., 2007). HRV appears to be a useful metric for distinguishing between a healthy baseline state and one with prevailing abnormal or underlying pathologies, making it a biomarker of particular interest in monitoring the cardiovascular health of racehorses. Like HR, an ECG is the gold standard for quantifying a horse's HRV (Frippiat et al., 2021; Stucke et al., 2015).

Heart sounds

Heart sounds are a natural product of the cardiac cycle (Reef, 1985). Commonly identifiable sounds include S1, S2, S3, S4, clicks varying in pitch and frequency and heart murmurs (Keen, 2019; Ware et al., 2021; Young et al., 2008). Cardiovascular auscultation allows trained practitioners to hear heart sounds with either an analogue or digital stethoscope, through which they can listen for heart sounds indicative of cardiovascular disorders. For example, cardiovascular auscultation of a horse with AF would typically reveal an irregularly irregular cardiac rhythm (Decloedt et al., 2021). While cardiac arrhythmias can be detected via auscultation, diagnosing their underlying aetiology also typically warrants an ECG (Schwarzwald, 2019; Welch-Huston et al., 2020).

Respiratory health biometrics

Respiration rate/frequency

A human's respiratory rate is sensitive to the onset of pathophysiological disorders, such as cardiac events, pneumonia, strenuous work, emotional and physiological stressors, as well as the heat and cold (Nicolò et al., 2020). Similarly, a horse's respiratory rate is a vital indication of its cardiorespiratory health and performance (Franklin et al., 2012; Gramkow & Evans, 2006). In particular, an elevated respiratory rate has been found to precede cardiac arrest (Churpek et al., 2012; Freel et al., 2010; Riond et al., 1992; Ware et al., 2021). At rest, horses are expected to have a respiratory rate of 6–24 breaths/min, where breaths taken should be slow, steady and inconspicuous (Arthur, 1990; Savage, 1997). However, during strenuous work, adaptive responses of a horse's respiratory system increase the delivery of oxidative fuels to active musculature, simultaneously facilitating the transport and removal of metabolic end products such as carbon dioxide and heat (Weber et al., 1987). In adaptation to strenuous exercise, horses increase their respiratory rate to maximise oxygen consumption (Franklin et al., 2012; Padilla et al., 2004), which can continue to exceed 120 breaths/min in the post-exercise period (Brownlow & Mizzi, 2022b). Therefore, anomalies in a racehorse's respiratory rate in reference to their level of exertion, particularly prior to racing, can signal the presence of or a precursor to a respiratory disorder.

Lung sounds

The intensity of adventitious lung sounds, such as crackles or wheezes, can indicate the presence and severity of airway obstruction (Arthur, 1990; Roy & Lavoie, 2003). Crackles have been attributed to collapsed lungs, where the sound is a product of airway reinflation or fluid secretions (Savage, 1997), whereas wheezes result from airflow narrowing or obstruction (Roy & Lavoie, 2003). In the same manner as detecting adventitious heart sounds, auscultation is

used to assess abnormal lung sounds and aids in diagnosing respiratory disorders (Arthur, 1990).

Thermometry biometrics

Thermometry has diverse applications within the field of equine sport and can present considerable insight into a racehorse's physiological status. Notably, thermometry has been applied in the diagnosis of distal limb and hoof conditions such as lameness, tendonitis and laminitis (Turner, 2001); detection of inflammation and musculoskeletal injuries (Soroko et al., 2017; Turner, 2001; von Schweinitz, 1999); as a proxy for stress (Rizzo et al., 2017; Soroko et al., 2016); analysing saddle pressure distribution (Siqueira et al., 2020; Soroko et al., 2018); as well as in detecting underlying pathological disorders (Hall et al., 2019).

Temperature

A horse's core temperature at rest oscillates between 37.8–38.9°C when measured by means of rectal thermometry (Piccione et al., 2002) and deviations from that baseline can indicate the presence of an underlying health disorder. The energetic demands of racing give rise to the build-up of metabolic heat in horses at rapid rates (Brownlow et al., 2016; Brownlow & Mizzi, 2022a). While horses have the capacity to dissipate heat through their skin, their cooling mechanisms are inherently limited by their low skin surface area to body mass ratio (Hodgson et al., 1993). Hence, racing under rigorous conditions for prolonged durations exposes horses to an increased risk of accumulating excess metabolic heat, which can potentially raise their core temperatures to critical levels (Brownlow & Brotherhood, 2021).

Central venous temperature, or arterial pulmonary blood temperature, is considered to be the gold standard for measuring core temperature in veterinary medicine (Hodgson et al., 1993; Kang et al., 2020). Typically, thermocouples are inserted into the pulmonary and/or carotid arteries via intravenous catheters, allowing for the measurement of venous blood temperature both at rest and during work (Hodgson et al., 1993). However, this procedure warrants the artery to be surgically elevated weeks prior to the exercise test (Evans & Rose, 1988), making it an invasive procedure with limited field applications.

Rectal thermometry is commonly used in the evaluation of a horse's body temperature (Collins et al., 2016; Hall et al., 2019; Ramey et al., 2011). However, the process of obtaining rectal temperature is both time-consuming and laborious, often putting handlers in danger of bites and kicks, in addition to being a stressful procedure for horses (Kang et al., 2020; Ramey et al., 2011). Obtaining accurate rectal temperatures post-exercise poses an additional challenge to handlers due to the horse's altered mentation and increased flaccidity of its caudal rectum in response to exhaustion (Brownlow et al., 2016). Furthermore, rectal temperatures have been reported

TABLE 1 Summary of commercially available technologies for racehorses and their reported capabilities.

Devices	Cardiovascular biometrics				Respiratory biometrics				Locomotor profile				Movement tracking				Device features			
	HR ^c (bpm)	HRV ^d	ECG ^e	Heart sounds	Blood oxygen saturation	Respiration frequency	Lung sounds	Body temperature	Stride length	Stride frequency	Sectional times	Gps ^f	Accelerometer	Wearable	Wireless	Real-time measurements	Remote monitoring	Scientifically validated	Battery life	
E-Trakka	✓	✓	✓						✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	10h
EKuore 1-lead digital cardiac monitor	✓	✓	✓						✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Not stated
Equimetre by Arianeo	✓	✓	✓	✓					✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	20h
Equinity by Equinity Technology	✓								✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	16h
Motion sport by Equisense	✓								✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	30h
Nightwatch	✓								✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	12h
Smart Bit by Equine Smart Bit	✓								✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	40h
Stridemaster									✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Not stated
Tail Tab by Epona Biotec									✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	480h
VetCheck by PonyUp Technologies	✓								✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Not stated

^aDevice needs to be connected via Bluetooth for data to be retrieved and, therefore, requires operators of the device to be in relatively close range.

^bRequires pairing with a phone application and the phone has to be carried by the rider at all times, which limits the real-time retrieval of data.

^cHeart rate.

^dHeart rate variability.

^eElectrocardiogram.

^fGlobal positioning system.

^gScientifically validated at rest.

^hScientifically validated at walk.

ⁱScientifically validated at trot.

^jScientifically validated at canter.

^kScientifically validated at gallop.

to lag behind core body temperatures, limiting their capacity for obtaining real-time temperature measurements (Hodgson et al., 1993). As rectal temperatures can only be obtained from horses at rest, this method does not allow for dynamic temperature measurements. Therefore, given the considerable drawbacks of this method, noninvasive measures of body temperature are of great interest.

Infrared thermography (IRT) is a noninvasive means of measuring skin surface temperature and functions by detecting and imaging the metabolic heat radiating from a horse's body surface (Brownlow & Mizzi, 2022a; Brownlow & Smith, 2021). IRT has multiple applications within the field of horseracing. Firstly, it can bring attention to areas of elevated temperature attributable to inflammation, the onset of injury and/or muscular fatigue and it is often detectable before the development of clinical signs of pathology (Prochno et al., 2020; Turner, 2001). IRT has also been used to confirm a range of back diseases such as thoracolumbar disease and sacral neuromuscular disease via the evaluation of the sympathetic tone in a horse's spine (von Schweinitz, 1999). Lastly, IRT measurements have been correlated to blood lactate concentration – a gold standard and objective biomechanical measure of a horse's response to physiological stress (Witkowska-Pilaszewicz et al., 2020). As such, it has been posited that coupled with other measures of physiological stress, IRT can be applied as an early detection tool for exertional heat illness (EHI) and as a measure of the deviation of a horse's health from baseline conditions (Brownlow & Mizzi, 2022a; Brownlow & Smith, 2021). It is important to note that temperatures measured by means of IRT are generally lower than that of rectal thermometry, can be influenced by environmental temperatures and vary depending on the body part where measurements are taken (Ramey et al., 2011).

COMMERCIALLY AVAILABLE WEARABLE DEVICES FOR BIOMETRIC MONITORING

Equimetre by Arioneo

According to Arioneo, the Equimetre contains electrodes, a 3-axis accelerometer, 3-axis gyroscope and a Global Navigation Satellite System (GNSS) module, allowing for the recording of a horse's heart rate, locomotion and stride characteristics and real-time location, respectively. The device is also equipped with a Radio Frequency Identification (RFID) antenna for recognising each horse's RFID chip, facilitating the digital identification of horses (Table 1). The device clips onto a harness, girth, or saddle pad, where it transmits live data to the Equimetre application, allowing for the real-time visualisation of cardiovascular biometrics (<http://training.arioneo.com/en/arioneo-home/>).

The Equimetre is one of few equine fitness trackers known to be scientifically validated against gold standard ECG measurements, having been reported to reliably measure HR and HRV at all gaits including at speeds of over 40km/h after the correction of data (Ter Woort et al., 2022). However, correcting data can be time-consuming and the validation trials were carried out at sub-maximal exercise intensities where symptoms of cardiac arrhythmias tend to be dormant (Navas

de Solis et al., 2016; Ter Woort et al., 2022). It is of interest for the device to be validated at top-range efforts where cardiac arrhythmias mostly present themselves in order to understand the Equimetre's potential application during racing (Navas de Solis et al., 2016).

Ekuore 1-lead Digital Cardiac Monitor

The Ekuore is a single-lead bipolar ECG device consisting of two electrodes connected by a micro-USB cable, reportedly capable of recording ECG traces in real-time (<https://ekuore.com/animal-health/veterinary-cardiac-monitor/>, Table 1). The device is said to adhere to the horse's skin via clips and transmits data to a mobile application, where it can be viewed in real time or recorded for further analyses. A study by Vitale et al. (2021) found a high level of agreement between the Ekuore and gold standard reference ECGs in the polarity of P-waves and QRS responses, duration of cardiac deflections and HR when validated on horses at rest. However, further trials are required to validate the device's measurements at all gaits and the current clip-style application of the electrodes is likely ill-suited for use during racing (Vitale et al., 2021). Furthermore, the device does not appear to flag anomalous ECG readings automatically, necessitating the interpretation of data by a trained practitioner.

E-Trakka

E-Trakka contains sensors and electrodes that reportedly capture HR and GPS data, providing fitness analytics such as sectional times, stride length, peak speed, HR, HR max and recovery HR (<https://www.etrakka.com.au/the-e-trakka-xv3/>, Table 1). The device has been marketed as a fitness analytic tool for racehorse trainers to monitor a horse's performance as well as make data-driven training and racing-related decision. Decisions may include determining an individual horse's training intensity, deciding when to scratch a horse and when and how long to spell a horse. The E-Trakka is embedded within a saddle blanket and reportedly allows trainers to access fitness analytics in real time via cloud software. Studies on equine physical fitness by Berkman et al. (2015), Buzas et al. (2008), and Gür and Matur (2013) have utilised the E-Trakka as a measure of a horse's HR. However, these trials were conducted during polocrosse competitions and sub-maximal training runs, with none of the studies validating the use of the device at maximal efforts such as those that would occur during racing (Berkman et al., 2015; Buzas et al., 2008; Gür & Matur, 2013).

Equinity by Equinity Technology

Marketed as a tool for monitoring a horse's physiological fitness, Equinity Technology states that the device contains an accelerometer, GPS and HR sensor, which accordingly allow Equinity to measure distance travelled, speed, sectional times, HR, HR max, recovery

time, stride rate, stride length, weather, going and altitude (<https://equinitytechnology.com>, Table 1). The wearable fitness tracker fits into a girth sleeve and transmits live data to its application. A study by Williams et al. (2019) did utilise Equinity to quantify effort zones as a percentage of HR maximum and to monitor a horse's HR in response to work at all gaits, but unlike some other commercially available devices, Equinity does not appear to have algorithms to raise alerts for cardiovascular anomalies.

Motion sport by Equisense

According to Equisense, the Motion Sport consists of a GPS, 9-axis motion sensor and electrode, which measure a horse's training intensity (using heart rate as a proctor), recovery, stride frequency and time spent on each rein (<https://equisense.com>, Table 1). The Motion Sport can reportedly detect lameness and boasts additional features tailored towards showjumpers, with algorithms measuring a horse's average rhythm between jumps and duration of flying phase. The device can be positioned on the girth via elastic attachments, further requiring the application of conductive gel between the attachment and electrode to obtain HR measurements. However, measured data can only be reviewed via mobile application after an activity has been recorded, limiting the device's use for detecting cardiorespiratory anomalies in real-time. Based on a pilot study by Alberda (2017), the Motion Sport has been used to quantify temporal and kinetic displacements in trotting warmbloods. Unfortunately, like many of these devices, the device has yet to be validated at maximal efforts, which limits its potential application for racehorses on race days.

Stridemaster

Stridemaster consists of GPS, infrared and inertial sensors, which reportedly capture data on stride characteristics such as stride length, stride duration, number of strides and stride efficiency (<https://www.stridemaster.com>, Table 1). The Stridemaster fits into the saddle cloth and allows for live data to be broadcasted. The device has been noted to employ machine-learning algorithms that detect anomalies in an individual's stride characteristics and raise alerts about the horse's risk of musculoskeletal injuries, based on the understanding that horses change their gait in response to injuries and pain. The Stridemaster has reportedly predicted 90% of race day injuries in advance when trialled on racetracks in the USA. Moreover, the device is further backed by a study from Wong et al. (2022) that successfully predicted horses' risks of musculoskeletal injury when trialled during racing. While the device does not appear to measure other biometrics of interest such as HR or temperature, the Stridemaster is one of few wearable devices currently used in racing, thus it has interesting potential for expanded applications that could potentially include other biometrics.

Other wearable commercially available biometric devices

While several other wearable technologies are commercially available for monitoring cardiorespiratory biometrics and temperature, they do not appear in the published peer-reviewed literature thus their potential applications in racing are limited at this time. Such biometric monitoring devices include: Nightwatch, which is reportedly fitted with a GPS, altimeter, an impulse radio ultra-wideband sensor, and 9-axis inertial measurement unit sensors embedded within a halter to monitor a horse's HR and respiration (Nightwatch Equine Distress and Wellness Monitor <https://www.smarthalter.com>, Table 1). The device is said to raise alerts for symptoms of a horse in distress such as lateral recumbency or a sudden spike in HR and respiration triggered by colic; VetCheq, a device which reportedly measures central venous blood pressure, HR, respiration rate and provides an ECG trace via a specialised wrap boot that lies on the horse's distal artery (<https://ponyutechnologies.com>, Table 1); Smart Bit, which measures temperature in addition to cardiorespiratory biometrics via a pulse oximeter, bio-algorithm sensor hub and clinical-grade thermometer (<https://www.esbits.com>); Sensors embedded in the bit lie on a horse's tongue to measure HR, respiration frequency, body temperature and blood oxygen saturation in real-time (Table 1); and Tail Tab, a temperature monitoring device that adheres to the skin on the underside of a horse's tail and records temperature at 5-min intervals (<https://www.eponabiotec.com>, Table 1). Unfortunately, without published peer-reviewed literature on these devices, the accuracy of their measurements and application in racing is difficult to substantiate.

APPLICATION OF WEARABLE BIOMETRIC MONITORING TECHNOLOGIES ON RACE DAYS

Horseracing at its core is a high-intensity sport requiring racehorses to be performing at maximal efforts. It is known that cardiorespiratory and temperature-related disorders mostly present themselves at top-range efforts rather than during training (Navas de Solis et al., 2016; Ter Woort et al., 2022). However, biometric data is rarely gathered from horses outside of training, limiting our understanding of cardiorespiratory and temperature-related disorders resulting in catastrophic events on race days.

Racehorses are generally prone to a range of cardiac arrhythmias especially during or immediately after exercise, with pathological cardiac arrhythmias indicative of underlying cardiovascular disorders (Marr et al., 2021; Navas de Solis et al., 2018; van Loon, 2019). For example, AF has been described as the most pervasive and clinically important cardiac arrhythmia found in racehorses (Broux et al., 2018; van Loon, 2019). Horses diagnosed with AF typically present symptoms ranging from a drop in performance (obvious

in races where horses abruptly decelerate), epistaxis, ataxia, distress and in the worst-case scenario, sudden collapse (Declerdt et al., 2020, 2021; Young, 2003). However, these symptoms are all retrospectively diagnosed post-racing (Navas de Solis, 2016).

Unfortunately, post-mortem examinations typically reveal not only cardiac but also pulmonary failure in these horses (Johnson et al., 1994; Lyle et al., 2011, 2012). Having been detected in 50%–80% of Thoroughbreds after racing (Arthur, 1990; Hinchcliff, 2004), exercise-induced pulmonary haemorrhage (EIPH) continues to be highly prevalent in racehorses and has been found to have definitive associations with SDs on race days (Lyle et al., 2011). Racehorses are also susceptible to thermoregulatory disorders such as EHI, which occurs due to a horse's failure to thermoregulate effectively (Brownlow et al., 2016; Brownlow & Mizzi, 2022a, 2022b). The accumulation of metabolic heat past the critical thermal maximum triggers the onset of a potentially fatal pathophysiological cascade, hence EHI is also regarded as a critical and life-threatening medical emergency requiring immediate treatment (Brownlow et al., 2016; Brownlow & Mizzi, 2022a, 2022b; Pryor et al., 2015).

In the interest of improving the welfare of racehorses and progressively reducing the prevalence of SD in racing, it is ideal for clinically relevant biometrics to be monitored in the lead-up to a race, during racing and in the immediate post-race period. Presently, as post-mortem examinations are not a requirement of most racing jurisdictions, causes of SD are commonly determined through observation by race day veterinary officials and are not always confirmed by necropsy, often resulting in inconclusive findings (Boden et al., 2005, 2006; Diab et al., 2017; Lucke, 1987; Lyle et al., 2011, 2012). The application of wearable biometric monitoring devices during racing could provide greater insight into physiological indicators that immediately precede sudden death on race days. Furthermore, by conducting retrospective analyses on horses that have suffered catastrophic events, it is plausible that precursors to catastrophic events can be pinpointed, thus enabling racetrack personnel (i.e. veterinarians and stewards) to better identify horses at risk. The possibility of such intervention by racetrack personnel would inevitably help to reduce the frequency of catastrophic events over time.

CONCLUSION

Despite the paucity of information defining the mechanisms of SD in racing, it is clear that monitoring cardiovascular biometrics, respiratory biometrics and the temperature of racehorses is relevant to ensuring the health and safety of racehorses and jockeys. Multiple companies have capitalised on the demand for data-driven racehorse training, creating technologies that are now 'invaluable' to racehorse trainers (Gardiner, 2022). Although the commercially available technologies discussed have been equipped with sensors measuring one or more health biometric(s), to our knowledge, the racing industry is still lacking a device with the capability of comprehensively

measuring cardiovascular, respiratory and temperature biometrics at clinical resolution on race days. The development of such a device and its application by racing stewards and veterinarians during racing could revolutionise the way racehorse health is monitored and potentially reduce the incidences of SD on race days.

AUTHOR CONTRIBUTIONS

P. Kee, N. Anderson, G. D. Gargiulo and B. D. Velie designed the project. P. Kee and B. D. Velie prepared the manuscript. P. Kee, N. Anderson, G. D. Gargiulo and B. D. Velie commented on and approved the final version of the manuscript.

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Not applicable for a review article.

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Approved by FDA under NADA # 141-458

Equioxx® Tablets

(firocoxib) 57 mg

Brief Summary: This information is not comprehensive. Before using Equioxx® (firocoxib) tablets, please consult the product insert for full prescribing information. The product insert may be obtained from your veterinarian or by visiting www.equioxx.com.

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

Indications:

Equioxx Tablets are administered once daily for up to 14 days for the control of pain and inflammation associated with osteoarthritis in horses.

Usage:

For use in horses only. Keep this and all medications out of the reach of children. Do not use in dogs and other pets in a secured location in order to prevent accidental ingestion or overuse.

Human Warnings: Not for use in humans. Keep this and all medications out of the reach of children. Consult a physician in case of accidental ingestion by humans.

Precautions:

Horses should undergo a thorough history and physical examination before initiation of NSAID therapy. Appropriate laboratory tests should be conducted to establish hematological and serum biochemical baseline data before and periodically during administration of any NSAID. Clients should be advised to observe for signs of potential drug toxicity and be given a Client Information Sheet with each prescription. See Information for Owner or Person Treating Horse section of this package insert.

Horses with Equioxx Tablets should be terminated if signs such as inappetence, colic, abnormal feces, or lethargy are observed.

As a class, cyclooxygenase inhibitor NSAIDs may be associated with gastrointestinal, renal, and hepatic toxicity. Sensitivity to drug-associated adverse events varies with the individual patient.

Horses that have experienced adverse reactions from one NSAID may experience adverse reactions from another NSAID. Patients at high risk for adverse events are those who are dehydrated, on diuretic therapy, or those with existing renal, cardiovascular, and/or hepatic dysfunction. Concurrent administration of potentially nephrotoxic drugs should be carefully approached or avoided. NSAIDs may inhibit the prostaglandins that maintain normal homeostatic function. Such anti-prostaglandin effects may result in clinically significant disease in patients with underlying or pre-existing disease that has not been previously diagnosed. Since many NSAIDs possess the potential to produce gastrointestinal ulcerations and/or gastrointestinal

perforation, concomitant use of Equioxx Tablets with other anti-inflammatory drugs, such as NSAIDs or corticosteroids, should be avoided.

The influence of coadministered drugs with Equioxx Tablets has not been studied in horses. The influence of concomitant drugs that may inhibit the metabolism of Equioxx Tablets has not been evaluated. Drug compatibility should be monitored in patients requiring adjunctive therapy.

The safe use of Equioxx Tablets in horses less than one year in age, horses used for breeding, or in pregnant or lactating mares has not been evaluated.

Consider appropriate washout times when switching from one NSAID to another NSAID or corticosteroids.

Adverse Reactions:

The safety and effectiveness of Equioxx Tablets was established in a relative bioavailability study comparing Equioxx Tablets and Equioxx (firocoxib) Oral Paste. Therefore, additional field studies were not conducted to support the effectiveness of Equioxx Tablets.

In a limited field study, 127 horses (ages 3 to 37 years) were evaluated for safety when given Equioxx Oral Paste at a dose of 0.045 mg/kg (0.1 mg/kg) orally once daily for up to 14 days. The following adverse reactions were observed. Horses may have experienced more than one of the observed adverse reactions during the study.

Table 1: Adverse Reactions Seen in U.S. Field Studies with Equioxx Oral Paste:

Adverse Reactions	EQUIOXX n=127	Active Control n=125
Abdominal Pain	0	1
Diarrhea	2	0
Excitation	1	0
Lethargy	0	1
Loose Stool	1	0
Polydipsia	0	1
Urticaria	0	1

In these field trials, Equioxx Oral Paste was safely used concomitantly with other therapies, including vaccines, anthelmintics, and antibiotics. The safety data sheet (SDS) contains more detailed information.

To report suspected adverse events, for technical assistance, or to obtain a copy of the SDS, contact Boehringer Ingelheim Animal Health USA, Inc. at 1-888-637-4251. For additional information about adverse drug experience reporting for animal drugs, contact FDA at 1-888-FDA-VETS or online at www.fda.gov/reportanimaladverse.

Animal Safety:

The safety of Equioxx Tablets was supported by a relative bioavailability study comparing Equioxx Tablets and Equioxx Oral Paste (see CLINICAL PHARMACOLOGY, Relative Bioavailability Study), pharmacovigilance information, and target animal safety data for existing firocoxib containing products in horses. No additional target animal safety studies were conducted with Equioxx Tablets.

Young, L., Rogers, K. & Wood, J. (2008) Heart murmurs and Valvular regurgitation in thoroughbred racehorses: epidemiology and associations with athletic performance. *Journal of Veterinary Internal Medicine*, 22, 418–426.

Young, L.E. (2003) Equine athletes, the equine athlete's heart and racing success. *Experimental Physiology*, 88, 659–663.

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In a target animal safety study conducted to support the approval of Equioxx Oral Paste, firocoxib was administered orally to healthy adult horses (two male castrates and four females per group) at 0, 0.1, 0.3 and 0.5 mg firocoxib/kg body weight (1, 3 and 5X the recommended dose) for 30 days. Administration of firocoxib at 0.3 and 0.5 mg/kg body weight was associated with an increased incidence of oral ulcers compared to the control group but, no oral ulcers were noted with 0.1 mg/kg.

There were no drug-related adverse events in the control group.

In another target animal safety study, firocoxib was administered orally to healthy adult horses (four males and four castrates and four females per group) at 0, 0.3 and 0.5 mg firocoxib/kg body weight (1, 3 and 5X the recommended dose) for 42 days. Administration of firocoxib at 0.1, 0.3 and 0.5 mg/kg body weight was associated with delayed healing of pre-existing oral (lip, tongue, gingival) ulcers. In addition, the incidence of oral ulcers was higher in all treated groups as compared to the control group.

Clinical chemistry and coagulation abnormalities were seen in several horses in the 0.5 mg/kg (5X) group.

In another target animal safety study, firocoxib was administered orally to healthy adult horses (three females, two male castrates and one male per group) at 0, 0.25 mg/kg, 0.75 mg/kg and 1.25 mg/kg body weight (1, 3 and 5X the recommended dose) for 21 days. Administration of firocoxib at 0.25 mg/kg body weight was associated with delayed healing of pre-existing oral (lip, tongue, gingival) ulcers. In addition, the incidence of oral ulcers was higher in all treated groups as compared to the control group.

Tubolointerstitial nephropathy occurred in one 3X female, two 3X male horses, and the 5X female horse discussed above with the prolonged BMBT. Papillary necrosis was present in one 1X male and the 5X female horse discussed above. Despite the gross and microscopic renal lesions, all of the horses were clinically healthy and had normal hematology, clinical chemistry and urinalysis values.

In another target animal safety study, firocoxib was administered orally to healthy adult horses (three females, two male castrates and one male per group) at 0, 0.25 mg/kg, 0.75 mg/kg and 1.25 mg/kg, 2.5 mg/kg and 12.5X the recommended dose for 92 days. Administration of firocoxib at 12.5X the recommended dose was associated with tubolointerstitial nephropathy in all horses and one male horse. There were treatment-related adverse events in all treated groups. These consisted of ulcers of the lips, gingiva and tongue and erosions of the skin of the mandible and head. Gross and microscopic lesions of the kidneys consistent with tubolointerstitial nephropathy were present in all horses. Papillary necrosis was present in one 1X male and one 5X group. In addition, several 12.5X horses had elevated liver enzymes (GGT, SGPT, AST and ALT). One 2.5X horse had increased urine GGT and urine protein levels which was due to renal hemorrhage and nephropathy. Gastric ulcers of the margo plicatus and glandular area were more prevalent in the 2.5X and 7.5X groups, but not seen in the 12.5X group. The group of horses that were monitored for 92 days (47–149) showed partial to full recovery from oral and skin ulcers, but no recovery from tubolointerstitial nephropathy.

Storage Information:

Store at room temperature, between 59°–86°F (15°–30°C). Brief periods up to 104°F (40°C) are permitted.

How Supplied:

Equioxx is available as round, beige to tan, half-scored tablets, containing 57 mg firocoxib. Equioxx Tablets are supplied in 60 and 180 count bottles.

¹ McCann ME, Rickles EL, Hora DF, Cunningham PK et al. In vitro effects and in vivo efficacy of a novel cyclooxygenase-2 inhibitor in cats with lipopolysaccharide-induced pyrexia. *Am J Vet Res*. 2005 Jul; 66 (7):1278–84.

² McCann ME, Anderson DR, Briderup C et al. In vitro activity and in vivo efficacy of a novel COX-2 inhibitor in horses. *Proceedings of the Academy of Veterinary Internal Medicine*. 2002. Abstract 114, p789.

³ Data on file. Made in France.

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¹EQUIOXX product labels and FOI summaries and supplements

²Kvaternik V, Pollmeier M, et al. Pharmacokinetics and metabolism of orally administered firocoxib, a novel second generation coxib in horses. *J Vet Pharmacol Ther.* 2007;30(3):208-217.

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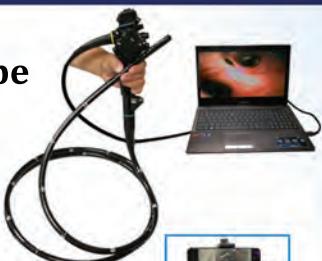
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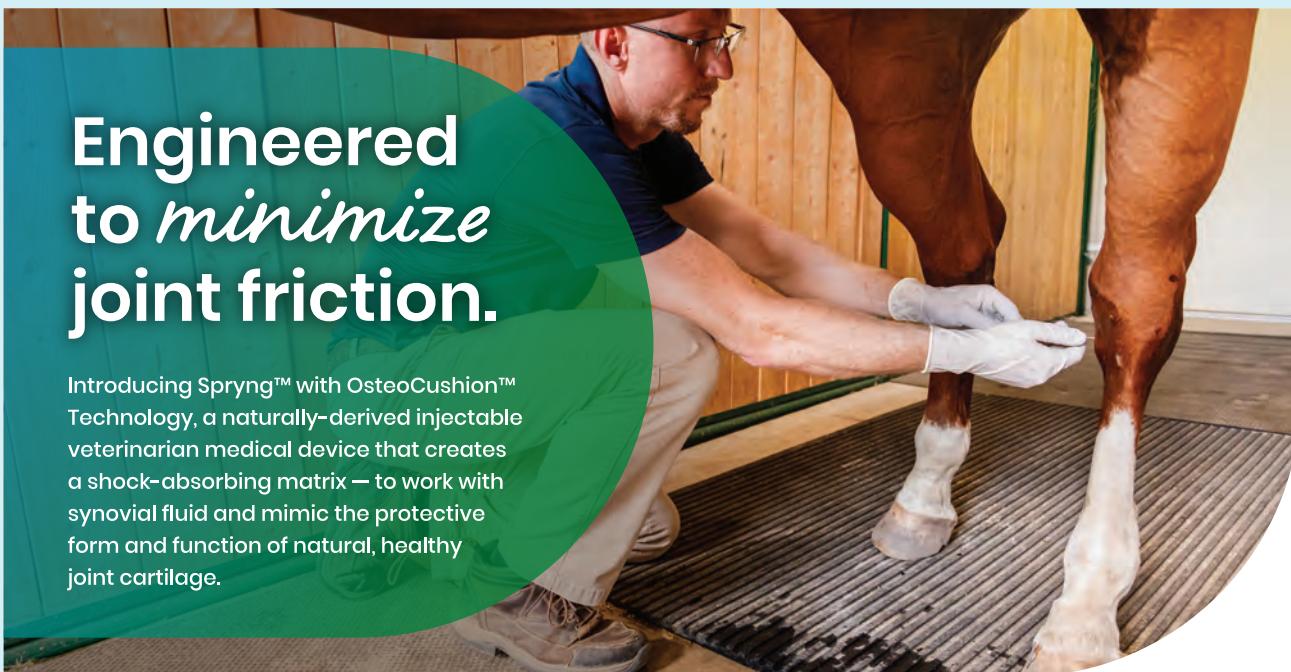


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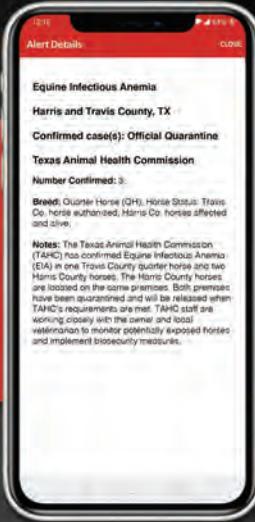
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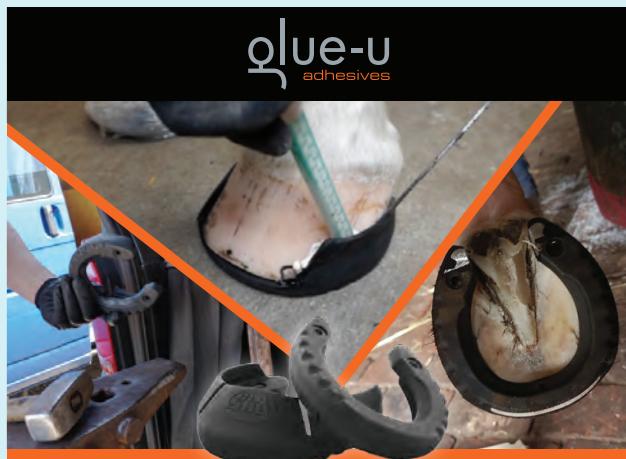
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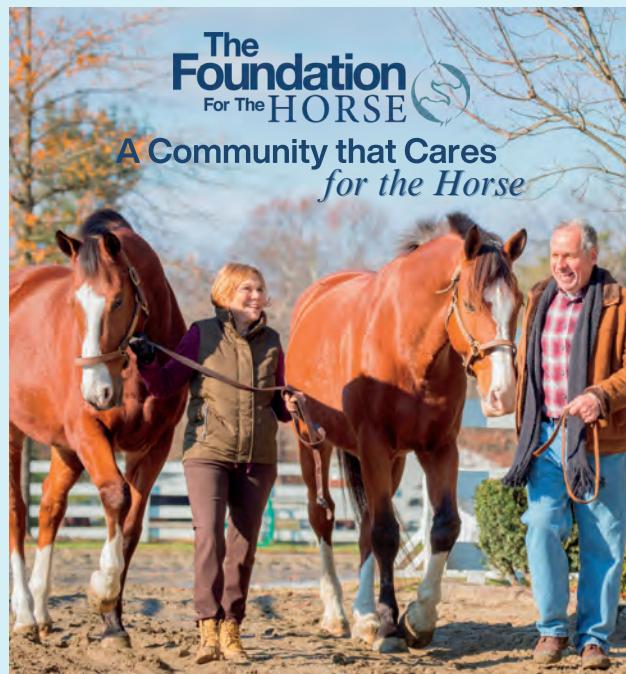
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References:

[1] Nogradi N, Couetil LL, Messick J, Stochelski MA, Burgess JA. Evaluation of an Omega-3 Fatty Acid Containing Feed Supplement in the Management of Horses with Chronic Lower Airway Inflammatory Diseases. *J Vet Intern Med* 2015; 29:299-306.

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